Book of Abstracts 2024

31st International Student Congress of (bio)Medical Sciences

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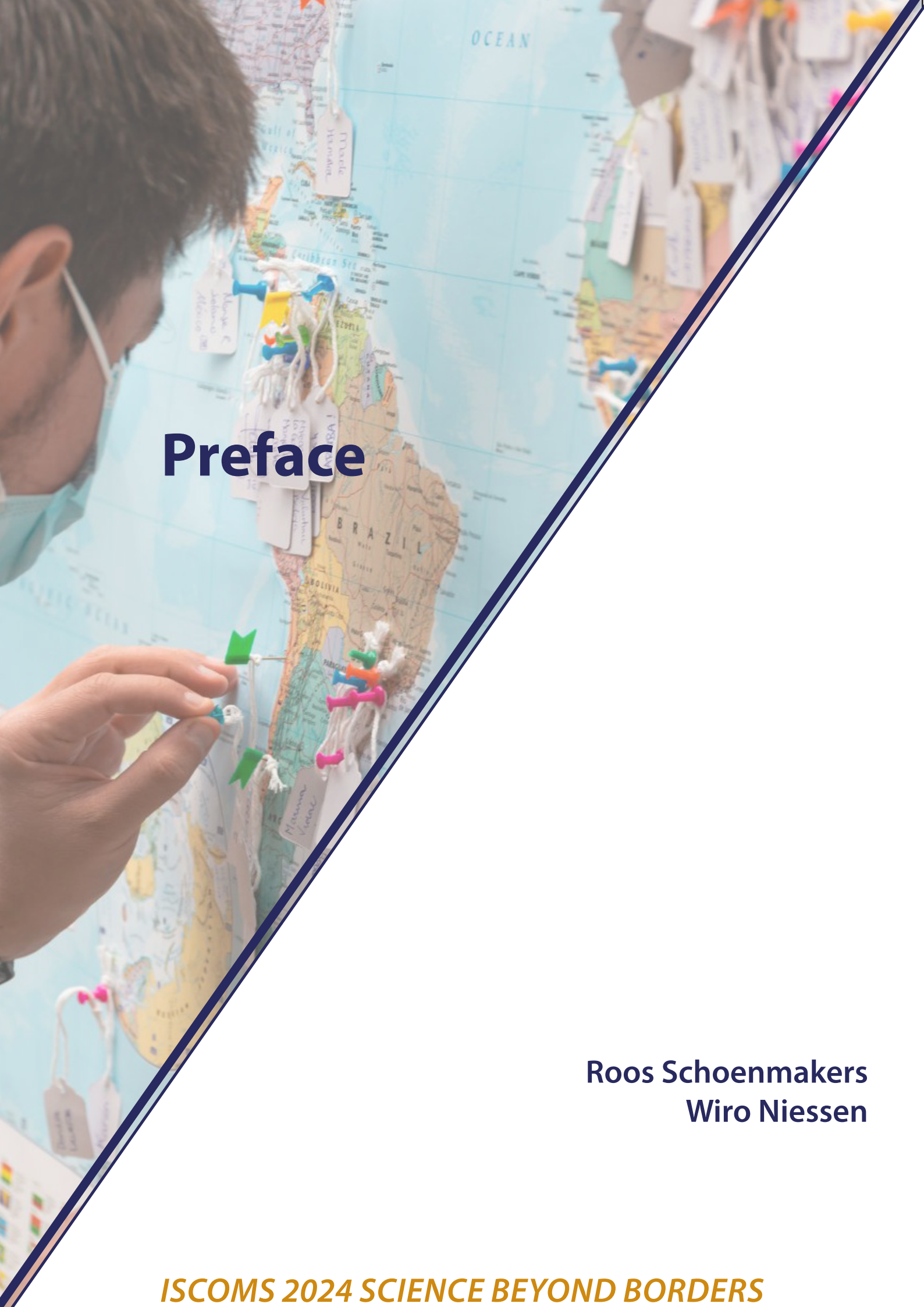


Preface

Roos Schoenmakers
Wiro Niessen

ISCOMS 2024 SCIENCE BEYOND BORDERS

Roos Schoenmakers
President ISCOMS 2024

Dear participants,

With great pleasure, I welcome you to the 31st edition of the International Student Congress of (bio)Medical Sciences (ISCOMS). I am proud that we are always handling according to our slogan; 'Science Beyond Borders'. We continue to provide students with the opportunity to present their research at an international platform, acquire knowledge by attending the scientific programme, and expand their network by interacting with other participants.

The theme of the congress is Future Medicine and for the first time, we will present daily themes, namely Inclusive Health, Artificial Intelligence: friend or foe, Molecular Mysteries, and Planetary Health. The themes are evident in the scientific programme, including day chairs, keynote lectures, and workshops. In addition, the theme will also be highlighted at the Fountain Patio.

On Monday, the 3rd of June, we start with the pre-course, a day in which enthusiastic students can improve their research skills by attending informative masterclasses. New this year are the ISCOMS Medical Talks, in which passionate specialists shed light on interesting topics in an interactive setting. During the following three congress days, participants are able to attend full days of inspiring lectures, hands-on workshops, and student presentations.

On Tuesday, keynote speaker Professor Michaela van der Schaar PhD, founder and director of the Cambridge Centre for AI in Medicine (CCAIM) and the most cited female AI researcher in the United Kingdom, will present a lecture about AI applications and Machine Learning in medicine. In addition, Professor Anne Schwerk PhD will speak on her expertise about the intersection of Artificial Intelligence and precision medicine. On Wednesday, Professor Dennis Lo Yuk Ming MD PhD, recipient of prestigious awards including the Lasker-Debakey Clinical Medical Research Award, will talk about his invention regarding Non-Invasive Prenatal Testing (NIPT). Also, Professor Brian Kobilka MD, Nobel Prize winner in chemistry, will give a lecture about his groundbreaking research on G-protein coupled receptors. On Thursday, keynote speaker Professor Mukesh Kapila MD PhD will speak on the prevention and management of genocides and recounts his experiences as a United Nations official.

There will be an interactive surgery where a vestibular schwannoma removal will be presented in an interdisciplinary way. In addition, the patient lecture is about an exoskeleton for people with a Spinal Cord Injury to allow them to stand up and walk again. After the congress, around thirty young and talented foreign (bio)medical students will start with the ISCOMS Research Fellowships where they will join the two-week research internships at the Research Institutes of the UMCG.

On behalf of the entire Organising Committee, I wish you all an inspiring experience and I hope you will enjoy ISCOMS 2024 as much as we did organising it.

Roos

Prof. Wiro Niessen PhD
Dean/Member of the Board of Directors
University Medical Center Groningen

Dear participants of the ISCOMS 2024 conference,

I would like to bid you a warm welcome to the International Student Congress Of bio(Medical) Sciences 2024. The beginning of June is always a beautiful time of the year in the city of Groningen. Spring turns into summer, the days are long, and the city is lively. And there is ISCOMS, the student conference that we at University Medical Center Groningen (UMCG) and the University of Groningen are immensely proud of. Fully organized by students for students, ISCOMS is one of the largest student conferences in the world and a truly unique event.

This year's theme of ISCOMS is Future Medicine. This theme greatly fits with the mission of the UMCG, where we aim to create the future of health; in all our activities, our main aim is to provide 'more healthy years'. More healthy years for citizens in our region, e.g. through prevention, by providing accessible, high-quality care, and by educating the next generation of health professionals. But also, more healthy years to people all over the world, by translating scientific discoveries and novel technologies into meaningful innovations.

In the ISCOMS programme, the Future of Medicine is explored in four thematic sessions: "Inclusive Health", "Artificial Intelligence, friend or foe", "Molecular Mysteries", and "Planetary Health. Around these theme's, this year's organization has managed to provide a wonderful programme, with great lectures, workshops, and activities. We are very proud to welcome renowned speakers such as Profs. Michaela van der Schaar, Anne Schwerk, Dennis Lo Yuk Ming, Brian Kobila (Nobel Prize Laureate), and Mukesh Kapila. And I here would like to express my great gratitude to the organizing committee for preparing this wonderful programme, and all the other hard work that is needed to organize such an event.

ISCOMS is a truly international meeting, and it is great to welcome people from such different places to Groningen. With * attendees form * countries, * of whom will be presenting their own work, we can have a truly global perspective on the Future of Medicine. Diversity and inclusion are important values for UMCG and the University of Groningen, and I am sure this diversity will increase the quality of the discussions and interactions at ISCOMS.

I invite you to take full advantage of the exciting programme of ISCOMS 2024. There can be such joy in learning new things, in getting inspired by the passion of professionals. In addition, I hope you will have an excellent time in Groningen. Conferences like these are also a place to meet people, to exchange ideas, to challenge each other how to create the best future for medicine, and, to have a good time. I myself met many people in my early career during conferences, and some of them have become dear friends.

Wiro

Organising Committee

Executive Board
Advisory Board
Junior Advisory Board
President, Secretary, Treasurer
Scientific Programme
Sponsors and Fundraising
International Contacts
Hosting and Logistics
Media and Branding
Research and Development
Ambassadors
Partners

Executive Board
ISCOMS 2024

The ISCOMS Executive Board consists of nine (bio)medical students of the University of Groningen and is working together with 24 members of the different committees to give you the best possible experience at ISCOMS. Our goal is to provide students with the opportunity to present their research on an international platform, acquire knowledge by attending the scientific programme, and expand their network by interacting with other participants. Since the Executive Board was formed in May 2023, we have accustomed ourselves to the functions and responsibilities. Throughout the meetings we had twice a week, we ensured that all tasks were completed and everyone was accurately informed.

In addition to our professional collaboration, we have also developed strong friendships. It is impressive how a group with such diverse personalities managed to complement and support each other whenever necessary. We have all learned a great deal during this challenging year and are very proud of the result. We extend our gratitude to the entire Organising Committee for their incredible efforts in organising this edition. Furthermore, we want to thank the advisory board, the junior advisors, and everyone else who supported us throughout the year.

We are honored to welcome you to the 31st edition of the International Student Congress Of (bio) Medical Sciences and we wish you an extraordinary experience!

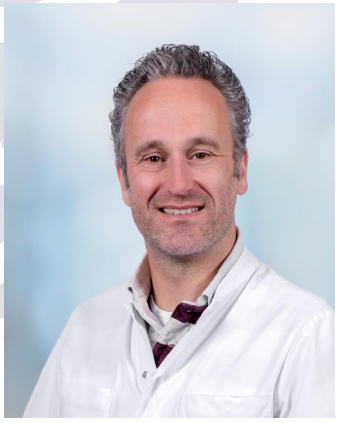
Roos Schoenmakers
Anke van Vliet
Adrian Naguib
Ali Eren Akkuş
Eva Hadderingh
Frederique Schimmel
Mas Arendsen
Iza de Wilde
Nick Meijer

Advisory Board

As the congress is organised every year by a new team of students, the advisory board can assist in the continuity of the congress. They have helped to organise ISCOMS for many years now. Their expertise, experience and contacts are of great support to the Organising Committee. The advisory board consists of three seniors from the University Medical Center Groningen (UMCG).

Prof. Paul de Vos PhD
Full professor of immune-endocrinology at the University of Groningen
Advisor since 2009

Prof. Matijs van Meurs MD PhD
Intensivist at the UMCG
Advisor since 2016



Robert A. Pol MD PhD
Vascular and transplant surgeon at the UMCG
Advisor since 2018

We would like to thank Paul, Matijs and Robert for their continuous support, advice and enthousiastic participation. We greatly appreciated and enjoyed our teamwork.

President, Secretary, Treasurer
ISCOMS 2024

The president, secretary and treasurer are responsible for overseeing the Organising committee, as head of the Executive Board.

The main task of the president, Roos Schoenmakers, is to lead the Executive Board. She is responsible for the whole organisation towards and during the congress. Additionally, her task is to find suitable day chairs and jury members.

The secretary, Anke van Vliet, is the contact person of the organisation. During this year she will work closely with the president. Besides that, she will be responsible for all of the registrations, both online and during the congress. She will manage the registration desk and will be happy to welcome you.

The treasurer, Adrian Naguib, is responsible for all of the budgetary aspects of the congress. As treasurer, he is in charge of the incoming and outgoing money and he will manage the budget estimate for the congress.

Furthermore, we will take care of the statistics of our congress, to improve ISCOMS for the coming years. We are looking forward to meeting you at ISCOMS 2024!

Roos Schoenmakers
Anke van Vliet
Adrian Naguib

Scientific Programme
ISCOMS 2024

The Scientific Programme committee consists of six young and enthusiastic (bio)medical students. It is their responsibility to organise the scientific part of ISCOMS 2024. They are in charge of the keynote lectures, workshops, pre-course, interactive operation and the ISCOMS Research Fellowships (IRF). Their aim is to make the scientific programme of ISCOMS challenging and diverse. Besides this, they also supervise the abstract selection and ensure that students can present their research in a plenary, oral or poster session.

During the pre-course, the Graduate School of Medical Sciences will tell you all about the research possibilities in Groningen at 'Your Future at the UMCG'. You will have the chance to improve your research skills in masterclasses and attend interesting speed-keynotes.

On three congress days five internationally well-established researchers will share their knowledge and experiences with us in keynote lectures. There are also a lot of exciting workshops you can participate in, ranging from practical workshops to patient demonstrations and interactive ethical workshops. Additionally, you will have the opportunity to attend an interactive operation. So even if you are not very familiar with research yet, you can visit the lectures, participate actively in hands-on workshops and gain new scientific skills.

For students who are interested in doing research in Groningen in the University Medical Center Groningen (UMCG), the Scientific Programme committee organises the two-week ISCOMS Research Fellowships. These short internships will take place directly after the congress and bring you into contact with researchers. Another possibility in order to come in contact with researchers from the UMCG is the workshop "Speeddating with Researchers". This workshop will be organised during the congress and will provide you the opportunity to talk to researchers of various Research Institutes of the UMCG.

We enjoy creating a challenging and diverse scientific programme for ISCOMS 2024 a lot and we are looking forward to meeting you all!

Ali Eren Akkuş
Georgina ter Haar
Jules van Eekeren
Wibine Roelants
Yfke van Doorn
Chris Remerij

Sponsors and Fundraising
ISCOMS 2024

ISCOMS cannot take place without its financial funding. The committee of Sponsors and Fundraising takes care of the financial resources. The Sponsors and Fundraising committee consists of five enthusiastic, dedicated students who will make every effort to make this congress financially possible. They do their very best to contact and inform companies in order to establish a good cooperation between the sponsors and ISCOMS.

Due to the fact that ISCOMS is one of the biggest student congresses for biomedical sciences within Europe and due to the numerous national and international students attending, ISCOMS has a great amount of sponsoring opportunities to offer. Besides students, there will also be scientists, professors, researchers and UMCG medical specialists attending the presentations, lectures and workshops. Hence making ISCOMS very attractive for potential sponsors.

Being a sponsor of ISCOMS allows extensive prospects for both large and small companies to create more awareness for the company, subsequently acquiring new business opportunities. Our purpose is to establish an agreement of mutual benefits. Companies can present themselves with an appearance of their logo on for example our website or our congress bag, a stand or giving interesting workshops.
Apart from contacting potential sponsors, the committee will also subscribe several funds to support ISCOMS. Besides that, one of the committee members is going to assist the treasurer with the finances during the congress. They are also responsible for the journal subscriptions which the presenting participants can win during the congress.

If you are interested in supporting biomedical research and if you want it to be able to reach hundreds of national and international motivated (bio)medical students or if you are willing to support ISCOMS as a high standing platform to exchange in international scientific knowledge, please take a good look around on our website! If you have any questions, please contact us and we are more than willing to give you all the information you need.

Eva Hadderingh
Raven Osinga
Dido Jakel
Loek de Esch
Sacha Snoek
Martijn Eshuis

International Contacts
ISCOMS 2024

The International Contacts committee takes care of the international part of ISCOMS. Their daily responsibilities include the worldwide promotion of the congress, and taking care of participants who encounter problems with their registration or experience other difficulties while preparing themselves for ISCOMS 2024.

The International Contacts committee takes care of the promotion by e-mailing, calling, and sending promotional materials across the globe. In this worldwide promotion they are supported by our highly motivated and valued ambassadors, who were inspired by their own ISCOMS experience. Click here to see what ambassadors do and which ambassadors you can contact in your own country.

All incoming emails of students who want to submit their abstract or who are seeking additional information about ISCOMS are answered by the International Contacts committee. They are also the committee that has contact with the embassies when aiding students in obtaining their Visa. Lastly, they are responsible for the Travel Grants for students that require financial aid in order to attend our congress.

As the International Contacts committee, we are constantly looking for new contacts around the world that would like to help us with promoting ISCOMS 2024. If you believe you can help, please send an email to iscoms@umcg.nl. If you have any other questions regarding promotion, Visas, ambassadors, Travel Grants, and so forth, please send us an email and we will be glad to help you!

We hope to see you at ISCOMS 2024!

Frederique Schimmel
Philip de Knijff
Julia Scholten
Xander Hegeman
Aniek Perdok
Nina Ruys

Hosting and Logistics
ISCOMS 2024

The Hosting and Logistics committee is responsible for hosting of participants, the social programme and the logistics during the congress.

When the participants come to Groningen, they need a place to stay. Next to providing discounts on various hotels and hostels in the city, the Hosting & Logistics committee can usually offer a cheap and fun alternative. In the stay with a student option, participants will sleep in a typical dutch student house. Next to it being cheaper than a hotel, participants will get to socialize with students from Groningen and see how they live.

Next to the scientific programme, ISCOMS offers a broad social programme for the participants to socialise and have fun with each other.

The Hosting & Logistics committee organises a city tour, a salsa workshop, a formal dinner on Tuesday, a "social evening" on which various activities were held and after the last day of the congress the World Wide ISCOMS night. A night on which everybody dresses up in a typical/classical outfit of their country and comes together to have a party to celebrate the amazing week they had. On Friday, one day after the congress, ISCOMS will go to another Dutch city. There, the Post Congress Tour is held, a day with activities and relaxing.

At last the Hosting and Logistics committee handles all the logistics at the congress. Together with the Scientific Programme committee they provide the programme for the congress, as well as the plan of action, a book in which every detail of the congress is laid out.

We hope you are as excited as we are and we are looking forward to seeing you at ISCOMS 2024!

Mas Arendsen
Anouk Vrouenaerts
Flip van Tongeren
Wietske de Boer

Media & Branding
ISCOMS 2024

The Media & Branding committee is responsible for the appearance of ISCOMS and the online promotion of ISCOMS. The committee consists of four creative and enthousiastic (bio)medical students who are constantly renewing the looks of the congress.

Their main task is to deliver the graphical design of all material that will be handed out at the congress and of all logo's, flyers, posters, booklets and cards that are spread all over the world by our colleagues from the International Contacts committee. Furthermore, they compose and design the Book of Abstracts that will be available online for all students. This book contains information about the congress and the people involved and contains all abstracts of participants who present their research at ISCOMS 2024. The presenting participant guide is also the responsibiilty of the Media & Branding Committee; this book contains tips and tricks to use while preparing for your presentation, the scientific programme, payment and visa information and important deadlins for presenting participants.

Besides the graphic design they are the creators of the ISCOMS Promotion Film, Trailer and Aftermovie. During the congress they will make sure every memorable moment is captured and shared with all the participants.

They are also responsible for keeping everyone updated with the latest news about the congress via social media platforms like Facebook, Tiktok, Instragram and LinkedIn and, of course, keeping you entertained!

We are very excited to welcome you to ISCOMS 2024.

Iza de Wilde
Bart Pastoor
Noor Brands
Marte Hamstra

Research & Development
ISCOMS 2024

The main goal of the Research & Development committee of ISCOMS is to innovate and improve every upcoming edition of the congress. They establish this by extensive evaluation that helps us determine what we can and should change. Also, they try to think of how it could be changed. The committee makes sure the improvements are implemented at the upcoming congress. Brainstorming is a great part of the committee's task. Thinking of new ideas that will enhance the congress. These ideas come from the evaluation sheets that participants fill out and, for example, brainstorm sessions with the entire organisation that our committee organises.

A good example of innovation of ISCOMS is the application for smartphones that has been set up and launched five years ago. In the meantime, it has been updated by the committee and is improving every year.

Furthermore, the Research & Development committee is responsible for the website. This means that, in addition to providing the website with its lay-out, they also keep the website up to date at all times to ensure you will receive the correct information.

Furthermore, they maintain partnerships with other student congresses, because these are vitally important to the improvement of medical congresses in general. Each year they evaluate these partnerships and look for possible new ones. As partners, ISCOMS tries to become an even more inspiring congress.

We would be delighted to welcome you to ISCOMS 2024!

Nick Meijer
Bauke Oostheim
Toon de Ruiter
Elise Verhees

Ambassadors
ISCOMS 2024

The ambassadors of ISCOMS are participants or presenters from a previous ISCOMS who were so enthusiastic about the congress, that they decided to apply to become a well-respected ambassador. They play a vital role in our international promotional campaign. Each year ambassadors are selected after the congress and maintain the ambassadorship for exactly one year, until the next congress takes place. However, some ambassadors can be reselected as they provided such devotion to ISCOMS that they cannot be missed.

The ambassadors start their main promotion in October. They share our social media posts and promote ISCOMS in their country by distributing posters and flyers. Some of the ambassadors even organise meetings or give presentations to explain how great their experience was at ISCOMS. The enthusiasm and excitement that we wish to bring across to everyone all around the world, is accomplished by this group of young excited scientists. We have ambassadors from over 35 countries worldwide, who we have close contact with. On the website you can find all of our ambassadors and their passion is evident in their words:

"I was privileged to attend ISCOMS in 2022 for the first time and I learned so much through the keynote lectures, oral and poster presentations, laboratory tours, and many other educational and recreational activities. ISCOMS is a great platform for students to present their research, and learn from fellow students and researchers from all over the world on different types of research they are conducting in their respective fields."

Alice Chimwemwe Mnyanga, a Master of Science student at the Kamuzu University of Health Sciences and a Research Assistant at Malawi Liverpool Welcome Trust.

For any question about ISCOMS, Visa applications, travelling to Groningen, or anything else, please do not hesitate to contact our ambassadors, as they will be more than happy to help you out. Their e-mail addresses can be found on our website.

If ISCOMS 2023 also excited you and makes you want to share your experience with others, you can apply to become an ambassador for ISCOMS 2025. Help us with our promotional campaign yourself!

Ambassadors
ISCOMS 2024

We would like to thank the following ambassadors for supporting us this year!

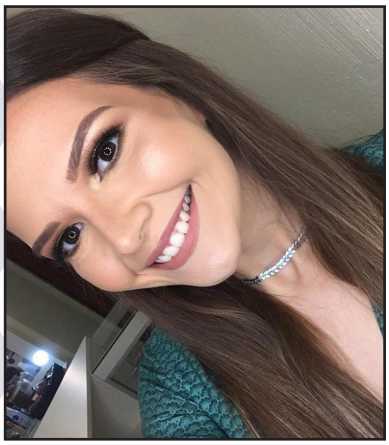
Sabina Hasanzade
Azerbaijan

Aghayarli Farida
Azerbaijan

Gabryella Cunha Aquino
Brazil

Gabriela Esteves de Jesus
Brazil

Luisa
Brazil



Ludimila Leite Marzochi
Brazil

Ambassadors
ISCOMS 2024

Usman Ali Khan
Bulgaria

Eduardo Villa
Chile

Kevin Saldarriaga Bedoya
Colombia

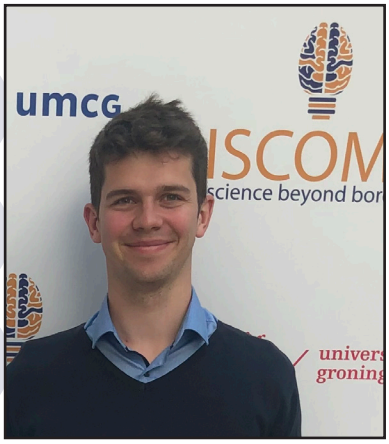
ADANNA Joyce Emenikeonu
Georgia

Rihana
Georgia

Elene Liluashvili
Georgia

Unzila Saifi
Georgia

Elene Lipartia
Georgia

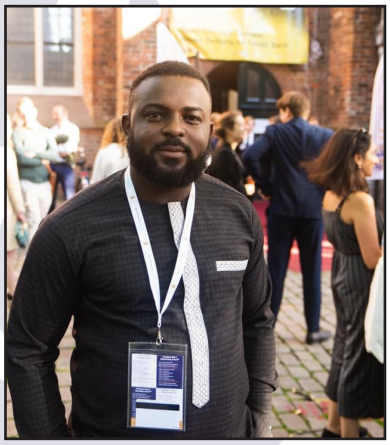


Maximilian Greiner
Germany

Ambassadors
ISCOMS 2024

Du Hanh
Germany

Yaa Owusuaa Offei Darko
Ghana



Bernard Annan
Ghana

Eirini
Greece

Dr. Pravina Kale
India

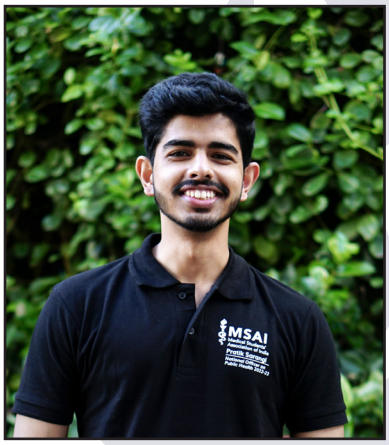
Perminder Singh
India

Kahan Mehta
India

Noora Jabeen
India

Prastuti Verma
India

Ambassadors
ISCOMS 2024



Pratik Sarangi
India

Dev Patel
India

Akriti Kumari Gupta
India

Nimrah Rehman
India

Pravina
India

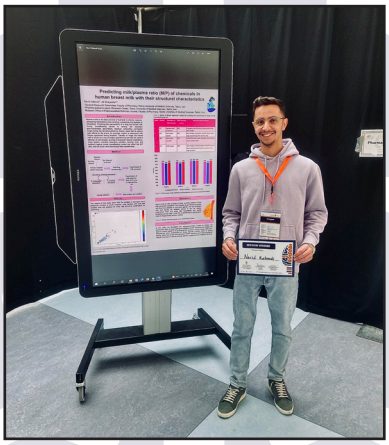
Masha
Iran

Mohammad Mobin Mirimoghaddam
Iran

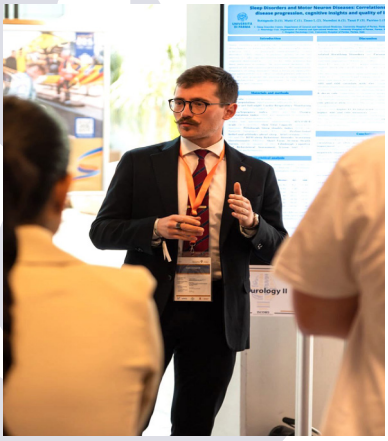
Niloufar Hazrati
Iran

Ambassadors
ISCOMS 2024

Niloufar Jafari
Iran



Navid Kaboudi
Iran

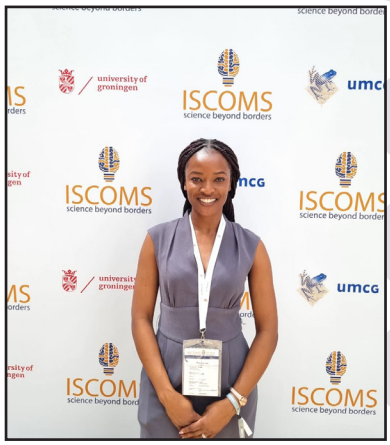


Dario Bottignole
Italy

Rami Edreis Gedo Abdalla
Kazakhstan

Ahmed Alsoufi
Libya

Taha Nagib
Libya



Alice Chimwemwe Mnyanga
Malawi

Glory Kaunda
Malawi

Saúl Rueda
Mexico

Ambassadors
ISCOMS 2024

Sara Arechavala
Mexico

Dashampreet Singh
India

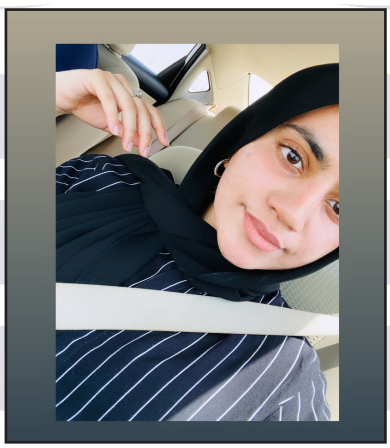
Theofanis Mavrepis
Netherlands

Samson
Nigeria

Savetka Drvarova
North Macedonia

Hristina Palazova
North Macedonia

Anna Bętkowska
Poland



Hafsa Khalid
Qatar

Mazga Isabela Andreea
Romania

Ambassadors
ISCOMS 2024

Vasiliki Antonopoulou
Romania

Syeda Sobiah Imad
Saudi Arabia

Yasir
Saudi Arabia

Okunola David Ayodele
Serbia

Ademeta Esther Oluwafeyisayo
Serbia

Pheladi Mokoena
South Africa

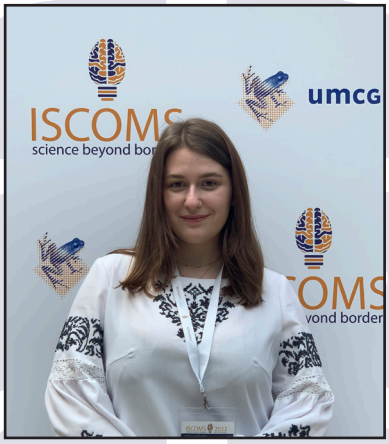
Sofía Cecilia García Soto
Spain

Rami Edreis Gedo
Sudan

Mert Egemen Çaliskan
Turkey

Ambassadors
ISCOMS 2024

Mukiza Prince Cesar
Uganda



Iryna Sokolnyk
Ukraine

Sofia Chala
Ukraine

Kapilraj Ravendran
United Kingdom

Dr Rizana Riyaz
United Kingdom

Krishin Yerabolu
United States

Zarnigor Umurzakova
Uzbekistan

Chenai Matowe
Zimbabwe

Partners
AIMS

The Annual International Medical Students (AIMS) Meeting is an international medical congress hosted at the Faculty of Medicine of the University of Lisbon, entirely held by students every year during the month of April. With renowned national and international speakers and a huge range of practical workshops on several medical fields, this is one of the most complete and alluring congresses for students in Europe. Since it is a three-day congress, each day is based on a subject module and all the scientific lectures are related to it. Besides this, there are also keynote lectures, Clinical and Scientific Competitions, a Research Competition (poster, oral and plenary sessions) and a science speed dating session with doctors and researchers. It is our main purpose to promote an enriching scientific setting for learning, interaction and communication among students, health professionals and researchers alike. As we deeply value the social and cultural dimensions of the human being, the AIMS Meeting also includes a social programme and a charity programme for all its participants.

Partners
AMSA

Student's Association (AMSA) International is a peak representative organisation for medical students from across Asia, the Asia-Pacific and beyond. Training doctors from 16 members Nations and 11 Associate/Observer Nations combine to share knowledge, undertake activities and create international and transcontinental friendships. AMSA awas officially founded in Manila, Philippines in 1985, and from this day it has been an active, dynamic and exciting student-led, not-for-profit, non-political organisation. Today, with members and friends spanning the glob AMSA has an active student-exchange programme, regularly undertakes national and regional projects, provides humanitarian assistance at times of need, produces quarterly student publications ans liaisies with the World Health Organisation, the Association of Medical Doctors of Asia and many other international and regional medical student organisations. Since it was first stablishes in1979 and the first conference was held in Mahidol University of Thailand, the Asian Medical Student Conferences have been a key focus for the organisation. Now it is held biannualy in January/February and July/August. These events see over 700 students from across the world to learn from each other, teach their fellow peers and develop lasting friendships. The AMSA Vision is Knowledge, Action and Friendship. Three areas we continuously strive to in our members and peers through our organisational missions:

- Knowledge: We promote scientific and medical activities to increase and expand our knowledge whilst training to become the medical professionals of the future.
- Action: As medical students, we are concerned for the community around us and endeavour to do things for the benefit and improvement of our fellow citizens.
- Friendship: As future doctors, we aim to build and maintain a good relationship among our colleagues of the Asia-Pacific and beyond.

AMSA
ASIAN MEDICAL STUDENTS' ASSOCIATION
SINCE 1985

AMSA INTERNATIONAL

Partners
AMSC

The Antwerp Medical Students' Congress is a project of the European Medical Students Association in Antwerp, Belgium. The AMSC has been organised yearly since 2006. Our congress is perfect for all students in the (para) medical field (medicine, pharmacy, dentistry, biomedical sciences and nursery) to share their knowledge with students from across the world. This year, AMSC will take place from the 12th to the 15th of September 2023. We will spend the first two days sharing all knowledge gathered by research conducted by medical students, using poster and oral presentations. Afterwards, we will inform you on the top medical practice, performed here in Antwerp and Belgium, through several interesting lectures and workshop

Partners
Braincoms

Braincoms is a unique opportunity for you to include yourself in the international medical context by listening to amazing internationally acclaimed speakers, practising and improving your skills at hands-on workshops, building up a network with other medical students from everywhere, and much more! All this in an engaging atmosphere with smart people, sense of humour, outstanding scientific quality and – why not? – great food and social events! This congress has everything to add a lot to your personal and medical formation. You couldn't spend these 3 days in a better way. You can't waste this chance!

The last edition of BRAINCOMS took place in São Paulo, at UNIFESP - Universidade Federal de São Paulo, Brazil, from the 17th till the 19th of November. Stay tuned for our next edition!

For more information, please, check our website: https://www. braincoms.com/

BRAINCOMS
BRAZILIAN INTERNATIONAL CONGRESS OF MEDICAL STUDENTS

Partners
CROSS

Croatian Student Summit – CROSS is a congress organized by the Student Council of the University of Zagreb, School of Medicine that has been continuously organised for 17 years in a row. The project was started in the academic year 2004/2005 and it also involved Dental, Veterinary and Pharmacy-Biochemistry Schools in the University of Zagreb. The eighteenth congress in a row will take place in 2023, at the School of Medicine University of Zagreb, Šalata 3. This year's topic is Body & Mind. (This topic is only regarding lectures.) Topics for poster presentations may differ. For more details about how to register and participate in CROSS 18 visit our website: https://cross.mef.hr/en

Partners
EMSA

The European Medical Students' Association (EMSA) is a politically neutral, non-governmental, nonprofit and independent organisation that represents students from individual medical faculties across geographical Europe. It was established in 1991 in Brussels, Belgium and is currently uniting 96 medical faculties in 24 different European countries. European Medical Students Association seeks to improve the health and quality of care of the European citizens, by acting as a conduit for increased interaction and sharing of knowledge between European medical students in the areas of medical education, medical ethics, medical science and European integration. The main objectives of EMSA are to establish a network between European medical students in order to facilitate European integration and develop a sense of European identity, to represent and voice the opinions of medical students of Europe and to promote the highest standards in European medical education, science and ethics.

Our webpage: www.emsa-europe.org Official BlueMist blog: www.bluemist.eu

Partners
ICHAMS

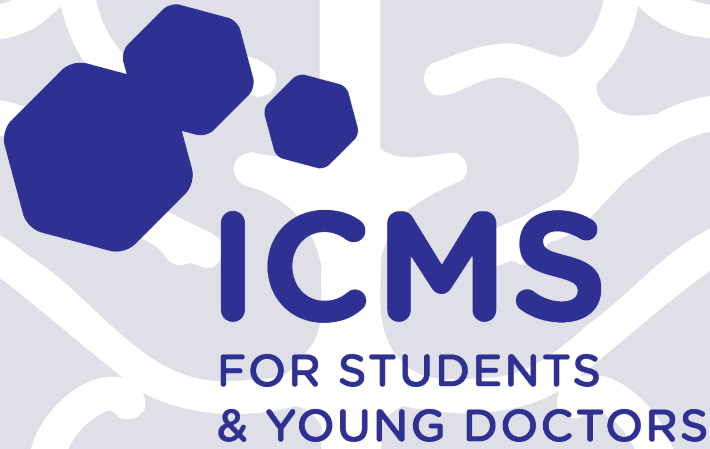
The International Conference for Healthcare and Medical Students (ICHAMS) is held annually at the Royal College of Surgeons in Ireland (RCSI) to allow undergraduate healthcare and medical students to present their research to peers and professionals in this field. Our mission is to create a platform for students across the globe to interact with one another in order to challenge conventional methodology and encourage innovation in medicine. The conference includes workshops offered on a variety of topics as well as keynote speakers representing incredibly impactful realms of medicine. Centred in the vibrant city of Dublin, Ireland, we also encourage our participants to embrace the rich culture via city walking tours and traditional Irish music. The first conference was held in 2011, and in 2013 the conference received the Irish Healthcare Award for student project of the year. As we continue to grow as an international conference, we are continuing to follow our mission of creating a global platform for innovation and medical research. For more information, visit our website www.ichams.org or contact us at ichams@rcsi.ie!

ICHAMS

International Conference for Healthcare and Medical Students

Partners
ICMS

ICMS – International Congress of Medical Sciences is an international event that welcomes more than 500 participants every year. The congress gives the opportunity to students and young doctors from all over the world to present their research in a set of Preclinic, Therapy, Surgery and Public Health poster and oral sessions. We aim to inspire innovation and promote academic quality through an outstanding list of hands-on workshops and keynote lectures by world-renowned scientists and doctors. The organiser of the forum is the Association of Medical Students in Bulgaria – Sofia (AMSB-Sofia).



Partners
IFMSA

International Federation of Medical Students Associations of the Netherlands (IFMSA-NL) is an organisation for Dutch medical students, situated at each of the eight medical faculties. Our mission is to offer future physicians a comprehensive Introduction to global health issues. Through our programming and opportunities, we develop culturally sensitive medical students, intent on influencing the transnational inequalities that shape the health of our planet. Besides being the Dutch member organisation of the worldwide federation called IFMSA, IFMSA-NL is also part of the European Medical Students Association (EMSA). More information at: http://www.ifmsa.nl/

IFMSA

Partners
LIMSC

The Leiden International (Bio)Medical Student Conference (LIMSC) is the largest biennial student conference in the world. LIMSC offers the opportunity for medical, biomedical and life sciences students worldwide to present their research, to participate in various state-of-the-art workshops, to be enlightened by prominent guest speakers and to engage in networking with fellow international students and researchers. Furthermore, anyone just interested in learning about cutting-edge research at the frontiers of science can attend the whole scientific and social programme without having to present their research. LIMSC takes pride in being able to provide a high-quality student conference since 1999 and we strive to improve LIMSC with every passing edition. This year's edition of LIMSC took place from the 15th till the 18th of March 2023

Partners
WIMC

We believe that there is a huge need of international meetings for medical students. Such events provoke discussion, lead to cooperation, provide inspiration and encourage young scientists to further endeavours. Therefore, we would like to invite you to Warsaw International Medical Congress (WIMC) 2023 edition. Students from all over the world are welcome to register and present their research, attend workshops, keynote lectures and thematic sessions. Students can choose to present their research in many different scientific sessions including a Dentistry Session, Case Report Sessions and PhD Students Sessions. WIMC offers a wide range of workshops – during the previous edition participants could choose out of 30 different fields. The rich social programme is another reason for joining the congress – the opening ceremony, gala dinner, medical students' party and "Warsaw by night" are events that should not be missed!

Please visit our website for more details: http://wimc.wum.edu.pl/

19th WIMC
WARSAW INTERNATIONAL MEDICAL CONGRESS

Partners
YES Meeting

The Young European Scientist Meeting (YES Meeting) is an annual international students conference which takes place at the Faculty of Medicine of the University of Porto, Portugal. After seventeen editions, the YES Meeting still aims to provide students with the opportunity to learn about groundbreaking and innovative discoveries from world-class scientists, and, more importantly, to hence their motivation in doing research! Therefore, the students have the chance to present and discuss their research projects on Oncology & Molecular Biology, Neurosciences, Physiology & Immunology, Internal Medicine, Surgery, Public Health & Medical Informatics. You'll also have the possibility to improve your skills with a wide variety of workshops and enjoy the beautiful city of Porto through various kinds of social programmes, where you can enjoy Porto's great weather and its vibrant culture. We invite you all to take part in the 18th YES Meeting, which will take place between the 14th and 17th of September 2023, whether as a Presenting or a Non-Presenting student. We are waiting for you!

YES MEETING

Partners
ZIMS

ZIMS is a medical congress that brings together medical students and young doctors worldwide. ZIMS gathers students of biomedical sciences and young doctors. Definition of „young doctor" is taken from the statute of EMSA Europe as a person who graduated from medical studies in the last 5 years. You can participate as active presenter (with poster presentation or oral presentation on MS PowerPoint), or as passive participant. ZIMS is one of few conferences where young students and not yet affirmed scientists have access to the world of publishing, thus becoming the only conference in Europe where the book of abstracts is published as a supplement to a prestigious medical journal, 'Liječnički vjesnik', which is indexed in EMBASE/Index Medicus. Moreover, the best works are published as full texts.

ZIMS
ZAGREB INTERNATIONAL MEDICAL SUMMIT

Partners
IBC

The International Biomedical Congress Sofia is an event, organized by students and aiming to unite a medical, dental and a pharmaceutical symposium. It gathers hundreds of participants each year.

We provide the participants with Medical, Dental and Pharmaceutical Symposium as well as Junior Pre-Course- a platform that allows students from all over Bulgaria with appearances and interests in the field of natural sciences to participate for free in this special program.

Participants have the opportunity to attend various workshops, lectures as part of the scientific program, divided in 4 clusters, Medical Universiade- a special competition, and last but not least the Opening Ceremony- a Gala dinner where participants have the possibility to immerse themselves in the motivational yet friendly, warm and supportive atmosphere we aim to create.

Organisation

Junior Scientific Masterclass
Graduate School of Medical Sciences
Research Institutes

Junior Scientific Masterclass Programme

Sonja Pyott
PhD, Associate Professor Department of Otorhinolaryngology/Junior Scientific Masterclass Programme Coordinator

About the Junior Scientific Masterclass (JSM) Programme

The Junior Scientific Masterclass (JSM) Programme organized by the Faculty of Medical Sciences at the University of Groningen and University Medical Center Groningen (UMCG) offers a unique opportunity for students enrolled in the bachelor's degree in Medicine and Dentistry to enhance their scientific training. Through the JSM Programme, students explore the integration of scientific research and clinical care, engage in hands-on research projects under the supervision of established (physician) scientists, deepen and develop their scientific knowledge and research skills, and gain the opportunity to tailor education and training to their individual interests and career goals, including preparation for the (D)MD/PhD trajectory.

Bridging the Gap: Training for Innovation in Healthcare

Physician-scientists play a crucial role in bridging research and clinical practice, both in translating research outcomes into advances in patient care as well as reverse-translating patient outcomes to understand their mechanistic basis. To fill the well-recognized shortage of physician-scientists, especially in the northern Netherlands, the JSM programme was created in 1999 with the mission to provide motivated and talented students opportunities to develop their research skills and ambitions and, thereby, train and ultimately embed talented physician-scientists in the northern Netherlands. Beginning in 2001, the (D)MD/PhD programme has given talented students the opportunity to pursue a PhD in parallel with their medical studies. Most recently, beginning in 2012, the Mandema stipend was initiated to enable new physician-scientists, (D)MD/PhDs, to combine their medical specialist training with research and establish their own lines of research. These initiatives have together trained numerous physician-scientists who now work successfully in the UMCG and surrounding hospitals.

Getting Involved in the JSM Programme

The JSM Programme offers numerous courses, research opportunities, and networking and mentoring activities to develop your scientific knowledge and skills. You can see the full range of available courses in Ocasys. If you're a student interested in joining the JSM Programme, please check out our website or email us. If you're a (clinician) scientist who would like to become (more) involved in the JSM Programme please also email us or check us out on the University Medical Center intranet.

Ocasys: **https://ocasys.rug.nl/current/catalog/programme/JSM1**
Website: **https://www.rug.nl/umcg/education/geneeskunde/junior-scientific-masterclass/**
Email: **j.s.masterclass@umcg.nl**
Intranet: **https://intranet.umcg.nl/c/portal/login?redirect=%2Fjunior-scientific-masterclass&refererPlid=38980&p_l_id=2**

Graduate School of Medical Sciences *(GSMS)*

Prof. dr/ Jolanda Smit, director GSMS

The Graduate School of Medical Sciences (GSMS) is the largest Graduate School of the University of Groningen. The GSMS is responsible for the selective masters and PhD education programmes within the University Medical Center Groningen (UMCG). Research within the UMCG ranges from fundamental to patient-oriented (clinical) research. The programmes available cover a wide range of research fields and are aimed towards students with a background in areas including biology, biochemistry, biomedicine, healthy ageing, healthcare, medicine, pharmacy, psychology and human movement sciences.
Prof. dr Jolanda Smit, director GSMS

Prof. dr Jolanda Smit, director GSMS

Graduate School of Medical Sciences (GSMS)

PhD programmes

The Graduate School of Medical Sciences (GSMS) offers different opportunities to prospective PhD students. Support ranges from locating potential supervisors to tailor-made advice in line with the funding structures you may have access to. Please consult our website to learn more about the types of PhD opportunities we have to offer.

Why pursue a PhD at the GSMS?

Internationally oriented

At the Graduate School of Medical Sciences, we are working with people from all over the world All of our postgraduate programmes are taught in English and almost half of our doctoral students are international! We encourage our students to complete parts of their programme in partner universities abroad and to build connections across national and cultural borders.

Personalised programme

We encourage our students to become critical and independent thinkers At the Graduate School of Medical Sciences, you will follow courses and do research in small groups where personal interaction with your supervisor is an important part of your education. As a result, our students design their research and their programme to meet their own personal interests.

World-class research

The University of Groningen is a top 100 University: our researchers come from all over the world and conduct groundbreaking research in an international environment Research within the GSMS ranges from fundamental to patient-oriented (clinical) research The GSMS has organized all its research in five research institutes and research programmes that each have developed research programmes around specific aims and objectives.

Degree awarded: PhD

Graduate School of Medical Sciences (GSMS)

Master programmes

The Graduate School of Medical Sciences administrates two master programmes:

1. **Clinical and Psychosocial Epidemiology**

Clinical and Psychosocial Epidemiology (CPE) is a selective two-year research master. This two-year selective research master's programme is designed to educate motivated students through a challenging and high-quality interdisciplinary curriculum. We focus on the prevention, development, and treatment of both physical and mental conditions. Biological, psychological, and social aspects all play a role in such conditions. In CPE students learn to unravel complex mental and physical health problems and how they can contribute to better solutions by applying innovative research designs and statistical techniques while making use of state-of-the-art facilities. Students will be situated within the University Medical Center Groningen (UMCG), and have the opportunity to work with unique data resources.

Track - Lifecourse Health Development

In this track, the focus lies on unraveling how chronic diseases and mental health issues develop and progress over a person's life through the application of a lifecourse perspective. Understanding the processes leading to changes in health and wellbeing and improving prevention and treatment strategies are key aspects of this track. While collaborating with renowned researchers and clinicians, you will learn how a person's age, stage of illness or stressful life events affects these processes.

Track - Health Systems and Prevention

In this track the focus lies on the application of a systems approach as a strategy for designing and evaluating population-targeted prevention programmes. Through the HSP track, you will acquire practical experience during an internship, allowing you to put research into practice to make a measurable impact on society.

More information: https://www.rug.nl/cpe

2. **MSc Molecular Medicine and Innovative Treatment**

The MSc Molecular Medicine and Innovative Treatment (MMIT) is a two-year selective programme designed to educate motivated students through a challenging and high-quality multidisciplinary curriculum. Whether students aspire to work in or outside academia, we will prepare them for a successful career in (bio)medical and pharmaceutical sciences. The programme is unique in that all the courses focus on how to become a successful independent researcher. Right from the start, students will learn to become a critical evaluator of current research, develop their own ideas, and define the kind of researcher they want to become.

MMIT offers a rare advantage by integrating clinical, medical, and pharmaceutical aspects. It covers a wide range of exciting topics in molecular and translational medical research such as Immunology and infectious diseases, drug innovation and development, neurobiology and neurodegenerative diseases, cancer biology and immune therapy, cardiovascular diseases, and bioinformatic and system medicine.
Track: Innovative Medicine (IMIM)

Research Institutes

Track: Innovative Medicine (IMIM)
Do you want to become an entrepreneur, start your own company to advance the research idea or medical device that you designed during your Bachelor or Master project? The Innovative Medicine track track offers training for students to patent a research idea, write and pitch a business plan and finally bring it to the market.

If you are interested in (applying for) one of these programmes? Please consult our webpages for more information:
www.rug.nl.cpe
www.rug.nl/mmit

Health in Context:
Research Institute for Prediction, Prevention, and Care
Director: Tineke Oldehinkel
Our mission is to promote public health and clinical care by facilitating high-quality research aimed at understanding and predicting health trajectories, preventing the onset, relapse or negative consequences of disorders and improving the treatment and care of patients. Much of our research focuses on contextual factors associated with health-related outcomes, including interventions. Together we envision shaping healthy futures for citizens, clients and patients.
Our institute covers fifteen research programs, which can be described by three research themes.

Clinical, cognitive, perceptual, and translational neuroscience
This research aims to better understand how the brain is involved in mental, cognitive, perceptual, and motor abilities, and to develop more effective treatments for current and future patients.

Individual, social, and environmental risk and resilience
This research focuses on how risk and resilience factors within individuals and in their social and physical environments influence the onset, course and consequences of disorders.

Movement, education, treatment, and care
This research focuses on how we can provide the best possible treatment and care. It involves, among other things, promoting lifestyle management, evidence-based training of health professionals, and treatments that are cost-effective and optimally geared to patients' needs.

MoHAD:
Research Institute for Mechanisms of Health, Ageing and Disease (MoHAD)
Director: Marco Demaria
The mission of MoHAD is to foster knowledge and promote collaboration among fundamental, translational and clinical researchers to understand and target disease mechanisms. With a deeper understanding of the mechanisms that regulate health and pathology, we strive to develop innovative therapeutic applications for multiple morbidities and for extension of healthy longevity.

Research Institutes

Themes:

- *Oncology* (Theme lead – Marcel van Vugt)
- *Cardiovascular and Renal* (Theme lead – Udo Mulder)
- *Aging and Development* (Theme lead – Ellen Nollen)

Precision:

Personalized medicine research institute Groningen (PRECISION)

Director: Debbie van Baarle

The mission of Precision is to foster innovative research in the development of diagnostic and therapeutic strategies aimed at advancing personalized care. To achieve this, we aim to create an open, inspiring, translational environment to facilitate multidisciplinary scientific excellence towards novel personalized treatments with scientific, economic and/or societal impact. Researchers from UMCG and GRIP actively participate within this institute.

The research is embedded in 3 themes:

1. *Innovative technologies for diagnostics, treatment and transplantation (Theme lead – Bart Cornelissen).*

Within this theme, we will develop novel medical technologies to identify and monitor disease, to improve (specificity of) treatments and to enhance survival after transplantation.

2. *Drug development and therapeutic strategies (Theme leads – Patrick van Rijn, Reinoud Gosens (GRIP)).*

We aim to improve drug therapies by discovery of novel drug targets, development of new (small molecule and biological) drug entities and therapeutic strategies, improved delivery of these drugs, and evaluation of drug use in the real world (from preclinical to application).

3. *Microbes, inflammation and immunity (Theme lead – Jill Moser).*

We will focus on conditions in which homeostasis is disturbed by pathogens or imbalances in host and inflammatory pathways in order advance immunomodulatory therapies and vaccine development.

Graduate School of Medical Sciences (GSMS)

European Research Institute for the Biology of Ageing (ERIBA)

Research in ERIBA is strongly connected with education and training of the future generation of Biology-of-Ageing researchers. ERIBA aims to be "the place to be" for the best students by offering comprehensive training in some of the top Biology-of-Ageing laboratories in the world. We have developed a cutting-edge graduate curriculum in Ageing biology in which students will be exposed to a wide variety of model systems and approaches. The extensive training experience of the international faculty at ERIBA in other research institutes worldwide ensures an optimal educational and research environment.

Undergraduate students

ERIBA welcomes applications from undergraduate (pre-BSc and MSc) students who wish to pursue an internship in one of the ERIBA labs. Students would typically be enrolled at a biomedical, chemical, pharmaceutical, medical or bioinformatic programme at their home University or University of Applied Sciences ("Hogeschool"). Prospective students are invited to explore the different research teams on the ERIBA website, and motivate in their application the interest for the lab of their choice. Although some short-term internships may be available, we prefer rotations that last for 5 months or longer.

PhD students

ERIBA offers an exciting environment to pursue a PhD degree in the Biology of Ageing. We aim to train PhD students to become independent, creative, multi-skilled scientists. Students devote most of their time to their own research project, but will be enriched by and benefit from the complimentary research activities in neighbouring labs. A large variety of courses, all taught in English, is available for PhD students to acquire additional skills. A PhD degree from one of the ERIBA labs will optimally prepare students for the next phase in their University or corporate career. PhD students in ERIBA will be enrolled in the Graduate School of Medical Sciences and defend their thesis at the University of Groningen. PhD projects in ERIBA typically will last 4 years.

Postdoctoral fellow

We are always searching for outstanding postdoctoral candidates with a proper training in molecular or cell biology who wish to solve scientific questions in ageing science We encourage postdoctoral candidates to directly contact one of the ERIBA Principal Investigators to explore job opportunities.

For more information, please visit https:www.eriba.umcg.nl

The Congress

Programme ISCOMS 2024
Day chairs
Jury chair + members
Awards
Focus: Future Medicine
Keynote lectures
Interactive Operation
Workshops
ISCOMS Corporate Member Meeting

Programme ISCOMS 2024

Monday 3rd of June 2024 – Pre-course (GMT +2)

08:15 - 09:00	Registration
09:00 - 09:30	Day opening
09:30 - 11:10	Masterclass
11:10 - 11:50	Break
11:50 - 13:20	Science Elective
13:20 - 14:20	Lunch + Meet the Expert
14:20 - 15:35	ISCOMS Medical Talks
15:45 - 16:45	Speed keynote lectures
16:45 - 17:15	Your Future at the UMCG
17:15 - 17:30	Day closing
19:00 - 23:00	Social programme

Tuesday 4th of June 2024 – Congress day 1 (GMT +2)

07:45 - 08:30	Registration
08:30 - 09:00	Opening ceremony
09:00 - 10:00	Keynote lecture I
10:00 - 11:05	Poster session I
11:05 - 11:50	Break
11:50 - 13:05	Workshops I
13:05 - 14:20	Lunch + Research & Academic Fair + Meet the Expert
14:20 - 15:45	Oral session I
15:45 - 16:15	Break
16:15 - 17:15	Keynote lecture II
17:15 - 17:40	Closing ceremony
19:30 - 23:30	Formal dinner

Programme ISCOMS 2024

Wednesday 5th of June 2024 – Congress day 2 (GMT +2)

08:30 - 09:00	Registration
09:00 - 09:15	Opening ceremony
09:15 - 10:15	Keynote lecture III
10:15 - 11:20	Poster session II
11:20 - 11:50	Break
11:50 - 13:05	Workshops II
13:05 - 14:05	Lunch + Career & Internship Fair + Meet the Expert
14:05 - 15:20	Operation: Vestibular Schwannoma Removal
15:20 - 15:35	Break
15:35 - 16:35	Plenary session I
16:35 - 17:35	Keynote lecture IV
17:35 - 17:50	Closing ceremony
19:00 - 22:30	Recreational evening

Thursday 6th of June 2024 – Congress day 3 (GMT +2)

08:30 - 09:00	Registration
09:00 - 09:15	Opening ceremony
09:15 - 10:15	Keynote lecture V
10:15 - 11:15	Plenary session II
11:15 - 11:45	Break: Meet the Expert
11:45 - 13:00	Workshops III
13:00 - 14:00	Lunch
14:00 - 15:25	Oral session II
15:25 - 15:55	Break
15:55 - 17:00	Patient Lecture: Spinal Cord Injury- Project MARCH
17:00 - 17:45	Award & closing ceremony
19:00 - 22:00	Buffet
22:00 - 02:00	World Wide ISCOMS Night

Day Chairs

Monday the 3rd of June

Derya Yakar MD PhD

Dr. Derya Yakar is an abdominal radiologist. Her academic journey began with a PhD in prostate MRI at Radboudumc, followed by a residency in radiology at the same institution. Dr. Yakar's dedication to research led her to complete a fellowship under the aegis of the European School of Radiology (ESOR) at the Memorial Sloan Kettering Cancer Center (MSKCC) in New York.

In 2016, she joined the University Medical Center Groningen (UMCG) and then, in 2021, the Netherlands Cancer Institute (NCI) as a staff radiologist. She specializes in the development and implementation of AI algorithms in radiology. Dr. Yakar has successfully secured several research grants from prestigious organizations such as Health Holland, NWO, and the Hanarth Fund. Her primary goal is to enhance the diagnostic accuracy of radiological techniques, such as CT and MRI, by streamlining imaging protocols and increasing the level of automation in radiologists' daily workflows. This approach aims to improve healthcare accessibility and affordability by optimizing the use of resources, including equipment and personnel.

In addition to her technical contributions, Dr. Yakar collaborates closely with social science experts and actively involves patients to ensure equitable healthcare practices. She is an editorial board member of international journals such as European Radiology and Diagnostics. In 2024, she will join the European Institute for Biomedical Imaging Research (EIBIR) as a Member of the Scientific Advisory Board (SAB). Her responsibilities in this role include providing expert advice and addressing policy-related questions from European Commission bodies and other international organizations.

Her research covers a broad range of topics including prostate MRI, AI in healthcare, patient-centric healthcare, and leadership. Dr. Yakar is committed to integrating these innovations into the education and training of residents. She is equally dedicated to promoting equity in the academic field, currently working on a mentor-sponsorship program aimed at elevating female physician-scientists into leadership roles. This initiative reflects her commitment to ensuring equal opportunities for all in climbing the academic ladder.

Day Chairs

Tuesday the 4th of June

Prof. Wiro Niessen PhD

Wiro Niessen is Dean of the Faculty of Medical Sciences, University of Groningen, and board member of University Medical Center Groningen since February 2023. He is also professor in AI in medical imaging and health. He has a background in physics and medical imaging, obtaining his MSc and PhD at Utrecht University. Part of this MSc/PhD trajectory was carried out at the University of Wisconsin, Madison, and Yale University, respectively. He previously worked at Erasmus MC, University Medical Center Rotterdam, and Delft University of Technology, leading a large research group on biomedical image analysis.

His research interests are in the development, validation and responsible implementation of AI in health. In this domain, he has primarily worked in the field of medical imaging, imaging genetics and computer-aided interventions. He supervised more than 60 PhD students in these fields. In 2023, he was named most influential researcher in Radiology in Europe by AuntMinnie. Wiro Niessen is fellow and, from 2016-2019 was president of the MICCAI Society, the premier international society in medical image computing and computer-assisted interventions.

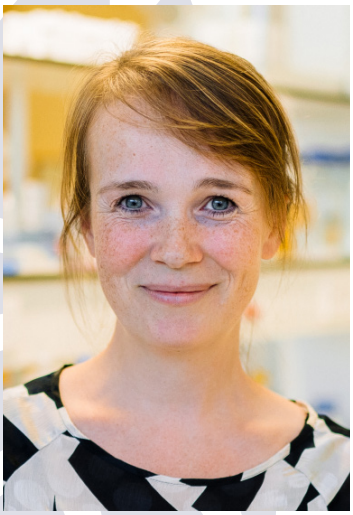
From 2020-2023, Wiro Niessen was CTO and board member of Health-RI, an initiative which aims to develop a national health data infrastructure for reuse of data for research and innovation; Health RI received a 69 MEuro Innovation grant of the Dutch government in 2021. In 2015 he received the Simon Stevin award, the largest prize in Applied Sciences in the Netherlands. In 2005 he was elected to the Dutch Young Academy and in 2017 he was elected to the Royal Netherlands Academy of Arts and Sciences. In 2023 he was elected to the Netherlands Academy of Engineering.

In 2012 Wiro Niessen founded Quantib, an AI company in medical imaging, where he acted as scientific lead until 2022. Quantib currently employs about 50 fte, and has multiple FDA approved products in MR brain image analysis, and MR prostate image analysis. In January 2022 Quantib was acquired by RadNet, the largest provider of outpatient radiological imaging services in the US.

Day Chairs

Wednesday the 5th of June

Prof. Marthe Walvoort PhD



Associate Professor of Chemical Glycobiology at the Stratingh Institute for Chemistry at the University of Groningen.

Marthe Walvoort obtained her PhD degree in 2012 (cum laude) at Leiden University (the Netherlands) on the organic chemistry of carbohydrates. This was followed by a postdoctoral period in the glycobiology group of Prof. Barbara Imperiali at Massachusetts Institute of Technology (Boston, USA). In the end of 2015, Walvoort joined the University of Groningen as Assistant Professor and Rosalind Franklin fellow in the Chemical Biology division at the Stratingh Institute for Chemistry, and she was promoted to Associated Professor in Chemical Glycobiology in 2021. She received the KNAW Early Career Award and NWO Athena Award (2021), and obtained a competitive ERC-Starting Grant (2022). In her research, Walvoort combines her expertise in (organic) chemistry with biochemistry to unravel the impact of sugars in health and disease.

Day Chairs

Thursday the 6th of June

Prof. Marie-José van Tol PhD

Marie-José van Tol (1980) is a cognitive neuroscientist, fascinated by how the brain contributes to getting stuck in enduring periods of depression. She works as a professor of Mood & Cognition at the Cognitive Neuroscience Center of the University Medical Center Groningen. She studied clinical- and health psychology at the University Utrecht, after which she worked as a psychologist in nursing home for people with psychogeriatric problems. In 2011 she obtained her PhD at the University of Leiden. Her thesis focused on the shared and unique brain abnormalities in people suffering from depression and anxiety disorders. After several post-docs at the universities of Leiden, Groningen and Magdeburg (Germany), she started her own research line focusing on understanding the neurocognitive mechanisms associated with the long-term course of depression in 2015. For her work she received multiple grants to study the neurocognitive effects of preventive treatments.

For understanding what causes one individual to suffer from psychiatric problems repeatedly and for long periods of time, while another individual seems resilient to massive disruptions of normal mood and behavior, she uses functional MRI, cognitive and behavioral testing, diary methods, and psychophysiological measures including pupillometry. She often designs and carries out randomize controlled intervention studies using non-pharmacological techniques. Current treatment trials involve interventions with cognitive therapy, behavioral activation, mindfulness, non-invasive brain stimulation, and complex skill training (including language and music).

Marie-José prefers to work interdisciplinary, because combining techniques and knowledge from different fields is in her opinion necessary to move forward in understanding the complex and multifactorial basis of psychiatric disorders (including major depressive disorder, anxiety disorders, schizophrenia) and psychiatric phenomena (including anhedonia, apathy, rumination, emotional dysregulation, and suicide). She collaborates with colleagues from clinical psychology, epidemiology, artificial intelligence, psychiatry, cognitive psychology, and applied linguistics.

She is a member and the chair of the Young Academy (De Jonge Akademie) of the Royal Netherlands Academy of Arts and Sciences (KNAW). In this role, she contributes to changing how we recognize and reward academic excellence and put more emphasis on team science and scholarship.

Jury Members

Jury Chair

Prof. Hjalmar Bouma, MD, PhD, EuCP

Consultant Internal Medicine, specialized in Acute Medicine and Pharmacology

Hjalmar Bouma is a physician-researcher with a strong dedication to improving the lives of acutely ill patients through research. He received his MD and PhD with honors and specialized in internist-acute medicine, with additional training in experimental and clinical pharmacology and immunology. During his PhD research, which he conducted in collaboration with Heidelberg University (Germany), the National Institutes of Health (Bethesda, USA), the University of Wisconsin (USA), and the University of Aberdeen (Scotland), he focused on the effects of metabolic stress induced by acute illness on the immune system, with relevance to acute kidney injury (AKI) and studied protective mechanisms of hibernating animals. His training provides him with extensive knowledge to successfully translate fundamental findings on the molecular mechanisms of disease into drug development.

His current work consists of caring for acutely ill patients at the Emergency Department (ED), including the coordination of the flow of patients at the ED to maintain acute care capacity. He is the course director of the Clinical Pharmacology training program and leads a translational research line dedicated to improving outcomes for patients with sepsis by improving recognition of early sepsis and developing personalized medicine. To learn from individual differences in early sepsis, clinical data, and biomaterials from thousands of acutely ill patients per year are collected by the Acutelines data-biobank (www.acutelines.nl) that facilitates the identification of (risk) markers predictive of response to therapy. Biomarkers associated with clinical outcomes in patients are further dissected in pre-clinical models to identify novel therapeutic targets. He is fascinated by hibernation: specific adaptations render the animals resistant to metabolic stress, which can serve as a blueprint for developing new therapies and has already resulted in a patented drug for sepsis. His research group is a dynamic blend of (technical) clinicians and experts in data and life sciences (more information: www.sepsisresearch.nl). He is a board member of the Dutch Sepsis Foundation (SepsisNet) and associate editor of Frontiers in Nephrology.

"Throughout my career, I have been intrigued by the molecular aspects of life and exploring the mechanisms that underlie human disease by fundamental and translational research. Already during my study in Medicine, I became involved in scientific research. Brainstorming about biomedical challenges with smart, dedicated, and creative people from different backgrounds is something that gives me a lot of energy. ISCOMS has contributed to my career at its early stage by allowing me to interact with peers and provide a lot of inspiration for my research!"

Jury Members

EmProf. Cees. Th. Smit Sibinga MD PhD

Expert Advisor World Health Organisation

EmProf. Cees Th. Smit Sibinga is a clinical haematologist and specialist of Transfusion Medicine. He is a special professor of International Development of Transfusion Medicine at the University of Groningen. He has been involved in the development of Transfusion Medicine, quality systems and management for developing economies since 1980 through his work with the World Health Organization (WHO). At the WHO, he has been the regional coordinator of the global Quality Management Project for the Europe region. For 25 years he has served as the Managing Director of Sanquin Division Blood Bank North Netherlands in Groningen. From 1993 until 2005 the Blood Bank incorporated the WHO Collaborating Center for Blood Transfusion and the WFH International Hemophilia Training Center in Groningen.

EmProf. Cees Th. Smit Sibinga is the founder of the Dutch Blood Bank Inspection and the Accreditation Program and the Hemovigilance system. Besides this, he is the founder of the Academic Institute for International Development of Transfusion Medicine at the UMCG. This institute used to provide a post-academic Master's in Management of Transfusion Medicine, which is now part of the Master's programme of the University of Groningen Graduate School of Medical Sciences. EmProf. Smit Sibinga is still deeply involved in transfusion medicine and related health sciences research focused on developing countries. He serves the WHO Eastern Mediterranean Region as a Lead Technical Adviser in their Strategic Framework for Blood Safety and Availability 2016-2025 and its priority interventions.

Jury Members

Prof. Joke Spikman PhD

Professor and head of the sub-department of Clinical Neuropsychology within the Department of Neurology at the UMCG

Professor Dr. J. M. (Joke) Spikman is a professor of Clinical Neuropsychology in Neurological Disorders at the UMCG, Groningen. In addition, she is a registered Clinical Neuropsychologist and serves as the head of the sub-department of Clinical Neuropsychology within the Department of Neurology at the UMCG. She studied Neuro- and Biopsychology at the University of Groningen (RUG) with Methodology and Functional/Cognitive Psychophysiology as minor subjects. In 2001, she earned her doctorate degree cum laude from the Faculty of Medicine at RUG, for her research on frontal damage and executive dysfunction following traumatic brain injury.

Since 1995, Professor Spikman has been employed at the UMCG, where she conducts neuropsychological diagnostics for patients with neurological disorders as part of patient care. At the same time, she worked at Rehabilitation Friesland for many years, where she conducted neuropsychological diagnostics and treatment for patients with brain injuries.

Her expertise lies in disorders of the 'prefrontally regulated' brain functions, such as attention, executive functions, and social cognition. Specifically, she focuses on how these relate to adaptive functioning in daily life and indicators of brain damage in patients with neurological disorders. Her research is about identifying determinants of such disorders and developing sensitive neuropsychological tests and effective neuropsychological treatments. It primarily involves patients with acute neurological disorders, in particular: traumatic brain injury, stroke, and subarachnoid hemorrhage. Professor Spikman is also engaged in research into other neurological disorders such as brain tumors, dementia, and movement disorders.

Jury Members

Sonja Pyott PhD

Associate Professor in the Department of Otorhinolaryngology at the UMCG

Sonja Pyott PhD is an Associate Professor in the Department of Otorhinolaryngology at the University Medical Center Groningen in the Netherlands. She is also involved in medical and graduate education at the University of Groningen.

Her research focuses on the molecular and cellular neuroscience of auditory and vestibular systems. It integrates investigation of 1) fundamental biology of sensory transduction in the inner ear; 2) pathophysiology underlying hearing and balance disorders; and 3) consequences of hearing and balance disorders on health and wellbeing. The goal of her research is to develop new strategies for prevention and treatment of hearing and balance disorders. To achieve this goal, Sonja Pyott PhD uses an interdisciplinary toolkit that leverages physiological, imaging, transcriptomic, genomic, comparative and evolutionary approaches to investigate the auditory and vestibular pathways in animal models and humans. Offering excellent scientific and academic training to students at various academic levels is central to her research.

Her academic training includes a Fulbright Scholarship at the Max Planck Institute for Biological Chemistry in Göttingen, Germany, a PhD from Stanford University, and postdoctoral research at Johns Hopkins School of Medicine. She has extensive experience coordinating interdisciplinary and international research collaborations and organizing top-tier scientific training. She serves as the Coordinator of the European MSCA PROVIDE doctoral network and oversees all network activities.

Jury Members

Ymke van Ginkel MD

A PhD candidate within the departments of Gastroenterology and Dermatology

Ymke van Ginkel is currently engaged in impactful research at the University Medical Centre Groningen (UMCG) as a PhD candidate within the departments of Gastroenterology and Dermatology. Prior to her current role, Ymke pursued her academic journey at the University of Groningen, where she attained her degree in medicine in 2023.

At UMCG, Ymke's research focuses on the application of fluorescent imaging in various diseases. She is particularly involved in clinical trials aimed at understanding the mechanisms of biological treatments like ustekinumab and adalimumab in conditions such as inflammatory bowel disease (IBD), rheumatoid arthritis (RA), and psoriasis. Additionally, she conducts research on esophageal cancer and the application of immunotherapy. Her aspiration is to enhance our ability to predict who will benefit from immunotherapy and who will not, ensuring that every patient receives personalized treatment.

Ymke's work showcases her dedication to advancing medical knowledge and improving patient care. The contributions she makes in her field hold the potential to generate valuable insights that may positively influence healthcare outcomes.

"it's great to see how students are already engaged in research and I can only encourage this. I look forward to meeting you at ISCOMS, where I'm eager to exchange insights and inspire each other with new ideas!"

Jury Members

Tom lieverse

President ISCOMS 2022

Dear participants,

My name is Tom Lieverse and I am a medical student at the University of Groningen. Currently, I am in my fourth year and doing my medical internships at the University Medical Center of Groningen. ISCOMS also inspired me explore a scientific career for myself. Therefore, I will begin a full-time research year in June at the Department of Internal Medicine!

As the president of ISCOMS 2022, I am honoured to be a jury member of the 31st edition of ISCOMS this year! After more than 30 years of experience, ISCOMS has grown to become the leading student congress in biomedical sciences. I am very proud of this year's organising committee because they have once again created a wonderful program that I am sure you will all enjoy. I am exceptionally proud of them for continuously enhancing ISCOMS, even after 30 years of experience, and for consistently raising the bar.

I am convinced that students can make a difference if we keep inspiring each other, exchange our scientific knowledge and start new collaborations, and ISCOMS offers a unique platform to do so. I would like to wish you all a great time at ISCOMS 2024, let's enjoy science together!

Awards

Plenary awards
Students who are selected to present their research during the plenary sessions have a chance of winning one of the three plenary awards. The first prize consists of 1250 euros, the second prize consists of 750 euros, and the third prize consists of 250 euros. You can spend this money on visiting (bio)medical congresses of your choice. The winners will be selected by a jury of renowned medical scientists and (bio)medical students.

Plenary presentation: Audience award
The winner of this prize will be determined by the audience and the First Year Crew. The plenary presenter most appreciated by the audience will receive a cheque of 150 euros to spend on visiting a (bio) medical congress of the presenter's choice.

World Health award
To stimulate and acknowledge students in the research of global health issues and their contribution to global health in general, the WHO-supported World Health award consists of a one-year online subscription to the Eastern Mediterranean Health Journal (EMHJ). This means that either the presenter comes from a developing country, or the subject of the research affects developing countries.

Best Oral Abstract awards
The best oral abstracts will be awarded for Basic Sciences, Clinical Sciences, or Public Health. Our official jury will select three winners out of all the different oral topics. Winners will receive a cheque of 150 euros to spend on visiting a (bio)medical congress of the presenter's choice.

Session winners
In each oral session, the best presenter will be selected. All session winners will receive an official certificate.

Sustainability award
Celebrating Responsible Travel: As part of our ongoing commitment to sustainability, ISCOMS hosts a sustainability award to recognize and celebrate participants who demonstrate exemplary efforts in sustainable travel. Participants are invited to submit an essay detailing their sustainable travel practices and the environmental initiatives they have undertaken to reduce their carbon footprint. By highlighting these commendable efforts, we aim to inspire others and foster a culture of sustainability within the scientific community. Three winners will be selected. The first prize consists of 200 euros, the second prize consists of 150 euros and the third prize consists of 100 euros. You can spend this money on travel costs or on visiting (bio)medical congresses of your choice.

Please note, all of the prizes which include money should be claimed in a maximum of three years after the 31st edition of ISCOMS. The awards can only be spent on visiting (bio)medical congresses, and only travel costs and the costs for the congress itself can be declared.

Please note, all of the prizes which include money should be claimed within a maximum of three years after

Focus: Future Medicine

Medical care is advancing towards greater personalization, digitization, and reliance on data. Much of this progress can be attributed to advancements in artificial intelligence (AI) and the growing feasibility of economically sustainable pathways for personalised and gene therapeutic medical approaches. The dynamics of politics, demographics, economics, and climate have a profound impact on all of us. Research plays a crucial role in addressing the significant challenges we encounter, but its effectiveness relies on the convergence of three key elements: science, innovation, and society. This convergence must occur in an environment that fosters the well-being of individuals and teams.

Today, we must seize the opportunity to influence the future development of the research culture for the next 25 years. ISCOMS 2024 will provide exclusive insights into the future of medicine. Various aspects of Future Medicine will be explored at ISCOMS 2024. For instance, we are honoured to welcome Prof. Mihaela van der Schaar, PhD, director of the Cambridge Centre for AI in Medicine, and who will present her research on AI combined with machine learning in healthcare. Furthermore, this year's surgical operation will involve the removal of a vestibular schwannoma using advanced planning for the operation, to minimise the risks of adverse events.

Moreover, the theme of Future Medicine will be unveiled in several interactive workshops, such as the 'CRISPR-Cas9' workshop or the science elective debate about AI in healthcare.

For this theme, we have a Future Medicine logo. This logo will be associated with keynote speakers, workshops, and presentations that incorporate Future Medicine in their research. The segments of the congress that embody the theme will be identified with this logo on our website.

Keynotes

This year we are happy to welcome five distinguished keynote speakers who will enlighten you about the impactful research they engage in. In their lectures they will share their knowledge and experiences with you. The speakers will delve into diverse subjects, spanning a wide range of fascinating research fields. We anticipate that their contributions will inspire and captivate you in your own research endeavors.

Professor Brian Kobilka MD

Professor Brian Kobilka MD received Bachelor of Science Degrees in Biology and Chemistry from the University of Minnesota, Duluth in 1977. He graduated from Yale University School of Medicine in 1981, and completed residency training in Internal Medicine at the Barnes Hospital, Washington University School of Medicine, St. Louis, Missouri in 1984. From 1984-1989 he was a postdoctoral fellow in the laboratory of Robert Lefkowitz at Duke University.

While in the Lefkowitz lab, he and his colleagues cloned the gene that encodes the receptor for the hormone adrenaline. They found that the receptor was similar to rhodopsin, the light-sensing receptor. It was later discovered that there is an entire family of receptors that look and act in similar ways. These receptors are known as G-protein-coupled receptors (GPCRs); they are responsible for the body's response to the majority of hormones and neurotransmitters.

In 1989 he joined the faculty of Medicine and Molecular and Cellular Physiology at Stanford University. Research in the Kobilka lab focuses on the structure and mechanism of action of GPCRs. They apply a spectrum of biochemical, biophysical and structural approaches to understand GPCR signaling at the molecular level. He is a member of the National Academy of Sciences, the National Academy of Medicine, and the American Academy of Arts and Sciences. In 2012, Brian Kobilka was awarded the Nobel Prize in Chemistry, along with Robert Lefkowitz, for his work in determining the structure of a GPCR in inactive and G protein-coupled states.

Structural insights into G protein-coupled receptor activation
G protein-coupled receptors (GPCRs) are a large family of membrane-bound receptors that mediate the majority of physiologic responses to hormones and neurotransmitters, as well as the senses of sight, smell, and taste. GPCRs are the largest group of pharmaceutical targets for a broad spectrum of diseases. The goal of my research over the past 33 years has been to characterize the dynamic process of GPCR activation by applying a spectrum of biophysical and structural approaches. I will discuss what these studies have taught us about GPCR signalling and how structural approaches can advance drug discovery.

Keynotes

Professor Anne Schwerk PhD

Anne Schwerk is a Professor of AI at the International University of Applied Sciences with a research focus on Medical AI applications and Natural Language Processing. At the same time, she works as the head of science management at the Berlin Institute of Health Center for Regenerative Therapies. After her studies in the Netherlands, at the VU Amsterdam, she conducted her Ph.D. at the Charité Berlin University Medicine. Then she worked for a few years at TNO, Leiden the Netherlands, before she moved back to Berlin to lead projects at the intersection of medicine and AI at the German Research Center of AI. Before her current position, Anne worked for a rare disease diagnostics company leading a team of 5 Machine Learning experts to develop omics driven diagnostics and therapies.

Artificial Intelligence in advancing precision medicine

In my lecture I will delve into my work at the intersection of artificial intelligence (AI) and medicine, emphasizing the pivotal role of AI in advancing precision medicine. I will explore how machine learning facilitates the discovery of personalized drugs, particularly for small patient cohorts, where complex, high-dimensional data from omics disciplines pose significant challenges. I will discuss the identification of patient-specific profiles using metabolomics data, tackling inherent difficulties due to data variability and quality issues.

Additionally, I shall cover the processing and analysis of real-time physiological data and multi-modal data sources. I will present a cutting-edge research project I lead, funded by the International University of Applied Sciences, investigating the use of affective computing to enhance and regulate stress and concentration through virtual reality, showcasing its potential impacts.

Given the critical importance of transparency, accountability, and trust in healthcare AI applications, I will provide insights into the application of explainability within medical models. I aim to unpack the complexity of these methods and their interactions with human and psychological factors, highlighting the essential balance between technical innovation and ethical considerations in the development of AI-driven healthcare solutions.

Keynotes

Professor Dennis Lo Yuk Ming MD PhD

A Professor Dennis Lo is the Associate Dean (Research) of the Faculty of Medicine of The Chinese University of Hong Kong, and the President of Hong Kong Academy of Sciences. His research interests focus on the biology and diagnostic applications of cell-free nucleic acids in plasma. In particular, he discovered the presence of cell-free fetal DNA in maternal plasma in 1997 and has since then been pioneering non-invasive prenatal diagnosis using this technology. This technology has been adopted globally and has created a paradigm in prenatal medicine. He has also made many innovations using circulating nucleic acids for cancer detection, including the screening of early stage nasopharyngeal cancer.

In recognition of his research, Professor Lo has been elected as Fellow of the Royal Society, Foreign Associate of the US National Academy of Sciences, Fellow of The World Academy of Sciences (TWAS) and Founding Member of the Academy of Sciences of Hong Kong. Professor Lo has won numerous awards, including the 2014 King Faisal International Prize in Medicine, the 2016 Future Science Prize in Life Science, the 2019 Fudan-Zhongzhi Science Award, the 2021 Breakthrough Prize in Life Sciences, the 2021 Royal Medal, the 2021 ESHG Mendel Award, the 2022 ISPD Pioneer Award and the 2022 Lasker~DeBakey Clinical Medical Research Award.

Non-invasive prenatal and cancer testing: from dream to reality

The presence of cell-free fetal DNA in the plasma of pregnant women was first reported by my team in 1997. Since then, we have been pushing forward the translation of this discovery into a new platform of non-invasive prenatal testing (NIPT). NIPT is now used worldwide, allowing the non-invasive screening of fetal chromosomal abnormalities and single gene disorders. A similar technology has also been used for the detection, monitoring and prognostication of cancer. Using an epigenetic-based approach, multiple types of cancer can be screened using a single blood test. In this talk, I shall talk about the journey through which this body of diagnostic technologies was developed and the challenges and impact of bringing such tests to the clinic.

Keynotes

Professor Mihaela van der Schaar PhD

Mihaela van der Schaar is the John Humphrey Plummer Professor of Machine Learning, Artificial Intelligence and Medicine at the University of Cambridge and a Fellow at The Alan Turing Institute in London. In addition to leading the van der Schaar Lab, Mihaela is founder and director of the Cambridge Centre for AI in Medicine (CCAIM).

Mihaela was elected IEEE Fellow in 2009. She has received numerous awards , including the Oon Prize on Preventative Medicine from the University of Cambridge (2018), a National Science Foundation CAREER Award (2004), 3 IBM Faculty Awards, the IBM Exploratory Stream Analytics Innovation Award, the Philips Make a Difference Award and several best paper awards, including the IEEE Darlington Award.

Mihaela is personally credited as inventor on 35 USA patents, many of which are still frequently cited and adopted in standards. She has made over 45 contributions to international standards for which she received 3 ISO Awards. In 2019, a Nesta report determined that Mihaela was the most-cited female AI researcher in the U.K.

Transforming Healthcare: The Impact of Machine Learning and Artificial Intelligence
During my lecture I will explore the transformative impacts of machine learning and AI on personalized medicine, clinical trials and healthcare delivery. I will introduce several breakthrough machine learning methods developed in our lab aimed to address some of the hardest and most complex challenges in medicine and healthcare. By integrating these methods in clinical practice together with clinicians, our lab is not only enhancing the precision of medical care for each patient, but also revolutionizing the efficiency of healthcare systems and of clinical trials. The lecture will showcase real-world examples of how machine learning and AI can redefine the entire healthcare landscape, providing insights into the current applications, challenges, and future directions of AI in medicine.

Keynotes

Professor Mukesh Kapila MD PhD CBE

Professor Mukesh Kapila MD PhD has extensive experience in global health, humanitarian affairs, conflict and security, international development, human rights and diplomacy, He has qualifications in medicine and public health from the Universities of Oxford and London. He is Professor Emeritus of Global Health and Humanitarian Affairs, University of Manchester, and Senior Adviser to the Parliamentary Assembly of the Mediterranean.

His previous leadership functions have included senior directorships at the World Health Organization and United Nations, and as Undersecretary-General at the International Federation of Red Cross and Red Crescent Societies. Previously he was Head of Conflict & Humanitarian A ffairs at what is now the UK Foreign, Commonwealth, and Development Office. Also he has served on several Boards, including chairing Minority Rights Group International, and Nonviolent Peaceforce which was nominated for the Nobel Peace Prize in 2016. Also advised many multilateral institutions including the World Bank. UN agencies, and international NGOs.

His many awards include a CBE from King Charles III, a Global Citizenship Award, the "I Witness!" award for human rights, and a special resolution of the California State Legislature for "lifetime achievements and meritorious service".His first memoir "Against a Tide of Evil" was shortlisted for the 2013 Best Non-Fiction Book award. His further book (2019) is entitled "Not a Stranger to Kindness". He is a public and media speaker, and his writings can be sampled on https://www.mukeshkapila.org.

Preventing and managing mass atrocities: what can humanitarian and health professionals do?
In my talk, I shall discuss the grim reality of today's armed conflicts, which often involve mass violence and even genocide. I will examine the factors that contribute to these international crimes against humanity and whether they can be prevented. Additionally, I'll delve into the important roles that humanitarians and health professionals play in these situations. They provide vital aid, stand up for human rights, and address the health needs of people affected by conflict. By exploring these issues, I aim to deepen our understanding of the challenges we face and how we can work towards a more peaceful world.

Workshops ISCOMS 2024

Basic life support, heroes are not born, they are trained

Department: Wenckebach Institute for Education and Training
Supervisor: Monique Timmer, Instructor ERC / NRR CPR-Instructor

During this workshop, participants will be invited to engage with fellow students (3-4 people) to demonstrate a perfect resuscitation (with AED) and continue the resuscitation for some time (5-7 minutes). Students who do not participate in the cardiopulmonary resuscitation-action (CPR) are invited to assess the resuscitation: what is going well and what could be better. If you are working as a doctor, it is necessary to take leadership in a resuscitation team and coach your CPR team. A good observation of skills is a requirement for doctors to make the CPR procedure perfect. During the CPR action, it is important to push hard (5-6 cm), push fast (100-120/minute), and minimize interruption. At the end of this workshop, participants can exercise their CPR skills with the AED. The workshop will end with a certificate of participation titled "Workshop: heroes aren't born, they are trained," given by the Wenckebach Training Institute of the UMCG. Participants can find the international guidelines for CPR on the site of the ERC:www.erc.edu. Furthermore, you can find a link about an international campaign for reanimation awareness: life-saver.org.uk.

Machine perfusion

Supervisors: Kirsten Francis Ma PhD, Kees Wieriks Msc, Minou de Bree MSc

Donor organ quality has recently been decreasing because of an ageing population and a rising BMI. Furthermore, in the coming years, more donor organs are expected to be declined for transplantation. Therefore, there is a need for a method to increase the pool of good-quality organs. Machine perfusion offers the possibility of viability testing and resuscitation of organs of suboptimal quality that would otherwise be discarded. In this way, machine perfusion can increase the quality of available donor organs and the number of viable organs. Machine perfusion of donor organs is becoming a standard way of organ preservation. The University Medical Center Groningen (UMCG) is leading in machine preservation. Many initially declined organs in the Netherlands are currently tested in the UMCG by machine perfusion. Many of the previously declined livers are now transplanted with good results. In this hands-on workshop, participants will learn about machine perfusion and the anatomy of perfused organs. They will practice preparing (porcine) donor organs for 'transplantation' and machine perfusion. Afterwards, they will see how well they had done the preparations when some of their organs are placed on the pump in a demonstration of machine perfusion.

Workshops ISCOMS 2024

Macroscopic Suturing

Department: Research Support Facility – Central Animal Facility
Supervisors: Annemieke van Oosten PhD, Michel Weij Ing, Daryll Eichhorn Ing

Microsurgical techniques have gained importance in recent years. The more delicate and sophisticated a surgical technique is, the more it requires training and education. The purpose of this workshop was to teach the students the proper way to handle their surgical instruments, how to tie a suture in the correct way, and to provide an opportunity to test their hands in the fine art and skill of suturing.

Guided Tour in the Central Animal Facility of the UMCG

Department: Research Support Facility – Central Animal Facility
Supervisors: Annemieke van Oosten PhD, Michel Weij Ing, Daryll Eichhorn Ing
Many major findings in the field of human medicine have been established following animal experiments. To date, animal experimentation is still a very important way to gain data and knowledge mandatory to develop new procedures in modern human medicine.

Within the UMCG all animal experimental work is organised in the Central Animal Facility.

The workshop consisted of a guided tour in this facility. During the tour the current status of laboratory animal experimentation within the UMCG is presented.

What if endless possibilities are no longer desirable..

Department: Geriatrics
Supervisor: Harianne Hegge PhD
About the future of healthcare. Despite the efforts of "healthy aging", everyone will grow older/ age. What does that mean? How does that feel? Try it yourself. In this workshop participants got acquainted with aging, frailty, and resilience. Furthermore, they could experience for themselves what it felt like to be an elderly person.

Workshops ISCOMS 2024

Gut anastomosis

Department: Surgery, UMCG
Supervisor: Arne de Niet, MD, PhD

In abdominal surgery bowel resections are often performed. In most cases an anastomosis is made. This means that the two ends of the bowel are attached to each other. In this workshop, different types of anastomoses are discussed and various techniques are explained. A large part of the program will consist of a hands-on workshop, in which actual intestinal anastomoses can be made by the students. After this workshop, the students will understand the different anastomoses, suturing techniques and pitfalls.

Rehabilitation through virtual reality

Department:
Supervisors: E. Wilhelm PhD

Over the last decades serious gaming has become increasingly more popular in physiotherapy and rehabilitation. Within this workshop participants will have the opportunity to experience a serious VR game that motivates patients with cervical dystonia to do their physiotherapy exercises. Furthermore, participants will learn about how games attempt to nudge patients into doing their exercises in the way the therapist wants them to do and discover how important the role of the therapist is in such a technology driven intervention. Finally they will get the opportunity to implement their own physiotherapy program in an interactive game.

Fracture management in trauma

Department:
Supervisors: George Volckmann

In this hands-on workshop, the supervisors will elaborate about various treatment possibilities for fractures. The biomechanical aspects of the different fixation methods will be covered. Moreover, you will be able to fixate implants on several kinds of fractures for the proximal femur, tibia and proximal humerus. The placement of the implants will be effectuated with medical drills, saws and operation sets.

Workshops ISCOMS 2024

The miracle of giving birth

Department: Clinical Training Center, UMCG
Supervisors: Marco A.C. Versluis MD PhD, Dennis Beekhuis MD

General childbirth, also known as labour, is an unique event showing the miracle and power of nature. Although it is a physiological event of itself, childbirth is one of the most fascinating aspects of medicine, which mostly deals with pathophysiological processes.

Childbirth is the culmination of the gestation and pregnancy period with the expulsion of one or more newborn babies from a women's uterus into a completely different environment. At that particular moment, being disconnected from the mother's circulation after cutting the umbilical cord, the newborn faces a very serious and complicated adaptation of his own circulation to the onset of his own respiratory system.

The process of a normal vaginal human childbirth is categorized into four stages:

Stage 1: The onset of birth is initiated by a metabolic change in the infant which causes the release of the hormones needed for uterine contractions.

Stage 2: The process of shortening and dilation of the uterine cervix is caused by uterine contractions. This process facilitates the head of the infant to enter the birth canal.

Stage 3: The continuation of uterine contractions with the help of the mothers pressing, pushing the baby through the birth canal into the baby's new world.

Stage 4: The delivery of the placenta. The expulsion of the placenta mostly starts spontaneously approximately twenty minutes after the occlusion and the cutting of the umbilical cord.

During this workshop more details will be given on monitoring labour, pain control, and problems that may happen before and during delivery including the therapeutic possibilities if these problems occur. You are also given the opportunity to deliver a baby using a mannequin, simulating the real situation.

Workshops ISCOMS 2024

State of the art radiotherapy: is it a game-changer in fighting cancer?

Department: Radiotherapy
Supervisor: Christian Hammer MD

Radiotherapy is one of the pillars of the treatment of oncologic patients, next to surgery and systemic therapy. In the Netherlands, this specialty is developing very fast, resulting in the treatment of new indications with state-of-the-art techniques to optimally treat cancer with minimal side effects. One of the most important innovations is proton therapy. The UMCG was the first institute that started this new technique in the Netherlands, back in 2018.

Proton therapy is a relatively new method to treat patients with radiation, as protons have special characteristics to inflict DNA damage without further passing through the body, as photons do. This makes it possible to inflict less damage to the healthy organs surrounding the tumor. The workshop entails an interactive presentation where input from the audience will be sought in a number of clinical urological cases in which new techniques were applied and provided basic insights into the treatment principles of cancer.

3D-Lab Groningen

Department: 3D-lab / Orthopedic Surgery / Trauma Surgery
Supervisors: Peter Pijpker, Anne Meesters, Nick Assink and Sander Tabernée Heijtmeijer (Technical Physicians and 3D specialists)

In the UMCG, 3D virtual surgical planning technology is used frequently for many interventions within various disciplines. The use of 3D technology assures safer, faster and more accurate surgical procedures. Within our institution the Technical Physicians of the 3D-lab are planning complex cases on a daily basis. Using 3D-printed patient specific instrumentation and implants, the virtual plan is transferred to the surgical theater with high accuracy.

One of many applications is the 3D guided patient-specific corrective limb osteotomy. Corrective osteotomy surgery for bony anomalies can be very challenging since the deformation of the bone is often in three-dimensions. The use of 3D planning and printing allows to visualize the anatomy in 3D and plan the osteotomy based on the CT scan. Additionally, patient-specific instrumentation can be manufactured to guide the cutting and reposition process, leading to a more predictive result.

This workshop consisted of two parts. Firstly, the participants would learn the basics of virtual surgical planning and tried to virtually plan a corrective limb osteotomy. Secondly, the workshop would continue with hands-on simulated surgery on sawbones. In this part the participants will learn how to use the patient specific 3D-printed instrumentation, aiming to correct the deformity.

Workshops ISCOMS 2024

State of the art radiotherapy: is it a game-changer in fighting cancer?

Department: Radiotherapy
Supervisor: Christian Hammer MD

Radiotherapy is one of the pillars of the treatment of oncologic patients, next to surgery and systemic therapy. In the Netherlands, this specialty is developing very fast, resulting in the treatment of new indications with state-of-the-art techniques to optimally treat cancer with minimal side effects. One of the most important innovations is proton therapy. The UMCG was the first institute that started this new technique in the Netherlands, back in 2018.

Proton therapy is a relatively new method to treat patients with radiation, as protons have special characteristics to inflict DNA damage without further passing through the body, as photons do. This makes it possible to inflict less damage to the healthy organs surrounding the tumor. The workshop entails an interactive presentation where input from the audience will be sought in a number of clinical urological cases in which new techniques were applied and provided basic insights into the treatment principles of cancer.

Surgical anatomy of the heart and invasive treatment of atrial fibrillation

Department: Cardiothoracic Surgery and Cardiology, UMCG
Supervisors: Dr. Y. Blaauw MD PhD and Dr. W. Bouma MD PhD

Atrial fibrillation is an increasing worldwide problem and is associated with significant morbidity and mortality. In this workshop, the basic anatomy of the heart and its relationship with the etiology and pathophysiology of atrial fibrillation will be discussed. A basic understanding of cardiac anatomy is essential in understanding atrial fibrillation and the different invasive treatment modalities. The different invasive treatment modalities for atrial fibrillation will be explained and shown during this workshop. Advantages and disadvantages of these techniques will be discussed. After this workshop, medical students will understand the basics of atrial fibrillation and its invasive treatment.

Workshops ISCOMS 2024

Transgender debate

Department: Genderteam UMCG
Supervisor: A. G. Schuringa

Transgender people experience a mismatch between their gender identity or gender expression and their assigned sex. Transgender is an umbrella term, because in addition to including trans men and trans women (whose binary gender identity is the opposite of their assigned sex), it may also include genderqueer people (whose identities are not exclusively masculine or feminine, for example: bigender, pangender, genderfluid, or agender).

Since the late '70s the University Medical Center Groningen (UMCG) in the Netherlands offers a treatment programme for transgenders, according to the professional standards of the World Professional Association of Transgender Health (WPATH). Once patients have been diagnosed with gender dysphoria by the psychiatrist, the 'real life phase' starts. This include living their gender identity and cross-sex hormone therapy. When the 'real-life phase' has been followed through with success, one can apply for sex reassignment surgery. After these operations, a lifelong continuation of cross-sex hormone therapy is needed to maintain secondary sex characteristics of the desired gender.

What does the transition contain and cause physically, mentally, and socially and how can we guide the patients in this process? During this workshop, participants will be able to ask questions to a member of the UMCG Gender team and a transgender patient.

Surgical anatomy and surgical treatment of end-stage heart failure LVAD

Department: Cardiothoracic Surgery, UMCG
Supervisors: Dr. Y.L. Douglas MD PhD and Dr. W. Bouma MD PhD

Heart failure is an increasing worldwide problem. Until recently, heart transplantation was the only effective option to prolong the survival of patients with end-stage heart failure. Nowadays it can be treated by implantation of a left ventricular assist device (LVAD). In this workshop, the problem of end-stage heart failure, the relevant cardiac anatomy, and concepts of different types of left ventricular assist devices will be discussed (emergency implantation and destination therapy). The implantation technique of an internal LVAD used for destination therapy will be shown. After this workshop, medical students will understand the entity of heart failure and the concepts and problems related to LVAD therapy.

Workshops ISCOMS 2024

Spinal cord injury: Able to walk or is that an illusion?

Department: UMCG Center for Rehabilitation, Physical and Rehabilitation Medicine
Supervisor: Dr. G.E. van der Wal, MD PhD

Spinal Cord Injury (SCI) is an event in which the individual experiences reduced or complete loss of mobility below the lesion level. Worldwide, SCI has an incidence of 3.6-195.4 cases per million persons. In the Netherlands the incidence of traumatic SCI is about 200 cases per year, the non-traumatic SCI is much higher.

Individuals with motor-complete SCI use, generally, have a wheelchair to move toward a destination in their daily activities. Most of the individuals with an incomplete SCI However, sitting in a wheelchair for a longer period leads to various medical and psychological problems. Standing and gait reconstruction to prevent these problems have been a key challenge within rehabilitation medicine.

In the past decades, science has improved and is developing methods to eventually cure SCI or at least improve the disability outcome. Herewith also a few gait and walking devices have been developed to improve or optimize remaining walking abilities or to provide standing and walking abilities for (in)complete SCI individuals.

In this workshop, we discuss the latest developments in trying to cure SCI/ improve the SCI outcome in the acute phase and the different possibilities to improve walking or make walking possible. We particularly focused on exoskeleton possibilities and when to use them.

After this workshop, medical students know what the state of the art science platform is now and when to indicate certain exoskeletons or other walking devices for individuals with a loss of mobility, especially individuals with a spinal cord injury.

Workshops ISCOMS 2024

Sustainable innovation; create your own innovation plan!

Department:
Supervisors: Femke van der Zant and Laura Ellérie

During this workshop, students will gain insight into the influence of healthcare on climate change and the paradoxical influence of climate change on the health of patients. The supervisors will illustrate the importance of the reduction of carbon emissions produced by health facilities. To reduce these carbon emissions in the healthcare sector sustainable innovations are essential.

Students will work in groups (4-5 people) and design their own sustainable innovation plan based on their experience in the hospital, lab or other (bio)medical department. An example of this is the "No risk, no glove" policy or the change from disposable to reusable materials. Students will be guided in the design of their plans by the supervisors. At the end of the session, every group gets to pitch their plan. Good ideas for sustainable innovations could be assessed and implemented in the UMCG, if possible!

Plastic Surgery: How do tissue expanders work?

Department: Plastic Surgery, University Medical Center Groningen
Supervisors: Vera van Aalst MD

Plastic surgeons perform a variety of different reconstructive and esthetic procedures. These vary from basic wound care to extensive reconstructions after tissue loss or removal due to trauma or disease, like cancer. Plastic surgeons at University Medical Center Groningen (UMCG), collaborate with many different medical specialists. Considering the high incidence of breast cancer (more than 1 in 8 women will have breast cancer in their lifetime) a large part of our practice focuses on breast reconstruction after cancer removal. We perform these reconstructions using a patient's own tissue, or implants. Tissue expanders are often used to expand skin and other soft tissues to create a pocket in which to place a permanent implant or to obtain more tissue to cover a defect.

The main goal of this workshop was to familiarize participants with different treatment options available for breast reconstruction. Specifically, they learned how to use tissue expanders for use in breast reconstruction.

Workshops ISCOMS 2024

Collaborating in Planetary Health

Department: Obstetrics & Gynaecology
Supervisors: Marco Versluis MD PhD, Girbe Buist PhD

Planetary health is about achieving the highest attainable standard of health, well-being, and equity worldwide through judicious attention to the human systems—political, economic, and social—that shape the future of humanity and the Earth's natural systems that define the safe environmental limits within which humanity can flourish. But what does this mean for the world we live in today and tomorrow, and how do we deal with the dauntingly complex problems characteristic of Planetary Health?

This workshop is for students of all disciplines. Participants collaborate on real world challenges within the domain of Planetary health such as draughts, floods, vector-borne diseases, microbial resistance, social justice and maintaining health equity. Using design thinking as an approach, they formulate simple solutions to elements that constitute these challenges. The workshop aims to teach participants about the concept of Planetary health and demonstrate that interdisciplinary collaboration offers opportunity to move forward.

Medical Statistics

Department: Statistics
Supervisors: Mostafa El Moumni MD PhD

In 90 minutes, an overview of statistical techniques will be given. Together with the participants, several questions will be answered including:

- What is the link between probability theory and statistics?
- Why is it important to use descriptive statistics?
- What is a statistical test? Why should we abandon null-hypothesis significance testing (NHST)?
- How to interpret effect sizes, confidence intervals and meta-analytic thinking?

The emphasis will not be on formulas and mathematics, but on understanding the logic behind the statistical tools to avoid biased conclusions. Prior to this masterclass participants will be asked to do a small homework assignment, so they are prepared for the masterclass.

Workshops ISCOMS 2024

Inside the psychotic experience

Department: Psychiatry, UMCG
Supervisor: F. D. van Es MD

Psychosis is a generic psychiatric term for a mental state often described as the loss of contact with reality. Patients experiencing psychosis may report hallucinations (seeing or hearing things that are not there) or delusional beliefs (false beliefs about what is taking place or who one is). The combination of both often causes a severe disruption of perception, thinking, emotion and behaviour. Depending on its severity, a psychotic episode may thus be accompanied by unusual or bizarre behaviour, as well as difficulty with social interaction and impairment in carrying out daily life activities. As a result, patients with psychosis are caught in a hostile environment. They are therefore in need of your dedication and medical skills: how can you meet their needs? How can you avoid stigma and promote health and social recovery?

During this workshop, participants are able to ask questions to a psychiatrist and a patient who had suffered from psychosis.

Dental implants in the aesthetic zone

Department: Oral Maxillofacial Surgery, UMCG Prosthetic Dentistry, UMCG
Supervisor: Prof. Henny J.A. Meijer DMD PhD, Prof. Gerry M. Raghoebar DMD PhD, Wim J.W.A. Slot DMD PhD, Charlotte Jensen DMD PhD, Gerdien Telleman DMD PhD.

Losing one or more teeth in the aesthetic zone has a great impact on a person. Inserting root-form dental implants and restoring them with ceramic crowns has proven to be a reliable method to solve this problem. The dental literature shows excellent survival rates of single-tooth restorations on dental implants, varying from 96.1% to 98.9% after 7.5 years in function. Studies that address aesthetics and patient satisfaction reveal it is a very sensitive method in the eye of the professional, but that patients are generally very satisfied. This workshop comprises a lecture with the possibilities of dental implants, different treatment steps and aesthetic results. The second part of the workshop is a hands-on training in which the participant actually places a dental implant in a model, imitating the surgical part of the treatment. The workshop is supported by Straumann Netherlands.

Workshops ISCOMS 2024

Measure my physiology!

An educational journey to determine pulmonary function

Department: Biomedical Sciences of Cells and Systems, section Anatomy and Medical Physiology
Supervisors: E. Sietsema

Pulmonary function tests, including spirometry, play an important role in the detection of asthma and Chronic Obstructive Pulmonary Disease (COPD). Measurements of pulmonary function help to chart the course of the disease and assess the risk of complications. As a doctor and clinical researcher, it is important to accurately interpret and analyse spirometry testing results. Therefore, practicals in performing these spirometry tests are an important part of the education provided by the medical faculty to its students. When attendees participate in this workshop, they experience one of the informative medical physiology laboratories about lung function testing as it is given to students of the University of Groningen Medical Faculty. Participants will learn to conduct lung function tests on their fellow students and generate their own physiological data. In addition, participants gain skills in performing lung function testing and learn to analyse and interpret their personalized data. Lastly, participants will have a chance to learn what these physiological concepts actually mean.

PULSE Racing - We stimulate to cycle

Department: Pulse racing
Supervisors: Kristel den Engelsman, Iris Kleinbog and Linda van der Klei

PULSE Racing was founded to advance functional electrostimulation (FES) for people with spinal cord injuries. Having a spinal cord injury causes several physical problems. Besides the inability to walk and reduced mobility, people with paraplegia (inability to voluntarily move the lower parts of the body) also have a reduced aerobic functioning, disturbed blood circulation and a high risk of pressure sores. This has a negative impact on their quality of life and personal well-being. FES has a proven positive influence on the physical and mental aspects of the life of people with spinal cord injury. The activity of the muscles induced by FES can improve the aerobic functioning, blood circulation and psychological state. In this workshop, participants will have the chance to gain a deeper understanding of how functional electrostimulation works and will have the ability to speak with paralympic athletes who uses this technology to cycle. They will even have the opportunity to try the bike for themselves!

Workshops ISCOMS 2024

Lab on a chip

Department: Research Institute of Pharmacy
Supervisor: Drs. Ing. P.P.M.F.A (Patty) Mulder, Prof. E.M.J. (Sabeth) Verpoorte, PhD

Over the past couple of decades Lab-on-a-chip technologies made inroads into laboratories focusing on the development of fast chemical and bioanalytical analyses using minute volumes of sample. Micro- and nanotechnologies are used to construct interconnected microchannel networks in planar substrates, forming microfluidic devices to replace more conventional chemical vessels such as beakers, and columns to achieve ultra-small-volume (from µL to nL) liquid handling. Small handheld analysers are one result, suitable for medical diagnostic, agricultural, environmental, and other applications.

The last fifteen years, lab chip technologies have also found increasing application for cell biological studies, as cell microenvironments can be exquisitely engineered to mimic in vivo environments. It has become possible to think about assembling tissue constructs or actual tissue samples in physiological configurations in specially designed lab chip systems, so-called "organ-on-a-chip" or "human-on-a-chip" systems. This may lead to an improved capability to study in vivo processes in vitro. Organ interactions can be revealed in these systems, giving insight not only into drug toxicity but also into more subtle regulatory pathways between organs.
This workshop will give participants a short glimpse into how a laboratory was actively involved in the realization of lab chip systems for sensing/analytical chemistry and cell culture and analysis. Participants will see the fabrication of those devices and learned the basic principles of microfluidics. Besides that, they will have an opportunity to discuss other possible medical uses of the lab-on-a-chip technologies with researchers in the lab.

Workshops ISCOMS 2024

Dissection of the human brain

Department: Anatomy &Amp; Medical Physiology, Biomedical Sciences of Cells &Amp; Systems, UMCG
Supervisors: Janniko Georgiadis, PhD

Dissection of the human body in general and of the brain in particular is an underexposed part of the average medical curriculum. In this context, the workshop "Dissection of the human brain" will address this omission. The workshop will be organised in the dissection room of the Anatomy Department of the UMCG and is especially intended for students with a special interest in the brain.

The workshop started with the inspection of the external parts of the human brain. The morphology of meninges, blood vessels, and neocortical areas were central topics. Subsequently, transversal and horizontal sections of fixated human brains were used to inspect the inner parts of the brain. Attention was paid to the three-dimensional location of the cortical, extrapyramidal, and limbic structures. At the end of the workshop, students had gained a better insight into the structure and function of the human brain.

Light up the tissue and brighten your patients odds

Department: Gastroenterology, UMCG
Supervisors: Andrea Sterkenburg TP PhD candidate, Lisanne van Heijst MD PhD candidate

The optical molecular imaging Groningen (OMIG) group aims to visualize and identify tissue and biodistribution of molecules in the near-infrared spectrum. In 2008 the first in human optical imaging trial was performed in the UMCG with a targeted FITC tracer in patients with ovarium carcinoma. This first success was followed by the foundation of the OMIG research group in 2015. Since then, more than 500 patients have entered clinical trials in both surgical and endoscopic fields. Before the procedure, patients are administered with the tracer and, with dedicated fluorescence camera systems, we can directly visualize these near infrared tracers intra-operatively and provide direct feedback. This provides information on the location of the tumor or biodistribution of a medicine. During this workshop, participants will track tumors in a phantom model and try to resect all of these with the aid of our dedicated fluorescence camera systems.

Workshops ISCOMS 2024

Gene editing Essentials: the CRISPR-Cas9 toolbox

Department: Genetics
Supervisors: Kai Yu Ma PhD & Willemien van Zwol PhD

Join us to unravel the complexities of gene-editing! Tailored for students with little to no background in gene-editing, this hands-on workshop demystifies the molecular mechanisms behind this groundbreaking technology. You will gain a foundational understanding of how gene-editing works, exploring its potential and limitations in a medical context. We'll address burning questions, such as the current state of gene-editing in health care, offering insights into what's currently possible and what remains science fiction.

Light up the tissue and brighten your patients odds

Department: Burn Centre, Groningen
Supervisor: M.E. van Eck MD

The treatment of patients with (extensive) burns remains a major challenge. Two main factors define burn severity: depth of burn injury and total body surface (TBSA) area burnt. In burn wounds, not only the thermally injured skin and the underlying anatomical structures are affected, but there are some pathophysiological changes that influence the whole body. This workshop entails an interactive presentation and a number of clinical cases in which the students could practice examining a burn wound.

An introduction in treating life-threatening situations in the IC

Department: Department of Critical Care, UMCG
Supervisors: A. (Annalies) de Bont-Prins and M. (Marije) Smit MD

Implementation of interdisciplinary teams in the ICU[IS1] to provide care in often life-threatening situations, focused attention on the relevance of leadership behaviour. Effective, coordinated, and safe patient care challenge even the most experienced ICU teams daily. Leadership behaviour is defined as the process of influencing others to understand and agree about what needs to be done and how to do it, and facilitating individual and collective efforts to accomplish shared objectives. Simulation training is useful for teaching team-based crisis management skills and is now considered essential in developing and maintaining competencies for ICU workers.
In our high fidelity simulation center, participants of the workshop will become familiar with some stepwise elements of the treatment, such as resuscitation and airway management of critically ill patients. The non-technical skills such as leadership, communication, and cooperation are also emphasised. The experiences may contribute to the development of knowledge and skills in decision-making and teamwork during the treatment of critically ill patients.

Workshops ISCOMS 2024

The miracle of ultrasounds in obstetrics

Department: Obstetrics & Gynaecology, Department of Prenatal Diagnosis
Supervisor: Ayten Elvan, MD PhD

In every pregnancy there is a risk for fetal anomalies. In the Netherlands pregnant women are offered a first and second trimester ultrasound examination to screen for fetal anomalies. With major improvement in image resolution and systematic anatomic assessment protocols, ultrasound evaluation of the fetal anatomy and anomalies with great detail is achievable.
In this workshop prenatal screening and diagnosis in the Netherlands will be discussed. What is different according to other countries?
Pictures of prenatal ultrasound findings will be shown, what do you see?
In the second part of the workshop we will show you the practice in our prenatal diagnosis department, hands on with pregnant women and you can practice with our ultrasound simulator.

Fix a mandibulair fracture yourself

Department: Oral and Maxillofacial Surgery, UMCG
Supervisors: Prof. Ruud R.M. Bos DMD PhD, Baucke van Minnen MD

The treatment of mandibular fractures has evolved greatly over the past 50 years. Biomechanical principles that have been developed in laboratory models are applied to clinical practice in order to allow for immediate mobilization and rehabilitation of the injured part. The goal of this workshop was to give insight into the widely accepted treatment modality of mandibular fractures: internal fixation with mini plates and screws. After a short introduction to the principles of mandibular fracture treatment, the participants will perform an osteosynthesis of mandibular fractures in a polyurethane mandible with mini plates and screws.

Pre-course

The pre-course will take place on Monday the 3rd of June. This day is focused on improving students' research skills and introducing them to new and different medical topics.

After registering for the pre-course day on our website, you will be able to attend a Masterclass, Science elective, IMED talks and Speed keynotes.

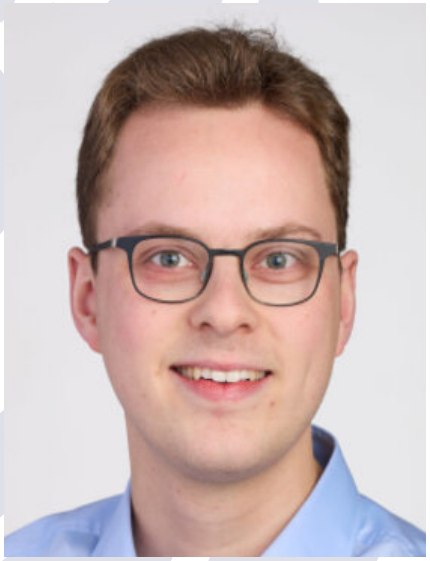
The pre-course starts with the masterclasses and are intended to improve your research skills. They will consist of masterclasses such as 'Preparing oral presentations', 'Scientific writing', and others. Besides the masterclasses, you can take part in several Science Electives, consisting of a debate about AI in health care, a patient lecture with a live patient and a trauma lecture about the HEMS: Dutch helicopter emergency medical services.

New to ISCOMS this year are the ISCOMS Medical talks. These six talks will be held by professors of the UMCG who are specialized in their different medical subjects. The talks will be followed by a discussion meant to broaden your knowledge on the subject and ask questions to these health professionals. During the pre-course day there will be two speed keynotes given by young and inspiring doctors who have written their PhD about the subject they will be presenting. These include 'Music therapy for neonates' and 'Biomarkers in IBD'.

Lastly there will be a lecture about 'Your Future at the UMCG', presented by a former ISCOMS Research Fellowship participant who will tell you more about the possibilities of doing research and the opportunities to gain a PhD position at the UMCG.

We will end the day with our social programme which will be a walking buffet followed by a salsa workshop in the cultural hall Dot in the city of Groningen.

Arno de Bourgonje



Inflammatory bowel diseases (IBD) are complex diseases of the gastrointestinal tract, characterised by chronic ulcerative inflammation and a relapse-remitting disease course. Since IBD is a complex, heterogeneous and unpredictable disease, there is an urgent need for biomarkers, which are objectively measured parameters of (ab)normal biological processes or -systems. Biomarkers may help to classify IBD, assess disease activity and disease complications, and accurately predict how a patient's disease course will develop and/or how a patient will respond to a particular treatment. Arno Bourgonje's research is focused on the discovery and application of novel biomarker signatures in patients with IBD, while also assessing their potential for therapeutic modulation (e.g., through dietary interventions) and their utility to predict clinical outcomes (e.g., response to established medical treatment). His strategy is to identify functionally relevant disease markers derived from different biological systems (e.g., the immune system) and -mechanisms (e.g., oxidative stress and redox signalling) and carefully examine these signatures through detailed phenotypic patient stratification. By adopting a "systems biology" approach and studying the interplay between different pathophysiological entities, his ultimate aim is to develop and validate clinically applicable biomarkers for personalised medicine, which could help improve patient outcomes.

Arno Bourgonje (27) studied Medicine at the University of Groningen (2020, summa cum laude) and obtained his PhD (2023, cum laude) at the Departments of Gastroenterology and Hepatology & Pathology and Medical Biology of the same university. Currently, he works as a postdoctoral researcher at the Icahn School of Medicine at Mount Sinai in New York, renowned as a world-leading centre for IBD.

Hanneke van Dokkum

Hanneke combined her medical studies at the University Medical Center Groningen (UMCG) with a PhD trajectory. The focus of this PhD was on neonatal stress in preterm-born infants admitted to the neonatal intensive care unit (NICU). She researched the effects of neonatal stress on neurodevelopment and behaviour, as well as underlying mechanisms of neonatal stress including DNA methylation of stress-related genes. Furthermore, she implemented and researched live-performed music therapy in the NICU as a stress-reducing intervention. During her MD-PhD trajectory, she lived in New York City, where she had the opportunity to witness this intervention in practice and study it in more detail. The findings of her research projects provide insight into care for the tiniest patients and their parents that will ultimately improve the quality of care in the NICU and the quality of life beyond the NICU.

Masterclasses

An abstract: A Gateway to get your attention

Prof. Harm Kampinga, PhD

The abstract of a scientific paper or grant is the gateway to being noted and read. If you do not roll out the red carpet, people will pass by! A good abstract should not only present the essential and sound features of your research and radiate its high quality, but also should advertise why your findings are relevant and how they are relevant.

In this Masterclass, we had an interactive discussion about the DOs and DONTs in writing a convincing scientific abstract.

Preparing an oral presentation

Prof. Anton Scheurink PhD

This masterclass provided strategies for preparing interesting and engaging presentations. The essence of an effective presentation was engaging the audience, capturing their interest by posing an intriguing question, spelling out a methodology for addressing that question, and then answering it. A successful presentation provided the audience with cues and information in an orderly structure, allowing them to form expectations on what they would hear and when they would hear it. Tips for doing so, along with tips on what not to do, were supplied. The presenter engaged participants in a highly interactive format by crafting storylines and structures from the material that they provided. The focus of this masterclass was on oral presentations, but at the end, some dos and don'ts on poster presentations were also given.

Do I see myself as a PHD student

Salome Scholtens PhD

You are all biomedical students with an affinity for research, but have you considered doing a PhD? This may be a tough decision. Maybe you already made up your mind and you are aiming for a PhD, but it could very well be that you struggle to decide because other career choices are luring as well. Perhaps you are hesitant, because of the many stories you heard about how stressful it is to be a PhD student. Or you simply don't know what a PhD trajectory really entails and therefore you find it difficult to decide on whether to go for it or not. During this masterclass, students will take time to think about a possible future as a PhD student and how to cooperate with stressful situations. We will guide them through some exercises to help you in finding out whether a PhD is something for you.

Masterclasses

Writing a Good Introduction for Your Research Article

Prof. Ton Lisman PhD (Professor of Experimental Surgery, UMCG)
Sjoukje van der Werf (Medical information specialist, Central Medical Library, UMCG)

The introduction is an essential part of your research article. It is the first thing that readers will see, and it needs to be engaging, informative, solid and well-written. In this workshop, we will discuss key elements of an effective introduction, share tips & tricks and address questions and challenges including:

When do you start writing the introduction?
How do you start?
How to summarize the literature (and make sure you do not miss anything)?
How do you motivate the relevance of your specific research question in the introduction?
Academic writing: structure and storytelling

Writing a Good Introduction for Your Research Article

Prof. Janette Burgess PhD

You have completed your experimental protocols, analysed the data and interpreted the results and written them down. Now you need to describe your findings in the context of the literature – how hard can that be? Well actually writing the discussion is often the hardest component of the manuscript to craft. What should you include and what not? How do you deal with conflicting data? How much can you speculate about the implications of your findings.
This interactive workshop aims to give you tools to help with crafting a compelling discussion that frames your new knowledge in the context of the state of the art in your field.

Medical statistics

Mostafa El Moumni MD PhD

In 90 minutes, an overview of statistical techniques will be given. Together with the participants several questions will be answered including:
What is the link between probability theory and statistics?
Why is it important to use descriptive statistics?
What is a statistical test? Why should we abandon null-hypothesis significance testing (NHST)?
How to interpret effect sizes, confidence intervals and meta-analytic thinking?

The emphasis will not be on formulas and mathematics, but on understanding the logic behind the statistical tools to avoid biased conclusions. Prior to this masterclass participants will be asked to do a small homework assignment, so they are prepared for the masterclass.

Title: "Doctor AI. A Debate about responsible use

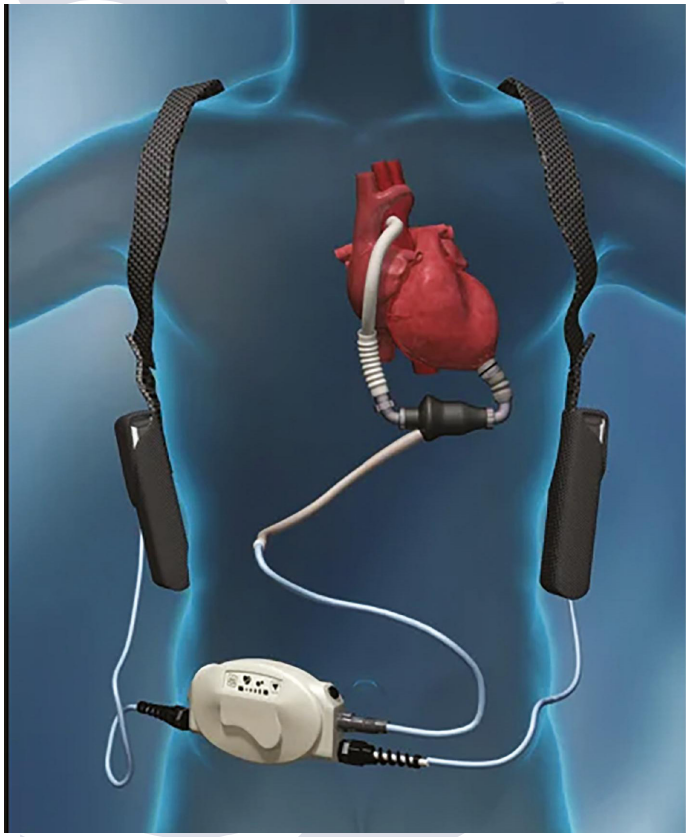
Els Maeckelberghe PhD, Associate Professor Ethics, UMCG

Imagine 2030: what types of medical professionals do we have? Has Artificial Intelligence (AI) taken over diagnosis and decision-making? Or has AI proven to increase health disparities, and therefore been consigned to the wastepaper basket long since?
Currently, the idea is that AI can profoundly disrupt human life and society. How can we effectively navigate and mitigate the disruptive impacts of AI in practical terms? How can we ensure AI is developed to serve humanity, promoting the common good, and enhancing human welfare, freedom, and particularly health? Healthcare institutions worldwide are increasingly using AI technologies to improve disease diagnosis, develop personalized treatments, and assist clinical decision-making. The inclusion of AI in the healthcare context is often motivated by the promise of efficiency gains, improved accuracy, mitigation of high costs and time in assessing healthcare data, as well as tackling the problem of personnel shortages and burdens faced by healthcare professionals. As such, rapid developments and implementation in AI offer an opportunity to transform healthcare by boosting its potential for providing patient care. The responsible development and implementation of AI thus raise a host of ethical, legal, and societal questions.

In this debate, we will try to tease out how AI is used in healthcare right now and how this can be done responsibly and trustworthily. Experts from the UMCG will share their experiences, knowledge, and insights, going into examples of how AI is used in neonatology (diagnostics and decision aid) and in genetics (accelerating genetic screening results).

Patient Lecture – Living with an LVAD of Artificial

Kevin Damman, MD, PhD



Heart failure is a disease characterized by severe symptoms of congestion, fatigue, limited exercise tolerance and impaired survival. When heart failure is severe, often medical therapy fails, and advanced therapies are necessary such as heart transplantation. Unfortunately, there is still a large shortage of donor hearts, and the time on the waiting list is long. Some patients are also not transplantable for other reasons.

For some of these patients, a left ventricular assist device (LVAD) is a treatment option that improves quality of life and survival. This therapy is essentially a pump that decreases intracardiac filling pressures and improve cardiac output. As a result, organ perfusion is restored and patients can mobilize, work, exercise and have a reduction of signs and symptoms. Unfortunately, this therapy also has its disadvantages, which are mostly related to the inherent risk of implanting a device that needs power into the bloodstream in a human body.

In this patient lecture we will meet a patient in whom an LVAD was implanted and discuss pro's and con's of this advanced heart failure therapy from a patient and medical perspective.

Scientific Electives

Trauma; a physician staffed helicopter emergency medical services (p-HEMS) in the Netherlands. Join the HEMS physician on a regular HEMS shift. of Artificial Intelligence in healthcare

Ellen Weelink MD, anaesthesiologist and HEMS physician

The Dutch prehospital care consists of highly skilled ambulance teams (nurse and driver). In severe cases where there is an immediate medical threat to a person, the ambulance team is joined by a physician staffed HEMS team.
In this science elective you will get an insight in the Dutch physician staffed HEMS (p-HEMS). By means of taking a regular HEMS shift to get you acquainted with the HEMS work. What is the role of the p-HEMS in the Dutch prehospital medical care system? What is a HEMS physician and what work do they do? You will learn about the technical and non-technical skills needed, the flight operations, medical decision making and of course what to do in between calls.

Learn all about the helicopter view of the acute prehospital patient care.

Patient Lecture
Exoskeleton

Imagine not being able to move your legs anymore – for the rest of your life. This is the result of a spinal cord injury. Now, imagine a future where you can walk again, using an exoskeleton that can take over the function of your lower body, thereby improving your physical health issues and giving you the opportunity to stand eye to eye with your friends and family again. How would that feel?

You most likely don't actively think about performing everyday activities, such as walking, climbing stairs or grabbing something from a high cupboard. However, those activities are hard(er) to perform while in a wheelchair. These tasks require more time, effort and preparation. Although rehabilitation learns you how to be mobile in a wheelchair again, the freedom of movement stays limiting.

Besides the evident impact on mobility, having a spinal cord injury leads to some secondary physical health effects as well. Muscle strength and bone structure declines, impaired cardiovascular issues result in affected blood flow and the control over bladder and bowel function is lost. These conditions lead to increased risks on for example osteoporosis, fractures and thrombosis. Besides the physical consequences, obvious mental challenges arise as well, such as feeling like people are always looking down on you. Daan van der Heyden is 32 years old and has a complete T5 lesion, which means that he is paralyzed from below his chest. In 2017, he suffered a spinal cord injury as a result of a sports accident and has been wheelchair bound ever since. Daan's expertise lies in orthopedic shoemaking. This gives him a better understanding of walking patterns. Daan also plays wheelchair basketball with team Ossnabrück, in Germany.

Daan rehabilitated at the Sint Maartenskliniek in Nijmegen, a hospital specialized in the field of motion disorders. Ilse van Nes and Hennie Rijken are both working at the spinal cord injury department of the Sint Maartenskliniek, Ilse as a rehabilitation physician and Hennie as a physical therapist. In 2020 Ilse participated in the Dutch tv-program 'Topdokters' and she is also editor of the Dutch textbook 'Dwarslaesierevalidatie'. Hennie has contributed to the development of gait training and the use of innovative gait training equipment at the Sint Maartenskliniek, from his position as a physical therapist and research associate. In this lecture they will share their experience with the use of exoskeletons for paraplegic patients, including the training program, patient characteristics and home use.

Project MARCH, a Dream Team from the TU Delft, builds an innovative exoskeleton for people with paraplegia. The team works together with Daan and the Sint Maartenskliniek to make this possible. An exoskeleton is a powered robotic suit attached to the outside of the body that takes over the functionalities of the lower part of the body. An exoskeleton enables someone with paraplegia to stand up and walk again, taking away a piece of dependency. Besides, regular standing and walking in an exoskeleton helps reducing the secondary health issues and, most importantly, gives people with paraplegia the ability back to stand eye to eye with their loved ones again.

Daan is extremely motivated to explore the limits of exoskeleton technology. He will showcase the innovations of Project MARCH to the world during the CYBATHLON 2024 in October, a worldwide competition for assistive technology mimicking the daily life activities we have to face everyday.

Social Programme

Sunday the 2nd of June 2024
Welcoming night: city tour & pub quiz
If you are already in Groningen on Sunday, you can participate in the city tour, which is organised on Sunday evening. We will walk through the historic city centre of Groningen and highlighting its most beautiful and enjoyable spots. The tour will end at a local pub where the welcoming night will take place. At this pub, we will join a pub quiz while enjoying a few drinks. It is a good opportunity for you to meet other participants, the ISCOMS Organising Committee and the First Year Crew! You are always welcome to join the welcoming night, regardless of your participation in the city tour.

Monday the 3rd of June 2024
Salsa workshop
Most of you will arrive on Monday. Throughout the day, you have the option to partake in the pre-course aimed at enhancing your research skills. Once the scientific programme concludes, we will guide you to DOT, a beautiful location close to the UMCG, where the dance class will take place. On arrival, an Italian pasta buffet will be served and we will have dinner together. After the buffet, you have the opportunity to blow off some steam and show everyone your dancing skills!

Tuesday the 4th of June 2024
Formal Dinner
After the second congress day, we will host a formal dinner at one of Groningen's most prestigious locations: 'Het Prinsenhof '. Situated in the heart of Groningen, near the magnificent 'Martinitoren,' this venue promises a memorable experience. Besides the organising comittee and the participants, UMCG officals and other notable people from the congress will attend. A delicious six-course dinner will be served. During the dinner a jazz band will be playing some music. This year, we are transforming the formal dinner into a walking dinner, fostering social interaction among all participants. It's a fantastic opportunity to connect with fellow ISCOMS participants and meet some of the professors who presented at the event. For an dazzling appearance, it would be great if you bring an elegant dress or your best suit.

Social Programme

Wednesday the 5th of June 2024
Recreational evening
We will start the evening by having dinner in different groups, so you can discuss the day and get to know each other. After that, we will move towards the various locations where the activities will take place. The choice of what you want to do this evening is all yours. You can decide what you want to do this evening; activities include a boat tour, a yoga class, laser gaming, bowling and pooling!

Thursday the 6th of June 2024
World Wide ISCOMS Night
After the conclusion of the last day of the congress and the closing ceremony, get ready for the World Wide ISCOMS Night! We are going to start with a delicious buffet with a lot of different dishes, something tasty for everyone! Afterwards, the great party will begin. this night is all about celebrating the different countries represented at ISCOMS. You can dress up in traditional clothes and bring a traditional snack from your country. We would love to play music specifically from your country, so ask the DJ if he can play your favourite music. It will be an unforgettable night!

Friday the 7th of June 2024
Post Congress Tour
Unfortunately, the congress will be over after the World Wide ISCOMS Night. But don't worry, we still have one activity for you: the Post Congress Tour! On this day we are going to Emmen. This day we will walk along one of the cultural highlights of the Netherlands, the Dolmens. After that, we will go to the zoo and enjoy the culture of the Netherlands in Emmen. We will finish off with a dinner in Groningen!

ISCOMS Research Fellowship

For students who are interested in doing research in Groningen in the University Medical Center Groningen (UMCG), we organize the two-week ISCOMS Research Fellowships. These short internships will take place directly after the congress.

The IRF allows students who present their research at ISCOMS to acquire a taste of conducting research in the Netherlands, and more specifically in the UMCG. The IRF will take place from, the 10th of June till the 21st of June 2024. In short, the IRF gives presenting participants of ISCOMS a chance to participate in a two-week research project at one of the UMCG Research Institutes. The IRF consists of a challenging programme, in which students are expected to actively participate in research and gather a great deal of knowledge related to the topic of their project. Top researchers will supervise the fellowships in the UMCG and they will expect fully motivated students.
As a student, you get the chance to perform research at a leading institute, meet top researchers, and learn about the possibilities of doing a PhD programme in the Netherlands. Many international students have been able to start a PhD-programme in the UMCG as a result of participation in the IRF!

All projects during the IRF 2024 are listed below.

ISCOMS Research Fellowship

Project A - The pathobiology of lymphoma

Supervisor: Lydia Visser MD PhD working with three PhD-students with an MSc
Field of research: pathology and medical biology

Description:
We will look at different aspects of lymphoma research by looking at the expression of proteins, drug sensitivity, combination therapy, or effect on the microenvironment. We can use techniques such as immunohistochemistry, cell culture, flowcytometry, western blot, elisa and metabolic assays. There will be different projects.
Experience from student: Looking for a student with interest in labwork

Project B – Nephrology

Supervisor: Jaap van den Born MD PhD, prof. Stefan P. Berger MD PhD
Field of research: Nephrology

Description:
In Nephrology Dept. various projects are running using diverse methodologies (see 1-6). You are invited to express your interests in one of these fields (being either clinical, epidemiological, human- or animal in vivo- or in vitro experimental) to indicate what sub-project interests you most. Please motivate your interest in the specific topic.

1. Patients with renal disease and progressive renal function loss, are being studied with respect to the mechanisms via which the urinary protein leakage results in renal function loss. We aim to modulate proteinuria-driven complement activation on endothelial and tubular cells.

2. Our center also has a large population of renal transplant recipients. These patients are monitored very closely, and regimens aimed at increasing the duration of graft function as well as patient survival are being studied currently. A large database including biobanked urine and plasma is available in TransplantLines. Within this cohort we try to entangle which factors associate/contribute to transplant loss and mortality.

3. General population cohorts are studied to detect which parameters lead to initiation of progressive renal function loss and its complications. The cohorts PREVEND and Lifelines from the general population are good examples. The natural course is followed to study possible causes of morbidity and mortality in relation to renal parameters.

4. Lifestyle and the kidney. Many lifestyle factors are involved in the risk of long term renal function loss. These include smoking as well as nutritional habits, such as excess caloric intake leading to obesity and diabetes, excess sodium intake and sedentary lifestyle. The mechanisms of renal damage induced by these lifestyle factors are being studied in patients as well as experimental animals, and the effect of lifestyle intervention measures on the course of renal disease is being studied. Nutritional monitoring is part of this project.

5. Endothelial dysfunction highly contributes to progression of renal and cardiovascular diseases. We are interested in the effects of uremic and/or transplantation conditions on the endothelial glycocalyx, and functional consequences of endothelial injury. This work is performed on human (renal) endothelial cells in culture and tissues from renal patients.

6. Immunity and the kidney. Within this research line we try to unravel the role of the immune system (complement system, leukocytes, endothelial cells) in chronic renal damage in proteinuric and transplanted kidneys. B-cell, endothelial and complement profiling will be associated with clinical outcome parameters.

Experience from student: Interest in nephrology

Project C - Immunofluorescent Staining of Human Liver Biopsies from Normothermic Machine Perfused Livers

Supervisor: Prof. Ton Lisman PhD, Silke Bodewes MD PhD-student
Field of research: Surgery

Description:
At the UMCG, we employ normothermic machine perfusion (NMP) for the evaluation of initially declined donor livers. NMP allows us to assess the viability of the liver and bile ducts, while the liver is fully metabolically active. To gain insights into these processes, we collect liver parenchyma biopsies before and after NMP. We aim to visualize multiple protein markers simultaneously using immunofluorescent staining and microscopy. During this project, students will learn the techniques of slicing liver biopsies, performing immunofluorescent staining, and evaluating the stained biopsies. If a liver perfusion is ongoing during the Research Fellowship, students may have the opportunity to observe the process.

Experience from student: Looking for a student with laboratory experience.

Project D - Association of automated myocardial blush scores and left ventricular diastolic function in STEMI patients

Supervisor: Prof. Adriaan Voors MD PhD, Erik Lipsic, MD PhD, Chris Lenselink BSc
Field of research: Cardiology

Description:
The employment of percutaneous coronary intervention (PCI) as first-line treatment for ST-elevation myocardial infarction (STEMI) has resulted in a preserved systolic function, as reflected by left ventricular ejection fraction, in the majority of patients. However, adverse diastolic remodeling is emerging as a predictor of clinical outcome as well. In spite of this, little is known about the pathophysiology of diastolic dysfunction after STEMI. In a prominent hypothesis, dysfunction of the coronary microcirculation, the tiniest vessels in the heart, is a pathophysiological hallmark of diastolic dysfunction. There is an unmet need to easily, objectively, and quickly assess the status of the coronary microcirculation during the PCI procedure of STEMI patients. The myocardial blush grade (MBG) is a potential marker for coronary microvascular dysfunction (CMD), yet it is not objective with high intra- and interobserver variability.

Methods
Non-diabetic STEMI patients from the GIPS-III trial will be analyzed. Automated MBG scores will be calculated using the QuBE software which semi-automatically determines MBG values using coronary angiograms as recorded during the PCI procedure. Diastolic function will be determined by abnormal results on echocardiography performed shortly after STEMI as well as after 4 months follow-up. Diastolic dysfunction will be defined as abnormal E/e' ratio and left atrial reservoir strain values, using 40 patients with diastolic dysfunction and 40 without. Using linear regression modeling, we will investigate whether automated MBG values are associated with abnormal diastolic function at baseline as well as change in diastolic function over the follow-up period.

Project E - Validation of a student engagement observation instrument in higher medical education

Supervisor: Alexandra Androni PhD-student
Field of research: Medical education

Description:
This project aims to validate a student engagement observation instrument by assessing its validity and inter-rater reliability. The student will work with previously collected data, whereby researchers used an observation instrument to score student engagement behaviour. Since this is a non-clinical project, emphasis is focused on educational theories, literature in educational models and instruments used to measure student engagement in higher education. We will begin by examining medical education literature and we will then discuss the current observation instrument that was used during data collection. The student will afterwards study the data and propose a method to validate sub-categories of the instrument. Validation strategies that we could work on might be content-related, construct-related or criterion-related.

The research question that the student will try to answer will be adapted according to the student's interests and competences, but will be related to the validation of the student engagement observation instrument. It is preferable that you are familiar with basic statistics (SPSS, STATA, etc.), and that you have some experience with quantitative research.

Finally, you will gain experience working in an inter-disciplinary team of medical education researchers, you will learn about the process of applying and attending medical school at the University of Groningen and you will work on your skills combining qualitative and quantitative research methods!

Experience from student: basic statistical knowledge and quantitative research.

ISCOMS Research Fellowship

Project F - Functional genetics to understand complex diseases

Supervisor: Sebo Withoff PhD
Field of research: Genetics ERIBA

Description:
The Immunogenetics group of the Department of Genetics within the UMCG investigates the role of genetic variation in health and the aetiology of autoimmune diseases (e.g. coeliac disease), the role of the gut microbiome therein, and is generating iPSC-based organ-on-chip models to investigate and validate 'omics' findings.

The data for these studies are mostly generated by next generation sequencing such as single-cell RNA-seq and ATAC-seq. The generation and analyses of the data requires a broad range of scientific expertise. In our group, a dynamic and highly interactive environment is created in which bioinformaticians, geneticists, statisticians, molecular biologists, stem cell biologists and immunologists work together closely.
Important findings published by the group are (a) the shared genetics of autoimmune diseases, (b) 95% of the autoimmune disease-associated single nucleotide polymorphisms (SNPs) affect gene expression rather than gene function, (c) eQTL effects of GWAS SNPs on long non-coding RNAs (lncRNAs), and (d) a range of environmental factors affecting the human microbiome.
The current ongoing research is for a large part focused on the prioritisation of SNPs, genes, pathways and cell types affected in autoimmune diseases, on in vitro experiments to validate the function of the prioritised candidates and on determining how host genetics affects microbiome composition.
Depending on the background and interests of the student, we will design a working plan for the two-week internship.

Project G - Evaluation of a smartphone based screening tool for neonatal jaundice

Supervisor: Hulzebos MD PhD
Field of research: Neonatology

Description:
Neonatal jaundice is a condition of elevated bilirubin level, also known as hyperbilirubinemia. Severe hyperbilirubinemia is potentially dangerous, and - when left untreated – may cause permanent brain damage. To prevent the harmless condition of neonatal jaundice from developing into kernicterus, it is highly important to identify the children at risk at an early stage. Jaundice can be identified by visual examination due to its ability to give yellowish colour to the skin and sclerae of the eye. However, visual judgement of jaundice severity has proven to be unreliable, even though performed by experienced health personnel. The measurement of bilirubin is traditionally done by blood samples. To reduce the need of drawing blood from the newborn, transcutaneous bilirubinometers have been developed to measure the bilirubin in the newborn skin. Both laboratory equipment and transcutaneous bilirubinometers are rather expensive, with a price of 6-10.000 US dollars, thus making them practically unavailable in low-income countries. Since most deaths due to jaundice occur in low-income countries, there is a large unmet need of simple, reliable and affordable technologies to identify at-risk newborns. There is a novel instrument that may fulfil these requirements: a smartphone-based application that estimates bilirubin levels based on the colour analysis of a digital image.

ISCOMS Research Fellowship

We hypothesise that the smartphone app in estimating bilirubin levels is highly correlated to transcutaneous or serum bilirubin levels, and that this new method is better than the visual estimation of neonatal jaundice. Following our hypothesis, the short-term goal for this project is to assess the user friendliness and hopefully demonstrate the ability of this novel screening method to identify newborns with neonatal jaundice.

Project H - Potassium correction for renin-angiotensin-aldosterone system optimization in chronic kidney disease (PROMISE)

Supervisor: Prof. M.H. de Borst, MD, PhD, C.J. van Lieshout, MD PhD
Field of research: Nephrology

Description:
Chronic kidney disease (CKD) forms a major medical, social and economic burden with a high risk of morbidity and premature mortality, affecting approximately 10% of the global population. Angiotensin converting enzyme inhibitors (ACEi) and angiotensin receptor blockers (ARB) are cornerstone therapy in patients with CKD. At the same time, <50% of patients with advanced CKD are on ACEi/ARB therapy. Several factors, including hyperkalaemia, can lead to discontinuation of ACEi/ARB in advanced CKD, and discontinuation of ACEi/ARB has been associated with an increased risk of cardiovascular disease, kidney failure or death. The main hypothesis of this trial is that the potassium binder patiromer enables up-titration of ACEi/ARB treatment in patients with CKD stage 3b/4 who are on suboptimal ACEi/ARB therapy and prone to hyperkalaemia, resulting in a reduction in albuminuria and blood pressure. We will investigate this hypothesis in a randomized, double-blind, placebo controlled cross-over trial. You will get familiar with all that it takes to perform a clinical trial.

Project I - Oncogenic expression of C/EBPβ-LIP in Breast Cancer

Supervisor: Prof. Cor Calkhoven MD PhD, PhD-student Clément Karch
Field of research: ERIBA, Ageing biology

Description:
Breast cancer is one of the most prevalent cancers worldwide. Breast cancer can be classified into different subtypes requiring different treatment, and despite the existence of treatments for most types of breast cancers, prognosis for metastatic breast cancer is still poor. To develop more specific and effective treatment it is crucial to understand the underlying cellular and molecular mechanisms that specify a certain breast cancer subtype.

The transcription factor C/EBPβ-LIP is specifically overexpressed in triple-negative breast cancer and was shown to be involved in cell migration, cancer metabolism and possibly immune evasion. The student will work on aspects of oncogenic functions of C/EBPβ-LIP. The project will likely involve cell culture, transfection, and immunoblotting techniques as well as assays for cancer cell proliferation and survival. Experience from student: some laboratory experience in molecular biology

ISCOMS Research Fellowship

Project J – How can medical students and professionals break the silence?

Supervisor: Sandra Hein MD

Description:
Research has shown that in the Netherlands deaf people have less access to health care. This limited access to healthcare probably arises from communication barriers and a lack of cultural awareness among medical practitioners. This innovative project aims to explore and compare the knowledge of medical students and health professionals regarding the healthcare accessibility of deaf individuals.

Project
During the spring 2024, we will conduct a survey among medical students and professionals. This survey will gather information about their knowledge about deaf peopl, their culture, if they think it is necessary to learn more about this barrier between the hearing and deaf culture in the curriculum etc.
In this research fellowship, you will conduct the same survey in your country with the same respondents. Also, you will do some literature research or local research on how the situation in your country is for deaf people.
This project differs from the others, as you should spread the survey among medical students and/or professionals before ISCOMS starts! (This will give you more time during the IRF and give you more time to discover the lovely city of Groningen).
We are looking for several students from different countries who are interested in this subject, so we can compare all the outcomes of the different situations/countries.

Practical
We can go to our local sign language bar and order food in Dutch sign language. You are welcome to our radiology/nuclear medicine department and have a look at multiple modalities. There will be an ultrasound workshop (you can perform the ultrasound at each other, try to give instructions in signs, not words). You can meet the research staff if you have any questions and work closely together with the anatomy section. You can make it your own project with supervision from researchers of the UMCG.

After this project, we hope that you can come up with suggestions about how we can improve the accessibility to medical care for deaf patients. How can we break the silence?!

Project K - Time spent in movement activities throughout the day and its association with mental health

Supervisor: dr. Nynke Smidt, Rosa Palazuelos Gonzalez PhD-student
Field of research: Epidemiology

Description:
Mental health is paramount for overall well-being, yet persistent conditions such as depression (affecting approximately 5% of adults) and anxiety disorders (impacting 4% of the total population) continue to challenge global preventive efforts. These conditions can significantly impact daily activities. While increasing physical activity is recognized as a beneficial strategy in preventing and treating depression and anxiety, current research often emphasizes in high-intensity exercises. Unfortunately, this focus often neglects the significance of other movement behaviors that might be performed in higher amounts of time throughout the day, such as sedentary activities and sleep.

This project aims to address this gap by examining the time allocated to various movement behaviors among adults in the Lifelines cohort. By exploring the prevalence of major depression and anxiety, the study seeks to identify specific activities associated with these mental health conditions. Recognizing the interrelation of daily activities, isotemporal substitution analysis will be employed to identify the impact of replacing time in one or other activity on mental health.

The research process involves a review of the latest literature, and regular meetings to discuss and interpret the results of the statistical analyses. The primary objective is to produce a draft manuscript. While prior experience in scientific writing is recommended (though not mandatory), this project provides a unique opportunity to contribute to the understanding of how daily movement behaviors impact mental health.

Experience from student: Basic statistical knowledge of logistic regression models is needed to interpret the obtained results from the performed analysis

Project L - Development of a nanogel library for drug delivery to the brain

Supervisor: prof. dr. Inge S. Zuhorn, Ginevra Mariani PhD-student
Field of research: Biomedical Technology

Description:
Glioblastoma is a highly aggressive type of brain cancer with a short survival period after treatment, which indicates a pressing need for better treatment options.
Nanoparticles (NPs) can be loaded with therapeutic molecules which significantly enhances their pharmacokinetics, biocompatibility and biodistribution, making NPs good candidates for the treatment of disease. However, to effectively reach the target site in the brain, NPs have to overcome many obstacles, like clearance from blood circulation, crossing of the blood-brain barrier and entering target brain cells. This project focuses on the development and characterization of a library of nanogels with different sizes and stiffnesses for the identification of optimal properties to overcome the above-mentioned obstacles. Nanogels are soft colloidal particles consisting of a crosslinked polymer network with tuneable properties, high biocompatibility and high loading capacity for hydrophilic drugs, such as DNA, RNA, proteins and peptides.

Poly(N-isopropylmethacrylamide) (p(NIPMAM)) nanogels are synthesized by precipitation polymerization. Nanogel properties such as size, charge and morphology will be investigated using different techniques, including dynamic light scattering, zeta potential measurement, atomic force microscopy and nanoparticle tracking analysis. Subsequently, the nanogels will be tested for increased blood circulation time, transport across the BBB and penetration into tumour spheroids.
Experience from student: Knowledge of nanotechnology or biology

ISCOMS Research Fellowship

Description:
Sex is still often considered a confounding factor rather than biological variation in cancer and aging studies, limiting our understandings of basic biological processes and differential sex-dependent responses to drug treatment. Sex chromosome-linked genes and sex-specific hormones play crucial roles in cancer- and aging-related phenotypes, but numerous data suggest that additional sex-associated cellular and molecular mechanisms are implicated.

Senescent cells play crucial roles in cancer and aging, and they are generally characterized by the upregulation of Cyclin-Dependent Kinase (CDK) inhibitor p16. Using this feature, our lab has developed the p16-3MR mouse model to selectively isolate, visualize and kill senescent cells. Using a chemotherapy-induced premature senescence/aging model and xenograft transplantation mouse models, we have shown that the temporal dynamics of senescent cell turnover are distinct between females and males. Our data clearly indicated that females have advantages in eliminating senescent cells, potentially providing improved health. With a proteomics approach, we have identified a profile of differentially expressed proteins to distinguish senescent female and male mouse dermal fibroblasts (MDFs). Based on the fold change and p-value, we identified the fatty acid binding protein FABP5 as a top hit, and decided to further study its role in mediating the sexual dimorphism in senescent cell turnover. Interestingly, knockdown (KD) of Fabp5 in male senescent MDFs made their immune clearance more efficient and these KD cells gained a gene expression profile that is more comparable to the female senescent cells.

In this project, using various cell culture models, we set to identify the function(s) of the target proteins that were affected by FABP5 KD in male cells and to explore the downstream mechanisms about how FABP5 mediates the sex disparity in senescent cells.

Experience from student: Hands-on experience with cell culture and molecular biology

Project N - Role of executive functioning and frontal cortex volume in cognition and daily functioning in elderly people

Supervisor: prof. André Aleman MD PhD
Field of research: Cognitive Neuroscience

Description:
Cognition is associated with daily functioning in elderly people, but inconsistent findings have been reported across studies regarding the precise nature of this association. This study aims to investigate cognitive predictors of independence in activities of daily living among community-dwelling older adults. A total of 187 Dutch participants aging from 51 to 92 years volunteered to the study. Their daily functioning was assessed using the Instrumental Activities of Daily Living scale and the Functional Activity Questionnaire, while multiple cognitive domains were measured using various neuropsychological tests (e.g., trail-making test, WAIS digit span, verbal fluency). The Geriatric Depression Scale was also included as a possible moderator variable. A specific question that will be addressed regards the role of executive functioning over and above other measures of cognition. MRI brain scans are available for a subset of participants. Related to this, the question can be addressed whether frontal cortex gray matter volume is associated with cognition and everyday functioning. Resting state connectivity of brain networks can also be investigated in relationship to cognitive measures.

ISCOMS Research Fellowship

Project O - Uncovering new onset diabetes after transplantation in kidney transplant recipients by nuclear magnetic resonance spectra

Supervisor: prof. Martin H. de Borst MD PhD, Tamas Szili-Torok MD PhD
Field of research: Epidemiology

Description:
The global incidence chronic kidney disease (CKD) has been steadily rising in the recent years resulting in a growing population of kidney transplant recipients (KTR). Acute rejection in the KTR population is now infrequent, attributable to high quality immunosuppressive medication regimens. Therefore, clinical focus has shifted towards preventing chronic complications. One such complication is new onset diabetes after transplantation (NODAT), which affects up to 50% of KTR. NODAT is associated with worse patient and kidney allograft outcomes. NODAT onset is possibly preventable, however, KTR at risk need to be reliably identified. At this moment, there are no good risk prediction algorithms available. Therefore, during this project you will use nuclear magnetic resonance (NMR) spectra to try to identify KTR at NODAT risk. The NMR spectra is represented as ~27 000 columns in a database which includes ~700 KTR. Working with such high dimensional data will require you to use machine learning/data science techniques such as feature selection and dimensionality reduction to successfully complete the project. Experience from student: background in one or more of the following topics: epidemiology, statistics, coding, and machine learning

Project P - Nanomedicines for cancer and cardiovascular diseases immunotherapeutic applications

Supervisor: prof. dr. Hélder A. Santos
Field of research: biomedical technology & immunotherapy

Description:
The recent cutting-edge advances on nanomaterials are anticipated to overcome some of the therapeutic window and clinical applicability of many drug/peptide molecules and can also act as innovative theranostic platforms and tools for the clinic in the future. In the last decade, research on cancer and cardiovascular diseases resulted in a new set of potential treatments with promising results in the clinics, which culminated with the development of the first nanovaccines for COVID-19. Amongst the different experimental treatments, active cancer and immunotherapy, and targeted to the injured heart, hold great promise for the future treatment of these diseases. The students will be introduced to prominent nanosystems, such as biohybrid nanocomposites made of different nanoparticles and cell-based membrane extracts as potential platforms for the individualization of medical intervention and biomedical applications. Examples on how biohybrid nanomaterials can be prepared and tested for immunotherapy, as well as how they can be used to enhance the drug's targetability, intracellular drug delivery for both cancer chemo- and immune-therapy applications as well as other applications, will be experienced.

ISCOMS Research Fellowship

Project Q - The prevalence of complications following Deep Brain Stimulation in Groningen.

Supervisor: Prof. J. Marc C. van Dijk MD PhD, D.L.Marinus Oterdoom MD PhD
Field of research: Neurosurgery

Description:
Deep brain stimulation (DBS) is a neurosurgical operation used for the treatment of various conditions, such as Parkinson's Disease (PD) and Obsessive Compulsive Disorder (OCD). In DBS, electrodes connected to an Internal Pulse Generator, are placed inside the brain. Electrical pulses can then influence the way a certain brain area functions. Many patients are treated with this technique for a disease which would otherwise be unmanageable. The DBS-operation has been modified over the years. E.g: a few years ago the procedure in the Universitair Medisch Centrum Groningen (UMCG), was performed whilst the patient was awake, allowing the neurosurgeon to make sure that no essential parts of the brain are harmed during the procedure. Currently the procedure in the UMCG is to place the patient under general anesthesia whilst the operation is performed. Besides this difference in anesthesia use changes were made in surgical technique and hardware. Complications that may arise as a result of the surgery and the effects of the DBS itself, are relevant. The aim of this retrospective study is to determine the prevalence of various complications that arise as a result of DBS surgery. This will be done by analyzing a patient cohort database from the UMCG.

Project R - Exploring cultural differences in health technology acceptance: a questionnaire study

Supervisor: E.I Metting PhD
Field of research: Epidemiology

Description:
Health organisation and the European union stimulates the development and implementation of digital healthcare by health programs and grants. Moreover, cross-border healthcare use can improve healthcare and accessibility. Collaboration between countries is needed to make this work. Unfortunately, there is nothing about go through differences regarding health, technology acceptance.
Aim of this study is to explore possible, cultural differences in health technology, acceptance of intern students.

Method:
the unified theory of technology acceptance will be used as basis for the questionnaire. During the conference, we will place QR codes with the link to an online questionnaire in the UMCG. Students can scan the code and fill in this short online questionnaire. We will also collect the country of the students and some basic demographics. The results of the questionnaires will be compared with the characteristics of the different countries (Hofstede dimensions). The data will be analysed using R or SPSS. Descriptive and inferential analysis will be performed with ANOVA's and T-tests or their non-parametric alternative.

Results:
the students will provide an overview of the technology, acceptance rate per country/continents and looks for cultural factors related acceptance.

ISCOMS Research Fellowship

Project S - Quantitative detection of peptidoglycan fragments in serum

Supervisor: Yanyan Fu PhD (postdoc) & Girbe Buist (Associate professor)
Field of research: Medical Microbiology and Infection prevention/Molecular Bacteriology

Description:
There is an urgent unmet need for reliable novel biomarkers for progression of chronic inflammatory disease and for therapy monitoring. Patient antibodies discriminating the wide chemical variety of bacterial peptidoglycans (PGN) represent a robust, new, and specific biomarker. PGN is an essential building block of the cell wall of all bacteria and has strong inflammatory actions. Since PGN peptide sequences differ between groups and individual species, we aim to develop methods for detection of PGN (fragments) in human samples. The various bonds in PGN can be cleaved using different types of PGN-hydrolases (PGHs). Depending on the specific cleavage sites, three main types of PGHs can be distinguished, including glycosidases, amidases, and endopeptidases (Wang, 2022). The general structure of PGN and predicted B-cell epitopes for antibodies are shown in the Figure. For Staphylococcus aureus, most of the biologically active PGHs have been isolated after heterologous production in Lactococcus lactis (Romero Pastrana, 2018).

Peptidoglycan will be isolated from different S. aureus strains and the concentration will be detected using fluorescently labeled Vancomycin. Through hydrolysis of purified PGN using different combinations of PGHs specificities, specific individual PGN fragments can be generated. PGN fragments are bound to membranes for dot-blot detection or to microtiter plates for ELISA approaches to determine quantitative responses of IgM, IgG or IgA against the various PGN fragments. Human sera will be used to determine the variation of natural responses against PGN fragments that are present in serum.

PLENARY SESSIONS

Presenters:

- Isaac Arango-Gil
- Ruben Zoodsma
- Yimeng Zhang
- Charlotte Brice
- Kapilraj Ravendran
- Tiara Dusselier
- Mohammed Hasan Almusrati
- Hannah J. Holstein

Methicillin Resistance and Its Effect on Clinical Outcomes in Staphylococcus aureus Bacteremia-Associated Sepsis: A Retrospective Cohort Analysis

Mr. Isaac Arango-Gil
University of Antioquia
Medellín, Colombia

Introduction

Staphylococcus aureus is a gram-positive pathogen associated with a broad spectrum of clinical illnesses, including relatively benign infections as well as life-threating conditions. Studies indicate that approximately >90% of patients diagnosed with Staphylococcus aureus bacteremia (SAB) will develop sepsis, which is associated with poor prognosis. It has been suggested that methicillin resistance may contribute to a dysregulated host response to infection. The aim of this study is to estimate the impact of methicillin-resistance on in-hospital mortality, length of hospital stay, and intensive care unit (ICU) admission in a group of patients with SAB and sepsis.

Method & Materials

This study is based on a retrospective cohort from two referral hospitals in the city of Medellín, Colombia. We analyzed patients with positive blood culture for Staphylococcus aureus with determined antibiotic susceptibility pattern and diagnosis of sepsis according to the 2016 Sepsis-3 consensus definition. To estimate the association between methicillin-resistance and healthcare outcomes, we employed two regression models adjusting for potential confounding variables. First, a logistic regression model was fitted to estimate the association between methicillin resistance and in-hospital mortality/ICU admission. Additionally, we fitted a multivariable Cox proportional hazard regression model, with death as a competing risk, to estimate the influence of methicillin-resistance on the length of hospital stay.

Results

Our study included 775 patients, of which 592 (76.4%) had MSSA-SAB and 183 (23.6%) had MRSA-SAB. The mean age was 56.4 years. Multivariable analysis showed that methicillin-resistance was not associated with increased in-hospital mortality (OR: 0.81, 95% CI: 0.52-1.26); but age, SOFA score and Friendman's classification of bacteremia were independent predictors of mortality. Appropriate initial empirical antibiotic treatment and adjusted antibiotic treatment following blood culture result were independent protective factors. In addition, methicillin-resistance showed a noteworthy impact on ICU admission (OR: 1.60, 95% CI: 1.06-2.4), along with community-acquired bacteremia. Methicillin resistance was not significantly associated with longer hospital stay (SHR: 0.92, 95% CI: 0.75-1.13).

Conclusion

In our study, methicillin resistance significantly increased ICU admission rates but was not associated with higher in-hospital mortality or extended hospital stays. These findings highlight the importance of tailored treatment strategies and early intervention in managing SAB.

Monitoring Complex Congenital Heart Disease: AI development & prospective use.

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Introduction

With an ongoing shift from Paediatric Intensive Care Unit (PICU)-wards to single person rooms, monitoring of the patient's condition can become challenging, especially when combined with the complex physiology of perioperative Congenital Heart Disease (CHD). Artificial Intelligence (AI) may facilitate early-warning and clinical decision-support in these data-rich and high-risk clinical wards through automated detection of ongoing clinical instability. Therefore, this study developed – and prospectively implemented – a data-driven, AI-based monitoring tool for patients with CHD at the PICU.

Method & Materials

"Data of four vital parameters and cerebral rSO2 of neonates with complex CHD admitted to the University Medical Center Utrecht, the Netherlands between 2002 and 2018 was used for training. Such data was integrated into an algorithm, combining a Support Vector Machine able to detect parameter combinations abnormal to the population, as well as an AI component analyzing significant patient-unique baseline deviations. Novel, unseen data was used for retrospective visualization of the model's performance as evaluated by a team of clinical experts.
Raw bedside monitoring data were prospectively transferred to a research server, where the developed AI-tool continuously assesses admitted patients for clinical instability."

Results

A respective 4600h and 229h in 78 and 10 neonates were used as training and testing dataset. Overall, the algorithm provided accurate detection in 90% of stable- and 71% of unstable episodes. Twenty-nine out of 101 expert-confirmed unstable episodes were missed in testing. The research server consists of several data pipelines aimed at per-minute data extraction, pre-processing and AI application for admitted CHD patients. AI output through dashboarding is accessible anywhere within the hospital, enabling bedside visibility and remote alarming while adherent to safety protocols.

Conclusion

In this study, an AI tool for clinical instability was developed and retrospectively tested for classifying clinical (in)stability for PICU patients with CHD – which achieved a reasonable performance taking the heterogeneous population into consideration. The dual analysis proofs to be promising with respect to enhancing applicability to heterogeneous pediatric populations. The tool was consequently, successfully implemented into the PICU dataflow, enabling prospective validation and unlocking the potential of data-driven monitoring support.

Identification and functional study of tumor microenvironment acquired super-enhancers in esophageal squamous cell carcinoma

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Introduction

Super-enhancers (SEs) are critical for gene transcription and histone 3 lysine 27 acetylation (H3K27ac) is a widely used method for the identification of SEs. Currently, studying the SE landscape is an effective way to discover new cancer target genes, especially for genes with frequent mutations. However, the mechanism of SE reprogramming in cancer remains incompletely understood. Interestingly, the enhancer landscape differs between cancer cell lines and tissues. This suggests that the extracellular microenvironment may influence the epigenetic landscape, contributing to tumor cell development and growth. Detecting dysfunctional SEs between primary tumors and normal tissues is still incomplete in many cancers. Additionally, downstream validation of the functional relevance of tumor-enriched SE in tumor growth is limited. It remains unclear whether the SE landscape of cancer cells is influenced by the local microenvironment of the tumor.

Method & Materials

This study integrated multiple pairs of H3K27ac ChIP-seq data, gene expression profiles and single-cell transcriptomics data from esophageal squamous cell carcinoma (ESCC) tissues and cell lines. High-throughput bioinformatics software was used to calculate tumor microenvironment SEs. Biological experiments and ATAC-seq data were used to investigate the specific mechanisms by which the tumor microenvironment activates SEs and thus influences malignant progression in ESCC.

Results

Histone modification mass spectrometry was used to analyze 122 paired esophageal cancers and adjacent tissues and showed that H3K27ac was overexpressed in esophageal cancer tissues. In addition, a specific type of tumor SE, was found in ESCC, which is tissue-specific and not present in cell lines, leading to abnormal gene expression. Single-cell transcriptome analysis reveals that acquired SEs highly regulate multiple genes involved in the immunosuppressive pathway, which differs from the typical SEs. Based on the constructed chromatin regulator regulatory network, a regulatory axis was predicted in which chromatin regulators and transcription factors synergistically activate super-enhancers leading to ESCC malignancy.

Conclusion

Genes that are regulated by tumor microenvironment acquired SEs are involved in immunosuppressive pathways and play a crucial role in the progression of ESCC. An in-depth study of the regulatory axis of transcription factors and chromatin regulators that synergistically activate super-enhancers in tumors is expected to facilitate precise diagnosis and treatment of tumors.

Developing a stem cell-based bioprinted in vitro pancreatic model

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Introduction

Diabetes mellitus, characterised by disrupted blood glucose homeostasis, constitutes a significant global healthcare burden. Type 2 diabetes is typically managed with lifestyle changes and medication, while in more severe cases, and type 1 diabetes, administration of exogenous insulin to avoid hyperglycaemic events is needed. However, diabetic complications still persist, with serious cardiovascular impairments due to prolonged exposure to elevated blood glucose levels, and potentially fatal hypoglycaemic events. Bioprinting allows for the creation of an enhanced in vitro endocrine pancreas, combining cells and biomaterials in a hierarchical structure to produce a more physiologically relevant model to improve drug development. Specifically, volumetric bioprinting (Bernal et al. 2022 Adv Mater) coupled with embedded extrusion bioprinting (EmVP) (Ribezzi et al. 2023 Adv Mater) provides a potential opportunity for the formation of such a complex multi-cellular and multi-material construct, revolutionising diabetes research.

Method & Materials

Pancreatic islets were generated from human induced pluripotent stem cells (iPSCs) following a seven-stage protocol (Balboa et al. 2022 Nature Biotechnology). iPSC-derived pancreatic progenitor cells (PPCs), at differentiation stage 4, were expanded as described elsewhere (Nakamura et al. 2022 Stem Cell Reports), and the passage-dependent efficiency for the differentiation and expansion was assessed using immunofluorescent characterisation. The islets underwent embedded extrusion bioprinting with 1% alginate bioink into 5% gelatine methacrylate (gelMA) microResin. The viability and metabolic activity of the printed constructs throughout a 21-day period in maturation culture was determined with CalceinAM/Ethidium homodimer-1 and Alamar Blue assays, respectively. Results were reported as mean+-standard deviation.

Results

The differentiation of iPSCs to PPCs resulted in 93.9+-2.2% pancreatic and duodenal homeobox 1 (PDX1, transcription factor necessary for pancreatic development)-positive cells at differentiation stage 4. After one expansion passage, the percentage of PDX1-positive PPCs was 86.8+-4.8%. Additionally, the generated islets exhibited production of insulin, glucagon, and somatostatin during stage 7. iPSC-derived islets were successfully bioprinted and kept in maturation culture for 21 days, showing high levels of viability and consistent levels of metabolic activity.

Conclusion

This study highlights successful, scalable iPSC-derived pancreatic islet production for complex in vitro models formed by embedded extrusion bioprinting, illustrating promising avenues for advanced pancreatic model development with the combination of volumetric printing.

Applying Cognitive Behaviour Therapy with a fully automated conversational agent (Woebot) to Bulgarian medical students: A Randomised Controlled Trial

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Introduction

Due to their prolonged exposure to stress, medical students frequently experience burnout, a syndrome marked by low self-accomplishment, depersonalization, and emotional exhaustion. Although they have shown promise, web-based apps for cognitive-behavioural therapy (CBT) are known for their low adherence. The study's objective was to ascertain whether a fully automated conversational agent could deliver a self-help program to people who self-identify as having symptoms of depression and anxiety and whether such an agent could be feasible, acceptable, and initially effective.

Method & Materials

In an unblinded trial, 138 participants from Bulgaria were randomly assigned to receive either self-help content derived from CBT principles in a conversational format over a period of 2 weeks (up to 20 sessions) with a text-based conversational agent (Woebot) (n = 69) or self-help leaflets as an information-only control group (n = 69). The participants were recruited online from a university community in Bulgaria. The participants' initial scores on the 9-item Patient Health Questionnaire (PHQ-9) and the 7-item Generalized Anxiety Disorder scale (GAD-7) prior to intervention was above 10 prior to intervention. Two weeks later, all individuals finished PHQ-9 and GAD-7 after intervention.

Results

"Initially 228 medical students from Bulgaria filled in the PHQ-9 and GAD-7 questionnaires. 60.5% (n=138) scored above 10 in either PHQ-9 or GAD-7 (60.5%), indicating moderate depression or anxiety.

The full 69 participants from the woebot group completed the PHQ-9 and GAD-7 following intervention. Only 34 (49.3%) from the control group filled completed the PHQ-9 and GAD-7 following intervention.

The woebot group showed an overall improvement in depression and anxiety. The mean score from GAD 7 reduced (SD)[CI 95%) by 1.78(1.697)[1,38-2.19], p-value <0.001. The PHQ-9 also had a reduced mean score (SD)[CI 95%] of 1.55(2.033)[1.06-2.04], p-value<0.001.

The control group however had a negative effect and saw an increase in depression and anxiety. The GAD-7 mean (SD)[CI 95%] increased by 0.18(2.645)[1.10-(-)0.75)], p-value<0.001. The PHQ-9 mean (SD)[CI 95%) also increased by 0.21(4.006)[1.16-(-)1.19], p-value<0.001."

Conclusion

It seems that conversational agents, such as Woebot are a practical, interesting, and successful method of delivering CBT.

IFN-Lambda-1 Associated with Inflammation in the Intestinal Epithelium: Insights from Lentiviral Integration within Organoids

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Introduction

IFN-Lambdas (IFNLs) are key responders in the intestinal, mucosal innate anti-viral response, playing a crucial role in defence that can be considered both protective and potentially pathogenic. Despite its potential therapeutic applications in conditions such as hepatitis, intestinal graft-vs-host disease, and SARS-CoV-2, the intricate regulatory system, and effects of each IFNL remain elusive. A lack of mechanistic understanding raises questions about its suitability and efficacy in different patient populations. We aim to unravel the role of IFNLs within the intestine, to understand the biology of intestinal IFNL signaling and thereby evaluate its therapeutic potential for patients with gastrointestinal disorders.

Method & Materials

A doxycycline-inducible IFNL-FLAG lentivirus was engineered and integrated into human intestinal organoids (hIOs) to investigate the intrinsic effects of IFNL. Successful integration and controlled expression were confirmed via Sanger sequencing and RT-PCR. Further evaluation involved synthetic dsRNA stimulation to mimic viral infection. Subsequently, morphological changes, inflammation, and gene expression in differentiated and undifferentiated cells were assessed using light microscopy and RT-PCR analysis.

Results

The generated IFNL1-FLAG lentiviral construct enabled precise temporal control of IFNL1 expression within hIOs. Following doxycycline stimulation, a significant exponential increase in IFNL was observed, correlating with a 3-6-fold upregulation of CXCL8 and CXCL10 compared to baseline in both differentiated and undifferentiated intestinal cells. Moreover, increased expression of pro-apoptotic markers BAK and BCLXL was noted.

Conclusion

In our study, IFNL1 expression promoted inflammation and apoptosis within the intestinal crypt and villus, necessitating careful consideration regarding its use in gastrointestinal disorders. Our research marks a significant advancement by establishing a novel, precise, and controllable system in hIOs, opening avenues to explore the spatiotemporal dynamics and functional effects of IFNL within a physiologically representative model. Further investigation into the post-transcriptional regulation of IFNL1 is needed to unravel the complexities of the intestinal innate immune response.

Development and Impact of a Custom AI-Enhanced Case Scenarios Simulation on Pulmonology Resident Training.

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Introduction

Effective training is critical in pulmonology, where decisions must be updated and evidence-based. This study evaluates the potential of AI-enhanced simulation training for pulmonology residents in Libya, focusing on its ability to improve the handling of complex conditions. By assessing how these simulations enhance clinical skills and identifying the challenges of integrating them into existing programs, our research seeks to advance medical training to better equip residents for demanding clinical environments.

Method & Materials

This cross-sectional study was conducted across pulmonology departments in various hospitals in Libya. Doctors administered a structured questionnaire to collect demographic information and assess participants' training backgrounds. Also, scales are used to measure attitudes regarding the usage of simulation in clinical practice to tackle weaknesses in decision-making and management. Also, a post-evaluation assessment after using an AI-enhanced platform to train the doctors in a simulation manner about the management of certain respiratory conditions. Analysis was performed using descriptive statistics, percentages, and correlation tests.

Results

In the study, 50 doctors (67.5% male, average age 36.7 years, SD = 8.0) participated. 76% of residents believed simulation could significantly enhance clinical skills, with 80% finding obstructive airway disease modules particularly useful. Following training, 66% reported improved emergency management skills. A significant positive correlation ($p = 0.04$) showed longer specialty experience linked to greater adoption of AI-enhanced training. Post-evaluation assessments ($p = 0.018$) confirmed improved clinical skills, endorsed by 80% of participants for enhancing practice quality without compromising patient care. However, approximately 70% of trainees express their worries about the need for additional time to integrate this method into their training schedules fully.

Conclusion

The findings indicate that AI-enhanced simulation-based training is valued by pulmonology residents, particularly those with greater experience in their specialty, for enhancing clinical skills, especially in emergency management and obstructive airway conditions. Despite the challenges related to time efficiency and high workload, the potential for this technology to transform medical education warrants further exploration and adaptation to meet learner needs and institutional capacities.

Exploring biomarkers of systemic oxidative stress and placental insufficiency in pregnant women with inflammatory bowel diseases

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Introduction

Inflammatory bowel disease (IBD), encompassing Crohn's disease (CD) and ulcerative colitis (UC), often manifest around the fertile age, yet its impact on pregnancy outcomes remains poorly understood. Both IBD and pregnancy complications are associated with oxidative stress, characterized by an imbalance between reactive oxygen species and antioxidants. Free thiols (FT) serve as biomarkers of oxidative stress, with reduced levels observed in both IBD and pregnancy complications. The behaviour of classical biomarkers of placental insufficiency, such as soluble FMS-like tyrosine kinase-1 (sFlt-1) and placental growth factor (PLGF), in pregnant women with IBD also remains unclear. This study aims to explore the relationship between FT, sFlt-1, and PLGF and pregnancy complications in IBD patients, along with their dynamics throughout pregnancy.

Method & Materials

In this retrospective pilot study, we investigated a cohort of pregnant women with IBD. Serum samples taken before (n=41), during (n=33), and after (n=25) pregnancy were analyzed for PLGF, sFlt1 and FT levels. Extensive clinical data were collected, including data about pregnancy complications and IBD disease parameters. Additionally, we included healthy pregnant women as controls (n=14).

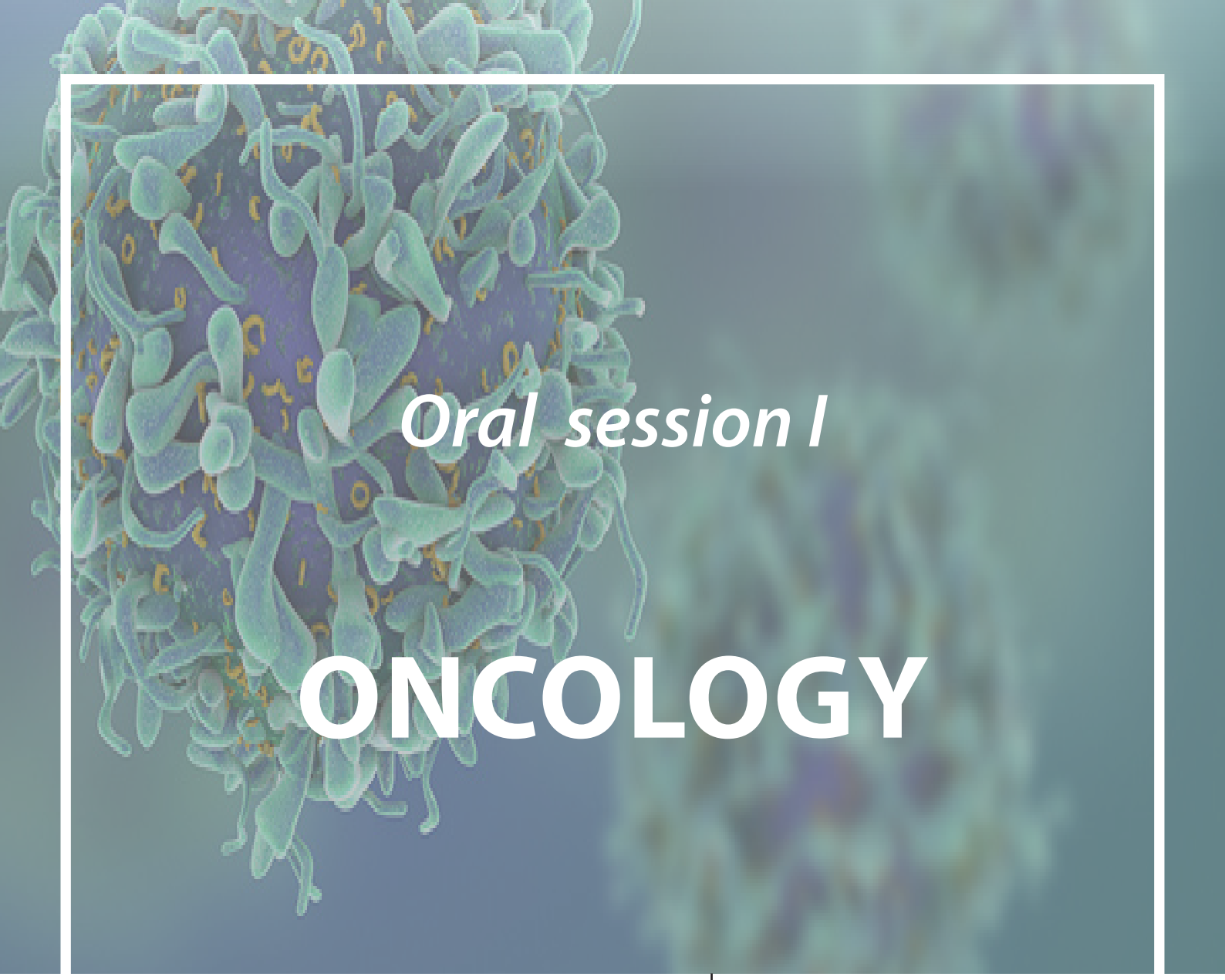
Results

In total, 40 patients (n=32 CD, n=7 UC, and n=1 IBD-U) with 47 pregnancies and 14 non-IBD control pregnancies were included. Comparing patients with IBD to controls during pregnancy, serum FT levels were significantly reduced in patients, even after adjustment for gestational age (p=0.043). FT levels significantly decreased during pregnancy compared to preconception (p=0.001), suggesting increased systemic oxidative stress during pregnancy. The sFlt-1/PLGF ratio was significantly higher in patients (p=0.011), which was partially due to a difference in gestational age. In total, 32 patients (56%) and 3 controls (21%) developed pregnancy complications. The sFlt-1/PLGF ratio was numerically higher in those developing maternal complications (p=0.053), while FT showed a trend towards decreased levels with maternal pregnancy complications (p=0.082).

Conclusion

This study provides evidence for increased systemic oxidative stress during pregnancy in IBD, when compared to both controls and their own pre-conceptional levels. Further research is necessary to substantiate these findings and evaluate the utility of these biomarkers in predicting pregnancy complications in IBD.

ORAL SESSIONS



Oral session I

ONCOLOGY

Presenters:

- Abdulrahma Alghamdi
- Sajjad Ali Mohammadvand
- Iris Barth
- Helena Wang

Effectiveness of Tachosil as sealant in lymphatic leakage of breast carcinoma with axillary dissection

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Introduction

Breast cancer is one of the most prevalent cancers in women. In 2020, it was linked to 15.5% of cancer deaths worldwide, 24.5% of all cancer diagnoses among women and an approximately 21.8% prevalence in Saudi women. Previous studies have indicated that, in many cases, axillary dissection is an essential part of the management of breast cancer. Following axillary dissection, postoperative lymphatic leakage as a lymphocele is possible, which is usually managed by drainage. TachoSil has also been shown to be useful in lowering the rate of lymphoceles following pelvic lymphadenectomy The aim of this study was to evaluate the use of TachoSil as a sealant for lymphatic leakage in breast cancer patients with axillary dissection.

Method & Materials

Breast cancer patients treated in the Department of Surgical Oncology at King Abdulaziz Medical City were enrolled to receive either Tachosil or undergo drain placement after axillary dissection. Repeated measures MANOVA was used to observe the difference in lymphatic drainage volume over time considering other covariates, such as age, sex, family history, neoadjuvant chemotherapy (NAC), and stage.

Results

The Tachosil group showed significantly lower lymphatic drainage volumes at 24 hours (106.5 Ò 11.3) than the control group (141.7 Ò 13.0) ($p<0.001$). There were no significant differences in lymphatic drainage volume at 3 days ($p=0.176$) and 7 days ($p=0.091$). However, at 10 days, the Tachosil group exhibited significantly lower lymphatic drainage volume (19.9 Ò 6.1) than the control group (44.5 Ò 9.2) ($p<0.001$). Repeated measures MANOVA showed a statistically significant difference in lymphatic drainage over time, with a moderate effect ($p<0.001$).

Conclusion

The findings suggest that Tachosil sealant effectively reduces early postoperative lymphatic drainage volume and maintains lower drainage rates up to 10 days following axillary dissection in breast carcinoma patients. The use of Tachosil sealant may have potential benefits in reducing the incidence of complications associated with lymphatic drainage and improving patient outcomes.

Aripiprazole-loaded niosome/AuNPs-chitosan for the chemo-photothermal therapy of breast cancer cells

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Introduction

Breast cancer (BC), a leading cause of mortality among women, exhibits unique cellular characteristics, including receptor overexpression and altered metabolism leading to an acidic tumor environment. Nanoparticles (NPs) are a promising approach for improved cancer treatments. Chitosan-coated gold nanoparticles (AuNPs-CS) an smart nanosystems that respond to the acidic cancer environment due to abundant amino groups in CS. Additionally, AuNPs possess photoacoustic and photothermal properties that make them suitable for hyperthermia-based treatment. Aripiprazole (ARI), known for antipsychotic properties, has shown promise for BC treatment. Niosomes (NIOs) possess unique properties, enabling simultaneous loading of hydrophobic and hydrophilic drugs. In this investigation, ARI was loaded into hydrophobic moieties and AuNPs-CS within and onto niosomes. The focus was the synthesis of AuNPs-CS for photothermal therapy (PTT) and ARI-loaded NIOs (NIOs/CS/AuNPs-CS/ARI) to facilitate a combinational chemo/phototherapy strategy to combat breast cancer.

Method & Materials

Key materials include chloroauric acid, chitosan, cholesterol, surfactants, Tween, MCF-7 cells, and RPMI 1640 medium. AuNPs-CS were prepared by dissolving chitosan and adding chloroauric acid. ARI-loaded NIOs/AuNPs-CS were synthesized using thin-film hydration. Characterization involved dynamic light scattering, FT-IR analysis, and UV-Vis spectroscopy. Drug loading, in vitro releases, cellular uptake, cytotoxicity, PTT assessment, and apoptosis/necrosis were evaluated.

Results

NIOs/AuNPs-CS displayed favorable properties, with a size of 54.77 nm and zeta potential of -0.836 mV. FT-IR and UV-Vis confirmed successful NP synthesis. ARI loading efficiency in NIOs was 75%. The pH-dependent drug release of NIOs/AuNPs-CS revealed their potential as a smart drug delivery system. The enhanced cellular uptake of NIOs/AuNPs-CS compared to NIOs demonstrated effective internalization by MCF-7. Cytotoxicity assays revealed NIOs/AuNPs-CS/ARI exerted a more potent inhibitory effect on MCF-7 cells than NIOs/ARI. The combination of PTT and drug-loaded NIOs/AuNPs-CS exhibited significantly higher cytotoxicity, outperforming individual therapies. Importantly, NIOs/AuNPs-CS/ARI substantially increased apoptosis/necrosis rates.

Conclusion

In this study, we successfully synthesized AuNPs-CS Niosomes loaded with ARI ((NIOs/AuNPs-CS/ARI)) for chemo-photothermal therapy of BC. These NPs exhibited pH-sensitivity behavior, efficient drug release, enhanced cellular uptake, and potent cytotoxicity. The combination of PTT and chemotherapy using these intelligent nanomaterials presents a promising approach to address the BC treatment challenges. However, further investigate their clinical applicability.

Sarcopenia and changes in skeletal muscle mass in patients with advanced gastrointestinal cancer following cytoreductive surgery and intraperitoneal hyperthermic chemotherapy

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Introduction

Cytoreductive-surgery (CRS) followed by intraperitoneal hyperthermic chemotherapy (HIPEC) offers potential benefits for patients with GI cancer. Patient selection to assess the fitness for surgery is crucial, yet patients often present with pre-surgical sarcopenia (low muscle mass). This study aims to investigate changes in muscle mass in patients undergoing CRS-HIPEC, before and after treatment, and explores potential predictors for long-term muscle mass.

Method & Materials

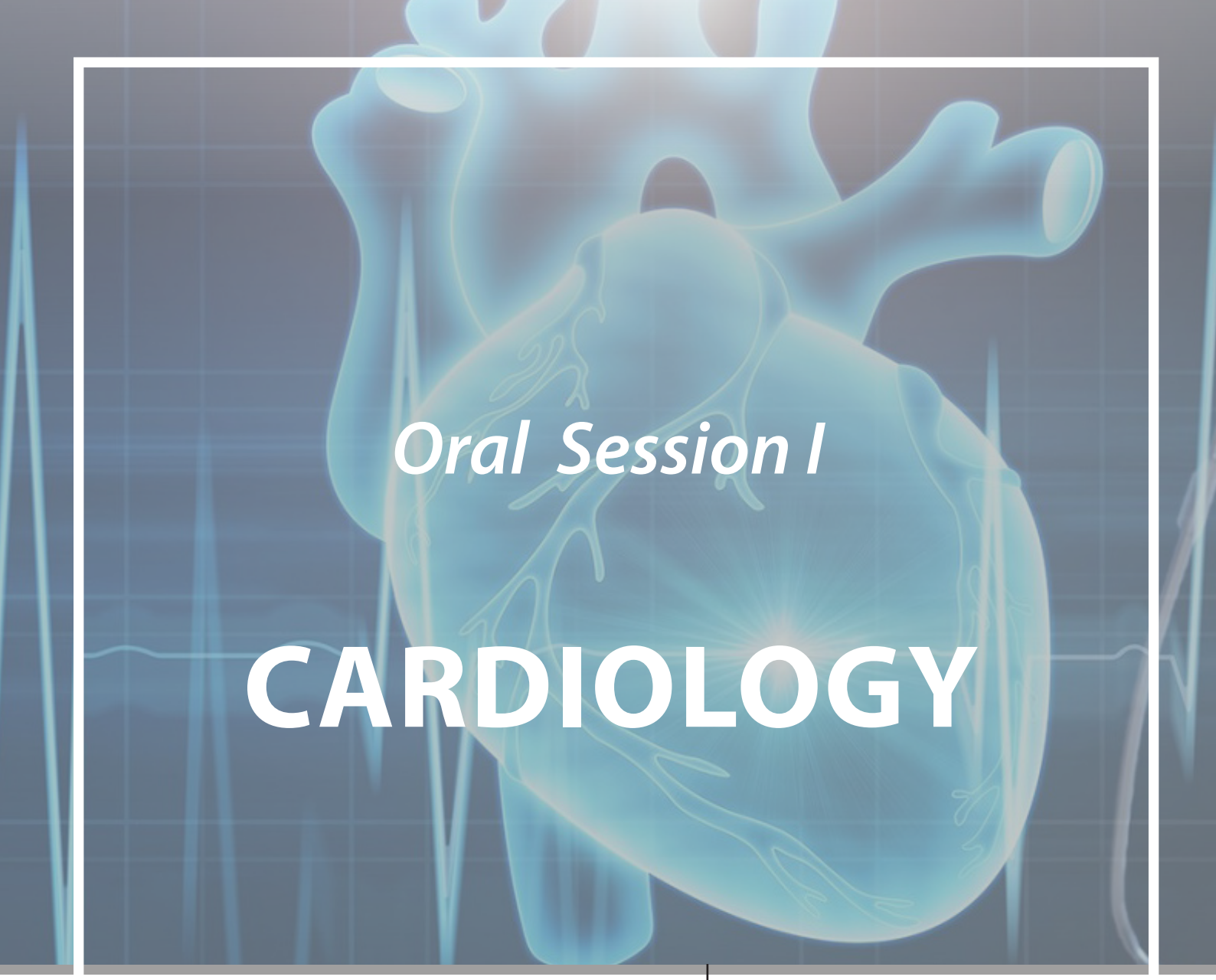
Adult patients scheduled for CRS-HIPEC were included between 2017-2022 and prospectively followed for one year. Skeletal muscle mass area (SMA) was measured on computed tomography (CT). Sarcopenia was determined using sex- and BMI specific cut-off values after calculation of the skeletal muscle mass index (SMI): SMA cm2/height m2. A paired t-test compared the difference in SMI at baseline (T0) and 12 months (T12). The relationship between predictor variables (handgrip strength [HGS], Time Up and Go, Charlson Comorbidity Index [CCI], American Society of Anesthesiologists score, Peritoneal Cancer Index, Completeness of Cytoreduction score, total cm removal of small intestine) and SMI at T12 was explored using univariate linear regression analysis.

Results

58 patients were eligible for analysis (median age 63; 67.2% female; 60.0% colorectal cancer) and 26 were lost to follow-up. In total, 56 and 44 routine CT-scans were analyzed at T0 and T12 respectively. Sarcopenia was present in 53.4% (n=31/58) patients at T0 and 61.4% (n=27/44) patients at T12. No significant difference was observed in SMI between T0 and T12 (mean difference -0.32; p=0.666; 95%CI -1.18, 1.83). Univariate regression analysis showed a significant relationship between CCI (_=0.395, SE=0.13, R2=17.6%, p=0.003), HGS (_=1.227, SE=0.42, R2=14.9%, p=0.005) and SMI at T12.

Conclusion

This explorative study shows that after CRS-HIPEC, muscle mass did not significantly change, and sarcopenia is still present in over half of the patients. Pre-surgical Comorbidity Index and handgrip strength have a predictive value in postoperative muscle mass. Further exploration of other key predictive variables is needed to enhance understanding of muscle mass development for targeted interventions in CRS-HIPEC patients.



Oral Session I

CARDIOLOGY

Presenters:

- Brian Poll
- Run Lin
- Michael Marterstock
- Mahsa Motiei
- Farnoush Sattari Pirsoltan
- Alicia del Carmen Yika

Validating Clinical Software for Precise Strain Measurement in Human-Engineered Heart Tissues: Predicting Disease Progression in Phospholamban P.Arg14del Patients

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Introduction

Cardiovascular diseases contribute to roughly one-third of global mortality, causing approximately 20.5 million deaths in 2021. Accurately assessing cardiac function is paramount in diagnosing wide-scale cardiac diseases, tailoring treatment, monitoring therapeutic progress, and predicting outcomes. The development of human induced pluripotent stem cell-derived cardiomyocytes and human-engineered heart tissues (EHTs) have enabled in vitro assessments of cardiac function. However, most current approaches focus on overall contractility, overlooking regional heterogeneity. Additionally, various laboratory-developed software tools yield disparate contractility parameters, with limited clinical relevance. In response to notable limitations, we propose an easily accessible methodology for contractility analysis in EHTs, capable of assessing multiple regions within a tissue and providing clinically relevant parameters.

Method & Materials

In this study, we used clinical echocardiography software (TOMTEC Imaging Systems GmbH) for precise longitudinal strain measurements in EHTs. We applied this method to EHTs derived from human induced pluripotent stem cells (hiPSC) from patients with the PLN p.Arg14del mutation and (isogenic) control subjects. We then compared the results to those obtained from current golden standard contractility analysis methods for EHTs (EHT Technologies and MUSCLEMOTION).

Results

Our results demonstrate consistency in "peak contractility" outcomes across different measurement methods, allowing clear differentiation between control and PLN EHTs. Moreover, PLN p.Arg14del EHTs displayed a reduced mean peak strain (8.468% vs. 12.65%; $p<0.05$) and a slower contraction as indicated by a less negative strain rate (-0.34 1/s vs. -0.46 1/s; $p<0.05$). Peak strain emerged as a significant parameter for distinguishing between control and PLN EHTs throughout the tissue, with differences particularly noticeable at the tissue's central points. Notably, PLN p.Arg14del EHTs exhibited greater mechanical dispersion compared to controls (24.48 ms vs. 11.99 ms; $p < 0.05$).

Conclusion

The use of clinical strain software allowed us to achieve a novel approach for sub-tissue-level functional cardiac measurements in EHTs expressed in clinically relevant parameters. Our findings indicate that this method provides consistent contractility assessments, mirroring clinical trends in strain, strain rates, and mechanical dispersion. This approach shows promise for bridging the gap between in vitro and in vivo contractility analysis, with potential applications in the diagnosis and treatment of cardiovascular diseases.

Relationships of Cumulative Resting Heart Rate with Cardiovascular Events and All-cause Mortality: A Post-hoc Analysis of STEP Trial Data

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Introduction

The long-term effects of cumulative resting heart rate (cumRHR) on the incidences of cardiovascular events and all-cause mortality in older hypertensive populations remain unclear.

Method & Materials

A total of 7,517 older patients with hypertension in whom RHR was measured at 0, 3, 6, 9, and 12 months were included in this post-hoc analysis. cumRHR exposure refers to the weighted mean of the RHR for each time interval. Participants were grouped into four quartiles based on their cumRHR.

Results

Over a median follow-up of 3.33 years, primary outcome events occurred in 206 patients. After adjustment for multiple potential confounders, the Q4 group (75.94?109.44 bpm) had higher risks of the primary outcome (hazard ratio [HR] 1.93, 95% confidence interval [CI] 1.23?3.02, p=0.004), MACEs (HR 1.74, 95% CI 1.04?2.90, p=0.03), and stroke (HR 2.97, 95% CI 1.19?7.43, p=0.02) vs. the Q3 group (72.19?75.88 bpm), and the Q1 group (44.50?68.44 bpm) were associated with increased risk of the primary outcome (HR 1.91, 95% CI 1.20?3.04, p=0.006) and MACEs (HR 1.84, 95% CI 1.10?3.10, p=0.02). However, this trend was not observed for all-cause mortality. Moreover, a U-shaped relationship with primary outcome was observed with higher risk in those with both very low or very high cumRHR levels compared with those with midrange values (p=0.008).

Conclusion

Both low and high cumRHR levels were associated with higher risk of cardiovascular events in older patients with hypertension. Thus, the monitoring and maintenance of an appropriate RHR may help with the treatment and prognosis of hypertension.

Acute systemic inflammation induced by lipopolysaccharides (LPS) initiates transient heart failure in mice

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Introduction

Patients experiencing systemic inflammatory response syndrome (SIRS) or septic shock often develop myocardial dysfunction, a condition associated with higher overall mortality compared to patients without such dysfunction. Bacterial lipopolysaccharides (LPS) have been identified as important trigger of SIRS and septic shock. Here we explore molecular mechanisms linking LPS exposure and the development of inflammation-induced myocardial dysfunction.

Method & Materials

C57/Bl6N mice were intraperitoneally injected with 5mg of LPS per kilogram of body weight or phosphate-buffered saline (PBS) as a control. Systolic (left ventricular ejection fraction, EF) and diastolic (isovolumetric relaxation time, IVRT) heart function were assessed at 6 hours, 24 hours, and 48 hours post-LPS injection using the Visualsonics Vevo 3100 cardiac imaging system. Additionally, we analyzed mRNA expression of cytokines and marker genes of neutrophils and macrophages to reflect the inflammation status in the left ventricle and quantified the cardiac metabolome at each time point. _id†k?s-multiple-comparison-test was used for statistical analysis (GraphPad Prism 10.0.3).

Results

Mice injected with LPS exhibited an initial decrease in EF and increase in IVRT at 6 hours post-injection compared to PBS-injected mice (EF: 20.9% vs. 51.7%, $p<0.001$; IVRT: 28.9ms vs. 14.7ms, $p<0.0001$), which improved at 24 hours post-LPS injection (EF: 39.5% vs. 56.1%, $p<0.03$; IVRT: 19.9ms vs. 12.6ms, $p=0.02$) and showed complete recovery after 48 hours post-LPS injection compared to PBS-injected mice (EF: 54.9% vs. 48.0%, $p=0.69$; IVRT: 19.4ms vs. 15.49ms, $p=0.46$). mRNA levels of pro-inflammatory cytokines, including Il6, Il1b, and INFg, were significantly upregulated at 6 hours post-LPS injection compared to PBS-injected mice, concurrently with an increase in Ly6c and Cxcr2 mRNA levels, indicating early neutrophil migration. Cxcr2, also expressed in macrophage subsets, exhibited another elevation in left ventricles at 48 hours after LPS injection compared to PBS-injected mice. Metabolomic analysis revealed a specific metabolic signature of innate immunity-driven inflammation in the left ventricles of LPS-injected mice, suggesting disturbances in the Krebs cycle.

Conclusion

LPS induces a temporary reduction in left ventricular systolic and diastolic function, consistent with the induction of pro-inflammatory cytokine expression. The accumulation of various immunometabolites in the cardiac tissue of LPS-treated mice is an intriguing observation that warrants further exploration.

A new era in cardiac monitoring: Integrating global longitudinal strain into routine care for chronic kidney disease patients

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Introduction

Cardiovascular disease has emerged as the main cause of mortality and morbidity in patients with chronic kidney disease (CKD). Traditional echocardiography methods including left ventricular ejection fraction (LV-EF) assessment cannot detect early stage of subclinical systolic dysfunction. So, we aimed to assess the potential of strain echocardiography in diagnosis the primary phase of systolic dysfunction in CKD patients and compare the results in subgroups of patients with diabetic kidney disease and those with non-diabetic kidney disease.

Method & Materials

One hundred CKD patients with normal LV-EF, were categorized into 2 subgroups, 50 with diabetic kidney disease and 50 with non-diabetic kidney disease. We compared findings of conventional echocardiography with strain echocardiography among these two groups. SPSS version 28 software was used for statistical analysis. The chi-squared test was used for the comparison of subgroups and the two-sample t-test was used to compare normally distributed continuous data. Mann?Whitney U test was used to compare non-normal continuous data. Results with a p-value < 0.05 were considered statistically significant.

Results

Assessment of echocardiographic parameters showed that E peak and E/A ratio were significantly lower in patients with diabetic kidney disease (P=0.005) than those with non-diabetic kidney disease. Also, left ventricular global longitudinal strain (GLS) values were significantly lower in the diabetic kidney disease patients, and 70.6% of patients in this group had abnormal GLS values even though with normal LV-EF (P=0.012). Linear regression analysis showed that only age significantly predicts the amount of GLS.

Conclusion

Lower values of GLS in diabetic kidney disease patients despite the normal range of LV-EF would suggest that systolic dysfunction is more probable in diabetic kidney disease patients than those with non-diabetic kidney disease. Also, measurement of GLS can help physicians predict the possibility of heart disease in asymptomatic patients with chronic kidney disease, sooner.

Association of dietary inflammatory index with cardiovascular diseases in adults: results of a prospective study of non-communicable psychiatric diseases

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Introduction

Cardiovascular diseases (CVD) are the first cause of death in the world and also the most important cause of disability and reduced quality of life all over the world. Diet and various food compounds are involved in the pathogenesis of chronic diseases, including CVD, through their inflammatory properties. Dietary Inflammatory Index (DII) is one of the methods that examines the inflammatory potential of diet and its relationship with various diseases. The purpose of this study is to determine the relationship between dietary inflammatory index and cardiovascular diseases.

Method & Materials

This cross-sectional study was conducted using the data of the initial phase of the non-communicable psychiatric diseases cohort study on 9824 adults. The food frequency questionnaire (FFQ) was used to evaluate the diet of the subjects. DII score was calculated using FFQ data. Data were analyzed using univariate and multivariate logistic regression tests in STATA 14.1 software.

Results

With the increase of DII quartiles, the risk of CVD increased (OR=1.7, CI=1.45-2.07). The level of education, economic and social status, physical activity and amount of energy, the percentage of calories received from protein and fat in the first quarter (the most anti-inflammatory diet) of DII was significantly higher than the fourth quarter (the most pro-inflammatory diet) ($p<0.001$). The incidence of high blood pressure and blood lipid disorders was significantly higher in the fourth quarter than in the first quarter ($p<0.001$). There was no significant difference in the incidence of diabetes between the first and fourth quartiles ($p=0.98$). The chance of CVD in women was higher than men (OR=1.8), socioeconomic status (OR=0.6) and physical activity (OR=0.47) were identified as protective factors against CVD. This study showed that overweight and obesity It increases the risk of CVD by 4.3 times.

Conclusion

In the present study, there was a linear relationship between the pro-inflammatory diet and the chance of developing CVD, so that with the increase in the DII score of the pro-inflammatory diet, the chance of developing CVD increased.

The Use of Statins and Their Long-Term Impact on Patients with Myocardial Infarction with Non-Obstructive Coronary Arteries (MINOCA)

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Introduction

Myocardial infarction with non-obstructive coronary arteries (MINOCA) is defined by general myocardial infarction criteria in the absence of atherosclerotic changes in coronary arteries. The 2020 ESC guidelines on acute coronary syndromes suggest that statin use may be beneficial in reducing mortality and major adverse cardiac events (MACE) among patients diagnosed with MINOCA. While previous data has been inconclusive, recent meta-analyses based on observational studies indicate that statin therapy resulted in a reduction of MACE and mortality.This study aimed to assess the impact of statin use on long-term mortality among patients diagnosed with MINOCA

Method & Materials

A total of 1011 patients hospitalized between 2012 and 2017 with a diagnosis of myocardial infarction based on clinical symptoms, EKG changes, and cardiac necrosis marker dynamics were included. Coronary angiography was performed for all patients upon admission. Seventy-two patients with coronary vessel changes narrowing the lumen by less than 50% were classified into the MINOCA group.

Results

Statins were taken by 54 patients (75.0%) in the MINOCA group. Among those treated with statins, a higher incidence of hypertension (P=0.001), dyslipidemia (P<0.001), lower Killip classification at admission (P=0.005), and higher LVEF (P=0.019) were observed compared to those not treated with statins in the MINOCA group. Higher LDL cholesterol levels in the MINOCA population influenced more frequent statin prescriptions (P=0.008). Long-term mortality was significantly higher in MINOCA patients untreated with statins (17.7%/year vs. 6.6%/year, P=0.009) compared to the statin-treated group.

Conclusion

The obtained results suggest that statins should be routinely prescribed in heterogeneous groups of patients diagnosed with MINOCA. Further research in this area is necessary.

Oral Session I

CELL BIOLOGY

Presenters:

- Henkie Isahwan Ahmad Mulyadi Lai
- Sophie Grigolo
- Kaiyuan Huang
- Eveiyn Weng Yan Phoon
- Hexing Sun
- Claudia Tesa
- Shimeng Wang

Developing Human iPSC-Derived Retinal Organoids for In Vitro Age-Related Macular Degeneration Studies

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Introduction

This study delineates significant progress in the in vitro modeling of retinal diseases, particularly focusing on age-related macular degeneration (AMD), using retinal organoids derived from human induced pluripotent stem cells (iPSCs). The iPSCs, sourced from peripheral blood mononuclear cells (PBMCs), offer a transformative avenue for understanding and potentially treating AMD. Through a strategic application of retinal-inducing factors and cell lineage-specific signaling molecules, we efficiently guided iPSCs to differentiate into key retinal cell types: photoreceptors, retinal pigment epithelium (RPE), and retinal ganglion cells (RGCs).

Method & Materials

Our approach involved differentiating iPSCs into essential retinal cells such as photoreceptors, retinal pigment epithelium (RPE), and retinal ganglion cells (RGCs). This was achieved by employing a combination of retinal-inducing factors and cell lineage-specific signaling molecules. The process of organoid formation began with the emergence of retinal cups around Day 30, gradually evolving into more complex structures with layered neuronal retinal cells, including RPE spheroids by Day 120.

Results

The organoids developed were subjected to thorough characterization using immunostaining and quantitative PCR. This maturation included the formation of RPE spheroids and brush-border-like morphologies. To verify the fidelity of differentiation, we conducted comprehensive characterizations using immunostaining and quantitative PCR. These analyses confirmed the presence of critical cell-type-specific markers: photoreceptor markers (such as opsin and rhodopsin), RGC markers (Brn3a and Thy1), and RPE markers (RPE65 and ZO-1).

Conclusion

Our development of retinal organoids from human iPSCs presents a significant advancement in the field of retinal research, particularly for conditions like AMD. These organoids not only serve as an effective platform for large-scale drug screening and studies on retinal development but also open up promising avenues for future applications in retinal cell transplantation, potentially offering new solutions for treating degenerative retinal diseases.

Interleukin-2 Acts Directly on Renal Cell Carcinoma Cells

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Introduction

Renal Cell Carcinoma (RCC) is the most common type of urogenital cancers. RCC includes various subtypes, clear cell carcinoma representing the most frequent type (75%). In some cases, RCC can become a sarcomatoid RCC, containing thus epithelial and mesenchymal features. Since many patients manifest the first symptoms at an advanced stage, immunotherapy is often considered a dominant treatment, such as high-dose interleukin-2 (IL-2). To date, it is known that IL-2 plays a role in the upregulation of the anti-tumor immune response. However, a direct influence of IL-2 on the kidney tumor cells has not yet been demonstrated. We aimed to investigate expression of the heterotrimeric IL-2 receptor _ (CD25), _ (CD122), _ (CD132) complex and the functionality on the RCC cells, as well as to reveal whether IL-2 acts directly on RCC cells.

Method & Materials

For this in vitro project, 4 kidney cancer cell lines where used: ACHN (adenocarcinoma with papillary and clear cell characteristics), A-498 (clear cell carcinoma), Caki-1 (clear cell carcinoma), and Caki-2 (clear cell carcinoma) (all from ATCC, USA). IL-2 receptor _, _ and _ gene expression was detected by quantitative real-time PCR and Western Blot. IL-2 receptor functionality was investigated by culturing the cells in the presence or absence of human recombinant IL-2 through MTT and BrdU-incorporation assays to measure proliferation and cell survival, and through Live-or-DyeTM Fixable Viability Staining to measure cell death.

Results

Quantitative real-time PCR showed mRNA expression of _ chain in 3 of 4 cancer cell lines, while at the protein level, Western Blot showed expression of the entire heterotrimeric IL-2 receptor ___ complex in all cell lines. We also observed that IL-2 enhances cell proliferation or cell death, depending on cell line and IL-2 concentration.

Conclusion

Overall, the expression of the IL-2 receptor complex was confirmed for the 4 cell lines. In addition, we conclude that the IL-2 receptor is functional, and that IL-2 could be used as a therapeutic option to act directly on the cancer cells. However, further investigation is required for better understanding the influence of IL-2 on the cancer cells.

Molecular Mechanism of CD146 Nanobody in Tumor Metastasis Inhibition mediating by IL-6/JAK/STAT3 signaling in Triple-negative Breast Cancer

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Introduction

CD146, an adhesion molecule involved in inflammatory regulation, is linked to increased aggressiveness in Triple Negative Breast Cancer (TNBC). Yet, the molecular mechanisms of CD1146-driven TNBC metastasis in an inflammatory context remain elusive. We synthesized CD146 nanobody (112-2), which degrades CD146, inhibiting IL-6-mediated JAK/STAT3 activation and suppressing TNBC metastasis. This study aims to elucidate the mechanisms of CD146 degradation by 112-2 and the role of CD146 in mediating inflammatory responses leading to TNBC metastasis.

Method & Materials

CD146 knockdown and knockout cell models were created using CRISPR/Cas9 or lentiviral techniques. Lung metastasis was evaluated by injecting luciferase-labeled cells into the tail veins of Balb/c-nu mice, monitored with the IVIS Kinetic system. The impact of CD146 on TNBC metastasis in inflammatory environment was explored through cell-adhesion assays and trans-endothelial migration assays using CD146 knockout models and HUVEC cells. Transwell assays assessed the influence of IL-6 and 112-2 on TNBC. To understand the molecular process of 112-2, CD146 mutants were generated to confirm the binding site. ELISA and immunofluorescence assays examined CD146 protein internalization. CD146 degradation by 112-2 was confirmed using proteasome inhibitor MG132 and lysosome inhibitor Bafilomycin A1, along with western blotting and immunofluorescence experiments.

Results

Stimulation of TNBC cells with IL-6 increased CD146 expression and tumor metastasis. CD146 knockdown significantly reduced IL-6 secretion by TNBC cells, leading to reduced tumor-endothelial cell adhesion and trans-endothelial migration. CD146 knockout or 112-2 treatment inhibited IL-6-mediated JAK/STAT3 activation and tumor metastasis. Experiments with CD146 mutants and molecular docking identified the specific 112-2 binding site at leucine positions 331-332 of CD146 protein. 112-2 treatment led to CD146 protein internalization and cleavage, resulting in an 80 kDa fragment recognized by both 112-2 and C-terminus-specific CD146 antibodies, ultimately inhibiting the activation of IL-6/JAK/STAT3 signaling. Notably, the inhibition of proteasome or lysosome activity failed to reverse the 112-2-induced reduction in CD146 protein levels. However, lysosome inhibition resulted in significant co-localization of CD146 with lysosomes, suggesting a potential role of lysosomes in 112-2-mediated cleavage of CD146.

Conclusion

CD146 regulates TNBC metastasis by modulating JAK/STAT3 activation through IL-6 signaling. The CD146 nanobody 112-2 induces proteolysis of CD146 protein, thereby inhibiting the tumor-promoting effect of IL-6.

BTYNB Alleviates ABCB1-Mediated Doxorubicin Chemoresistance in Uterine Sarcoma and Breast Cancer via IGF2BP1 Inhibition

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Introduction

Overexpression of ATP-binding Cassette Sub-family B Member 1 (ABCB1) is a mechanism of multidrug resistance (MDR), a primary cause of chemotherapy failure. Currently, no clinically approved inhibitor is available for ABCB1. Dysregulation of N6-Methyladenosine (m6A), a prevalent mRNA modification has been linked to chemoresistance. Yet, the role of m6A dysregulation in ABCB1-mediated chemoresistance in uterine sarcoma and breast cancer remains unexplored. We aim to elucidate the role of m6A modifications in the development of ABCB1-mediated chemoresistance in uterine sarcoma and breast cancer and to discover alternative ABCB1 inhibitors.

Method & Materials

Differential expression analysis of common m6A regulators was performed using RT-qPCR. We validated the expression of the highest differentially expressed m6A regulator via RT-qPCR and western blot in both parental and MDR cells of uterine sarcoma and breast cancer. In silico analysis of RNA sequencing results in GEO datasets was performed to determine the correlation of the candidate m6A regulator and ABCB1 in clinical samples. The effectiveness of the inhibitor of our candidate m6A regulator in reducing chemoresistance was studied using colony formation assays.

Results

Both MDR variants of uterine sarcoma and breast cancer exhibited significant upregulation of Insulin-like Growth Factor 2 mRNA-binding Protein 1 (IGF2BP1), an m6A reader. Gene counts of IGF2BP1 were positively correlated with gene counts of ABCB1 in in silico analysis, indicating a possible participation of IGF2BP1 in ABCB1-mediated chemoresistance. We are currently establishing protocols to demonstrate the IGF2BP1-ABCB1 interaction and elucidate the mechanisms by which IGF2BP1 regulates ABCB1 expression. An inhibitor of IGF2BP1, BTYNB, effectively mitigated chemoresistance in the MDR uterine sarcoma by significantly reducing the half-maximal inhibitory concentration of doxorubicin, a commonly used chemotherapeutic drug used in both uterine sarcoma and breast cancer. Furthermore, BTYNB induces the downregulation of ABCB1 in both MDR uterine sarcoma and breast cancer.

Conclusion

Inhibiting IGF2BP1 with BTYNB effectively reduces doxorubicin chemoresistance in MDR uterine sarcoma and breast cancer. Therefore, BTYNB may be a potential ABCB1 inhibitor.

CD146 mediates intimate crosstalk between adipocytes and triple-negative breast cancer cells and drives tumor metastasis through lipid metabolic reprogramming

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Introduction

In the tumor microenvironment, the adipocytes enhance the invasiveness of breast cancer (BC) by remodeling the lipid metabolism, especially in triple-negative breast cancer (TNBC). The cell adhesion molecule CD146 was highly expressed in TNBC and predicted poor distant metastasis free survival (DMFS) in patients. Meanwhile, CD146 was known to alter the obesity process by regulating the metabolic level. In this study, we aimed to explore the molecular mechanism of CD146 in tumor metastasis mediating by lipid metabolic reprogramming between adipocytes and TNBC cells.

Method & Materials

CD146 knockout or overexpression cell models were constructed by CRISPR/Cas9 or lentivirus. Cells labeled with luciferase were injected in tail vein of Balb/c-nude mice and monitored lung metastasis by IVIS Kinetic system. We synthesized anti-CD146 nanobodies, which significantly degrade CD146 protein and inhibit its function. RNA-seq and Lipidomics in CD146 knockout models were performed to analyze the role of CD146 in metabolism. Immunofluorescence was used to detect the intracellular content of Lipid Droplet (LD) and protein localization.

Results

CD146 was highly expressed in TNBC and predicted poor DMFS survival. Inhibition of CD146 suppressed tumor aggressiveness and lung metastasis in vitro and in vivo. According to the bioinformatics and RNA-Seq analysis, we showed that CD146 was intimately involved in the lipid metabolic pathway, particularly fatty acid metabolism, and revealed that inhibiting CD146 in TNBC elevated the intracellular triglyceride level through lipidomic study. Meanwhile, knockout of CD146 promoted LD accumulation and decreased fatty acid oxidation (FAO) and mitochondrial ATP levels. In molecular mechanism, we found that adipocytes secrete high level of IL6 and fatty acid, which activated JAK/STAT3 signaling and FAO mediating by CD146 in TNBC cells. Blocking CD146 by nanobody inhibited IL6/JAK/STAT3 activation and ACADM, leading to impairment of FAO and lung metastasis suppression in vitro and in vivo.

Conclusion

We demonstrated the crucial role of CD146 in the crosstalk between tumor cells and adipocytes in the tumor microenvironment. CD146 promotes the utilization of fatty acids through FAO and activates the inflammatory pathway response with adipocyte-secreted IL-6, thereby driving BC aggressiveness. Our studies have important implications for the development of TNBC therapeutics to block CD146-driven FAO process and inflammatory response.

Pluripotent stem cell-derived salivary glands models in regenerative medicine

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Introduction

The irreversible hypofunction of salivary glands (SGs) is a characteristic feature of various systemic diseases such as Sjîgren's syndrome, granulomatous diseases, graft-versus-host disease, cystic fibrosis, uncontrolled diabetes, human immunodeficiency virus infection, thyroid disease, and radiation therapy for head and neck cancer. The hypofunction of SGs leads to xerostomia, a common disorder that severely hampers a patient?s quality of life. Artificial saliva and many pharmacological approaches have been used, but do not restore salivary gland function and, in the case of radiotherapy for head and neck cancer, the stem cell niche in the field of radiation can be severely affected resulting in patients with no remaining salivary gland stem cells. Therefore, the establishment of Pluripotent-stem cell (PSC)-derived salivary gland progenitors for autologous transplantation to restore salivary gland hypofunction represents a promising strategy in regenerative medicine. This project focused on translating the embryonic development of the salivary gland into a PSC differentiation protocol that can yield putative salivary gland stem cells.

Method & Materials

PSCs (hES9 cells) were used as a starting point and were characterized at the different stages of differentiation, from PSCs, to definitive ectoderm, oral ectoderm, and putative salivary gland precursors, that could be further differentiated to start the expression of (pre)-acinar cells markers (PIP, PRH2, BPIFA1, AQP5), the cell type responsible for saliva production.

Results

Sequential down-regulation of pluripotent and endoderm markers, the absence of mesoderm markers, and prominent non-neural ectodermal differentiation were observed, characterizing the process of organogenesis. Furthermore, the expression of some SG progenitor markers, such as FOXC1 and SOX9 was observed and validated at transcriptional and protein level. Maturation markers KRT5 and KRT14 emerged in later stages, and acinar cell markers displayed distinct expression patterns, particularly a significant increase in PIP in the final stage. STATH and HTN3 were consistently undetected.

Conclusion

This project successfully directed PSCs towards salivary gland pre-acinar cells. Further studies are necessary to investigate the functionality of these cells in vivo.

RNA binding protein RBMS1 promotes aggressiveness of triple-negative breast cancer by modulating YAP1 signaling

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Introduction

RNA-binding proteins (RBPs) refer to a cluster of proteins that regulate RNA expression in post-transcriptional manner and in various cancer cells exists disorders in RBP expression. RNA-binding motif single-stranded interacting protein 1 (RBMS1) has been identified as a RBP upregulating in triple-negative breast cancer (TNBC) and associated with anti-tumor immunity. Moreover, YAP1 drives tumor progression as a critical role in Hippo pathway in TNBC. However, the molecular mechanism of RBMS1 promoting the progression of TNBC remains unknown. Our study aims to investigate the regulatory mechanism of RBMS1/YAP axis and clarify its regulatory role in invasion and migration of TNBC cells.

Method & Materials

RBMS1 knockdown or overexpression cell models were constructed by lentivirus plasmids. Wound healing assay and transwell assay were implemented to observe the impact of RBMS1 on migration and invasion of TNBC cells. RBMS1 and YAP expression levels were determined by quantitative real time polymerase chain reaction (qRT-PCR) and western blot. RNA stability assay was performed to analyze the influence of RBMS1 on YAP1 mRNA degradation. Immunological fluorescence assay was utilized to explore the protein locations of RBMS1 and YAP.

Results

RBMS1 was upregulated in TNBC cell compared to cells of other subtypes and normal breast cells, and by using the Bioinformatics technology and TCGA database, the high expression level of RBMS1 suggested poor prognosis of breast cancer patients. After scan YAP1 mRNA full-length sequence, we found multiple short sequences which were reported to bind with RBMS1 directly. Knockdown of RBMS1 suppressed the migration and invasion of BT549 and HCC1937 cells. Mechanistically, RBMS1 knockdown significantly leaded to declined YAP expression only in protein level, with no significant change in mRNA level. RNA stability assay showed that knockdown of RBMS1 destabilized YAP1 mRNA. Immunological fluorescence assay revealed that RBMS1 knockdown attenuated YAP signal in the nucleus.

Conclusion

Our findings suggest that RBMS1 activates YAP expression through post-transcriptional manner and drives cell migration and invasion in TNBC. RBMS1 could be a novel potential target for TNBC treatment. We will screen for chemicals targeting RBMS1 and further explore the molecular mechanism and therapeutic significance of RBMS1 in organoid and animal models.

Oral Session I

FUTURE MEDICINE

Presenters:

- Ahmed Alsoufi
- Samin Emaminia
- Marta Hanczar
- Mohammad Reza Hatamnejad
- Radvilė Kadytė

Optimizing Mental Health Disorder Screening Post-Disasters: Examining AI-Enhanced Human-in-the-Loop Application for Volunteer Accuracy and Effectiveness in Crisis Environments.

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Introduction

In disasters, the rise of mental health disorders presents a critical challenge, necessitating effective identification and referral by volunteers, especially in the lack of access to massive trained mental health specialists. Our study assesses the effectiveness of an artificial-intelligent-Enhanced Human-in-the-Loop application we developed to help volunteers during a real natural disaster in Libya in 2023 for the identification and referral of disorders such as Post-Traumatic Stress Disorder (PTSD), Major Depressive Disorder, Anxiety Disorders, and Grief and Bereavement, with a focus on the impact of volunteers' backgrounds and training.

Method & Materials

Our study applied a cross-sectional survey of volunteers using a mobile application for mental health screening after a disaster situation in Libya, the data included volunteers? demographics, educational level, and previous mental health care training, the study's main focus was on evaluating the volunteers' capability of utilizing the application, and the application?s ability in screening multiple mental health disorders, with paying attention on identifying the most significant correlations. Statistical analysis was performed using descriptive statistics, percentages, and correlation tests.

Results

In this study, 62 predominantly male volunteers (76.47%) with an average age of 28.71 years (Ò8.27), demonstrated high proficiency in using the app (82% accuracy). From the application database, we find that the effectiveness varied across disorders, with accuracies of 76% in Post-Traumatic Stress Disorder (PTSD), 70% in Major Depressive Disorder screenings, and 58% in Anxiety Disorders. We find Two key correlations emerged as particularly significant: a strong positive correlation ($r = 0.77$, $p < 0.01$) was found between medical students and accurate human final judgment, and a notable positive correlation ($r = 0.53$, $p < 0.01$) between higher educational levels and good decision and action taken.

Conclusion

Our study highlights the significant role of new AI-Enhanced Human-in-the-Loop applications as tools for identifying and referring mental health disorders conducted by nonmedical volunteers. The effectiveness of these technologies is considerably influenced by the volunteers' educational background, suggesting the need for targeted training programs and specialized app functionalities. Further research is essential to explore the long-term impact of these novel technologies on post-disaster mental health outcomes.

Harnessing the power of retrieval augmentation generation (RAG) for enhanced dermatological knowledge acquisition

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Introduction

Dermatologists face the challenge of acquiring accurate and accessible information to make informed diagnosis and treatment decisions. Conventional methods often lack comprehensiveness and efficiency, hindering timely and informed decision-making. Retrieval Augmentation Generation (RAG), a novel approach that integrates retrieval-based techniques with generative models, presents a promising avenue for revolutionizing dermatological knowledge acquisition. This study explores RAG's potential in dermatology, evaluating its effectiveness against established models like Claude and GPT-3.5.

Method & Materials

A comprehensive dataset of textual information from medical journals, textbooks, along with a collection of dermatological images encompassing various dermatological facets formed the foundation for refining the RAG model. Careful annotation ensured the accuracy and relevance of the information. RAG model underwent fine-tuning using a combination of retrieval-based and generative techniques. The retrieval component was trained to identify and retrieve relevant dermatological information from the curated dataset. The generative component was trained to synthesize retrieved information and generate detailed, context-specific outputs in response to user queries. A series of dermatological queries, ranging from common skin conditions to complex diagnostic dilemmas, were formulated to evaluate the RAG model's performance.

Results

Overall accuracies for RAG, Claude and GPT-3.5 models were 82%, 64% and 63.5%, respectively. The evaluation demonstrated a remarkable 18% increase in accuracy for the RAG model compared to Claude and GPT-3.5 in providing specific and pertinent dermatological information. The RAG model also exhibited superior performance in terms of relevance and comprehensiveness, generating detailed, context-specific outputs tailored to the specific needs of users.

Conclusion

The integration of Retrieval Augmentation Generation methodology in dermatology marks a significant advancement in information retrieval and generation. RAG's impressive performance, characterized by a substantial increase in accuracy compared to Claude and GPT-3.5, underscores its potential to revolutionize dermatological knowledge acquisition. Empowering dermatologists and patients with accurate and accessible knowledge, RAG holds the promise of transforming dermatological care, leading to improved diagnosis, treatment outcomes, and patient education.

Modelling Blood Vessel Disorder Hereditary Hemorrhagic Telangiectasia in a Vessel-on-a-Chip model using patient-derived isogenic induced pluripotent stem cells

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Introduction

Human induced pluripotent stem cell (hiPSC)-derived vascular cells in combination with advanced microfluidic in vitro models, also referred to as Vessel-on-Chip (VoC), can be used to study hereditary vascular diseases and provide a better representation of human vasculature in vitro. One disease of interest is hereditary haemorrhagic telangiectasia type 1 (HHT1), an autosomal dominant genetic disorder characterized by weak blood vessels and organ-specific abnormalities. Orlova et al. 2022 differentiated endothelial cells (hiPSC-ECs) using hiPSCs from a mosaic HHT1 patient, along with isogenic controls with genetic correction of the mutation. The group also established a self-assembled VoC model recapitulating the disease phenotype in 3D. While parts of the phenotype representative of the disease have already been recapitulated in these systems, additional inflammatory triggers are suggested to further enhance the disease phenotype in vitro. Therefore, this study aims to investigate the effect of proinflammatory triggers on the HHT1 phenotype using established VoC models.

Method & Materials

hiPSC lines derived from mosaic HHT1-iPSCs and isogenic control lines were differentiated into ECs. The VoC model was generated by integrating HHT1 hiPSC-ECs with mural cells into a microfluidic chip. Following microvasculature formation inside of the microfluidic chip, cells were stimulated with the proinflammatory cytokine TNF-_ to induce inflammatory responses. Subsequently, immunofluorescent staining will be performed, and structural analysis of the vessels will be conducted using confocal microscopy. Additional analyses will include cytokine and gene expression assessments.

Results

We successfully developed a perfusable microvascular network within our VoC platform by integrating hiPSC-derived HHT1 hiPSC-ECs and hiPSC-derived mural cells. To trigger proinflammatory responses, we subjected the microvasculature cultures to overnight stimulation with TNF-_. Preliminary results revealed that the microvasculature formed by mutant HHT1 hiPSC-ECs exhibited elevated levels of proinflammatory cytokines and chemokines, such as IL-8, CCL2, CXCL1, and CXCL5, in response to TNF-_ stimulation.

Conclusion

The established VoC model allows for investigating the proinflammatory responses of HHT1 disease. Our preliminary results align with existing literature, indicating an increased inflammation associated with HHT1. These findings hold promise for replicating the complex disease phenotype in vitro. Future experiments aim to resolve the HHT1 phenotype by applying targeted anti-inflammatory drugs.

The utility of SYNTAX score predictability by electrocardiogram parameters in patients with unstable angina

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Iran

Introduction

SYNTAX score is one of the risk assessment systems to predict cardiac events in acute coronary syndrome patients. Despite the large number of SYNTAX score benefits, invasive methods such as coronary angiography are necessary to perform the scoring. We hypothesized that ECG parameters could predict the SYNTAX score in unstable angina patients.

Method & Materials

During the retrospective cohort study, a total number of 876 patients were diagnosed with unstable angina. After applying the exclusion criteria, 600 patients were divided into tertiles based on the SYNTAX scores as low (0?22), intermediate (23?32), and high (Ú_33). The association between ECG parameters and SYNTAX score was investigated.

Results

The study included 65% men and 35% women with a mean age of 62.4_Ò_9.97 years. The delayed transition zone of QRS complex, ST-depression in inferior-lateral territories or/and in all three territories, and T-wave inversion in lateral territory were significant (p_<_0.05) independent predictors of intermediate SYNTAX score. High SYNTAX score was predicted by the presence of prolonged P wave duration, ST-depression in lateral territory or/and anterior-lateral territories, ST-elevation in aVR?III leads or/and aVR?III?V1 leads. Among those, all three territories ST-depression (AUC: 0.611, sensitivity: 75%, specificity: 51%) and aVR_+_III ST-elevation (AUC: 0.672, sensitivity: 50.12%, specificity: 80.50%) were the most accurate parameters to predict intermediate and high SYNTAX scores, respectively.

Conclusion

The present study demonstrates that accompanying the STE in the right side leads (aVR, III, V1) with ST-depression in other leads indicates the patients with high SYNTAX score; meanwhile, diffuse ST-depression without ST-elevation is a marker for intermediate SYNTAX score in unstable angina patients and can be applied for early risk stratification and intervention.

Sentante - the first fully robotic endovascular thrombectomy procedure.

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Introduction

Strokes are the leading cause of disability and the second cause of mortality and morbidity in Europe. Mechanical thrombectomy and blood flow restoration to the brain is the most cost-efficient procedure. However, only 10% of all stroke patients are treated invasively, because of short time window. An endovascular robot Sentante was tuned to perform cerebral thrombectomies remotely, using stent retrievers. The ability to perform the whole procedure robotically enables stroke thrombectomies in hospitals without a dedicated doctor on-site. The aim of study was to assess a latency of teleoperated system for thrombectomy stent procedure, in a vascular model.

Method & Materials

Two remote sites (more than 100 km apart) were chosen. The ability to robotically reach the target vessel with a guiding catheter, change to a 0.014?? platform, deploy the stent retriever with the help of a microcatheter and pull it back to the guiding catheter was counted as a technical success.

Results

An attempt of the remote thrombectomy procedure with a stent retriever in a vascular model was done. All three attempts were successful. The stent was placed and retracted flawlessly - the technical success rate was 100%. Also, the latency for streaming images, endovascular instruments movement and haptic feedback was measured. The delays for video, movement, and haptic feedback signals were 350 Ò 47 ms, 50 ms Ò 38 ms, and 55 Ò 43 ms, accordingly.

Conclusion

Endovascular robotic remote thrombectomies proved to be feasible within a 100 km distance. Mechanical movement and haptic feedback delays are small and barely detectable with human hands. However, the latencies for video signals are more significant and require dedicated solutions.

Oral Session I

IMMUNOLOGY

Presenters:

- Maximilian Griesbaum
- Ayidana Hayierhan
- Hosein Kouchaki
- Sandra Murawska
- Ali Tabatabaei

Fatigued patients with Inflammatory Bowel Disease exhibit distinct systemic antibody epitope repertoires

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Introduction

Patients with inflammatory bowel diseases (IBD) frequently experience fatigue, affecting up to 80% of those with active disease and approximately 50% with quiescent disease. The exact cause of IBD-associated fatigue is often unknown, making clinical management challenging. This study aims to explore whether patients with IBD reporting fatigue exhibit specific systemic antibody responses, which could elucidate immune reactivities underlying fatigue.

Method & Materials

Systemic antibody epitope repertoires were profiled in 327 patients with IBD (156 Crohn?s disease [CD]; 171 ulcerative colitis [UC]) leveraging phage-display immunoprecipitation sequencing (PhIP-Seq) against 344,000 rationally selected peptide antigens. Fatigue severity was assessed on a 10-point Likert scale, based on severity of fatigue. Multivariable logistic regression analyses, allowing adjustment for potential confounding factors e.g. age, sex, and smoking, were performed to identify associations between fatigue and systemic antibody responses.

Results

A total of 105 different antibody-bound peptides were associated with fatigue (nominal P-value <0.05), albeit none passed adjustment for multiple comparisons. Among these antibodies, 50 (47.6%) were found to be less frequent in highly fatigued patients (fourth quartile, Q4), while 55 (52.4%) were identified as more frequent in highly fatigued patients compared to those with low fatigue scores (first quartile, Q1). Among highly fatigued patients, antibody responses were primarily directed towards viral antigens, notably several antigens from Epstein-Barr virus (EBV), as well as bacterial antigens, including functional proteins from Streptococcus and Staphylococcus species. Fatigued patients with CD exhibited elevated systemic antibody responses against allergens, Adenovirus and Pseudomonas aeruginosa species. Fatigued patients with UC showed higher frequencies of antibody responses against herpes simplex virus (HSV), Influenza viruses, and few responses against allergens and H. influenzae bacteria.

Conclusion

This study may suggest a potential role of viral antigens, particularly EBV, in the pathophysiology of fatigue in patients with IBD. However, larger confirmatory studies are needed to validate these findings. PhIP-Seq may represent a valuable strategy to approach the investigation of immune responses underlying complex symptoms such as fatigue.

GRM4 as a Prospective CAR-T Cell Therapy Target in Breast Cancer

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Introduction

Chimeric antigen receptor T (CAR-T) cell therapy is a promising form of engineered immune-cell immunotherapy, selectively targeting membrane antigens on cancer cells. This innovative approach is designed to precisely target membrane antigens on cancer cells, showcasing notable therapeutic efficacy in addressing both hematologic and solid malignancies. But in breast cancer (BC), the application of immunotherapy is still limited, and one of the reasons is the discovery of a lack of specific antigens for breast cancer. Nowadays, tumor associated target exesit in breast cancer using clinically remain rare, even in CAR-T therapy for breast cancer. Targets widely used in clinical include PD-L1(20%-30%), and HER-2_15%-20%), but not all patients expressed these two targets. Here, we identified a target that is expressed more in breast cancer, with our primary aim being to assess GRM4 as a potential CAR-T-associated antigen in BC.

Method & Materials

Bioinformatic analyses assessed GRM4 expression in breast carcinoma and normal tissues using RNA-seq data from The Cancer Genome Atlas (TCGA). Additionally, GRM4 expression was evaluated via the Human Protein Atlas database. Immunoblotting Western Blot(WB) characterized GRM4 expression in BC cell lines (MCF7, MDAMB-231). Immunohistochemical (IHC) staining for GRM4 was performed on tumor specimens from 36 BC patients.

Results

TCGA data revealed significant upregulation of GRM4 in BC, with elevated expression in cancer tissues compared to normal breast tissues. WB confirmed increased GRM4 expression in BC cell lines. IHC demonstrated positive GRM4 staining in approximately 90% (33/36) of BC specimens. Considering the role of GRM4 in the central nervous system and its association with neurological disorders, we will explore its correlation with breast cancer and psychiatric diseases.

Conclusion

Our study provides the first evidence of elevated GRM4 expression in breast cancer, suggesting its potential as a prognostic biomarker and a prospective CAR-T therapy target for BC. Further large-scale studies and clinical trials are essential to validate its utility in CAR-T therapy within the constraints of limited therapeutic options for BC patients.

Prognostic Significance of Basal and Luminal Related Markers in Bladder Cancer

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Introduction

Bladder cancer (BC) is a prevalent genitourinary malignancy with diverse clinical and pathological manifestations. These heterogeneities arise from distinct molecular expression signatures, which play a crucial role in cancer progression, metastases, and overall survival. Based on transcriptional evaluations, researchers have classified BC into two primary molecular subtypes: luminal and basal. The luminal group is characterized by expressing markers of urothelial differentiation such as Forkhead box A1 (FOXA1) and GATA-binding protein 3 (GATA3). On the other hand, basal types predominantly express high molecular weight keratins, including cytokeratin 14 (CK14) and CK5/6. Notwithstanding a growing number of recent molecular studies, the role of basal and luminal markers in BC tumorigenesis remains a subject of controversy. Therefore, herein, we aimed to investigate the relationship between the expression of these markers and clinicopathological parameters of disease progression.

Method & Materials

Eighty-seven BC tissues obtained from curative operation were evaluated by an expert pathologist to document the patients' pathological data. Furthermore, immunohistochemistry staining was conducted for markers associated with luminal (GATA3 and FOXA1) and basal (CK5/6 and CK14) phenotypes. Following that, two clinical-blinded pathologists independently assessed the stained slides and reported the mean percentage of each marker. Associations between variables were investigated in the entire cohort using SPSS software version 27.

Results

Our findings indicated that lower expression of GATA3 was significantly associated with advanced tumor stage ($P = 0.005$), higher histologic grade ($P = 0.005$), non-organ-confined tumors ($P = 0.001$), as well as invasion to the muscle ($P = 0.002$), perivesical fat layer ($P = 0.009$), and perineural region ($P < 0.001$). Additionally, high expression of CK5/6 positivity correlated with perineural invasion ($P = 0.031$) and involving the muscle layer ($P = 0.026$). Moreover, increased levels of CK14 expression showed a positive association with perineural invasion ($P = 0.004$). No significant relation, however, was observed between FOXA1 expression and clinicopathological parameters.

Conclusion

The present study underscores the prognostic importance of BC-related molecular markers, particularly GATA3. Notably, these markers may assist in selecting appropriate therapeutic plans for patients with BC, as they could accurately predict the clinical outcomes.

Significance of peripheral blood monocyte subsets in the couse of newly-diagnosed Type 1 Diabetes in pediatric patients

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Introduction

Type 1 diabetes mellitus (T1DM) is an organ-specific autoimmune disease characterized by the destruction of insulin-producing beta cells in the pancreas. Although numerous studies have been conducted, the network of immunological interactions in T1D is still not fully understood. Recently, scientific reports have shown the potential involvement of peripheral blood monocytes in the pathogenesis and outcome of that disease. That particularly applies to the existence of functionally diverse monocyte subpopulations. Thus, we aimed to evaluate variations in monocyte subsets in patients with newly diagnosed type 1 diabetes and their relation to the clinically relevant diagnostic parameters.

Method & Materials

The study involved 51 newly diagnosed T1D pediatric patients and 31 age- and sex-matched healthy children as a control group. Peripheral blood monocyte frequency was evaluated in venous blood through the detection of CD14 and CD16 surface markers using flow cytometry. In accordance, monocytes were divided into three subsets: classical (CD14++CD16-), intermediate (CD14++CD16+), and non-classical (CD14+CD16++). Additionally, substantial clinical parameters (glycated hemoglobin, c-peptide, insulin usage) were collected for two years of follow-up.

Results

Diabetic patients demonstrated significantly higher levels of intermediate monocytes compared to the healthy control group. Increased levels of anti-GADA autoantibodies were present in a subset of those CD14++CD16+ monocytes. Noteworthy, patients with initially increased values of intermediate monocytes revealed higher values of c-peptide after two years of therapy. Additionally, odds ratio assessment showed that patients with low frequency of intermediate and non-classical monocytes at the time of diagnosis have a significantly lower chance of achieving optimal c-peptide values in the course of T1D management.

Conclusion

Peripheral blood monocytes seem to be involved in the outcome of type 1 diabetes in a subset-dependent manner. We demonstrated the substantial association between the frequency of intermediate monocytes and c-peptide concentrations. The diagnostic value of the obtained monocyte data as prognostic biomarkers in monitoring the treatment of T1D would be investigated in subsequent studies.

Machine learning as a solution to improve systemic lupus erythematosus subtype classification

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Introduction

Systemic Lupus Erythematosus (SLE) is a multifaceted autoimmune disease that has historically challenged clinicians with its diverse symptomatology, necessitating advancements in precise subtyping to tailor individual treatment plans effectively. We present a machine learning model that leverages the capabilities of Bidirectional Long Short-Term Memory (Bi-LSTM) networks and Gradient Boosted Decision Trees (GBDT) to improve the accuracy of diagnosing SLE subtypes. This integrative approach signifies a pivot towards a more personalized and adaptive therapeutic framework for SLE patients.

Method & Materials

Our study lies in its comprehensive application of Bi-LSTMs to use complex patterns from unstructured patient narratives?a narrative encompassing a decade?s worth of clinical evaluations, serological assessments, and medication histories. Concurrently, GBDTs, renowned for their predictive strength, provided a structured, analytical layer for identifying subtle SLE subtypes from systematic data. We ensured model robustness by fine-tuning critical GBDT hyperparameters, exploring learning rates between 0.05 to 0.20 and increasing tree counts from 100 to 500 through cross-validation. The collated dataset included over 1,200 anonymized patient records from dual institutions, which were partitioned, maintaining an 80% training and 20% validation split, to ascertain model efficacy across unseen data.

Results

The results of our dual-model framework were remarkable. The integrated Bi-LSTM and GBDT model demonstrated an overall precision rate of 95.3%, with a specificity of 93.2% and a sensitivity of 94.8%, indicating a significant upgrade in subtype discrimination over baseline models. Notably, distinct SLE manifestations such as lupus nephritis, which traditionally complicate diagnosis, were identified with an accuracy of 92%, a number exemplifying the capability of our model against traditional diagnostic methods, which fall around the 65-75% range.

Conclusion

The implementation of Bi-LSTM, and GBDT-based machine learning models guide in a new era for the diagnostic and treatment of SLE. Our findings not only elevate diagnostic accuracy but also underscore the vital role that machine learning can reduce the uncertainties prevalent in SLE subtype classification. Looking ahead, pursuing external validation with a broader dataset spectrum is essential as we continue to refine our algorithms?thereby consolidating their relevance, extensibility, and adoption for clinical applications.

Oral Session II

INFECTIOUS DISEASE

Presenters:

- Ketema Bizuwork
- John Bester Kalumbi
- Adriel Loekito
- Mina Rahmati

Urinary Tract Infection among People Living with HIV in Addis Ababa Ethiopia

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Introduction

Urinary tract infections (UTIs) are the most important public health problems among people living with HIV (PWH) globally. The higher the prevalence of UTIs in developing countries ratifies the importance of conducting studies among vulnerable populations. This study aimed to investigate prevalence of UTIs, associated factors, bacterial causal agents and antibiotic susceptibility profile among PWH in Addis Ababa, Ethiopia.

Method & Materials

Hospital-based cross-sectional study was conducted among PWH. Midstream urine samples were collected aseptically and a loopful (0.01ml) of serially diluted well-mixed urine was inoculated on plate count agar and incubated for 24 hours at 37 Degree Celsius. Diagnosis of UTI was based on detection of microbial count of at least 105 colony forming unit per milliliter (cfu/ml) for study participants without symptoms of UTIs while at least 102 cfu/ml for those with symptoms of UTIs. Standard conventional microbial culture methods and matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF) were used to identify the bacterial isolates at the species level. Kirby Bauer?s disc diffusion method was used to determine the antibiotic susceptibility profile of the bacterial isolates. Logistic regression was used to examine factors associated with the occurrence of UTIs.

Results

Out of 518 PWH involved in the current study, 102 (19.7%) were positive for UTI and the majority 86 (84.3%) of them were acquired asymptomatic UTIs. High HIV RNA load was significantly associated with the occurrence of UTIs ($P<0.02$). The dominant bacterial species isolated were Escherichia coli 43 (40%), Enterococcus faecalis 16 (15%), Proteus mirabilis 7 (6%), Klebsiella pneumoniea 6 (6%), and Staphylococcus aureus 7 (6%). All of the Staphylococcus aureus isolates were methicillin-resistant (MRSA). Over three-fourth of Escherichia coli and all the isolates of Enterococcus faecalis and Enterococcus faecium were resistant to multiple antibiotics.

Conclusion

Considering the higher rate of UTIs and antibiotic resistance in this study population, there is a need for public health interventions: educating PWH about UTI and its risks associated, resistant organisms, proper antibiotic use, and consequences of misuse or overuse of antibiotics. Healthcare providers should also adopt antibiotic stewardship programs to promote and ensure the appropriate and judicious use of antibiotics

Evaluating the implementation of prevention of mother to child transmission of HIV in Mwanza District, Malawi

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Introduction

Research has shown that with introduction of prevention of mother to child transmission of HIV(PMTCT) the cases of MTCT are reduced to global targets of less than 5% as we aim for elimination. This study evaluated the implementation of PMTCT program focusing on the treatment impact, strengths and challenges in relation to the guidelines provided by WHO towards the global targets. The objectives were to assess the impact of ART treatment defaulting on the PMTCT program and to determine the challenges and gaps in the implementation of PMTCT services that hinder elimination of pediatric HIV infections at Mwanza district.

Method & Materials

This was a retrospective study and data was collected at Mwanza hospital. The quantitative component involved data collected from women enrolled in the PMTCT program for 24 months, from June 2020 to June 2022. The study included pregnant women with HIV and exposed infants who were followed up from first result at 6 weeks to the time the child reached 24 months. We analyzed different variables using bivariate and logistic regression. Thematic and fish bone analysis were also used to analyze qualitative data

Results

The MTCT transmission rate is 1.7% for Mwanza district compared to the 6% national transmission rate as recorded by UNAIDS 2020. Women who had a higher transmission of HIV (5.56%), were those that had defaulted visits to collect ART treatment unlike those that didn?t (0.6%). Bivariate analysis of the variables that were considered to influence the outcome of infants HIV status, only defaulting of ART treatment was significantly influencing the transmission of HIV from the mother to the child ($x2=9.6521$, $p= 0.002$).

Conclusion

Managing clients to return for treatment is a breakthrough which could significantly lower the number of HIV positive infants who get the virus from their mother. Getting to zero number of transmissions of HIV from the mother to the child is possible if ART treatment could be 100% for all women if they adhere to ART treatment

Inappropriate Antibiotic Dosing in Pneumonia Patients with Chronic Kidney Disease is Associated with Longer Length of Stay

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Introduction

Pneumonia remains one of the most prevalent infectious diseases worldwide. Unfortunately, patients with preexisting comorbidities such as chronic kidney disease (CKD) are at a higher risk of hospitalisation and death due to pneumonia. The use of antibiotics in pneumonia patients with impaired kidney function often requires dosing adjustments, as many antibiotics are eliminated in the kidney. However, adjustments remain substandard in many patients, resulting in a worse therapeutic regime. This study aims to evaluate the appropriateness of antibiotic dosing in pneumonia patients with CKD and its impact on mortality and length of stay (LOS).

Method & Materials

A cross-sectional retrospective study was done at a major respiratory hospital in Jakarta. Reviews were done on patients' medical records with ICD-10 codes for pneumonia and CKD between 2021 and 2023. Lab results were used to determine eGFR values, while pharmacy instructions were referred to determine the antibiotics prescribed. Dose adjustments were compared against hospital antibiotics guidelines and Lexicomp. Statistical analysis was done using the _2 and Mann-Whitney test for categorical and continuous values, respectively.

Results

230 antibiotics were prescribed to 111 patients. Antibiotic dosing was found to be inappropriate in 51.4% of patients observed. Patients with improper antibiotic dosing had longer lengths of stays compared to those with appropriate dosing (median 8 vs. 12 days, $p < 0{,}001$). No statistically significant association were found between proper antibiotic dosing and mortality.

Conclusion

Inappropriate antibiotic dosing in pneumonia patients with CKD appears to lengthen the length of stay of patients, potentially causing a negative impact on patient outcomes and increasing healthcare costs.

Rosuvastatin intervention in patients with chronic hepatitis B (CHB) expands CD14+ CD16- classical monocytes via aryl hydrocarbon receptor (AHR)

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Iran

Introduction

Chronic Hepatitis B (CHB) is difficult to treat and the immune response, especially mononuclear phagocytes, determines the treatment response and disease outcome. Monocytes can develop different subpopulations and AHR is involved in altering their phenotypes. Statins modulate inflammation and could also affect monocyte function through AHR activation. This study investigated the effects of rosuvastatin (RSV) on monocyte subtypes, inflammatory markers, and its relation with AHR in CHB patients.

Method & Materials

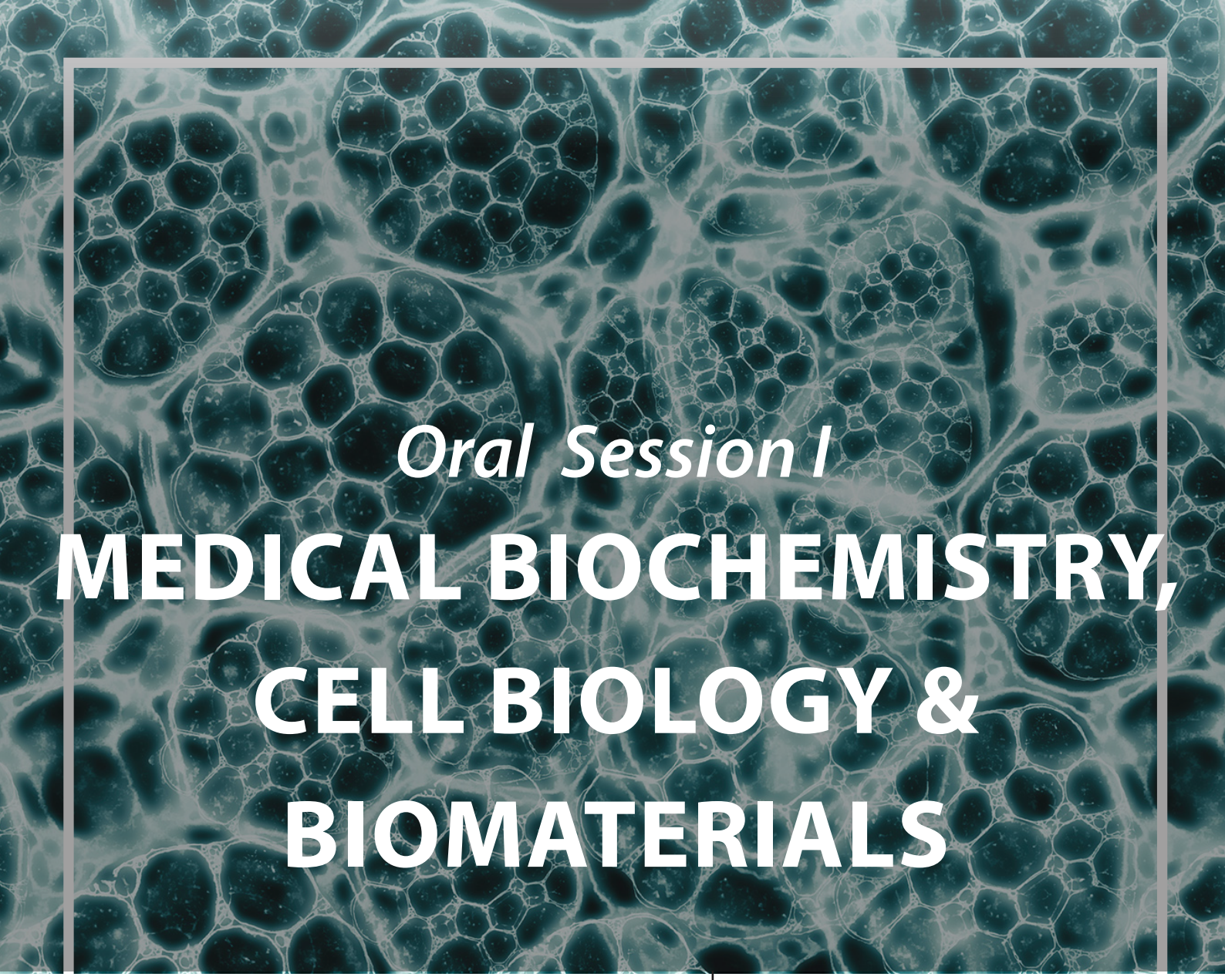
Patients diagnosed with CHB were allocated randomly into two sets of 15 individuals each. Over a period of three months, the initial set was administered a daily dose of 20mg RSV, while the second set was given a placebo. The CD14+CD16- (Classical), CD14+CD16+ (Intermediate), CD14dimCD16+ (Patrolling) monocyte subtypes, and the levels of AHR in each subset, were assessed by flow cytometry. The levels of IL-6, IFN-_, IL-12, IL-10, TNF-_, TGF-_, and IL-1_ cytokines were quantified through the application of ELISA.

Results

Our findings showed that RSV administration was in favor of expanding the CD14+ CD16- classical and decreasing CD14+ CD16+ intermediate monocytes among CHB patients. Moreover, RSV intervention increased the percentages of AHR+ cells among all subpopulations of monocytes. The administration of RSV to patients with CHB led to a reduction in the serum concentrations of pro-inflammatory cytokines such as IL-6, IFN_, IL-12, and TNF-_, while elevating the levels of anti-inflammatory cytokines IL-10 and TGF-_.

Conclusion

RSV could be introduced as a modulator of immune response, by altering the subtypes of monocytes in CHB patients, via AHR.



Oral Session I

MEDICAL BIOCHEMISTRY, CELL BIOLOGY & BIOMATERIALS

Presenters:

- Sem Geertsema
- Attila Tamás György
- Jiaqi Lin
- Joaquín Torres-Núñez
- Zhisheng Wu
- Jinling Zhong

Systemic redox status associates with disease activity and clinical phenotypes in inflammatory bowel disease

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Introduction

Oxidative stress is a key pathophysiological mechanism in inflammatory bowel diseases (IBD). Systemic levels of oxidative stress are reflected by reduced levels of free thiols (FT) in circulating proteins, especially those in albumin, which associates with disease activity in IBD. Yet, clinal value of circulating FT level as biomarkers of disease and therapy response remains largely unexplored. Here we investigated the association between plasma FT levels and clinical parameters, the plasma inflammatory proteome and medication use.

Method & Materials

Plasma samples from 1,028 patients with IBD (567 Crohn's disease [CD] and 461 ulcerative colitis [UC]), and 500 healthy controls (HCs) participating in the 1000IBD and LifeLines projects were profiled for free thiols (FT), uric acid, bilirubin and 92 inflammation-related proteins (Olink Inflammation panel). All biomarkers were associated with clinical phenotypes using general linear models adjusting for age, sex, body mass index, smoking and medication use.

Results

Plasma FT levels were significantly lower in IBD compared to HCs ($p<0.05$), with patients with UC showing even lower levels than patients with CD ($p<0.05$). Patients with UC on induction therapy had lower FT levels compared to patients on maintenance therapy ($p<0.05$). Furthermore, FT levels of patients with IBD were strongly associated with systemic inflammation (C-reactive protein [CRP], $p<0.05$). In both patients with CD and UC, reduced FT levels were associated with elevated levels of inflammation-, apoptosis-, and growth factor-related proteins, including C-X-C motif chemokine 9 (CXCL9), CUB domain-containing protein 1 (CDCP1) and caspase-8 (CASP8), proteins that have been previous associated with preclinical IBD. Furthermore, specifically for patients with UC, reduced FT levels were associated with elevated eotaxin-1 (CCL11), monocyte chemotactic protein-1 (MCP-1), and several cytokine biomarkers like Interleukine-6 (IL6) and Interleukin-17A (IL17A).

Conclusion

Systemic FT levels associate with inflammatory disease activity and clinical therapy and may offer potential utility in clinical assessments. This study highlights the intricate involvement of oxidative stress in various inflammatory pathways and components, particularly in innate/adaptive immune balance, cell damage, and apoptosis. These findings contribute to a deeper understanding of the interplay between oxidative stress, inflammation, and IBD.

Investigation of protein-protein interactions in the pathogenesis of colorectal and prostate cancer using artificial intelligence

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Introduction

Although several previous studies have highlighted the potential role of arylsulfatase B in the pathogenesis of malignant colorectal and prostate tumors, the exact pathomechanism of this remains unknown. In silico examinations of the protein-protein interactions can be very effective with the application of artificial intelligence in this field. The objective of our research is to investigate the potential involvement of arylsulfatase B in the development of colorectal and prostate cancer, using interaction predictions by artificial intelligence.

Method & Materials

The interaction network of arylsulfatase B was examined using the STRING database. The recommended confidence value of 0.400 was used to determine the strength of the interactions. Two bioinformatics tools based on artificial intelligence were used to analyze the interactions of the proteins in the most optimal pathway, using different methods. The proteins' amino acid sequence was inputted into the PEPPI system, and the HDOCK Server tool utilized their tertiary structure.

Results

The strongest interaction pathway between ARSB and proteins involved in tumor development was represented by GUSB (0.77) and HSP90AB1 (0.62) proteins. For colorectal cancer, the PEPPI system predicted the most likely interaction of HSP90AB1 with AKT1 (log(LR) = 1.78), TP53 (log(LR) = 0.96) and EGFR (log(LR) = 0.87) proteins. Meanwhile, the HDOCK Server showed the highest confidence score for connection of HSP90AB1 with RAF1 (0.92), BRAF (0.91), and EGFR (0.90) proteins. For prostate cancer, the PEPPI system predicted the most likely interaction of HSP90AB1 protein with ERBB2 (log(LR) = 0.99), TP53 (log(LR) = 0.96) and EGFR (log(LR) = 0.87) proteins. In contrast, the HDOCK Server showed the highest confidence score for connection of HSP90AB1 with BRAF (0.91), EGFR (0.90), and TP53 (0.87) proteins.

Conclusion

For both tumor types, the strongest association between ARSB and the proteins involved in tumorigenesis is found to be GUSB and HSP90AB1. Furthermore, TP53 and EGFR are the most likely interaction partners for HSP90AB1 according to the PEPPI system, while BRAF and EGFR according to the HDOCK Server. Our results illustrate the benefits of using artificial intelligence in the field of molecular biology and highlight the ways in which these analytical methods can help guide experimental research.

Wound Healing Effects of Hyaluronic Acid-Poloxamer Hydrogel Loaded with PDGF Expressing Enucleated BMSCs

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Introduction

The treatment of chronic refractory skin wounds still remains a serious clinical challenge. Stem cells embedded in hydrogels are widely used for the healing of various types of skin wounds. As a promising vehicle for biomaterial delivery, enucleated cells have a wide range of therapeutic applications. This study aimed to demonstrate the wound healing effect of a hydrogel loaded with enucleated stem cells expressing platelet-derived growth factor (PDGF).

Method & Materials

An injectable hydrogel was developed based on hyaluronic acid and poloxamer. A PDGF-B transgenic cell line was generated from mouse bone marrow mesenchymal stem cells (BMSCs), which were enucleated and embedded in hydrogel. The healing effects of the mixture was tested in a full-thickness skin wound model of healthy mice.

Results

The RT-qPCR, immunofluorescence staining and Western blot analysis were carried to verify the expression of PDGF-B in the transgenic cell line. Cells were enucleated and embedded in hydrogel. The viability revealed by Calcein-AM and TMRE staining reduced steadily post enucleation but still maintained about 54.29% at 48 h. Intra- and extracellular PGDF-BB concentration was assayed by ELISA, which showed that the hydrogel we developed can secrete more PDGF-BB in 48 h. 5_105 cells were mixed with 50 mL of hydrogel, which was then applied to a full-thickness skin wound murine model. After 3 days, wound area reduced 64.71%. In contrast, mice without treatment and treated with hydrogel or BMSC hydrogel alone reduced 11.98%, 23.48% and 40.71%. In addition, overexpressed PDGF enucleated stem cell hydrogel enhanced the regeneration of neovascular, skin appendages and collagen fibers, and down-regulated the expression of TNF-_, IL-1_, IL-6, MMP-3, and MMP-9 in the wound epithelial tissues.

Conclusion

Overexpressed PDGF enucleated stem cell hydrogel significantly improved wound healing and reduced wound inflammatory factor expression in Balb/c mice. This biomaterial-based hydrogel provides a new powerful reference for the treatment of chronically wounded skin.

Frequency of Antibiotic Resistance in Helicobacter pylori Strains in Pediatric Patients Undergoing Upper Gastrointestinal Endoscopy

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Introduction

In pediatric patients, Helicobacter pylori infection commonly presents as asymptomatic chronic gastritis, which does not necessitate treatment. However, some patients progress to peptic ulcer disease, justifying the need for antimicrobial eradication therapy. International pediatric consensus guidelines recommend tailoring each patient's regimen based on the antibiotic susceptibility of the involved strain. Nevertheless, implementing this approach is impractical in the Latin American reality, leading to empirical treatment. Eradication rates below 80% have been reported, primarily attributed to the emergence of resistant strains, a problem seemingly on the rise. The aim of this study was to describe the molecular resistance profile of H. pylori strains isolated from pediatric patients undergoing upper gastrointestinal endoscopy (UGIE) and compare the frequency over two time periods.

Method & Materials

A multicenter, descriptive, cross-sectional study was conducted with approval from the institutional ethics committee. DNA extraction from gastric antrum biopsies was performed, followed by PCR-RFLP and ASP-PCR to identify clarithromycin (CLR) and levofloxacin (LEV) resistance-conferring mutations, respectively, in patients recruited during the periods 2010-2015 and 2019-2022.

Results

A total of 59 samples were analyzed, 34 from the 2010-2015 period and 25 from the 2019-2022 period. A 22.3% resistance to CLR was detected, with no significant difference between the two periods (23.5% in samples from 2010-2015 and 20.0% in 2019-2022, respectively; p=0.7465). Molecular resistance to LEV was 78.9% overall (81.8% in samples from 2010-2015 and 73.7% in 2019-2022, respectively; p=0.4892)

Conclusion

Molecular resistance rates to CLR and LEV exceeding 15% were obtained, the recommended cutoff in consensus guidelines for discouraging the use of these antibiotics in empirical regimens. CLR and LEV resistance remained stable over time. Continuous surveillance of H. pylori antimicrobial resistance rates is crucial for informed decision-making in the empirical treatment of patients.

FOXM1 protects cells from ferroptosis by regulating the expression of SESN2 in esophageal cancer

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Introduction

Reactive oxygen species (ROS) play a crucial part in the process of cell death, including ferroptosis. FOXM1 is a key transcription factor usually highly expressed in many tumors, promoting tumor initiation and development. However, the regulation mechanism of FOXM1 in oxidative stress in esophageal cancer remains unclear. Therefore, this study aims to explore the role of FOXM1 in oxidative stress in esophageal cancer.

Method & Materials

Firstly, the expression pattern of a total of 402 genes involved ROS were evaluated in expression profiles of esophageal cancer. Then, Lasso-Cox regression analysis was used to construct a prognostic model. Next, the cell function was analyzed through CCK-8, cell clone formation, cell cycle assay, as well as the levels of ROS, malondialdehyde (MDA), GSH, and mitochondrial membrane potential were detected, after overexpression or knockdown of FOXM1 in esophageal cancer cells. Then RNNA-seq and luciferase reporter gene assay were applied to search for potential transcriptional downstream targets for FOXM1. The biological effects and molecular mechanism of the target gene on the cell death were evaluated as well.

Results

FOXM1 was highly expressed in esophageal cancer clinical samples, and the patients with a high expression of FOXM1 had a better prognosis. After knocking down FOXM1, the levels of GSH and total antioxidant capacity were decreased, while the intracellular levels of ROS and MDA were increased, and cell cycle arrest was occurred in the G2/M phase. The overexpression of FOXM1 led to an opposite effect. The potential target genes were selected from the differentially expressed genes of RNA-seq results. Luciferase reporter gene assays were conducted to confirm that SESN2 was a target gene for downstream regulation of FOXM1. when both knocking down FOXM1 and SESN2, the mitochondrial membrane potential was decreases and cell apoptosis were increases. The result from transmission electron microscopy shown the mitochondria become smaller, mitochondria membrane density increases, and mitochondrial cristae decrease after the knockdown of FOXM1 and SESN2. The expression of ferroptosis-related protein GPX4 and p53 were decreased as well after FOXM1 and SESN2 knockdown.

Conclusion

FOXM1 protects cancer cells from ferroptosis by regulating the expression of SESN2 in esophageal cancer.

Molecular mechanism and drug intervention of Fascin mediating DNA damage repair in response to radiation through interaction with PARP1

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China

Introduction

Fascin 1 (Fascin), a protein known for its role in bundling actin filaments and enhancing cellular invasion, has emerged as a significant biomarker in various cancer types, including esophageal cancer. Despite extensive studies of its cytoplasmic function, Fascin was found not only to be localized within the nucleus of cancer cells, but also to be associated with chromatin remodeling. Fascin also exhibited a unique response to DNA damage and co-localized with _H2AX, a hallmark of DNA double-strand breaks following exposure to ionizing radiation, yet the precise molecular mechanisms remain unclear. This study aims to elucidate the intricate molecular mechanisms governing the interaction between Fascin and PARP1, a pivotal player in DNA damage repair.

Method & Materials

Our research employed a bioinformatics approach by combining esophageal cancer proteomic data with Uniprot datasets to identify candidate interacting proteins of Fascin. Subsequently, we substantiated these interactions through a series of biochemical experiments, including immunoprecipitation, Pull Down assays, and the construction of truncated eukaryotic expression plasmids. Further investigations encompassed immunoblotting, immunofluorescence, and in vitro PARylation experiments, shedding light on the role of Fascin in early DNA damage signal responses. Finally, we conducted clonogenic assays to assess the impact of combination therapy on esophageal cancer cells.

Results

Through immunoprecipitation and Pull Down assays, we confirmed a direct and robust the interaction between Fascin and PARP1. Transient transfection with truncated eukaryotic expression plasmids further established their interaction across various structural domains of Fascin. Immunoblotting and immunofluorescence experiments unveiled the pivotal role of Fascin in early DNA damage response, specifically in PAR signal generation. Our subsequent investigations demonstrated that Fascin significantly enhances PARP1 enzyme activity. Notably, co-administration of Fascin and PARP inhibitors heightened the radiosensitivity of esophageal cancer cells.

Conclusion

Fascin amplifies intracellular PAR signals by promoting PARP1 enzyme activity, thereby recruiting DNA damage repair factors to the damaged site for DNA damage repair. Fastin and PARP1 inhibitors combined with radiotherapy will contribute to the potential development of innovative therapeutic strategies for cancer cells.

Oral Session I

NEUROLOGY

Presenters:

- Abdulrahman Almulla
- Bart Wijntjes
- Changwei Guo
- Abdulrahman Krayim
- Veneesha Liyanage
- Omar Mochtar Syarif

Optic Neuritis: A Key Determinant of Outcome and Prognosis in Multiple Sclerosis

Abdulrahman Almulla
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Saudi Arabia
Co-authors: AlHussein M. (Maha), AlHelal F. (Fatimah), Al Qhtani M. (Muhanned)

Introduction

Multiple Sclerosis (MS) is a widespread neurodegenerative disorder affecting the central _nervous system, with an estimated 2.8 million people worldwide. Optic neuritis (ON), an _ inflammatory disease affecting the optic nerve, is commonly associated with MS. ON typically _presents as unilateral painful vision loss and blurry vision. This study aims to investigate the _outcomes of MS patients with and without ON, contributing to the development of tailored _treatment plans for MS patients and ultimately reducing disease progression and axonal _injury._

Method & Materials

This cross-sectional study held at King Abdulaziz Medical City in Riyadh, Saudi Arabia. A total _of 481 MS patients were included, and data were collected from medical records and _telephone interviews. The collected data included demographic information, MS _characteristics, CSF findings, MRI results, and scores from four scales (EDSS, MSIS-29, smRSq, _IVIS) obtained through interviews. Statistical analysis was performed using SPSS version 24, _including T-tests, one-way ANOVA, and chi-square tests._

Results

Among the 481 patients, 256 responded to the study. The average age was 36.26 Ò 9.67 years, _and the majority were females (67.2%). Of the respondents, 113 (44.1%) had optic neuritis __(ON), with 31 (27.4%) having non-optic neuritis onset MS (NONOMS) and 82 (72.6%) having _optic neuritis onset MS (ONOMS). Patients with ON had an average physical MSIS score of __26.78 Ò 25.96 and an average IVIS score of 2.78 Ò 3.70, compared to 27.67 Ò 27.41 and 1.67 Ò __2.98 in patients without ON, respectively (P = 0.008). The smRSq score average was 3.61 Ò __4.04 for patients with ON, compared to 4.15 Ò 4.38 for patients without ON. The EDSS score _was Ú 6 in 48 patients with non-optic neuritis MS and 38 patients with optic neuritis MS._

Conclusion

The study reveals a significant disparity in the impact of visual impairment scale (IVIS) _between patients with and without optic neuritis (ON). While no substantial variations were _observed in the outcomes of other scales, except for the Modified Rankin Scale (smRSq). It is _crucial to note that MS patients without optic neuritis (ON) demonstrated a heightened risk of _disease progression and accumulating disability.

Revealing Positive Perceptions and Accessibility Challenges in Virtual Reality Rehabilitation for Stroke Patients and Caregivers in Indonesia: A Qualitative Study

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Introduction

Assessing the risk of falling in People with Parkinson's Disease (PwPD) is typically carried out by a combination of neuropsychological and dynamic movement tests. EEG-derived measures would allow clinicians to probe neural activation patterns, which may be indicative of falls risk. Wireless EEG systems allow for such neural activity to be simultaneously recorded along with gait-related movement data, allowing for a better understanding of the origins of gait abnormalities in PwPD.

Method & Materials

EEG data and movement data, obtained from inertial movement sensors (IMU) placed on the lower limbs, are recorded synchronously. However, applying ASR to the position of the EEG signal during known specific periods where the signal is corrupted by movement artefact (heel strikes, etc.) can prove to be more effective in artefact removal while maintaining the quality of neural information contained in the data. The performance of this artefact removal strategy is objectively quantified by metrics such as SNR. Testing is underway in a convenient sample of PwPD cohort (3) and aged-matched controls (3) as they follow a specific out-patient protocol to assess their balance and movement.

Results

Expected: The applied filtering method has a higher SNR than conventional EEG filtering methods..

Conclusion

Expected: The application of an optimal filtering algorithm to remove gait-induced movement artefacts will allow improved clinical interpretation of neuromotor ability of PwPD and possibly other neuro-motor diseases during different dynamic movement tasks.

Tirofiban for Stroke without Large or Medium-Sized Vessel Occlusion: a Double-blind, Randomized Control Trial

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Co-authors: Zi W. (Wenjie), Li F. (Fengli), Song J. (Jiaxing), Li F. (Fengli)

Introduction

The effects of the glycoprotein IIb/IIIa receptor inhibitor tirofiban in patients with acute ischemic stroke but who have no evidence of complete occlusion of large or medium-sized vessels have not been extensively studied.

Method & Materials

In a multicenter trial in China, we enrolled patients with ischemic stroke without occlusion of large or medium-sized vessels and with a National Institutes of Health Stroke Scale score of 5 or more and at least one moderately to severely weak limb. Eligible patients had any of four clinical presentations: ineligible for thrombolysis or thrombectomy and within 24 hours after the patient was last known to be well; progression of stroke symptoms 24 to 96 hours after onset; early neurologic deterioration after thrombolysis; or thrombolysis with no improvement at 4 to 24 hours. Patients were assigned to receive intravenous tirofiban (plus oral placebo) or oral aspirin (100 mg per day, plus intravenous placebo) for 2 days; all patients then received oral aspirin until day 90. The primary efficacy end point was an excellent outcome, defined as a score of 0 or 1 on the modified Rankin scale (range, 0 [no symptoms] to 6 [death]) at 90 days. Secondary end points included functional independence at 90 days and a quality-of-life score. The primary safety end points were death and symptomatic intracranial hemorrhage.

Results

A total of 606 patients were assigned to the tirofiban group and 571 to the aspirin group. Most patients had small infarctions that were presumed to be atherosclerotic. The percentage of patients with a score of 0 or 1 on the modified Rankin scale at 90 days was 29.1% with tirofiban and 22.2% with aspirin (adjusted risk ratio, 1.26; 95% confidence interval, 1.04 to 1.53, P = 0.02). Results for secondary end points were generally not consistent with the results of the primary analysis. Mortality was similar in the two groups. The incidence of symptomatic intracranial hemorrhage was 1.0% in the tirofiban group and 0% in the aspirin group.

Conclusion

In this trial involving heterogeneous groups of patients with stroke of recent onset or progression of stroke symptoms and nonoccluded large and medium-sized cerebral vessels, intravenous tirofiban was associated with a greater likelihood of an excellent outcome than low-dose aspirin. Incidences of intracranial hemorrhages were low but slightly higher with tirofiban.

Efficacy of Intermittent Theta Burst Stimulation (iTBS) on Post-Stroke Cognitive Impairment (PSCI): A systematic review and meta-analysis

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Introduction

Stroke is a significant global cause of mortality and morbidity, and post-stroke cognitive impairment (PSCI) affects up to half of stroke patients. Despite the availability of pharmacological and non-pharmacological interventions, there is a lack of definitive effective treatments for PSCI. Non-invasive brain stimulation (NIBS), particularly intermittent theta burst stimulation (iTBS), has emerged as a promising therapy for ameliorating cognitive impairment post-stroke.

Method & Materials

A comprehensive search was conducted across multiple databases, including PubMed, Web of Science, Scopus, Cochrane Library, and CNKI, to identify relevant randomized controlled trials (RCTs) published before April 2023. The primary outcome measured changes in global cognitive scales, while the secondary outcomes focused on improvements in attention, orientation, visual-spatial perception, and activities of daily living.

Results

The meta-analysis encompassed six studies involving 325 patients. The results demonstrated that iTBS led to a significant improvement in global cognitive scales (SMD = 1.12, 95% CI = [0.59 to 1.65], $P < 0.0001$), attention (SMD = 0.48, 95% CI [0.13 to 0.82], $P = 0.007$), visual perception (SMD = 0.99, 95% CI [0.13 to 1.86], $P = 0.02$), and activities of daily living (SMD = 0.82, 95% CI [0.55 to 1.08], $P < 0.00001$). However, there was no significant effect on orientation (SMD = 0.36, 95% CI [-0.04 to 0.76], $P = 0.07$). Subgroup analyses based on the number of sessions were conducted, revealing a significant improvement in global cognition among patients with PSCI across the three categories (10 sessions, 20 sessions, and 30 sessions) with no between-group difference ($P = 0.28$). None of the included studies reported any serious adverse effects.

Conclusion

In conclusion, iTBS appears to be a safe and effective non-invasive treatment that can enhance the cognitive abilities and daily living skills of patients with post-stroke cognitive impairment. However, our conclusion is constrained by the limited number of studies. Further high-quality, large-sample RCTs with extended follow-up periods are necessary to validate these findings. Integrating iTBS with brain imaging techniques, such as functional MRI, could aid in elucidating the mechanism of iTBS action.

Visuospatial Memory in International Chess Federation-rated Chess Players: A Controlled Study.

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Introduction

The board game of chess encompasses multiple cognitive domains. It is thought to be predominantly a visuospatial endeavor, demanding adept analysis of the arrangement of pieces. The FIDE rating, a dynamic evaluation system, assesses players? performance and competitiveness, reflecting their overall standing in competitive chess. Here we aimed to determine the predominant memory facet in FIDE-rated chess players compared to non-chess players.

Method & Materials

Using a counterbalanced cross-sectional design, we evaluated visuospatial and verbal memory in 64 FIDE-rated chess players and 64 controls individually matched for age, sex, and education. All participants were 15 years or older and were native Sinhala speakers. They underwent standard neuropsychological assessment of visuospatial memory (Rey-Osterrieth Complex Figure test, ROCF) and verbal memory (the Sinhala version of the Rey Auditory Verbal Learning Test, RAVLT). General intelligence was also assessed using the Raven?s Progressive Matrices (RPM).

Results

Outcome measures, except RAVLT trial A3 and the learning rate, favored better performance in chess players. However, significant differences were observed only in RAVLT trial A6 ($p = 0.028$), A7 ($p = 0.031$), and retroactive interference ($p = 0.005$). In a subsidiary analysis, we noted a negative correlation between ROCF delayed recall and FIDE rating, and no significant correlation between RAVLT trial A7 and FIDE rating, even after adjusting for age and years of education.

Conclusion

Despite the hypothesis that chess predominantly engages visuospatial elements, our findings suggest that chess players have better memory in general (where verbal memory was significantly better, whereas any advantage in visuospatial memory was not significant). As evident in some previous studies, this could be attributed to chess improving visuospatial memory primarily in game-related scenarios, rather than leading to a general improvement in visuospatial memory. Additionally, it is also possible that visuospatial memory of chess positions is not the most critical factor for chess players. Simultaneously evaluating various other cognitive functions, particularly executive functions, alongside memory in future studies, will provide further evidence for the association between chess and cognitive functions.

Revealing Positive Perceptions and Accessibility Challenges in Virtual Reality Rehabilitation for Stroke Patients and Caregivers in Indonesia: A Qualitative Study

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Introduction

Stroke is one of the biggest global health issues, causing both short-term and long-term implications for affected individuals. The aftermath of a stroke often results in disability, emphasizing the critical need for effective rehabilitation strategies. Virtual reality (VR) is one of the recent treatment approaches developed for stroke rehabilitation. However, little is known about patients' perceptions of VR due to a lack of studies. Investigating how patients view and engage with VR is vital for improving VR and ensuring a patient-centered approach. This study aims to explore stroke patients' perceptions of virtual reality implementation and the potential for further development of VR in rehabilitation, particularly in Indonesia.

Method & Materials

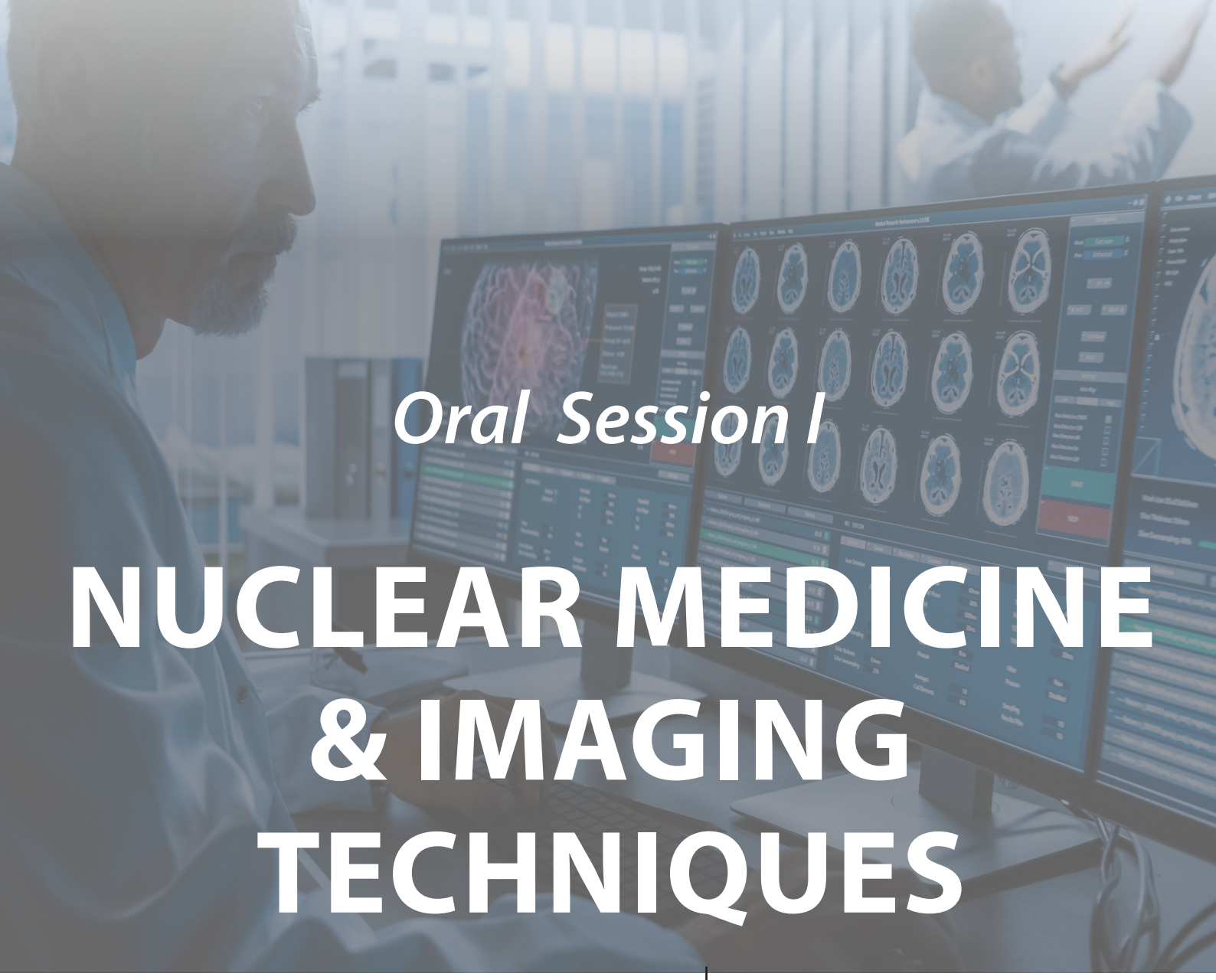
This is a qualitative descriptive study, utilizing interviews with patients undergoing rehabilitation at Universitas Indonesia's Hospital (RSUI) and their caregivers. Patients experienced a VR game specifically designed for rehabilitation, followed by interviews with a semi-structured approach. All data were audio-recorded and transcribed verbatim.

Results

A total of 10 stroke patients and 4 caregivers participated in the study. The collected data were analyzed to explore three main topics: perceptions of VR, accessibility to VR, and preferences and recommendations for VR. The majority of the patients reported positive feelings toward VR rehabilitation. Despite facing some challenges in adjusting the headset and pressing buttons, participants generally found VR convenient. They believe that VR is beneficial for hands' motoric training, memory training, and emotional support in stroke rehabilitation. The patients prefer traditional therapies over VR, but they see value in combining the VR for maximum benefit if it's freely available in the hospital. However, the high cost of purchasing VR alone is still a barrier. Suggestions for VR therapy include adding sensitivity options to VR controllers, expanding selection of the games and levels to involve more body movements, and enhancing safety measures for VR tools.

Conclusion

Stroke patients show positive perceptions toward VR rehabilitation, acknowledging its benefits for optimizing their rehabilitation. However, the high cost of VR equipment remains a significant obstacle in the accessibility of VR. To improve VR therapy, incorporating patient-centered modifications and ensuring affordability are crucial for optimizing its integration into stroke rehabilitation programs.



Oral Session I

NUCLEAR MEDICINE & IMAGING TECHNIQUES

Presenters:

- Zifan Sang
- Ali FathiJouzdani
- Tina Gabriel

Histogram Metrics of Contrast Clearance Analysis for Enhanced Glioma Genotyping

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Introduction

Little is known on the role of MRI contrast clearance analysis (CCA) in glioma genotyping and distinguishing glioma IDH and 1p/19q genotypes.To confirm whether the percentage of active tumor component and the histogram analysis of CCA, which could be acquired within a single scan additionally, correlate with IDH genotypes and 1p/19q codeletion, and to assess the proliferative activity in enhanced gliomas.

Method & Materials

This prospective study comprised 42 glioma patients who underwent preoperative delayed MRI. The histogram metrics, including mean, median, maximum, minimum, 10th percentiles (C10), 90th percentiles (C90), kurtosis, skewness, and variance were extracted from the blue and red regions in CCA map. A two-tailed Mann-Whitney U test was used for all two-group comparisons according to IDH genotype and 1p/19q codeletion status. Receiver operating characteristic curve analyses were undertaken to assess the diagnostic performance. The correlations between the Ki-67 labeling index and all CCA histogram metrics were evaluated by using the Pearson correlation coefficient. Statistical analysis was performed by using software (SPSS, version 26.0), and two-sided P values less than 0.05 were considered to indicate statistical significance.

Results

The proportion of blue lesions in the CCA was significantly higher in IDH wild-type and 1p/19q codeletion as compared to IDH mutation and 1p/19q non-codeletion. The histogram parameters of red and blue component in CCA differentiated IDH genotype with AUCs of 0.700-0.888. And the 90th percentile of blue/tumor region was the most useful metric. Collectively, the metrics of the blue region outperformed those of the red region in IDH genotype classification. The skewness of blue region showed a significant difference for predicting 1p/19q codeletion in gliomas. Significant correlations were identified between Ki-67 and histogram parameters of blue region (energy and kurtosis).

Conclusion

Collectively, the metrics of the blue region outperformed those of the red region in IDH genotype classification. Besides, the energy and kurtosis showed great potential in evaluating the proliferation activity of gliomas. CCA histogram parameters may represent in vivo biomarkers for predicting enhanced glioma isocitrate dehydrogenase and 1p/19q genotyping, and proliferative activity of glioma.

Machine Learning for Survival Time Prediction in Lung Cancer: The Application of CT-based Radiomics and Clinical Features

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Introduction

This study aims to predict overall survival (OS) time for lung cancer patients by combining clinical and imaging features. Clinical features describe the specific traits of each patient's disease, while imaging features show the cancer's behavior and progression. The study uses handcrafted radiomics (RF) with machine learning, to deal with the diverse and complex nature of lung cancer. The study hopes to enhance the reliability of OS predictions and suggest customized treatment plans for better patient outcomes.

Method & Materials

This study enrolled 199 patients with lung cancer who had both Computed tomography (CT) and clinical data from the Vancouver General Hospital. The study examined clinical features and their combination with 215 RFs that were obtained from tumors manually segmented using the standardized ViSERA software. Different types of clinical features, such as surgical, biopsy, clinical history, tumor staging, chemo and radiotherapy, and demographics information, along with RFs, were used to predict OS outcomes. The study used various machine learning methods that consisted of 3 feature selection methods (limited to selecting 20 relevant features) connected with 10 regression methods. The parameters of the regressors were fine-tuned using 5-fold cross-validation and grid-search methods. The data was divided into 80% for 5-fold cross-validation and 20% for external nested testing.

Results

In the CT-RF framework, the lowest mean absolute error (MAE) was 0.38Ò0.07 years for 5-fold cross-validation, with external nested test of 0.44Ò0.42 years in Matual info feature selection combined with Gradient boosting regressor (GBR). The clinical feature provided an MAE of 0.17Ò0.01 with external nested test of 0.42Ò0.11 by R-regression feature selection and Extra trees regressor. Adding clinical features to RF enhanced performance when both 5-fold cross-validation and external nested tests were used, resulting in an MAE of 0.1Ò0.03 by external nested test of 0.24Ò0.19 in F-regression feature selection and GBR. Recurrence status and weight loss were the most clinical features selected by machines for better prediction.

Conclusion

Our study showed that we could use clinical features integrated with imaging data to predict the survival time of lung cancer patients, and CT features combined with clinical features enhanced predictions.

Differentiation between low and high grades of steatosis using H-Scan, based on raw ultrasound data in a handheld device

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Co-authors: Chaghaneh O. (Omid), Naas A. (Antje), Herzog M. (Moritz), Hampe P. (Jochen), Fettweis P. (Gerhard)

Introduction

Handheld ultrasound presents a lightweight, globally accessible option for future medicine. Utilization of all frequencies in raw signals poses options for simple add-ons to these devices. An example for this is called H-Scan, the convolution of raw signal with Gaussian weighted Hermite-polynomials of the n-order (GHn). The filtering of low (GH2) and high frequencies (GH8), enables the differentiation of small and large scatterers. This could help staging pathologies like steatosis, one of the leading pathologies among western population, in which fat vacuoles accumulate in the cells thereby changing the scatter size. Up to date, staging of liver steatosis often relies on Fibroscan?, an unwieldy and time-consuming device. This study therefore explores quantification of liver steatosis with handhelds based on H-scan analysis. It is aimed to differentiate low CAP (value < 248 dB/m) and high CAP (value > 280 dB/m) using the ratio of GH8/GH2.

Method & Materials

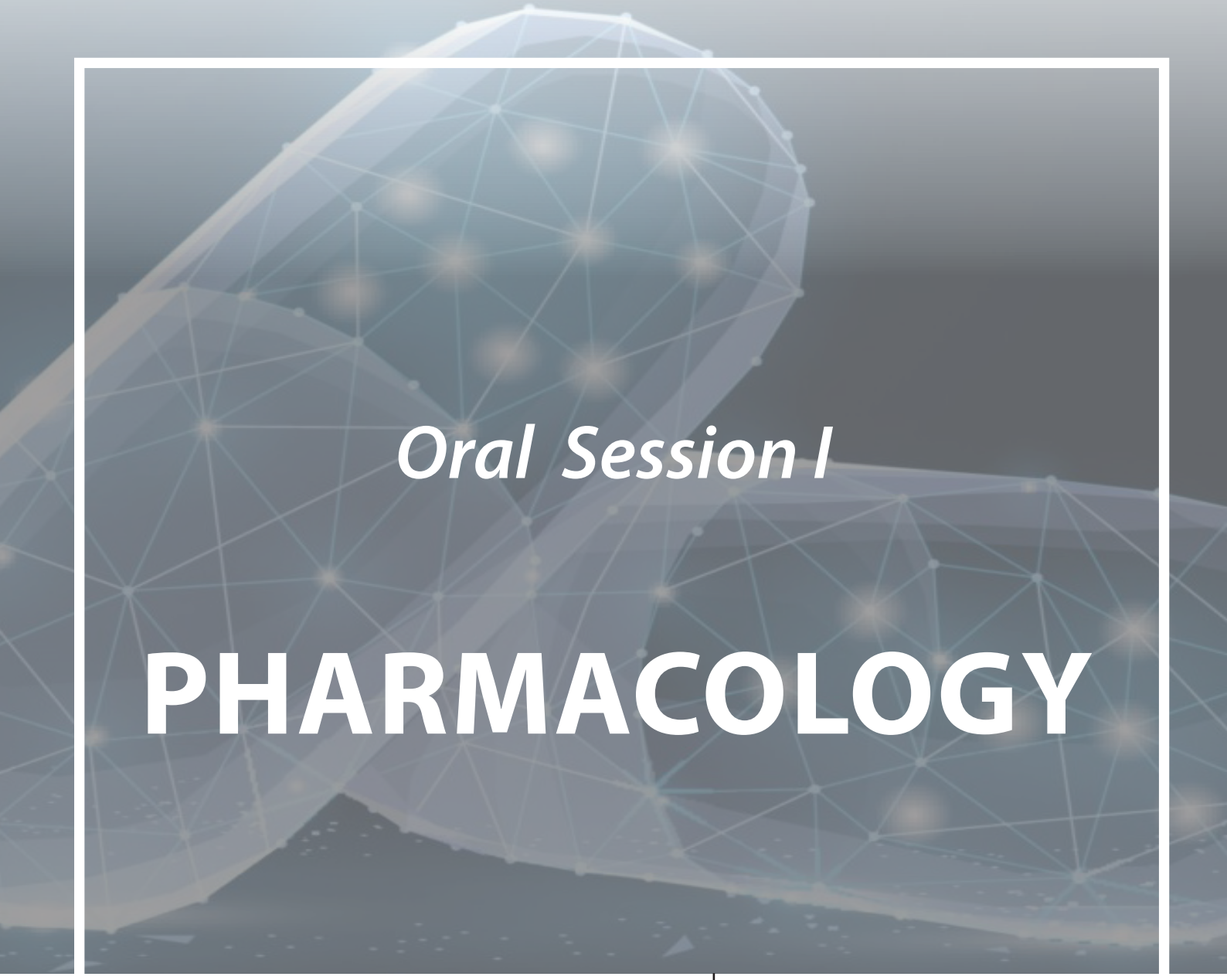
388 patients undergoing sonographic liver examination at the University Hospital Dresden were involved. The CAP value of Fibroscan? and raw data of two handheld devices (Clarius HD3C3, 2-6MHz and HD3L15, 5-15MHz) were recorded. H-Scan analysis was conducted by: 1. Defining the gaussian weighted hermite polynomials as filters 2. Applying the filters through convolution 3. plotting the result in a logarithmic RGB coded image with blue encoding GH8 and red encoding GH2. Border for outliers was defined beyond by 2 standard deviations. The resulting GH8/GH2-ratios were compared between patients showing low and high CAP levels using the Mann-Whitney-U-Test.

Results

A total of 280 patients were enrolled. After analysis of data 139 subjects were included in low CAP and 126 in high CAP group. A significant difference ($p<0.05$) was found between low CAP and high CAP for GH8/GH2-ratio in the L15 probe. There was no significant difference of GH8/GH2-ratio for the C3 probe.

Conclusion

This study demonstrates the differentiation between high and low CAP values as a surrogate for severity of liver steatosis, using H-Scan. Considering the limited availability of FibroScan?, H-Scan inside a simple handheld device might offer an alternative tool. Future research may extend the application of H-Scan to assess liver fibrosis and focal lesions.



Oral Session I

PHARMACOLOGY

Presenters:

- Mahsa Fakhraee
- Taravat Hedayati
- Gabriela Jesus
- Levon Kharatyan
- Wiktor Kruczek
- Melika Naji

Evaluation of Antinociceptive and Antioxidant Activities of Carvacrol in Alloxan-induced Diabetic Mice

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Co-authors: Shokrzadeh M. (Mohammad), Zamani E. (Ehsan)

Introduction

Introduction: Diabetes, a prevalent metabolic disorder, is widespread across many countries. One of the major complications of this condition is neuropathy, primarily characterized by hyperalgesia. There is a broad consensus that oxidative stress significantly contributes to the development of diabetic neuropathy. Carvacrol, known for its potent antioxidant properties, may have the potential to mitigate oxidative stress. This study aims to explore the effects of carvacrol on reducing brain oxidative damage and hyperalgesia in diabetic mice.

Method & Materials

Methods: In this experiment, thirty-six mice, weighing between 20 to 25 grams, were allocated into six groups (n=6): control, diabetic, and diabetic treated with Carvacrol at dosages of 50, 25, and 100 mg/kg, along with a group receiving vitamin E at 200 mg/kg. Diabetes induction was achieved through the intraperitoneal injection of 200 mg/kg alloxan. Following a six-week treatment period, nociceptive behavior in the animals was evaluated using two methods: the formalin test (0.5%) and the hot plate test. Additionally, this study measured the lipid peroxidation index, glutathione levels, and protein carbonyl content in the brain tissue of the mice.

Results

Results: The hot plate test and formalin injection in the paws of diabetic mice revealed a significant reduction in pain threshold compared to the control mice ($P<0.01$). Treatment of diabetic mice with Carvacrol effectively reduced this index, bringing it to levels comparable to those of non-diabetic mice ($P<0.05$). Additionally, there was an observed increase in lipid peroxidation and protein carbonyl content, coupled with a decrease in glutathione levels, in the homogenized brain tissue of diabetic mice relative to the control group. The administration of Carvacrol to diabetic mice moderated these indices, indicating a potential therapeutic effect.

Conclusion

Conclusion: The findings of this study highlight the role of oxidative stress in the development of hyperalgesia in diabetes. Moreover, Carvacrol, with its antioxidant properties, demonstrates the capability to alleviate pain in both acute and chronic stages, as well as reduce oxidative damage in diabetic mice. This suggests the potential therapeutic efficacy of Carvacrol in managing neuropathic pain associated with diabetes.

Exploring NaTxAK: A Novel Scorpion Toxin Targeting Sodium Channel 5-1 with Therapeutic Potential

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Introduction

The lethality of scorpion toxins has recently attracted significant scientific attention for potential therapeutic applications. There has been recognition that scorpion toxins may target voltage-gated sodium channels, particularly sodium channel 5-1, to treat various diseases, such as autoimmune disorders and cancer. In this study, a novel toxin with the potential to block sodium channel 5-1 was identified, extracted, and analyzed from one of Iran's deadliest scorpions named Odontobutous doriae.

Method & Materials

The research methodology involved the identification of toxins similar to Lqh-_IT in Odontobutous doriae. Sequencing-specific primers were developed to extract the toxin's coding gene, which were then cloned in bacteria and sequenced. Comparative analysis assessed the toxin's sequence identity with Lqh-_IT and its similarity to other toxins, focusing on alpha toxins. Its potential interaction with sodium channel 5-1 was investigated using bioinformatics.

Results

A novel toxin named NaTxAK was identified and characterized, whose sequence has a substantial 69% similarity to Lqh-_IT. In addition, NaTxAK showed a significant 76% sequence similarity to NaTx11, a related toxin from Odontobutous doriae. NaTxAK is highly similar to alpha toxins, and bioinformatics analysis indicates its potential to interact with sodium channel 5-1's inactivation gate. As a result of these findings, it seems that the toxin can effectively block this channel, thereby opening up possibilities for medical application.

Conclusion

Hence, the present study has identified NaTxAK, which shows potential for therapeutic intervention as a toxin closely related to Lqh-_IT. Its sequence identity to Lqh-_IT and its potential to block sodium channel 5-1 positions it as a valuable candidate for treating autoimmune diseases and cancer. Similar to alpha toxins in insects, it might be a potential pesticide. The discovery highlights scorpion toxins' versatility in medical and agriculture, offering new research opportunities.

Mesenchymal stem cell and empagliflozin treatment regulatory actions on the expression of mouse kidney-derived c-Kit stem cell population

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Albert Einstein Israeli College of Health Sciences
Brasil

Introduction

Diabetes mellitus affects 1 in 10 adults worldwide. Approximately 30%-40% of diabetics develop diabetic kidney disease (DKD). Metabolic changes such as glomerular hypertrophy, tubulointerstitial inflammation, and fibrosis constitute its pathophysiology. Thus, mitigating the occurrence of these changes compounds the search for new treatments. Empagliflozin is a renal sodium-glucose cotransporter 2 inhibitor and one of the available therapies that reduces tubular reabsorption of glucose, promoting better glycemic control and fluid overload, as well as a lower oxidative stress environment. Mesenchymal stem cells (MSC) treatment is an emerging therapy, whose reparative and immunomodulatory behavior is combined with anti-oxidative, anti-fibrotic and anti-apoptotic effects. The clonogenic, multipotent, and self-renewal capacity of kidney cell populations that present the c-Kit+ proto-oncogene has been proven. However, studies in animal models are seeking to establish its potential for recovering damaged kidney tissue. We aimed to verify whether MSC-based cell therapy or empagliflozin modulate the c-Kit+ cell population in the kidney of diabetic and obese BTBR ob/ob mice.

Method & Materials

We included four groups of male BTBR ob/ob mice (n=6 animals/group) according to treatment: (a) BTBR ob/ob animal with no treatment, (b) wild-type BTBR animal with no treatment, (c) BTBR ob/ob animal on empagliflozin treatment, and (d) BTBR ob/ob animal on MSC treatment. At 10, 14, and 20 weeks, animals from each group were euthanized for tissue sample collection. We performed immunohistochemical (IHC) analysis and quantification using CellSens (Olympus) software. Quantitative PCR is ongoing. We used two-way ANOVA, considering the variables of time and treatment. $P<0.05$ was considered significant.

Results

Preliminary results indicate an increase in the detection of c-Kit+ cells in distinct compartments after MSC and empagliflozin therapies, including Henle?s loop, distal tubules, and collecting ducts, but not in proximal tubules. Strikingly, c-kit cells were found within the glomeruli. The two-way ANOVA analysis revealed a significant p-value for the treatment variable in the cortex and medulla (p-value=0.0001 and 0.0133 respectively), but not for the time variable.

Conclusion

MSC-based cell therapy and empagliflozin can regulate the c-Kit+ stem cell pool within the mouse kidney, indicating important biological properties.

Novel molecular framework generation approach to identify PLK1 selective inhibitors

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Introduction

Molecular frameworks (a combination of ring systems and linkers in the molecule) are useful representations of molecules for drug design and discovery applications, such as fragment-based drug design and structure-activity relationship models. Molecular frameworks can act as a seed for medicinal chemists to create new ideas for identifying a drug candidate. PLK1 is an attractive target for drug discovery as it has been pre-clinically validated as an anticancer target. Also, evidence shows that PLK2 and PLK3 act as tumor suppressors through their functions in the p53 signaling network. Thus, desired molecules need selectivity against the PLK1. Thus, we have developed a framework generator that identifies promising scaffolds from databases of molecules with examples on PLK enzymes.

Method & Materials

The first step of the algorithm is to generate Bemis-Murcko scaffolds for the molecules of a given database. Next, the molecules are clustered with a Butina clustering algorithm based on Tanimoto similarity. All pairwise most common substructures within each cluster are determined, and their frequency (Score = Count of generated Framework/Count of generated all Frameworks) within the group is calculated. The implementation also can identify the most common frameworks between multiple databases. Databases of active molecules against PLK enzymes were retrieved from the ChEMBL.

Results

Compound databases targeting PLK1, PLK2, and PLK3, have 26,001, 564, and 1,336 unique compounds correspondingly. After framework grouping, there are 124, 15, and 19 groups for compounds correspondingly. In the PLK1-targeting framework groups, 94.35% of the frameworks are not present in PLK2 and PLK3 databases, while 1.38% of the frameworks overlap across all three group frameworks. Some of PLK1-targeting frameworks, like 1,2,3-oxathiazinane-2,2-dioxide or 4-(4-phenyl-4H-1,2,4-triazol-3-yl)morpholine; demonstrated score 1.0, suggesting their selectivity.

Conclusion

We have developed an advanced framework generator that can be utilized for drug discovery and the analysis of compound databases. The algorithm can be used to identify promising ideas for the development of drug candidates. The algorithm was tested on compound databases targeting PLK enzymes to find potentially selective scaffolds.

Bimekizumab ? efficacy and safety in the treatment of psoriasis. Are biologics the future of dermatological pharmacotherapy?

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Introduction

Psoriasis known as a chronic systemic inflammatory disease leads to uncontrolled keratinocyte differentiation and proliferation. Affects up to 3% of the population worldwide, does not only compound patients? quality of life but also is associated with comorbidities such as psoriatic arthritis, inflammatory bowel disease and depression. Increasing understanding of the molecular pathogenesis of psoriasis has escalated the development of targeted biological treatments. Bimekizumab is the newest humanized, monoclonal IgG1 antibody that selectively inhibits interleukin-17A and interleukin-17F. The aim of the study was to evaluate the safety and efficacy of bimekizumab in psoriasis treatment.

Method & Materials

Patients meeting the drug programme criteria for the treatment of moderate to advanced psoriasis with bimekizumab were included in the study ? failure of two previous therapies and PASI >10 (Psoriasis Area and Severity Index). From July 2023 14 patients have been included to the cohort. Bimekizumab has been administered subcutaneously at a dose of 320 mg every 4 weeks. PASI, BSA (Body Surface Area) and DLQI (Dermatology Life Quality Index) have been evaluated before every administration. Statistical analysis were conducted. Observation is still pending.

Results

The median age was 45,1 years (range, 19-73 years) with 78,6% men and 21,4% women. 2 patients have concomitant psoriatic arthritis. Average chronicity of the psoriasis in all patients equals 16,86 years. 85,71% of patients underwent treatment with cyclosporin A, 78,57% with methotrexate and 57,14% with acitretin without positive clinical outcome. Before first bimekizumab dose the mean PASI was 15,63, BSA yielded 22,32 and DLQI 20,1. After first bimekizumab administration PASI-75 (75% or more PASI reduction from baseline) has been achieved by 92,86% of patients. 85,71% of patients? DLQI score reduced to 0, 14,29% patients from the study group have moderately reduced quality of life (DLQI range 6-10). No significant side effects were observed in patients. Further analysis is pending.

Conclusion

Bimekizumab exhibited good tolerance, safety profile and fast clinical response in psoriasis treatment. Convenient posology assures patient?s adherence to medication which is connected with long-term efficacy. The preliminary results suggest that biological systemic therapy with bimekizumab could provide remission and significantly improve quality of life.

The comparative efficacy of bentonite and sodium polystyrene sulfonate in acute lithium toxicity in animal study

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Introduction

Lithium poisoning is a major concern owing to its narrow therapeutic index. Treatment approaches, including sodium polystyrene sulfonate (SPS, cation-exchange resin), which is restricted due to its hypokalemia and activated charcoal (AC), are ineffective. Bentonite is the best-known clay and a long-forgotten adsorbent. This study aimed to evaluate the potential effects of bentonite as a novel gastrointestinal absorbent on the reduction of serum lithium levels by comparing it with AC and SPS.

Method & Materials

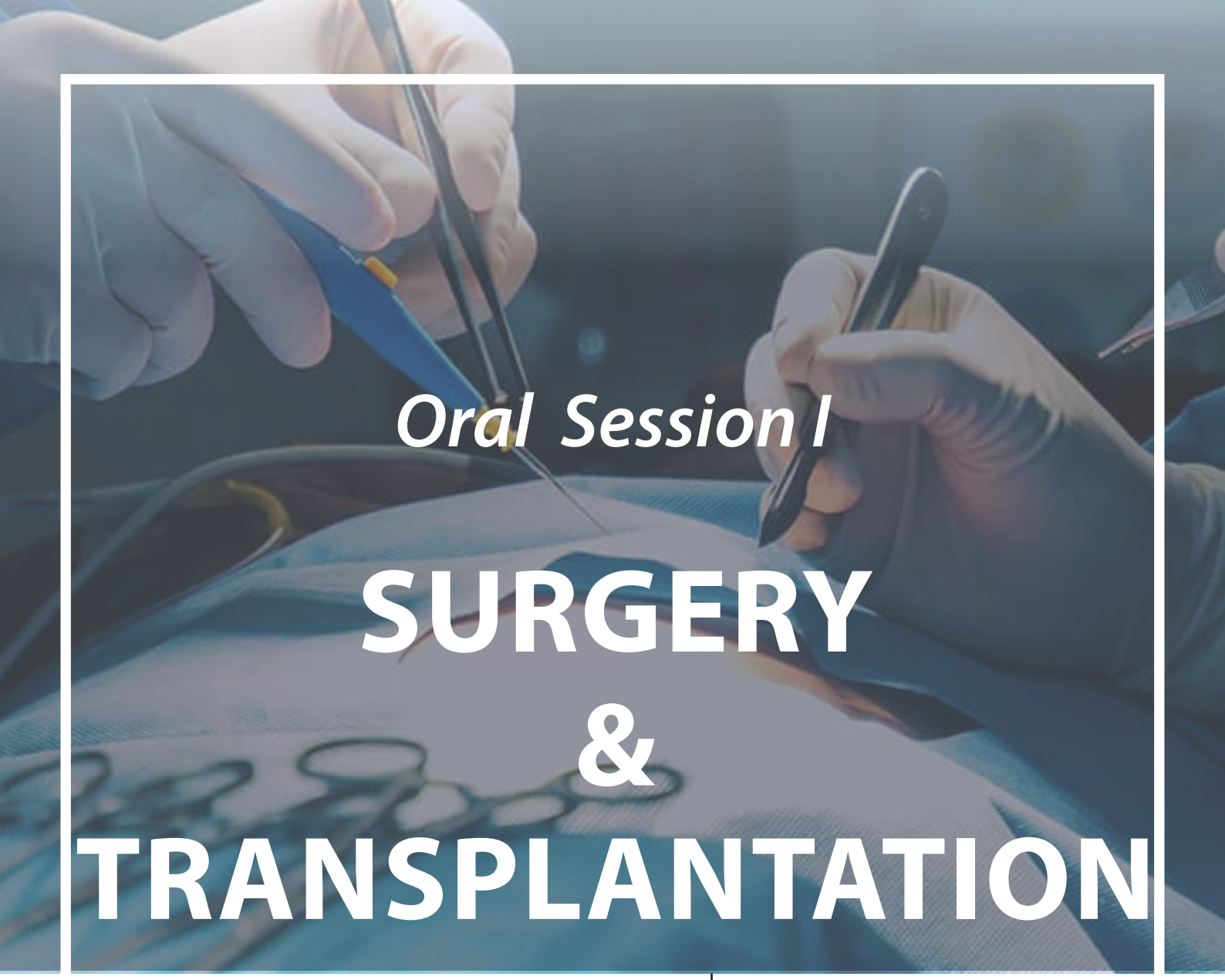
We developed an acute poisoning model by oral administration of lithium carbonate (400 mg/kg) in male Wistar rats (n=30), followed by oral gavage with 1 g/kg bentonite, SPS, and AC. Hematological and biochemical parameters including serum Li, WBC, neutrophil counts, and Na+ and K+ levels were evaluated. Motor coordination and strength were determined using the Rotarod, the Grip strength, and locomotor activity tests. All tests were performed 2 and 24 hours after treatment. A repeated-measures model was performed using RStudio software, followed by Tukey?s HSD for parametric and Aligned Rank Transform for nonparametric tests.

Results

The results indicated that administration of bentonite ($p<0.01$) and SPS ($p<0.05$) significantly reduced the serum lithium levels. Moreover, both resins showed similar effects ($P=0.9967$). In addition, AC did not reduce the lithium concentration ($P=0.99$). Surprisingly, leukocytosis, which occurs during lithium toxicity, did not correlate with serum lithium concentration. Therefore, the analyses broadly supported the insignificant differences in the WBC and neutrophil counts. Bentonite did not cause any electrolyte abnormalities but SPS reduced K+ levels in comparison with bentonite ($p<0.001$). According to the behavioral tests, both absorbents improved coordination and balance ($P<0.001$) compared with lithium and AC. Furthermore, there were insignificant differences between the bentonite and SPS.

Conclusion

These results reveal that bentonite clay can compete with SPS without significant side effects, such as hypokalemia. Although further analyses are needed, these findings provide a step forward towards a good candidate for lithium gut decontamination and a possible substitute for other similar substances that are not well absorbed, such as AC.



Oral Session I

SURGERY & TRANSPLANTATION

Presenters:

- Łukasz Banaszek
- Felipe Gonçalves
- Kexi Liao
- Sabrina Stimmeder

The influence of body dysmorphic disorder on perception patterns of own and model faces - A cross-sectional eye-tracking study

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Co-authors: Rudziska M. (Monika), Wojtkiewicz M. (Marta), Krysiak P. (Piotr), Stachura A. (Albert), Paskal W. (Wiktor)

Introduction

Body dysmorphic disorder (BDD) is a mental health condition centered around excessive concerns about self-image, impacting approximately 15% of plastic surgery patients. The influence of BDD on perceptual patterns related to one's own or others' bodies is poorly understood. This study aimed to investigate whether positive BDD screening, using the Body Dysmorphic Disorder Questionnaire (BDDQ), influences the perception of the human face.

Method & Materials

Participants were recruited from a Psychotherapeutic Clinic of the Institute of Psychiatry and Neurology, Warsaw, Poland, where stable patients with mixed personality disorders were hospitalised (28 patients). This cohort was chosen due to a likely high prevalence of BDD. Moreover, 51 medical students volunteered to take part. Firstly, all participants completed the BDDQ. Next, a facial photography was taken of those who consented. Then, participants were asked to look at the computer screen displaying standardised photographs of model male and female faces, as well as their own ? all in frontal and lateral view. An eye-tracking device was used to collect data on gaze fixation patterns using pre-determined areas of interest (AOIs) encompassing key facial structures.

Results

Of 79 participants (60.8% females), 18 (22.8%) screened positive for BDD. In general, participants focused most frequently on nose (21.8Ò13.9%), eyes (20.9Ò13.8%) and eyebrows (19.2Ò13.8%). Compared to same-sex model faces, participants spent more time looking at their own chin (3.9%Ò6.2% vs 1.9Ò3.3%, p=0.01) and cheeks (9.6Ò9.3% vs 6.6Ò7.3%, p=0.014). Surprisingly, BDDQ screening result did not influence perception patterns of either self or model faces. Moreover, Bland-Altman plots revealed broadly overlapping levels of agreement between perception patterns of self and same-sex model face for each AOI when both BDDQ groups were compared. Total number of fixations, their mean duration and frequency were similar for those who screened positive and negative for BDD. However, participants from the heterogenous psychiatric cohort had higher total fixation counts (74.9Ò15.8 vs 34.3Ò5.1, p<0.001), more frequent (5.74Ò1.2 vs 2.64Ò0.4 fixations/second, p<0.001) and shorter (118.8Ò19.7ms vs 193.8Ò43.6ms, p<0.001) fixations than students.

Conclusion

Positive screening for BDD is not associated with significant alterations in facial perception patterns. BDD may be associated with distorted stimuli processing rather than altered perception.

Unlocking the Potential: Adipocyte Stem Cells and their Impact on Reducing Inflammation in Silicone Implant Capsules

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Introduction

Breast reconstruction offers various options, and one of them involves the use of silicone prostheses. Following immediate breast reconstruction surgery, some patients undergo radiotherapy, but approximately 80% may encounter capsular contracture. Among the numerous strategies to address this issue, stem cells have shown promising outcomes. This study aims to evaluate the impact of adipocyte stem cells (ASC) in the treatment of silicone capsular contracture.

Method & Materials

We analyzed 30 female Rattus norvegicus weighing 200?250g. All the animals were undermined by mini-silicone prosthesis implanted in the dorsal region. The rats were divided into three groups: the control group (receiving saline solution injection in the surrounding tissue of the silicone implant), the radiotherapy group (RDT), and the radiotherapy + adipocyte stem cell (ASC) injection group. After three months, we performed a macroscopic analysis. Furthermore, capsule samples were collected and subjected to histological analysis using H&E staining, evaluating inflammatory cell counting, vascular density and collagen fibers. Additionally, we analyzed the gene expression of TNF_alpha 1, IL-1, CD-68, IL-10, MMP-3, and MMP-9 through Real-Time Polymerase Chain Reaction (qRT-PCR).

Results

In the macroscopic analysis, the Radiation Therapy Oncology Group (RTOG) Score revealed a 2-point reduction in the ASC group compared to the RDT group. Histologically, the ASC group exhibited less than 50% of inflammatory cells compared to the RDT group, resembling the reaction observed in the control group. Interestingly, this study demonstrated that the IL-1 rap gene expression was comparable between the RDT and ASC groups. In comparison to the control group, the ASC treatment led to a 30% reduction in IL-1 rap, although no significant difference was observed. Additionally, CD-68 and MMP-3 levels were similar in the control and ASC groups, without significant distinctions.

Conclusion

The findings of this study suggest that treatment with adipocyte stem cells (ASC) can reduce inflammation reaction of silicone prosthesis capsules post radiotherapy.

Laparoscopic Anatomic Versus Non-anatomic Hepatectomy in the Treatment of Hepatocellular Carcinoma: A Randomised Controlled Trial

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Introduction

The choice of surgical modality for laparoscopic hepatectomy for hepatocellular carcinoma (HCC) has not been supported by high level of medical evidence hitherto. A prospective randomized controlled trial was conducted to compare the perioperative and follow-up outcomes of patients with HCC treated by laparoscopic anatomic hepatectomy (LAH) and non-anatomic hepatectomy (LNAH) .

Method & Materials

Between March 2013 and Jan 2018, eligible patients undergoing LAH and LNAH were enrolled and divided randomly into LAH group and LNAH group in this study. The perioperative and follow-up outcomes of both groups were compared and analyzed.

Results

A total of 385 patients with HCC were randomly divided into LAH (n=192) and LNAH (n=193) groups. The groups were evenly matched for age, sex, liver background, segment involvement, tumor size, Child-Pugh grade and preoperative liver function. The operative time in LAH group was longer than that of LNAH group ($p = 0.003$). No significant between-group differences in intraoperative blood loss ($p = 0.368$), transfusion rate ($p = 0.876$), conversion to laparotomy rate ($p = 0.365$), overall complication rates ($p = 0.054$) were observed. The 1-year, 3-year and 5-year overall survival rates (OS) in LAH group were 91.1%, 67.2%, 43.2%, respectively. The corresponding data in LNAH group were 89.1%, 63.7%, and 35.2% respectively. No significant difference was observed with regard to the 5-year OS rate ($p = 0.054$) between the two groups. The 1-year, 3-year and 5-year disease-free survival (DFS) rates in the LAH group were 87.0%, 54.7%, 33.9%, respectively. The corresponding data in LNAH group were 70.5%, 34.7%, and 30.1%, respectively. The 5-year DFS rate in LAH group was significantly higher than that in LNAH group ($p = 0.009$).

Conclusion

LAH versus LNAH for selected HCC patients was associated with increased DFS, lower intrahepatic ipsilateral recurrence rate, comparable long-term OS and postoperative complications. LAH is therefore recommended for selected HCC patients. Registration number: NCT02009176 (https://www.clinicaltrials.gov/).

Cytokine adsorption during subnormothermic liver perfusion potentially reduces cytokine levels and inflammation

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Introduction

Ex vivo machine perfusion methods have emerged as a promising tool for organ preservation, reconditioning and repair. However, the underlying process triggers inflammatory processes. Especially ECD grafts are more vulnerable. An approach to counteract the release of cytokines and thus mitigate the inflammatory response, is the inclusion of an adsorption device into a machine perfusion circuit. Furthermore, cytokines may be promising as additional biomarkers for graft assessment.

Method & Materials

In the first experiment cytokine dynamics of porcine ECD (n = 6) and healthy (n = 4) liver grafts were evaluated during machine perfusion. The feasibility and effect of cytokine adsorption was assessed in a follow-up experiment by connecting the CytoSorb? adsorber to the circuit and perfusing additional livers either with (n = 5) or without (n = 3) this adsorber. All liver grafts were subject to 24 h static cold storage and subsequently perfused for 24 h in a subnormothermic oxygenated perfusion circuit. Throughout perfusion perfusate was collected for analyzing perfusion parameters (pH, glucose, lactate) and snap frozen for post hoc assessment of liver function and cytokine levels. Tissue biopsies were taken every 3 h and bile production measured throughout perfusion.

Results

Baseline cytokine levels (IFN-gamma, IL-10, IL-12, IL-18, IL-1alpha, IL-1beta, IL-1ra, IL-2, IL-4, IL-6, IL-8, MMP1, TNF-alpha) were comparable in all healthy liver groups. ECD grafts showed higher levels of pro-inflammatory cytokines after 24 h static cold storage. Levels of pro-inflammatory cytokines IL-1alpha, IL-1beta, IL-12, IL-18 increased over time in ECD and healthy livers and were significantly higher in the ECD livers from 6, 24, 1 and 1 h of perfusion onwards, respectively. Calgranulin levels were significantly higher in the ECD grafts. Overall perfusion performance in terms of glucose metabolism and lactate clearance was comparable in both groups. The inclusion of an adsorption device resulted in lower levels of both pro- and anti-inflammatory cytokines. Especially, levels of IL-12 but also MMP-1 were significantly lower in the adsorption group throughout perfusion. Bile production was numerically higher in livers perfused with the CytoSorb?. Over time all machine perfusion performed showed a tendency towards rising cytokine levels.

Conclusion

These preliminary results provide insight into cytokine dynamics of ECD and healthy liver grafts during subnormothermic machine perfusion. Especially, long term machine perfusion of 24 hours increased pro-inflammatory cytokine levels. The inclusion of an adsorption device is feasible and has the potential to not only reduce elevated cytokine levels but also optimize organ performance. Thus, further investigations on cytokine adsorption during ECD graft perfusion may offer additional insights into cytokine dynamics.

Oral Session II

IMMUNOLOGY

Presenters:

- Zaniar Farhang
- Irakli Khuntsaria
- Weinian Liao
- María Sánchez-Blázquez
- Juan-Francisco Silva Agüero

RA-EnsemblePrognosis: Predictive Modeling for Individualized Arthritis Care

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Iran

Introduction

Rheumatoid arthritis (RA) presents a complex challenge in treatment due to its varied response to medications among patients. This study aims to estimate drug response in 500 RA patients by analyzing extensive parameters encompassing demographics, disease markers, joint information, drug details, and blood test results.

Method & Materials

Ensemble learning techniques, including CatBoost, LightGBM, and XGBoost, were employed iteratively and for stacking to create a predictive model. The study utilized SHapley Additive exPlanations (SHAP) to aid in feature selection. The ensemble model utilized gradient boosting algorithms, with CatBoost and LightGBM repeated twice and XGBoost once as base models. XGBoost was used as the meta-model for stacking. The response metric was based on monitoring the decrease in Disease Activity Score (DAS28) over a 9-month period.

Results

The ensemble model demonstrated exceptional predictive performance specifically on the subset of 150 patients, achieving 92% accuracy on the test set and 89% accuracy in cross-validation. Additionally, ROC analysis indicated an AUC of 0.94, demonstrating the model's capability in understanding drug response. Crucial features impacting drug response, identified using SHAP, included ESR, hemoglobin levels, RF, anti-CCP, and ANA. These factors explain the relationship between specific markers and treatment outcomes in RA. The classifications based on DAS28 changes aligned with response categories: Û 0.6 for "No Response," 0.6 < ? Û 1.2 for "Moderate Response," and ? > 1.2 for "Good Response."

Conclusion

The ensemble approach, combining multiple iterations of CatBoost, LightGBM, and XGBoost as base models and leveraging XGBoost for stacking, refined through hyperparameter tuning and feature selection, provides valuable insights into personalized treatment strategies for RA. This research signifies a significant leap in modeling for RA therapy, laying the groundwork for tailored interventions and improved treatment outcomes.

The immunosuppressive nature of neutrophils and novel indicators of neutrophil behavior

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Introduction

Neutrophils play diverse roles in diseases such as infectious, metabolic, autoimmune, and aging-associated conditions. While their pathological effects are extensively studied, further exploration of their immunosuppressive role, marked by reduced response to chemokines and inhibition of T cell immunity, is needed. Identifying the key determinant of neutrophil activity is crucial for this investigation, with human neutrophil lipocalin (HNL) being a potential candidate due to its association with neutrophil presence and secretory activity. Understanding the functional responsibility of neutrophils requires considering the status of other immunocompetent cells. The cytokine-specific G-protein coupled receptor CXCR3, expressed by T and B lymphocytes and NK cells, is of interest due to its evolutionary significance and its role in controlling neutrophil-mediated severe pulmonary inflammation.

Method & Materials

Our study aimed at the quantitative determination of NGAL and CXCR3 in peripheral blood samples of 200 participants via the ELISA method. The number of participants includes 50 patients with acute respiratory infection, 50 patients with clinically documented COVID-19 (recovered), 50 oncology patients, and 50 donors (as a control group).

Results

According to our data CXCR3 levels remain stable across acute respiratory infections, including COVID-19, suggesting consistent expression during infections. Within acute respiratory infections, subgroup identification implies heterogeneity, possibly reflecting diverse infection stages or types. In COVID-19, lower HNL levels compared to general respiratory infections may indicate a unique inflammatory response or neutrophil activation. Donors exhibit higher HNL levels than COVID-19 patients, suggesting elevated baseline neutrophil activity. CXCR3 levels in donors are stable, mirroring patterns seen in acute respiratory infections and COVID-19 groups. Oncology patients show CXCR3 and HNL levels similar to acute respiratory infections, suggesting shared inflammatory or immune responses. Prostate cancer patients exhibit higher CXCR3 and HNL levels than breast and colorectal cancer patients, indicating distinct immune responses in prostate cancer.

Conclusion

we presume that neutrophil activation, characterized by elevated HNL levels, might be immunosuppressive for cells expressing CXCR3 receptors. This proposed immunosuppressive role of neutrophils may potentially prevent the development of a cytokine storm. Our findings align with the evolving understanding of neutrophil functions, although further investigations are required to determine the neutrophil-induced immunosuppressive mechanisms.

Aged hematopoietic stem cells entrap regulatory T cells to create a prosurvival microenvironment

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Co-authors: Ye L. (Lilin)

Introduction

Immune cells constitute the majority of cells surrounding hematopoietic stem cells (HSCs) in the bone marrow (BM), it appears likely that HSCs are more readily to take their cues from immune cells under physiopathological conditions including aging. Despite that the promotive roles of innate and adaptive effector cells in HSC aging have been well documented, there is almost no evidence regarding the role of immunosuppressive components of immune cells in stem cell aging.

Method & Materials

Mouse models of pathological and physiological premature aging were built by using mice exposed to radiation and at middle age. Phenotypes and functions of HSCs and regulatory T cells (Tregs) were determined by flow cytometry and multi-omics analysis. HSC?Treg interaction was determined by coculture and adoptive transfer systems. Comparisons between two groups were determined by Student?s t-test. Three or more groups were compared by one-way ANOVA. $P < 0.05$ was considered statistically significant.

Results

Both mouse models exhibited features of HSC aging including expansion, impaired reconstitution capacity, and myeloid-biased differentiation, accompanied by exclusive clonal expansion and TCR activation of Tregs in the BM. Meanwhile, a distinct and dramatic upregulation of MHCII probably provoked by DNA mutation accumulation was detected on aged HSCs. Then, bidirectional interaction established between aged HSCs and BM Tregs via MHCII?TCR engagement, by which BM Tregs were expanded through TCR recognition of MHCII on aged HSCs whereas the apoptotic priming of aged HSCs was diminished through gap junction (GJ)-mediated transfer of cyclic adenosine monophosphate (cAMP) from BM Tregs. Importantly, targeting HSC?Treg interaction by depleting Tregs or intervening GJ with inhibitors prevented HSC aging from an early age.

Conclusion

This study identifies an active self-protective mechanism for aged HSCs to obtain clonal advantage by entrapping local Tregs to construct a pro-survival niche. These findings not only afford promising candidates to extend human hematopoietic health span, but also extend our understanding of the non-canonical regulatory roles of Tregs in stem cell homeostasis.

The TBK1 inhibitor amlexanox has the potential to become a therapeutic option for systemic autoimmune diseases

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The Netherlands
Co-authors: Bjîrk A. (Albin)

Introduction

Systemic autoimmune diseases such as systemic lupus erythematosus (SLE), primary Sjîgren?s syndrome (pSS) and systemic sclerosis (SSc) have as hallmark increased systemic levels of type I interferon (IFN-I) and B-cell hyperactivation. TANK-binding kinase 1 (TBK1) is an important signaling hub which controls production of IFN-I, and therefore constitutes a potential therapeutic target. Amlexanox is a TBK1 inhibitor which has been used to treat aphthous ulcers and asthma. The aim is to determine the capacity of amlexanox to inhibit IFN-I and to determine potential direct effects of the drug on B-cells.

Method & Materials

Inhibiting effects of amlexanox on IFN-I pathway activation was assessed using qPCR of the IFN-I stimulated gene MX1 in PBMC cultures. Intracellular amount of phosphorylated TBK1 (pTBK1) in peripheral B-cells was assessed by phosphoflow. Blood-derived CD19+ B-cells from patients and healthy controls (HC) were co-cultured in vitro on CD40L-expressing NIH3T3 fibroblasts together with IL-21 to simulate germinal center-like conditions. Cultures containing various concentrations of IFN-I, BAFF, and amlexanox, were established for 6 days. Proliferation was quantified by CellTrace staining. Differentiation was assessed using spectral flow cytometry. Cell supernatants were collected for IgG and IgM measurement by ELISA.

Results

MX1 expression was significantly decreased by amlexanox in patients with systemic autoimmune diseases compared to HC (childhood-onset SLE (cSLE): $p=0.0001$, SLE: $p=0.0159$, pSS: $p=0.0051$, SSc: $p=0.0052$). Analyzing CD20+ B-cells, CD27+IgD- switched memory B-cells, CD27+IgD+ unswitched memory B-cells and CD27-IgD+ naãve B-cells, a trend of higher pTBK1 levels was observed in SLE compared to HC. Amlexanox decreased B-cell differentiation into antibody secreting cells (ASCs) using both HC and SSc samples (HC: $p<0.01$, SSc: $p<0.05$,) as well as B-cell proliferation using HC samples ($p<0.001$). Amlexanox also inhibited differentiation of memory B-cells into ASCs using HC and cSLE samples (HC: $p<0.001$, cSLE: $p=0.002$), which corresponded with less production of both IgG and IgM (HC-IgG: $p=0.002$, HC-IgM: $p=0.0006$, cSLE-IgM/IgG: $p<0.001$).

Conclusion

This study provides evidence for inhibitory effects of amlexanox on expression of interferon stimulated genes as well as on B-cell differentiation and proliferation in primary human cells in vitro. TBK1 inhibition is a promising therapeutic option to tackle IFN-driven autoimmune diseases.

B-Cell Lymphoma Protein 6: A Novel Transcription Factor Involved In Cardiac Hypertrophy Revealed Through Human Transcriptional Regulatory Networks

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Introduction

Heart failure (HF) is a complex condition where the heart cannot pump enough blood to the body. HF onset precedes cardiac hypertrophy (CH), an adaptative response to increased workload characterized by cardiomyocyte enlargement. Cardiac stressors, such as Norepinephrine (NE), activate a global transcriptional response of different signaling cascades of master transcription factors (TFs, e.g., NFAT, GATA4, MEF2). However, these already-known TF do not account for all the gene expression changes observed during the HF and CH process.

Method & Materials

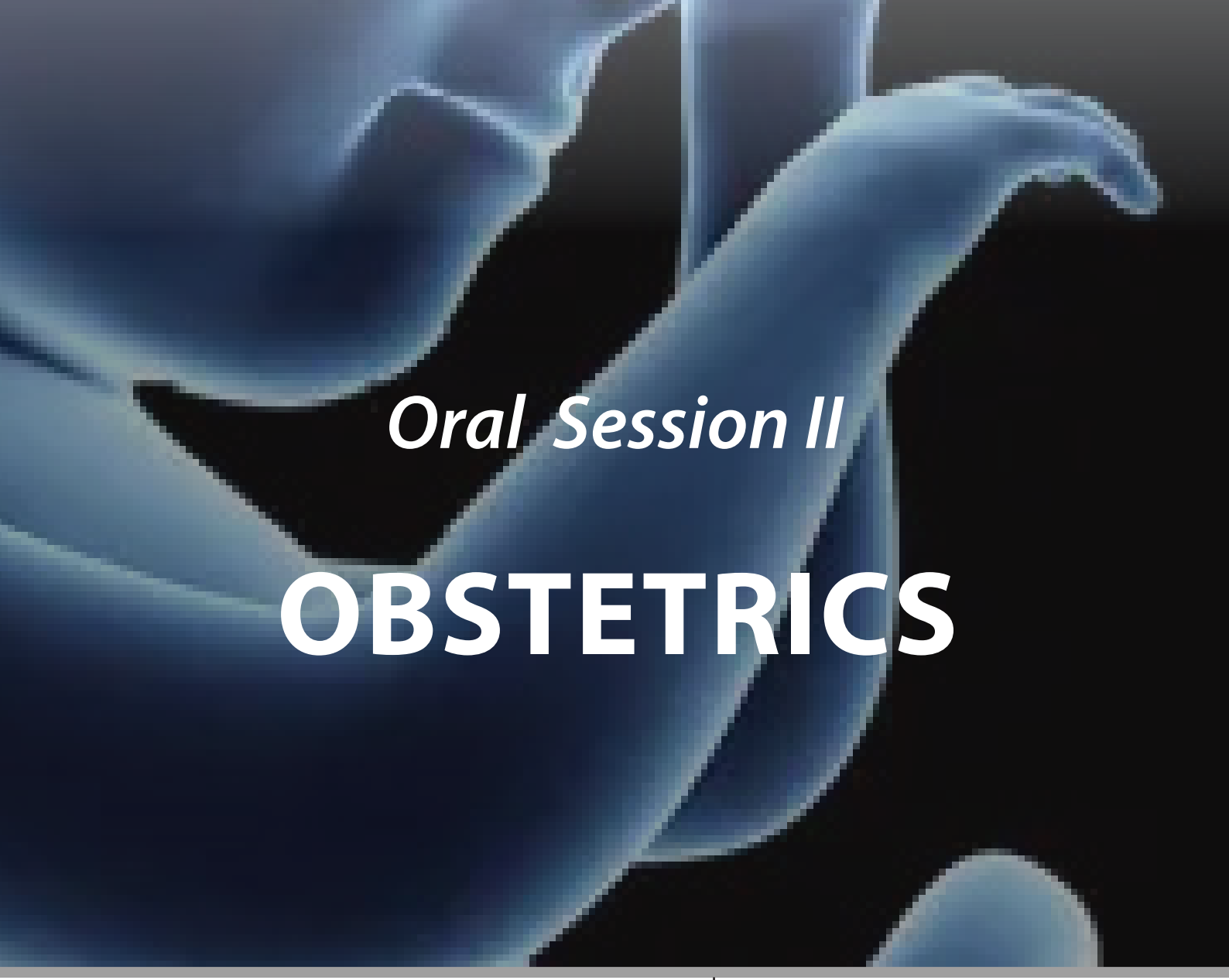
Using a systems biology approach, we build a transcriptional regulatory network (TRN) activated by HF. Noteworthily, the network contained several TF involved in CH/HF in addition to uncharacterized factors, thus selecting BCL6 as a potential new regulator. To evaluate BCL6 function, we treated neonatal rat cardiomyocytes (NRVM) with NE. Data were analyzed by unpaired t-test or ANOVA; values corresponded to mean Ò SEM (N = 3-6).

Results

BCL6 mRNA and protein levels increased on NE-treated NVRM. BCL6 expression and nuclear distribution correlated with the overexpression of cardiomyocyte hypertrophy markers (ANP and BNP) and cell growth. In addition, BCL6 knockdown (KD) on NE-treated NVRM ameliorated ANP and BNP increase and inhibited cardiomyocyte hypertrophic growth. Mitochondrial dynamic analysis revealed that BCL6 KD prevented mitochondrial fragmentation, reverted Drp1 phosphorylation, and upregulated Mitofusin-2 (Mfn2) levels; all characteristics of the mitochondrial fragmented phenotype and metabolic switch observed in CH/HF. Finally, the BCL6 inhibitor FX-1 ameliorated ANP overexpression and cardiomyocyte cell growth on NE-treated NVRM.

Conclusion

To our knowledge, this is the first report showing a TRN activated by HF, a model capable of identifying new TF involved in CH. Finally, our results suggest that BCL6 may exert a critical pro-hypertrophic role. Future studies will be needed to evaluate BCL6 pro-hypertrophic mechanisms, potential therapeutic role on HF, and additional potential targets derived from HF-activated TRN.



Oral Session II

OBSTETRICS

Presenters:

- Ghadah AlQarni
- Nora El Moussaoui
- Laura Ellérie
- Gaurang Narayan
- Jaime Plane

Molecular and Microscopic Insights into Fetal Nucleated Red Blood Cells: Advancing Early Pregnancy Diagnostics

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Introduction

Background: Since the initial discovery of fetal nucleated red blood cells (fNRBCs) in maternal circulation, their isolation for in-depth genomic analysis has garnered significant attention. This method allows for extensive genetic diagnostics with the prioritization of maternal and fetal well-being. The detection of fetal genetic abnormalities may lead to the contemplation of terminating the pregnancy at an early stage. Objective: This study seeks to establish a set of standardized protocols that utilize advanced techniques in microscopy and molecular analysis to accurately identify and characterize the morphological attributes of fNRBCs during the early stages of pregnancy.

Method & Materials

At King Fahd University Hospital in Khobar, Saudi Arabia, umbilical cord and maternal blood samples were collected from willing mothers after delivery and during early pregnancy, respectively. Double density gradient method was used to enrich fNRBCs. Various nuclear stains, including a specially developed in-house fetal hemoglobin stain (HbF stain), were applied for light microscope visualization. Additionally, RBCs were prepared for examination using fluorescence confocal microscopy. This involved using fNRBC-specific CD235a monoclonal antibodies and a secondary antibody labeled with FITC fluorophore. Scanning electron microscopy (SEM) was also used for further analysis. To confirm that the isolated fNRBCs originated from fetal cells, a molecular approach was employed by performing gender multiplex PCR and nanopore whole genome sequencing (WGS) on the extracted DNA from the isolated fNRBCs and the cell-free fetal DNA (cffDNA) obtained from the plasma of the same samples.

Results

The in-house HbF stain was the most effective nuclear stain for visualizing fNRBCs under a light microscope. Fluorescence confocal microscopy confirmed the presence of fNRBCs in cord blood samples through robust fluorescent signals identified by CD235a markers. Conversely, blood samples from adults were negative. SEM analysis showcased distinct cellular characteristics, variations in size, shape, and surface texture, between blood samples from maternal and cord origins. The diameter of fNRBCs was 42% larger than RBCs. Gender multiplex PCR and nanopore sequencing consistently confirmed the fetal origin of fNRBCs, including the presence of the Y-chromosome.

Conclusion

The identified morphological and molecular features can be effectively utilized to accurately separate fNRBCs from maternal blood samples obtained during early pregnancy, thereby facilitating early non-invasive prenatal diagnosis.

eCTG vs. CTG monitoring during term labour: the effect on analgesic use

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Introduction

Conventional cardiotocography (CTG) has been a cornerstone in obstetrics for half a century. However, CTG is prone to signal loss and its application is uncomfortable limiting women's freedom of movement during labour. These shortcomings led to the development of a new non-invasive monitoring method; electrophysiological CTG (eCTG). Next to a better signal one of the largest advantages of the eCTG in comparison with the conventional CTG is its wireless and beltless character giving patients the ability to move and change positions throughout labour. Freedom of movement is well known for its positive effects on (perception of) pain. The objective of the current study is to investigate whether the use of eCTG leads to a reduction in analgesic use during labour when compared to conventional CTG monitoring.

Method & Materials

The current study is part of a large single-center cohort intervention study (NIEM-II) taking place at the women, mother, and child center of M†xima medical center (The Netherlands). Pregnant women with an indication for continuous fetal monitoring during delivery are being screened for eligibility and a random sample (90.9%) is offered eCTG monitoring. The remaining eligible women receive CTG monitoring together with historical controls they will form the comparison group. The primary outcome measure is the use of analgesics during labour: epidural or remifentanil. Descriptive and inferential analyses will be performed accordingly.

Results

Preliminary results Data collection is taking place until the 31st of March. Baseline characteristics and study parameters are being retrieved from the electronic patient records. The aim is to include at least 100 women in each group. Currently, 28 women are included in the intervention arm and 3 in the prospective control arm.

Conclusion

It is hypothesized that the eCTG reduces the use of analgesics during labour when compared with conventional CTG monitoring because it allows freedom of movement during labour which in return positively influences pain perception. Therefore eCTG has the potential to revolutionize obstetric care. Further studies should investigate its impact on patient satisfaction and operative interventions during labour. *This study is still ongoing, all results and a more elaborate conclusion will be available at the time of the congress.

Placental morphometry and fetal size in the Lifelines NEXT birth cohort: an algorithm-based analysis

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Introduction

In fetal growth restriction (FGR), the fetus is unable to achieve its intrinsic growth potential. Placental supply of nutrients and oxygen is impaired, which leads to growth restriction and hypoxia of the fetus. FGR is associated with increased risks of stillbirth, preterm birth, neurodevelopmental delay and cardiovascular disease in adulthood. Currently used tools for detection of FGR are limited and conventional clinical monitoring does not prevent a high proportion of placenta insufficiency related stillbirths. More specific and clinically useful tools are needed to improve the antenatal and postnatal detection of impaired growth of the fetus. Impairments in placental size, volume and shape appear to be contributing to placental dysfunction. This study aims to determine the inter-relationships between placental morphometry, fetal size and the occurrence of adverse perinatal outcomes.

Method & Materials

This study will use placenta photos and additional maternal and fetal data of 600 singleton pregnant women, collected within the Lifelines NEXT birth cohort. To determine the association between placental morphometry, fetal size and adverse perinatal outcomes, we will analyze placenta photos with an image processing algorithm created in MATLAB programming platform. Initial code was written for analysis within the Pregnancy Outcome Prediction (POP) study. In the current study, a revised version of this code will be used. Intra-observer repeatability and reliability of placental morphometry will be assessed with blinded and repeated measurements of the same placentas. Associations between placental morphometry, fetal size and adverse perinatal outcomes will be assessed with correlation analysis and regression analysis.

Results

Since this study is still being conducted at the time of abstract submission, no final results can be given yet. However, the algorithm is fully developed and is currently being used for image analysis.

Conclusion

Since this study is still being conducted at the time of abstract submission, no conclusions can be drawn yet.

Genetic Insights: Exploring the Impact of MTHFD1G1958A Polymorphism on the Risk of Gestational Diabetes Mellitus

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Introduction

The MTHFD1 (Methylene Tetra Hydro Folate Dehydrogenase 1) gene is pivotal in folic acid metabolism, catalyzing sequential process in tetrahydrofolate (THF) conversion. MTHFD1's role in supplying one-carbon units for methylation reactions and producing 10-formyl-THF is crucial for nucleotide formation and DNA synthesis. A polymorphism at nucleotide 1958 G > A in the MTHFD1 gene has been associated with adverse pregnancy outcomes, including recurrent pregnancy loss, congenital heart diseases, intrauterine growth restriction, preeclampsia, abruptio placenta, and fetal death. Moreover, this polymorphism can lead to potentially neural tube defects (NTD) during embryonic development. With an increasing prevalence of gestational diabetes mellitus (GDM), a condition linked to significant morbidity and mortality, understanding gene polymorphisms, particularly in folate metabolism, is vital. This study aimed to investigate the association between MTHFD1G1958A polymorphism, folate metabolism, and GDM risk.

Method & Materials

A case-control study involving 304 pregnant women (152 GDM cases, 152 controls) aged 25-35 years was conducted in a tertiary care teaching hospital. GDM diagnosis followed the IADPSG criteria, with exclusion criteria such as pre-existing diabetes, multiple gestations, and other complications. Ethical approval and written informed consent were obtained. Genomic DNA was isolated, focusing on the MTHFD1G1958A polymorphism, using PCR-RFLP techniques. Statistical analysis included genotype and allele frequencies, chi-square tests, and student-t test.

Results

Significant differences were observed in the baseline parameters categorizing as risk factors (age, normal pregnancy) between GDM cases and controls (p-0.0000). Genotype frequencies showed a significant association (p-0.005), with the G-allele more prevalent in controls and the A-allele in GDM cases. The recessive model revealed a high risk in mild GDM cases (p-0.0000). Association was also significant in the overall group and group with severe form (p-0.031, p-0.011, respectively). Though, allele frequencies alone did not show statistical significance, both severe and mild forms demonstrated a strong link between the homozygous AA genotype and increased susceptibility to GDM.

Conclusion

This study establishes significant associations between MTHFD1G1958A polymorphism and GDM risk, providing insights into potential genetic influences on this condition, in an Indian setting. The findings emphasize further research, to confirm and expand our understanding of this association and its clinical implications.

Bone Marrow Mesenchymal Stem Cells Therapy for Premature Ovarian Insufficiency: a systematic review and meta-analysis of preclinical studies

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Introduction

Premature ovarian insufficiency (POI) is a prevalent condition in women under 40, characterized by elevated gonadotropin levels, diminished estradiol (E2), compromised follicular production, irregular menstrual cycles, and infertility. Mesenchymal Stem Cell (MSCs) transplantation particularly utilizing Bone marrow-derived MSCs (BM-MSCs) has emerged as a prospective treatment in preclinical studies. Therefore, we aimed to perform a systematic review and meta-analysis of the efficacy of BM-MSCs in ameliorating POI within animal models.

Method & Materials

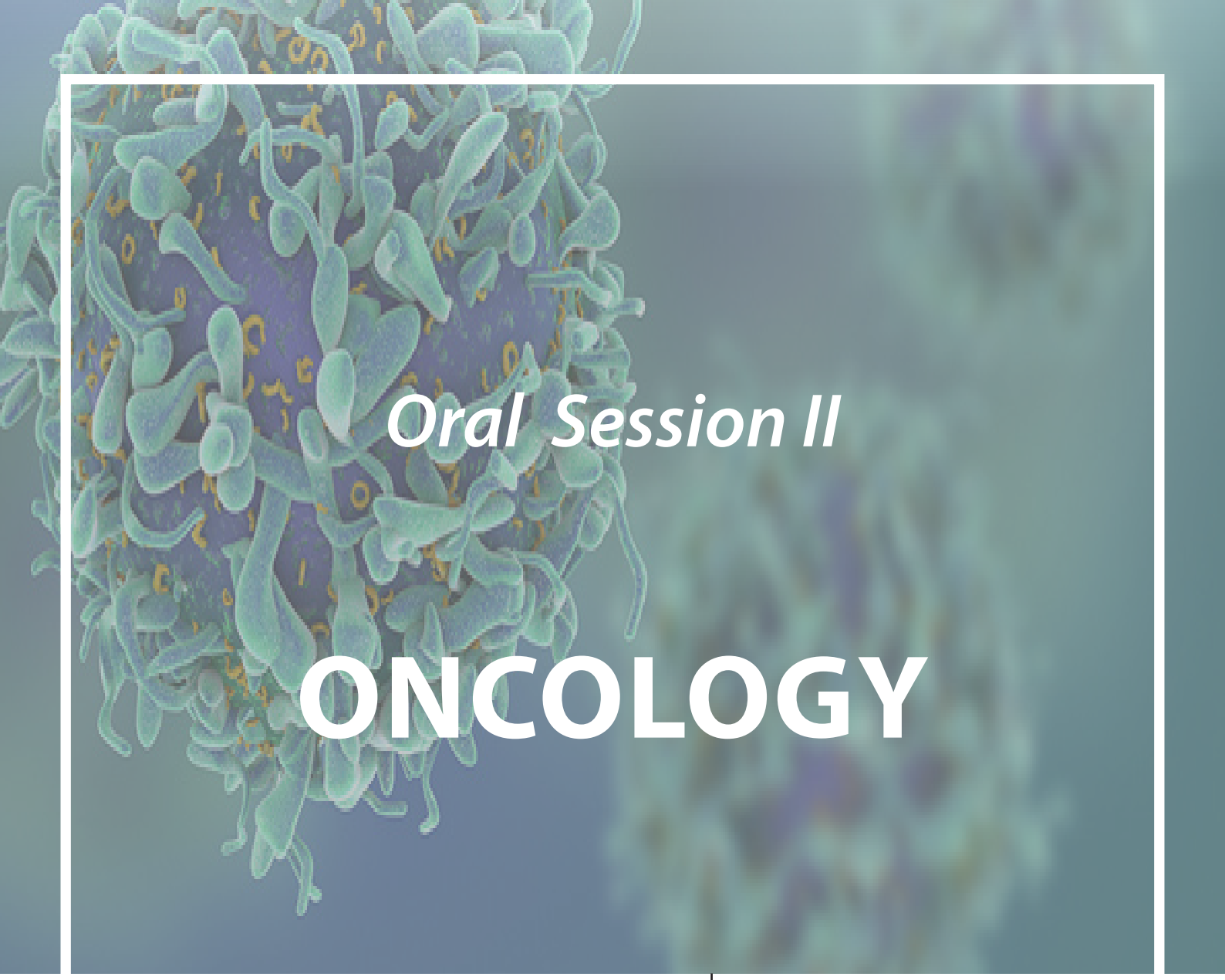
Pubmed, Web Of Science, SCOPUS, ScienceDirect, and Cochrane Library were searched for preclinical studies involving BM-MSCs therapy, including MSCs and MSCs-derived exosomes trials, compared to placebo and non-treatment control in POI animal models. The endpoints were centered on serum hormone levels, estrous cycle, follicular production, and fertility outcomes.

Results

Twenty-four articles involving 561 animals were included. Animals treated with BM-MSCs therapy had a significant improvement in hormonal function, increasing E2 (mean difference [MD] 13.60 pg/ml; 95% confidence interval [CI] 10.28,16.91; $p<0.00001$), decreasing follicle-stimulating hormone (FSH) (standardized mean difference [SMD] -2.80; 95% [CI] -3.19,-2.42; $p<0.00001$), and presenting associated a higher proportion of animals conserving normal Estrous Cycle (risk ratio [RR] 11.44; 95% [CI] 2.83,46.17; $p=0.0006$). Follicular production was significantly increased in the BM-MSCs therapy group, including primordial, primary, secondary, and total number ($p=0.002$; $p=0.002$; $p=0.0008$; $p<0.00001$, respectively). Concerning fertility, there was an improvement in pregnancy rate ([RR] 3.12; 95% [CI] 1.64,5.91; $p=0.0005$) and number of offspring ($p<0.0001$) compared to the control group.

Conclusion

In summary, these findings suggest that BM-MSCs therapy in POI preclinical studies ameliorates ovarian function, improving hormonal and follicular production, estrous cycle, and fertility. Further clinical studies are needed to confirm its efficacy in patients suffering from POI.



Oral Session II

ONCOLOGY

Presenters:

- Saif Ahmed
- Zhen Lin
- Hosein Kouchaki
- Mehul Saxena
- Kapilraj Ravendran

The Impact of Artificial Intelligence on Advancing Cancer Diagnostics: A Comprehensive Meta-Analysis

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Introduction

The analysis of vast genomic and clinical data through the integration of AI into imaging technology has the potential to transform cancer diagnosis. This comprehensive meta-analysis evaluates the precision and efficacy of AI-assisted diagnosis in diverse types of cancer, intending to provide valuable knowledge for future research and practical implementation.

Method & Materials

An extensive search was conducted across various medical databases to identify relevant studies. 25 studies met inclusion and exclusion criteria. Sensitivity and subgroup analyses were performed to ensure robust results. Funnel plots addressed potential bias. Meta-analysis was performed using Comprehensive Meta-Analysis Software (CMS).

Results

The meta-analysis of AI-based diagnostic assessments for various cancers unveiled substantial accuracy improvements. In bladder cancer, AI demonstrated noteworthy effectiveness, yielding an F1 score of 0.88, with substantial sensitivity (95.77%, 95% CI: 95.53%?96.00%) and specificity (87.84%, 95% CI: 87.59%?88.09%). For breast and colorectal cancers, it maintained consistent and accurate diagnostic capabilities, achieving balanced F1 scores of 0.77 (95% CI: 0.77?0.78) and 0.79 (95% CI: 0.78?0.79), respectively. In renal cancer, it showcased high performance, achieving an F1 score of 0.89 (95% CI: 0.89?0.90), alongside impressive sensitivity (95.80%) and specificity (88.80%). AI excelled in oral cancer, reflected in an outstanding F1 score of 0.98, with remarkable sensitivity (97.76%) and specificity (99.26%). For pancreatic and prostate cancers, it attained F1 scores of 0.83 (95% CI: 0.82?0.83) and 0.90 (95% CI: 0.90?0.90), respectively. In uterine cancer diagnosis, it demonstrated balanced sensitivity (99%) and specificity (86%), achieving an F1 score of 0.86 (95% CI: 0.85?0.87). In hepatic cancer, AI delivered notable performance, with an F1 score of 0.82 (95% CI: 0.81?0.83), emphasizing its diagnostic effectiveness across diverse cancer types.

Conclusion

The results obtained from the meta-analysis indicate that the efficacy metrics of artificial intelligence (AI) in detecting, diagnosing, and treating cancer were either higher or very close to the benchmark. This provides convincing evidence supporting the effectiveness of AI-powered imaging modalities in cancer diagnosis. The use of AI has improved accuracy, facilitated personalized precision treatment approaches, and advanced cancer care.

The role of Carbonic anhydrase IX on Extramural venous invasion in esophageal squamous cell carcinoma patients

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Introduction

Extramural venous invasion (EMVI) has an independent adverse effect on survival in esophageal squamous cell carcinoma (ESCC) patients. Carbonic anhydrase IX (CAIX) is involved in hypoxia and anoikis. Here we examine its role in promoting dissemination in ESCC.

Method & Materials

CAIX expression was investigated immunohistochemically in tumor and EMVI tissues from 53 patients with locally advanced ESCC and EMVI+ after surgery only (period 2009-2013). Photomicrographs were evaluated with Aperio Image scope. H-score was used as a mathematical product of proportion score (% positive cells) and intensity score (estimated fraction-stained tumor cells), resulting in a low/high level according to the median H-score.

Results

Of the 23 EMVI tissue (23/53, 43%), 12 showed high CAIX expression. CAIX expression in ESCC and its EMVI tissues was insignificant for gender, age, lesion location, pT stage, pN stage, differentiation grade, lymph-vascular invasion and perineural invasion. CAIX expression level in ESCC seemed to influence CAIX expression in EMVI (Logistic regression, $P = 0.002$), but not its level. The univariate Cox regression analyses showed high CAIX in primary tumor and EMVI correlated with worse overall survival ($P = 0.04$) although this was insignificant when CAIX expression in primary tumor and its EMVI tissues was correlated with prognosis. In multivariate analyses, lymph node metastasis was the only independent adverse factor.

Conclusion

High CAIX expression in both primary tumor and EMVI tissues is associated with a worst survival in ESCC patients. Inhibition of CAIX might reduce the potential of tumor cells to establish disseminated disease.

Efficacy and Safety of Brentuximab Vedotin in Pediatric Patients with Relapsed or Refractory Hodgkin Lymphoma: A Systematic Review and Meta-Analysis

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Introduction

Although Classical Hodgkin Lymphoma (cHL) is highly curable in children, 10?20% of patients experience poor outcomes of relapsed or refractory disease (R/R). Brentuximab vedotin (Bv), a CD30-targeting antibody-drug conjugate, has demonstrated promising therapeutic effects in adults with R/R cHL. However, its safety and efficacy in pediatric patients remain uncertain, primarily due to limited sample sizes in existing studies. To address this gap, this meta-analysis aims to evaluate both therapeutic outcomes and adverse events associated with Bv in under-eighteen patients with R/R cHL.

Method & Materials

Electronic databases were systematically searched in PubMed, Scopus, Web of Science, Embase, Google Scholar, and Cochrane Library until December 31, 2023. The quality assessment of included studies was performed using the Newcastle-Ottawa Scale. Additionally, we applied the chi-squared test and I2 statistics to evaluate potential heterogeneity across eligible studies. The random-effects model obtained pooled percentage estimates and associated 95% confidence intervals (CI). All statistical analyses were conducted through STATA version 16.0 with the "metaprop" command.

Results

Out of 1704 citations, 18 articles (11 clinical trials and 7 observational studies) with a total of 592 patients were included. Our meta-analyses revealed that the overall response rate (ORR), complete response (CR), and partial response (PR) rates were 86% (95% CI, 74%; 95%), 65% (95% CI, 50%; 79%), and 20% (95% CI, 10%; 32%), respectively. In subgroup analysis, patients receiving Bv combined with Doxorubicin, Vinblastine, and Dacarbazine demonstrated higher ORR and CR rate compared to the Bv monotherapy group. Regarding survival, the progression-free survival at 1-year was 88% (95% CI, 73%; 98%), while 13% (95% CI, 4%; 24%) of patients experienced progressive disease. Severe (Grade Ú3) treatment-emergent adverse events were reported in 49% (95% CI, 32%; 65%), and mortality occurred in only 1% (95% CI, 0%; 4%) of the entire population. Overall, 11% (95% CI, 3%; 22%) of patients discontinued their treatment due to the development of adverse events or progressive disease.

Conclusion

As a valuable rescue therapy, the Bv-contained regimens exhibit a notably high clinical response rate and favorable survival outcomes in pediatric patients with R/R cHL. However, further prospective studies are warranted to provide adequate information on their safety.

Impact of Adjuvant Chemotherapy in Patients with non-metastatic Pancreatic Ductal Adenocarcinoma in Bulgaria - A Population-wide Observational Study

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Introduction

The number of patients receiving neoadjuvant chemotherapy (NAC) for pancreatic ductal adenocarcinoma (PDAC) is on the rise. Adjuvant chemotherapy (AC) may have additional benefits for these patients according to NCCN guidelines, but this is yet unknown. Our study's objective was to assess the relationship between AC and overall survival (OS) in PDAC patients who underwent surgery after receiving multiagent NAC.

Method & Materials

This is a retrospective population wide observational study of 1128 cases registered with PADC who underwent surgery after receiving multiagent NAC in the Bulgarian National Cancer Registry (BNCR) in 2013-2014. The mean age of according to stage at diagnosis and gender were calculated. The median OS was analyzed according to the stage at diagnosis and for patients registered with stage 1 or stage 2, PADC, the effect of AC on the median OS was examined. The statistical significance was estimated using the ANOVA tests and the Kaplan-Meier curve with log rank.

Results

The mean [SD] age at diagnosis was 65.64 [10.426] years, with males have a lower mean age at diagnosis compared to females (64.55 [10.143] vs 67.04 [10.622] years). The mean age at diagnosis according to stage at diagnosis was 64.89, 64, 66.39 and 65.97 for stage 1, 2, 3 and 4 respectively, p-value <0.001. The median OS according to stage at diagnosis for PADC was 12.066 vs 10.356 vs 6.214 vs 2.729 months for stage 1, 2, 3 and 4 respectively, p-value <0.001. Males had a lower median [95% confidence interval] OS compared to females (4.044 [3.565-4.523] vs 4.636 [3.980-5.311] months), p-value = 0.102. A total of 283 patients were registered with stage 1 or 2 PDAC who underwent surgery after receiving multiagent NAC, of which only 42.8% received AC. The median [95% confidence interval] OS was higher for patients who received AC than those who did not receive AC (12.888 [10.434-15.341] vs 8.942 [6.573-11.312] months), p-value=0.004

Conclusion

Patients may benefit from AC to have a longer survival even after receiving multiagent NAC and resection as their survival was higher than those who did not receive AC. Bulgaria may benefit from diagnostic modalities such as CT-guided or EUS-guided biopsy.

Comparison of Hyperthermic Intravesical Chemotherapy (HIVEC) using Mitomycin C and Intravesical BCG following Transurethral Resection for Superficial Bladder Cancer

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Introduction

The standard approach for treating non-muscle invasive bladder cancer (NMIBC) involves transurethral resection of bladder tumor (TURBT), but this method alone is linked to a higher recurrence rate. To mitigate this issue, intravesical therapies like Bacillus Calmette?GuÇrin (BCG) are recommended, with Mitomycin C emerging as a viable alternative.

Method & Materials

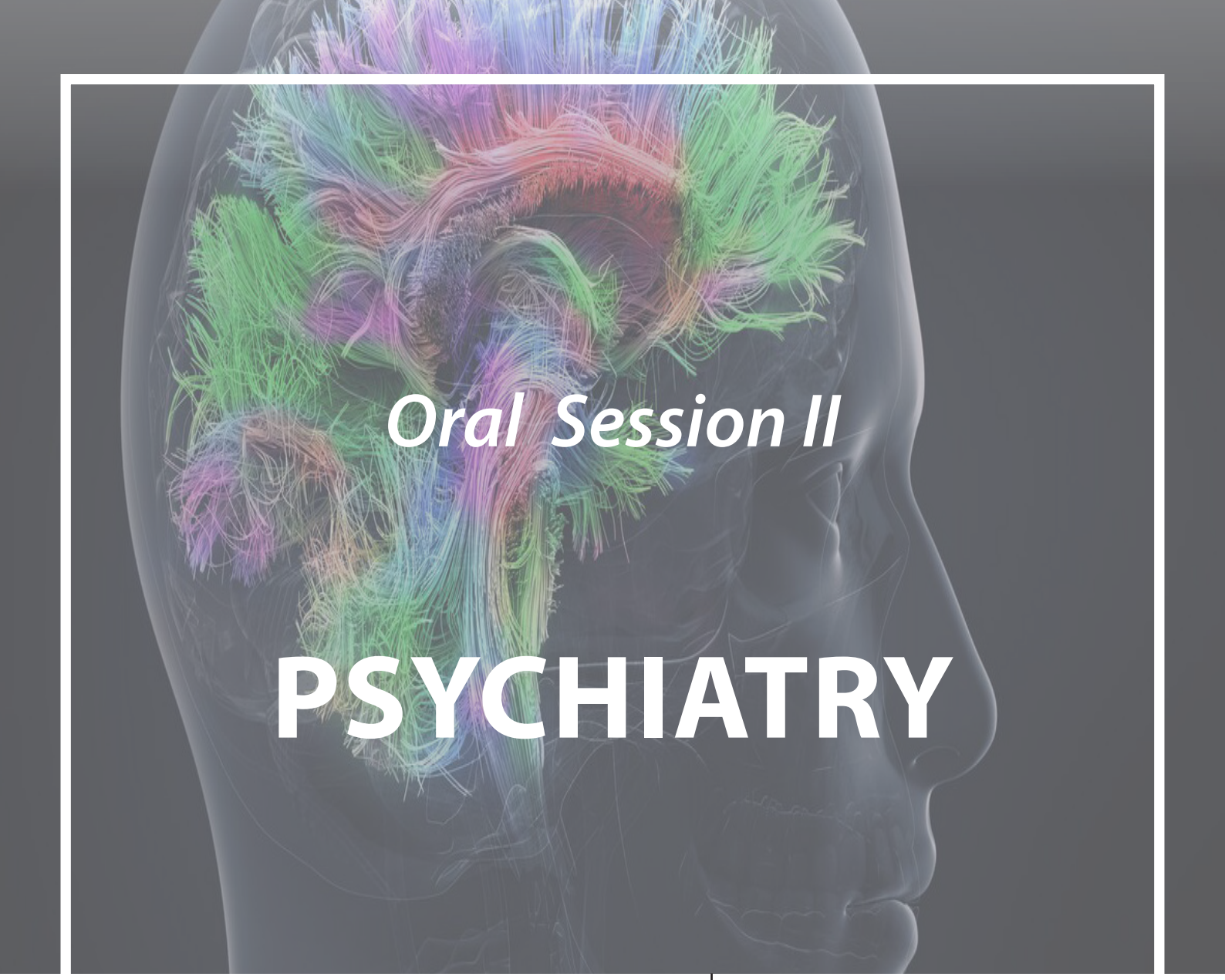
In a randomized study conducted over 2 years at a tertiary-care North-Indian hospital, 200 patients with histologically confirmed NMIBC?Transitional cell carcinoma (ECOG performance status < 2) were enrolled. Following TURBT, patients were randomly assigned to two groups: Group A received hyperthermic intravesical chemotherapy (HIVEC) with Mitomycin C, while Group B received intravesical BCG 2-4 weeks post-TURBT. Both groups were monitored for 6 months, and comparisons were made regarding therapy-related side effects, follow-up observations, and recurrence.

Results

Similarities in age, gender distribution, urine cytology, Bladder Tumor Antigen status, and tumor grades were observed between the two groups. Group B exhibited significantly higher occurrences of adverse effects during the procedure, including burning micturition ($p < 0.001$*), bladder spasm ($p < 0.014$*), urinary tract pain ($p = 0.012$*), and cystitis ($p = 0.005$*). Conversely, Group A showed a significantly higher prevalence of burning sensation in the abdomen ($p = 0.003$*). These adverse effects also demonstrated notable differences in severity according to the CTCAE 5.0 Scale. The incidence of adverse effects such as hematuria, urethral stricture, urgency, urticaria, dry skin, and fever were comparable between the two groups. On follow-up, only the burning sensation in the abdomen was significantly higher in Group B, while the remaining observations were similar in both groups. No recurrence was observed in either group based on urine cytology, ultrasound, or cystoscopy during the 6-month follow-up.

Conclusion

HIVEC with Mitomycin C displayed significantly fewer side effects compared to the conventional BCG treatment, despite similar recurrence rates, which were zero in our case.



Oral Session II

PSYCHIATRY

Presenters:

- Sena Lemma
- Abdulkader Mohammad
- Zablon Sewalem
- Dandan Zheng

Effect of gene-drug interactions on antidepressant treatment side effects among patients with MDD, Anxiety and Bipolar disorders

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Introduction

In real-world clinical practice, optimizing outcomes for individuals using antidepressant (AD) remains challenging, with only 30% achieving remission and 43% discontinuing treatment due to side effects. Genetic variations play a substantial role, accounting for 42% of the variability in individual responses to AD. Utilizing polygenic risk scores (PRS) has the potential to enhance treatment decision-making. This study goes beyond previous research by exploring multiple pharmacogenomic (PGx) variants and their interactions with AD, while considering both subjective responses and objective metabolic outcomes within a longitudinal cohort.

Method & Materials

This longitudinal naturalistic cohort study includes participants from the Netherlands Study of Depression and Anxiety (NESDA) cohort. Both subjective and objective side effects are assed using validated questionnaires and laboratory findings. PRS will be calculated using previously identified PGx SNVs. The analytical approach involves descriptive analysis, missing data imputation, and sensitivity analyses. Following initial univariate analyses, a multivariate regression will examine the association between PGx-PRS and AD outcomes. An ANCOVA mixed-effect model will assess the longitudinal association between PGx-PRS and AD side effects overall and for different AD classes. Four models will be compared: I) baseline covariable effects, II) incorporation of additional genetic factors (PGx-PRS), III) interaction effects between PGx-PRS and drug, IV) sensitivity analysis exploring independent effects of TCAs and SSRIs alongside genetic factors.

Results

Preliminary results will be ready in 3 weeks

Conclusion

This study investigates gene-drug interactions and their impact on antidepressant side effects. The findings have the potential to improve personalized treatment approaches for mood disorders.

In the Minds of Future Doctors: Unveiling Mental Health Stigma and Help-Seeking Behavior among Medical Students

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Introduction

Stigma denotes an unjust and negative belief within a society or group towards something, often leading to rejection, isolation, and discrimination. Persistent stigma surrounding mental illness poses a substantial obstacle to optimal treatment and recovery, notably when emanating from healthcare providers. This issue is particularly pertinent among medical students, as their attitudes can significantly impact patient care in the future. In this research, we aimed to explore the mental health-related stigma among medical students.

Method & Materials

A cross-sectional study utilizing The Opening Minds Stigma Scale for Health Care Providers (OMS-HC) was conducted. The scale comprises 15 questions, each scored on a scale from 1 to 5, with higher scores indicating greater stigma. The survey was distributed to students of the Faculty of Medicine in Novi Sad-Serbia through social media platforms. Subsequently, the results were analyzed using SPSS, version 26.0. Independent samples T test was used to compare different participants according to demographic characteristics.

Results

A total of 222 medical students participated, with 50.9% being males. Most participants (62.6%) reported exposure to mental health education in their curriculum. The survey was divided into three subscales: Attitude, Disclosure and Help-seeking, and Social Distance. In the Social Distance and the Disclosure and Help-seeking subscales, most participants scored 4 (34.86% and 27.13% respectively), indicating a higher level of concern compared to the attitude subscale (15.4%). In both questions, regarding whether healthcare providers need to be advocates for people with mental illness, and the struggle to feel compassion for individuals with mental illness, preclinical respondents exhibited more positive attitudes with average scores of 2.69 and 2.40 out of 5, for the respective questions. In contrast, clinical year respondents had lower average scores, with 2.27 (P=0.004) for advocacy and 2.03 (P=0.018) for compassion, respectively.

Conclusion

The results revealed a pronounced stigma towards mental health patients, particularly among pre-clinical years students. This underscores the importance of integrating comprehensive mental health education into the medical curriculum to promote understanding, empathy, and destigmatizations among future healthcare providers. Additionally, a call for further research is essential to delve deeper into the stigma held by medical students towards patients with mental health concerns.

: Polygenic and Exposome Risk Loading Predict Long-term Clinical and Functional Outcomes in Schizophrenia Spectrum Disorders

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Introduction

Schizophrenia spectrum disorders (SSDs) are severe and highly heritable psychiatric illnesses that typically emerge during adolescence or early adulthood and exhibit a diverse course characterized by varying long-term outcomes. Recent research underscores the notion that SSDs arise from the complex interplay between genetic and environmental factors. The objective of this study is to investigate the individual and combined effects of the polygenic risk score (PRS) and exposome risk score (ES) for schizophrenia spectrum disorders (SSDs) on long-term clinical outcomes, including symptom severity, functioning, and cognitive outcome.

Method & Materials

In this 6-year prospective cohort study, baseline, three- and six-year follow-up data of 1,119 patients with SSDs from the Genetic Risk and Outcome of Psychosis (GROUP) cohort was used. Weighted PRS was constructed using PGC summary statistics. ERS was calculated using the weighted combined effect of cannabis use, childhood adversity, and bullying. Positive and negative symptom severity was assessed using Positive and Negative Syndrome Scale (PANSS), cognitive trajectories were used to assess cognitive outcomes. and functioning was assessed using Global Assessment of Functioning (GAF). Linear regression models were employed to examine the associations of PRS and ERS with clinical and functional outcomes adjusting for covariates.

Results

1,119 participants with SSDs (mean age 27.4 years, 63% male). ERS was significantly associated with severe positive symptoms (_ = 1.2 ; 95% CI =1.1-1.3 ; p=0.02), and we anticipate an association with cognitive outcome and a significant interaction with PRS.

Conclusion

Higher polygenic and exposome risk scores may contribute additively and synergistically to adverse outcomes in SSDs. Assessing joint genomic and environmental loading could augment prognostic models to guide early interventions and improve long-term trajectories.

Characteristics of the relationship between sleep, gut microbiota, and fecal short-chain fatty acids in shift workers: a cross-sectional study

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Introduction

Shift workers (SWs) have a higher risk of sleep complaints. Meanwhile, gut microbiota and short-chain fatty acids (SCFAs) have a bidirectional relationship in sleep regulation, via the brain-gut axis. This study aimed to examine the relationship between sleep, gut microbiota, and SCFAs in SWs.

Method & Materials

A total of 41 SWs and 47 controls were recruited from June 2018 to July 2021 (mean age=28.10Ò4.61 years, female 73.86%). SW was defined as working time outside 7:00 to 18:00 for Ú 3 years and the shift frequency Ú 3 times/month. Sociodemographic characteristics and the Beck Depression Inventory (BDI) score were collected. Subjective sleep was assessed via questionnaires and a 7-day sleep diary. Objective sleep was assessed via polysomnography (PSG) and a 7-day actigraphy. The fecal samples were collected during the PSG recording and immediately stored at -80_ until 16S rRNA sequencing and SCFA analyses. Comparisons between groups were performed by independent t-test, Mann?Whitney U-test, or the _2 test according to the variable type. Spearman?s correlation analyses were performed between sleep, gut microbiota, and SCFAs in SWs. Correlation heatmaps were performed by OmicStudio tools (https://www.omicstudio.cn).

Results

Compared to controls, SWs showed higher BDI scores (8.07Ò7.78 vs. 10.98Ò7.71, p <0.001) and worse sleep, such as shorter subjective (sleep diary, 383.56Ò66.60 min vs. 413.62Ò47.76 min, p=0.016) and objective total sleep time (TST) (actigraphy, 352.19Ò55.26 min vs. 380.94Ò41.19 min, p=0.010). Regarding gut microbiota at Family and Genus levels, SWs showed relative abundance alterations, such as Sutterellaceae decreasing (p=0.016) and Oribacterium increasing (p=0.033). Regarding SCFAs, SWs had decreased butyric (p=0.007) and valeric (p=0.026) acid levels. Correlation analyses suggested that in SWs, both sleep, such as objective TST (r=0.28, p=0.009), and butyric acid level (r=0.32, p=0.002) were related to Sutterellaceae.

Conclusion

Sleep, gut microbiota, and SCFAs have altered in SWs. SW made sleep worse, which decreased the relative abundance of Sutterellaceae, and ultimately led to the butyric acid level decreasing.

Oral Session II

PUBLIC HEALTH

Presenters:

- Fareezah Abdul Karim Siddique
- Fatemeh Babadiyousefi
- Baina Lavginova
- Precious Mastala
- Hamrish Kumar Rajakumar
- Gadise Regassa
- Suvd-Erdene Uurdmunkh

Determinants To Cervical Cancer Screening Uptake In Resource-Constrained Settings: A Cross-country Comparison

Fareezah Abdul Karim Siddique
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Introduction

Cervical cancer (CC) is a significant global health concern, causing 350,000 deaths in 2021, primarily affecting women in low- and middle-income countries and ethnic minorities in high-income countries. The PREvention and SCReening Innovation Project Toward Elimination of Cervical Cancer (PRESCRIP-TEC) centres on cervical cancer screening (CCS), and specifically addresses the World Health Organization's (WHO) second elimination initiative target. The project aims to assess the efficacy and uptake of high-risk Human Papillomavirus (hrHPV) self-sampling, aligning with the initiative's objectives to reduce mortality and enhance participation. The study will further explore the applicability of WHO guidelines in diverse health systems. Objectives: PRESCRIP-TEC aims to implement self-sampling as the primary tool in underserved populations in Uganda, Bangladesh, and the Slovak Republic. This study seeks to conduct a multinational investigation, examining the determinants that impact self-sampling uptake, encompassing both individual and health-system factors.

Method & Materials

This cross-sectional study integrates individual- and country-level data from the PRESCRIP-TEC project. Surveys examine individual-level factors among women and male household decision-makers, in conjunction with assessing country-level health system readiness. A multilevel logistic regression, clustered by country, will analyse determinants affecting self-sampling uptake. Interaction analyses between individual and health-system determinants will inform strategies for enhancing CCS participation in varied socioeconomic contexts.

Results

Ongoing data collection targets rural areas of Uganda, Bangladesh, and the Roma community in Slovakia. Initial analysis of available WHO data indicates a 3.6% prevalence of HPV-16/18 in Uganda, with around 57% attributed to invasive CCs. Specific estimates for Bangladesh and Slovakia are pending, but regional data approximates 4.4% HPV-16/18 prevalence in Southern Asia and 9.7% in Eastern Europe. Notably, around 80.3% and 84.7% of invasive cervical cancers in Southern Asia and Eastern Europe, respectively, are linked to HPV-16/18. A forthcoming multilevel logistic regression will identify key determinants impacting self-sampling uptake.

Conclusion

The study aims to guide multi-level determinants to guide effective strategies for enhancing CCS participation in diverse socioeconomic settings. These findings will help diminish barriers and facilitate the scaling-up of self-sampling programs, ultimately reducing the global burden of cervical cancer. The research is ongoing, with an anticipated conclusion in early 2024.

Glucosamine and chondroitin sulfate combination in osteoarthritis patients of Mashhad, Iran: a long-term observational study

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Introduction

Patients with osteoarthritis who experience moderate to severe knee pain may benefit from oral treatment with glucosamine (GA) and chondroitin sulfate (CS). Although GA and CS are effective on both clinical and radiological findings, few high-quality trials have been conducted. It remains controversial whether they are effective in real-world clinical practice. A study was conducted to determine the impact of GA + CS on clinical outcomes in patients with knee and hip osteoarthritis.

Method & Materials

A prospective observational cohort study conducted in Mashhad involved 950 patients with knee or hip osteoarthritis (Kellgren & Lawrence grades I-III). From November 20, 2019, to March 20, 2023, patients received glucosamine hydrochloride 500 mg and chondroitin sulfate 400 mg orally, following a specified dosage regimen. Over the observational period of 54-64 weeks, including 4 visits, changes in KOOS and HOOS questionnaire scores were assessed. Additionally, treatment satisfaction, concomitant NSAID use, and adverse events were investigated. The study aimed to evaluate the effectiveness and safety of glucosamine hydrochloride and chondroitin sulfate in managing osteoarthritis.

Results

The study included 950 patients with knee and hip osteoarthritis. In this study, patients averaged 64.5 years old, 78.7% were women, and 27.49 kg/m2 was their average body mass index. A clinically and statistically significant improvement was shown in all KOOS and HOOS subscales. Pain, Symptoms, Physical Function (KOOS-PS), and Quality of Life (QOL) subscales increased from baseline to end of Week 64 by 32.87, 19.87, 14.40, and 22.77, respectively. On the Pain, Symptoms, Physical Function (HOOS-PS), and Quality of Life (QOL) subscales (P 0.001), patients with hip osteoarthritis had mean score improvements of 21.81, 17.93, 17.74, and 23.71. For the study, patient use of NSAIDs decreased from 42.9% to 12.4% (P 0.001). 2.4% of patients experienced treatment-related adverse events, primarily gastrointestinal disorders [25 AEs in 24 (1.9%). Almost all (78.1%) patients were satisfied.

Conclusion

The effects of long-term oral GA and CS on joint function and QOL were positive in patients with knee and hip osteoarthritis in routine clinical practice

Predictors of suboptimal peak inspiratory flow in patients with acute exacerbation of chronic obstructive pulmonary disease in real clinical practice

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Introduction

Incorrect inhalation technique is one of the most common reasons for the ineffectiveness of Chronic Obstructive Pulmonary Disease (COPD) therapy, increasing the frequency of exacerbations. Selection of treatment based on Peak Inspiratory Flow (PIF) measurements or predictors of suboptimal PIF (sPIF) could optimize therapy in patients with COPD.

Method & Materials

The goal of this study was to investigate a prevalence and predictors of sPIF in hospitalized patients with acute exacerbation of COPD in real clinical practice. The study involved 72 patients hospitalized with acute exacerbation of COPD. The analysis included demographic and clinical and lung function parameters. PIF was measured at the resistance level of patients? inhalation device using the In-Check DIAL G16 before and after explaining the inhalation technique, as well as at R2 and R5 at admission and on discharge.

Results

Upon admission and before explaining the inhalation technique, sPIF was observed in 52.7% of patients, while after the explanation, the proportion of patients with sPIF decreased to 19.4% ($p < 0.0001$). ROC analysis revealed that independent predictors of suboptimal PIF were age >70 years; FVC <73% pred.; FEV1< 35 % pred.; RV > 194% pred.; RV/TLC > 70%; DLco < 36% pred. The most significant predictors of sPIF were age (OR 0.89) and FEV1 (OR 0.59).

Conclusion

When choosing dry powder inhaler for the maintenance therapy in patients with acute exacerbation of COPD, it is important to consider the patient's ability to generate the optimal PIF taking into account the patient's age and the severity of functional impairments.

Assessment of Human Rabies Incidence and Post-Exposure Prophylaxis (PEP) Accessibility in Southern Malawi

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Introduction

Rabies, a major public threat with a 100% fatality rate, remains costly due to premature deaths and expenses related to post-exposure prophylaxis (PEP) procumbent and access. Despite endemicity in most Low- and Middle-Income Countries (LMICs), there is a PEP access barrier. Furthermore, there is a paucity of research to collect and adequately present information on disease burden, risks, and susceptibilities, an important aspect needed for planning, optimizing, and implementing control strategies. This study evaluated the incidence of human rabies, assessed PEP access routes, barriers, issuance patterns, and measured the accessibility and availability of anti-rabies vaccine.

Method & Materials

A mixed methods study was undertaken in public hospitals and District Health Offices spanning Blantyre, Zomba, Machinga, and Chiradzulu districts. This research involved retrospective data analysis and qualitative approaches. The data collection process included examining human rabies clinical records, reviewing anti-rabies stock records from 2008 to 2023, and conducting interviews with 8 District Health Officers and 16 patients. Data analysis was performed in R and NViVO.

Results

A total of 94 people has died from rabies; 19(20.2%), 8(8.5%), 38(40.4%), and 29(30.8%) of the deaths happened in Chiradzulu, Machinga, Zomba, and Blantyre, respectively. While no documentation of the storage of rabies immunoglobulins (HRIG) exists, all DHOs store and offer anti-rabies vaccine. The monthly consumption was: 91.4 (71.5-111.), p=<.0001 in Blantyre, in 32.5 (22.8-423) p=<.0001 in Chiradzulu, 149 (110-188) p=<.0001 in Machinga, and 570 (476-664), p=<.0001 in Zomba. The mean annual stock-out days was 18.55 (10.78-26.31), p=.00001, with no difference between the DHOs (p=0.0663). Additionally, vaccination schedules, injection techniques, and fundamental procedures for giving patients successive doses vary throughout DHOs. In addition to stockouts, we report how distance and lack of finances impedes exposed people in accessing rabies PEP.

Conclusion

This study underscores the continual loss of human lives to rabies. The absence of storage for human rabies immunoglobulins, coupled with frequent shortages of anti-rabies supplies, increases this risk, particularly during rabies outbreaks. Addressing PEP shortages and adopting a harmonized intradermal route has the potential to significantly reduce vaccine usage by up to 80%, thereby markedly reducing rabies-related human mortality associated with PEP stockouts.

Evaluating the Diagnostic Accuracy and Reliability of Mobile Audiometry for Screening Hearing Loss in Adults in Comparison to Pure Tone Audiometry.

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Introduction

Hearing loss affects 1.5 billion people globally and 430 million people require rehabilitation. According to a Forbes Health Survey, 80% of adults are undiagnosed and untreated for hearing loss due to a lack of adequate screening facilities leading to late presentation to the physician at an advanced stage when the hearing loss cannot be treated adequately. Pure tone audiometry (PTA) is the gold standard for audiometric assessments but faces limitations in accessibility, especially in underserved regions. Mobile audiometry (MA) emerges as a potential solution, leveraging smartphones for cost-effective hearing assessments. This study aims to evaluate MA?s diagnostic accuracy, specificity, and sensitivity in adults for hearing loss screening. Additionally, we aim to investigate the interpretation of MA results in elderly individuals.

Method & Materials

After obtaining ethical approval and informed consent, patients were recruited excluding minors and individuals with tinnitus. Audiometric assessments were conducted using both PTA and MA. with the former employing calibrated audiometers, trained audiologists in a soundproof room, and the latter utilizing an open-source app on smartphones. Hearing thresholds were measured for air and bone conduction at frequencies from 250Hz to 8kHz. Data was statistically analyzed for correlation, agreement, diagnostic accuracy, sensitivity, and specificity. The reliability of MA is assessed using the Intraclass Correlation Coefficient. Furthermore, we stratified participants into four age groups to explore and investigate MA accuracy across different age cohorts.

Results

Our study consisted of 250 participants. MA demonstrates a strong correlation with PTA across all frequencies. Bland-Altman analysis indicates good agreement. MA achieves 70.67% diagnostic accuracy in categorizing the degree of hearing loss. Sensitivity and specificity for hearing loss screening are 94.51% and 70.96% respectively. The kappa statistic indicates excellent agreement (_ = 0.659). MA shows high consistency and agreement in test-retest reliability. We also found that the accuracy of MA declines with advancing age.

Conclusion

MA emerges as a cost-effective, accessible, and patient-centered method for hearing evaluations. While not replacing PTA, MA's positions it as a valuable tool for hearing loss screening in resource-poor settings and epidemiological studies. The use of affordable, generic headsets enhances its practicality. MA results need to be carefully interpreted in the elderly.

Feasibility and acceptability of a family-led postnatal care (FPNC) service delivery model to increase PNC coverage in Ethiopia

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Introduction

Postnatal care (PNC) can prevent maternal and neonatal deaths. Existing PNC services are not reaching mothers and newborns in Ethiopia. Using human centered design to address key barriers to PNC uptake, we developed the family led postnatal care (FPNC) model which is based on self-care principles. FPNC provides an improved discharge process that involves family members and gives access to user-friendly self-monitoring devices and resources for families to use at home for one week. Selected community members distribute and manage the devices. This study aimed to explore if FPNC would increase postnatal checks in the first week, and also assess its feasibility and acceptability.

Method & Materials

A pre-intervention survey was employed among 119 postnatal women who delivered in in four health centers in Ada district from November 2022 to January 2023. A post-intervention survey was then conducted from February 2023 to April 2023 with 110 postnatal women. Descriptive analysis and chi-square tests were conducted. Qualitative data was also collected from husbands, family members, custodians and health workers and thematically analyzed.

Results

The PNC check between 24-72 hours in the pre-intervention period was 10.9% (13/119) for neonates and 9.2% (11/119) for mothers and increased to 95.5% for both neonates and mothers (105/110) ($p<0.0001$). A similar trend was seen for PNC checks between 73 hours to 7 days. All neonates and 80% of women with an identified danger sign sought care. Majority of women preferred FPNC approach over the traditional PNC. Women appreciated the involvement of their husbands and reported that they felt they were receiving good PNC care.

Conclusion

The FPNC model increased coverage of postnatal checks for mother and newborn and the use of the homecare kit and checklist was acceptable and feasible. Testing FPNC in different contexts can provide insights on the scalability of the model.

Investigation of Enterobiasis and Associated Factors in Mongolia Using Adhesive Tape Sampling

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Introduction

Enterobiasis is a widely prevalent parasitic infection affecting many children worldwide, with 5-12-year-olds accounting for 70-90% of cases. Although most countries utilize adhesive tapes to diagnose infection of Enterobius vermicularis, traditional swabbing methods in our country pose challenges, including time consumption and causing undue stress and discomfort for children. Therefore, introducing adhesive tape methodology for E.vermicularis detection is necessary.

Method & Materials

The research employed a cross-sectional survey design that involved 207 children from 42 groups in six kindergartens located in six districts of Ulaanbaatar city. Additionally, 70 kindergarten teachers and doctors participated in the study, examining risk factors that affect infections and satisfaction with diagnostic methods. To detect E.vermicularis infections, the adhesive tape method involved placing the tape on the anal swab of the child after they wake up or the organs' relaxation. After the pinworm actively compresses its eggs, the tape adheres without gas, and the child's code and age are noted. The laboratory uses a microscope with 100x and 400x magnification to detect E.vermicularis eggs. The study was conducted with the support of the Parasitology Laboratory of the National Center for Communicable Disease and the School of Bio-Medicine, Department of Biology.

Results

This study investigated the infection rate and risk factors of E.vermicularis infections among children attending various kindergartens and daycare centers in six districts of Ulaanbaatar city. Of the 207 children studied, 56% were male, and 44% were female. E.vermicularis infection was found in 15% of the children, with Chingeltei (39%) and Songinokhairkhan (16%) districts reporting the highest rates. The infection of E.vermicularis varied across kindergarten types, with rates of 24% in 24-hour daycare centers and 12% in home-based kindergartens and portable water centers. Children aged five years had the highest infection rates, while 0.05% of children attending special and middle-of-the-building kindergartens were affected. The study identified several risk factors for E.vermicularis infection, including poor personal and environmental hygiene, substandard living and learning environments, inadequate parental attention, and heavy workloads for kindergarten teachers. Additionally, the adhesive tape method for diagnosing enterobiasis was highly satisfactory among 80-90% of the teachers surveyed, as it was less invasive, more practical, and less time-consuming than alternative diagnostic techniques.

Conclusion

The adhesive tape method detected E.vermicularis eggs in 15% (31) of the children studied. Poor personal and environmental hygiene, inadequate parental attention, substandard living and learning environments, high workload for kindergarten teachers, non-early detection of infection, and using specific, less-sensitive detection techniques were identified as major risk factors for infection of E.vermicularis spread.

Oral Session II

RADIOLOGY & RADIOTHERAPY

Presenters:

- Job van den End
- Taravat Hedayati Kalourazi
- Jerzy Krzeszowiak
- Alsideg Nweir

ISCOMS 2024 SCIENCE BEYOND BORDERS

Evaluation of local side effects of radiotherapy in patients with thyroid cancer

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Introduction

Locoregional external beam radiotherapy (EBRT) is selectively used in thyroid cancer patients to obtain locoregional control in extensive disease or in high-risk patients after incomplete surgical resection. Despite technological advances, EBRT is still associated with acute and late toxicities, but data on thyroid cancer-specific toxicities are limited. Acute and late toxicities, long-term quality of life (QoL) and the correlation of this QoL with treatment characteristics were studied in this cohort of thyroid cancer patients.

Method & Materials

Thyroid cancer patients treated with locoregional EBRT at Universal Medical Centre Groningen (UMCG) from 2007 to 2023 were studied. Patient and treatment characteristics were extracted from patient files retrospectively, after local ethics committee approval. Acute (<6 weeks) and late (Ú3 months) toxicities and QLQ-H&N35 results, collected as standard part of patient care, were extracted from a prospective database of the Department of Radiotherapy. Additionally, living patients were asked to complete two questionnaires (QLQ-H&N43-renewed version of QLQ-H&N35- and SF-36-RAND-36), allowing a longitudinal comparison, using the Wilcoxon signed-rank test. Correlations were evaluated between questionnaire scores and EBRT techniques, using the Mann Whitney U test and other treatment characteristics, using the Spearman Rank correlation.

Results

For the retrospective analysis, 66 patients were studied. In a subset of 31 patients that completed the questionnaires during EBRT prospectively, acute toxicities included: dermatitis (100%), dysphagia (83%), pain (74%), hoarseness (74%), tough mucus (55%), xerostomia (52%), change of taste (37%), and mucositis (26%). Late toxicity presented as persisting acute toxicity and fibrosis (65%). In these 31 patients, after six months, only the QLQ-H&N35 domains ?social eating? ($p=0.031$) and ?dry mouth/sticky saliva? ($p=0.025$) were impaired, in comparison to pre-radiation. 25 out of the 66 patients were alive and 17/25 filled in the two additional questionnaires. Long-term mitigation was not observed for the 10 patients that completed both QLQ-H&N35 and QLQ-H&N43. For the treatment characteristics, only the EBRT technique correlated with an improved QLQ-H&N43 score ($U=5.5$, $p=0.047$).

Conclusion

EBRT results in acute and late toxicities in most patients and in a diminished QoL. Therefore, there is a compelling need for more refined radiation techniques, such as proton therapy.

Computer aided diagnosis (CAD) system for detecting breast cancer masses in mammographic images based on YOLO deep learning algorithm

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Introduction

Breast cancer, which is the second leading cause of death in women worldwide, requires early and accurate diagnosis. Although mammography is vital in early detection, its interpretation may vary with radiologist expertise. Using artificial intelligence (AI) and the YOLO (You Only Look Once) deep learning algorithm, this study introduces a computer-aided analytical (CAD) approach, which aims to reduce human error and speed up diagnosis.

Method & Materials

The basic of our methodology is carefully selecting of a diverse dataset from the Digital Database for Screening Mammography (DDSM) and INBreast datasets. These images represented various breast types, ages, and malignancy levels. Before training, data preprocessing such as pixel density standardization, and contrast enhancement was employed to ensure uniformity of the data. The YOLO deep learning model, with repeatable training and validation for model development, and validation metrics, including accuracy, sensitivity, specificity, area under curve (AUC) for receiver operating characteristic (ROC) curve, and cross-validation were used in this study.

Results

Our model demonstrated an accuracy of 94.5% to correctly detect cancer masses in breast images. A sensitivity of 89.2% and a specificity of 96.3% confirm its capability in breast cancer masses detection. Moreover, the area under the receiver operating characteristic curve (ROC-AUC) reached the value of 0.96, indicating the strong performance of our model. This consistent performance in cross-validation proves the model's reliability for further prediction.

Conclusion

Using artificial intelligence for breast cancer masses detection would lead to early diagnosis, reducing the mortality rate and saving significant costs for the patients. The final accuracy of our model with different validation metrics shows the eligibility of our model to perform as a promising diagnostic tool.

The investigation of individual and composite radiological markers of frailty in CT scans in elderly patients undergoing abdominal surgery.

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Introduction

Frailty syndrome has been proved to be an important risk factor of poorer outcomes in older patients undergoing abdominal surgery. Currently a gold standard of its evaluation is the Comprehensive Geriatric Assessment (CGA). Unfortunately this method is time-consuming and is associated with a significant risk of bias. The hypothesis of the study assumed that the measurement of the parameters of the ageing on the CT scans could provide a more objective and replicable method of frailty assessment and the postoperative outcomes prediction.

Method & Materials

Consecutive patients Ú65, operated in our Department, were included for CGA evaluation. Within this group CT measurement was performed in patients whose scans were available in the internal hospital system, including sarcopenia, osteoporosis, renal atrophy, abdominal aorta calcification (AAC) and sarcopenic obesity. These factors were analyzed both individually and together as a Radiological Component Frailty Score. Clinical data such as length of stay, postoperative complications, and ICU admissions were also collected. The statistical analysis was performed using IBM SPSS Statistics version 29.0.0.0 (241).

Results

97 patients were included to the study, with the median age of 72 years. The prevalence of frailty syndrome was 81.44%. Most common procedures type of surgery were colorectal resections (30.93%), but the group was heterogenous in terms of the types of surgery. Individually, only AAC was a factor significantly determining the occurrence of frailty syndrome (OR 1.412; IC 1.123-1.776; p=0.003) and postoperative complications (OR 1.128; IC 1.034-1.230; p=0.007), while the other analyzed radiological factors did not have a significant impact. A component score, which included all five radiological domains, had a significant efficacy in frailty detection (AUROC=0.652; p=0.039), but it was not useful in terms of morbidity prediction.

Conclusion

CGA is still the most valuable tool of frailty evaluation. A component score of CT parameters of ageing could be used for frailty detection, but it has no significant value for postoperative complication prediction. The usefulness of the Radiological Component Frailty Score should be analyzed on a larger, more homogenous group of patients.

Evaluating Analytical Competency in Shoulder X-ray Interpretation Among First-Year Family Physicians

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Introduction

The accurate interpretation of radiological images is an important skill for primary care physicians, directly affecting the diagnosis and subsequent care of patients. This study evaluates the proficiency of first year family doctors in interpreting shoulder X-rays. Recognizing the importance of early exposure and training in radiology for general practitioners, our research aims to identify areas of strength and weakness in their diagnostic capabilities, with a specific focus on shoulder imaging.

Method & Materials

In this cross-sectional study, 48 first-year family doctors from various primary care centers in Libya participated, with a mean age of 28 years Ò1.34; 83% were female. The physicians analyzed 16 different shoulder X-rays, to identify abnormal structures and provide comments on their findings. The study used descriptive and inferential statistical analyses to assess their interpretations, with a focus on their ability to recognize various pathologies and the occurrence of false interpretations of normal structures.

Results

Our primary results showed that 97% of participants were able to successfully identify foreign bodies in the X-rays. However, only 33.3% were able to correctly identify abnormal relationships between structures. Additionally, 3.2% and 2.5% were able to identify diseased acromioclavicular joint and surgically removed scapula respectively. also, 3% of the doctors recognized osteophytes, and 7.5% correctly identified a Hill-Sachs lesion. The most common normal structures that were interpreted as abnormal are the clavicle 13.5%, coracoid process 11.3%, and acromion process 9.37%.

Conclusion

Our study shows a significant proficiency in recognizing basic abnormalities among first-year family doctors. But also points out major gaps in identifying more complex conditions. The high rate of certain false positives suggests a need for enhanced training in shoulder radiology among family physicians. As accurate radiological interpretation is important in primary care settings, these results could inform decision-makers to improve the local educational program, ultimately improving patient outcomes.

Oral Session II

NEUROLOGY

Presenters:

- Ghazale Angaji
- Motahareh Bagheri
- Hadil Diab
- Changwei Guo
- Mariana Luna Alvarez
- Manon Stern

Advancements in seizure prediction through graph neural networks modeling EEG structures

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Co-authors: Togha M. (Mansoureh)

Introduction

Seizure, a debilitating neurodegenerative disease affecting millions of people, is generally resistant to conventional treatment in 30% of cases. Predicting the pre-ictal state, a brief state before seizure occurrence, provides a promising intervention strategy. Previous studies have shown that EEG signals can be used for early detection, but there are still gaps in achieving greater accuracy. This study investigates using deep learning and EEG data for seizure prediction.

Method & Materials

Our study introduces a groundbreaking approach leveraging Graph Neural Networks (GNNs) designed to capture the complex nature of EEG data. We establish two novel EEG graph structures to encapsulate critical aspects of brain activity: the Electrode Geometry Graph and the Dynamic Brain Connectivity Graph. The Electrode Geometry Graph captures spatial relationships among EEG electrodes, encoding the physical proximity and layout of scalp electrodes. In contrast, the Dynamic Brain Connectivity Graph models the evolving functional connections between brain regions, capturing temporal dynamics in neural activity.

Results

Implementing these graph structures significantly enhances seizure classification. Our model achieves an Area Under the Receiver Operating Characteristic Curve (AUC-ROC) of 0.875 for seizure detection and a weighted F1-score of 0.749. Crucially, it demonstrates unprecedented efficacy in accurately identifying and classifying rare seizure types, marking a substantial improvement over previous methodologies. The model's interpretability analysis precisely localizes 25.4% of focal seizures within EEG data, a critical advancement in understanding seizure onset regions.

Conclusion

Our study introduces a pioneering approach that revolutionizes EEG-based seizure prediction. By integrating EEG graph structures into deep learning frameworks, our model achieves remarkable accuracy in seizure classification, particularly in identifying rare seizure types. This breakthrough holds immense promise for clinicians, offering a deeper understanding of seizure onset regions and paving the way for more targeted and effective treatment strategies in neurology.

Cognitive Decline in Parkinson's Disease: A Machine Learning Study of DAT SPECT and Clinical Biomarkers

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Introduction

Parkinson's disease (PD) is an age-related unprogressive neurodegenerative condition characterized mostly by motor symptoms. Although a wide range of non-motor symptoms (NMS) are frequently experienced by PD patients. One of the important and common NMS is cognitive decline, which is measured using different cognitive scales. In this study, we aim to identify the optimal combination of cognitive assessment scales and biomarkers that can provide the most accurate and robust prediction of cognitive decline in PD.

Method & Materials

Hybrid Machine Learning Systems (HMLS) have previously shown superior performance in image and clinical data classification and detection. In this study, we investigated the prediction of cognitive decline in a 4-year interval in de-novo PD patients using HMLS with Dopamine Active Transporter Single-Photon Emission Computed Tomography (DAT SPECT) imaging and clinical biomarkers. We collected 390 DAT SPECT images and their clinical data in years 0 and 4 from Parkinson's Progression Markers Initiative (PPMI). We then designed a 3D Autoencoder to extract deep radiomics features (DF) from DAT SPECT images, and we then concatenated it with five clinical features (CF) to predict cognitive decline based on four cognitive scales, including Montreal Cognitive Assessment (MoCA), MDS Task Force guideline (MDS-TFG), The Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPRDS-I) and Site Investigator Diagnosis (SID).

Results

In this study, different subsets of features were evaluated using multiple classifiers for the detection of cognitive decline using four scales, namely MDS-TFG, SID, MDS-UPDRS, and MoCA. The CF subset demonstrated the highest performance for MDS-TFG scale, achieving a cross-validation test accuracy of 91.4 Ò 1.2% with K-Nearest Neighbors+Mutual information (MI) and 100 selected features. For SID scale, the combined CF+DF subset exhibited the best results, attaining a cross-validation test accuracy of 91.4 Ò 4.8% with Artificial Bee Colony+-MI and 20 selected features. In the case of MDS-UPDRS scale, the CF subset outperformed others, yielding a cross-validation test accuracy of 79.4 Ò 1.2% using Support Vector Classifier (SVC)+F regression and 10 selected features. However, for MoCA scale, the combined CF+DF subset showed superior performance, achieving a cross-validation test accuracy of 61.9 Ò 4.5% with SVC+MI and 50 selected features.

Conclusion

The study findings indicate that the MDS-TGF scale may be a more effective predictor of 4-year cognitive decline when using HMLS, imaging data, and clinical biomarkers compared to the MDS-UPDRS, MoCA, and SID scale.

Cerebral Small Vessel Disease and All-cause Mortality in Geriatric Outpatients: The Amsterdam Aging Cohort

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Introduction

Introduction: Cerebral Small-Vessel Disease (CSVD) is an age-related multifactorial condition that affects the small blood vessels supplying the brain?s white matter and deep structures. It is associated with adverse outcomes in geriatric patients including vascular cognitive impairment. This study investigates the association between CSVD and all-cause mortality using the Amsterdam Ageing Cohort, a study in patients attending the geriatric outpatient clinic at the Amsterdam University Medical Center.

Method & Materials

Methods: In this prospective cohort study, 1170 geriatric outpatients (mean age, 79.5 Ò 6.6; 50.6% women) were included. CSVD diagnosis relied on MRI (n=800) or CT (n=370) scans, identifying white matter hyperintensities (Fazekas score Ú 2), cerebral microbleeds(n Ú 3), or lacunar infarctions (n Ú 1). Mortality data spanning from 2016 to 2022 was obtained from the Dutch Municipal Register. The association between CSVD and all-cause mortality was examined using a Kaplan-Meier curve and Cox proportional-hazards models. Model 1 adjusted for age and sex, Model 2 included additional adjustments for a history of cardiovascular diseases and risk factors, and Model 3 additionally adjusted for cognitive functioning.

Results

Results: we analyzed data from 1170 patients with a median follow-up of 1301.5 (IQR, 491.5 ? 1462.5). Among these patients 750 (64.1%) had CSVD, of whom 257 (34.3%) died, whereas among the 450 (35.9%) patients without CSVD, 92 (21.9%) died. Cox regression analyses showed a significantly increased mortality risk for patients with CSVD (HR 1.42, 95% CI 1.11 ? 1.81) following adjustments for age, sex, a history of cardiovascular diseases and risk factors, and cognitive functioning. Interaction term analyses for CSVD and age, sex, a history of cardiovascular diseases, and cognitive diagnosis revealed no effect modifiers.

Conclusion

Conclusion: CSVD is associated with increased mortality risk in geriatric outpatients, independent of confounding factors. This underscores the impact of CSVD on elevated mortality, emphasizing the role of effective cardiovascular risk management in delaying or preventing CSVD development in this population.

The Golden 75 Min And Black 120 Min For Acute Basilar Artery Occlusion Embolectomy: Effect Of Procedure Time On Outcome

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Introduction

Previous studies have demonstrated the association between the procedure time (PT) and outcomes for patients with proximal large vessel occlusion; however, whether the relationship remains for patients with acute basilar artery occlusion (ABAO) was not clear. We aimed to characterize the association between PT and other procedure-related variables on clinical outcomes among patients with ABAO who underwent endovascular treatment (EVT).

Method & Materials

Patients with ABAO who underwent EVT with a documented PT in the EVT for Acute Basilar Artery Occlusion (BASILAR) study from January 2014 to May 2019 among 47 comprehensive centers in China were included. Multivariable analysis was performed to reveal the association between PT and 90-day modified Rankin Scale score, mortality, complications, and all-cause death at 1 year.

Results

Of the 829 patients from the BASILAR registry, 633 eligible patients were included. Longer PT were associated with a lower rate of favorable outcome (by 30 minutes, adjusted OR 0.82 [95%CI 0.72?0.93], p = 0.01). In addition, a PT Û 75 minutes was associated with a favorable outcome (adjusted OR 2.03 [95% CI 1.26?3.28]). The risk of complications and mortality increased by 0.5% and 1.5% with every 10 minutes increase in PT, respectively (R2 = 0.64 and R2 = 0.68, p < 0.01). The cumulative rates of favorable outcomes and successful recanalization plateaued after 120 minutes (2 attempts). Restricted cubic spline regression analysis for the probability of favorable outcomes had an L-shape association (p nonlinearity = 0.01) with PT with significant benefit loss before 120 minutes and then appeared relatively flat.

Conclusion

For patients with ABAO, procedures that exceeded 75 minutes were associated with an increased risk of mortality and lower odds of a favorable outcome. A careful assessment of futility and the risks of continuing the procedure should be made after 120 minutes.

Assessing immune and DNA repair spatial status of multi stage glial tumors

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Introduction

The tumors of the central nervous system (CNS) encompass a broad group of brain and spinal neoplasms. Approximately 80% of malignant brain tumors are gliomas, ranging from low-grade to high-grade gliomas and glioblastoma multiforme (GBM). Understanding the DNA repair pathways, cell proliferation dynamics, and the tumor microenvironment can help assess whether there is a difference among various types and grades of gliomas. Emerging methodologies in cancer research, such as the adoption of spatial proteomics at the single-cell level using formalin-fixed and paraffin-embedded samples (FFPEs) from solid tumors, are opening promising avenues for novel therapeutic perspectives.

Method & Materials

We conducted a comprehensive analysis of the tumor-immune microenvironment in glial tumors of different WHO grades through single-cell spatial profiling. This was achieved using highly multiplexed tissue cyclic immunofluorescence (t-CyCIF) on 20 formalin-fixed and paraffin-embedded (FFPE) tumor samples, encompassing astrocytoma, oligodendroglioma, and glioblastoma from patients. The FFPE blocks underwent deparaffinization, dehydration, and rehydration in citrate buffer. Subsequently, slides were subjected to multiple staining cycles using a panel of 23 fluorochrome-tagged antibodies and were imaged in each cycle using a Rarecyte Scanning System. The resulting multidimensional images were then analyzed using computational techniques, such as Napari, StarDist, and MCMICRO to assess immune microenvironment, spatial tissue architecture and protein expression relative to DNA repair pathways and cell cycle dynamics.

Results

Computational analysis was performed on the images of 4 low-grade astrocytomas, 4 high-grade astrocytomas, 4 glioblastomas, 4 low-grade oligodendrogliomas, and 4 high-grade oligodendrogliomas. We found phenotypic heterogeneity among the different types and grades of gliomas, demonstrating specific tumor and stromal immunologic compositions. The histological grade is correlated with the infiltration of immune cells. Comparisons were also made between primary tumors and recurrent ones that had received radiotherapy. The differences in the tumor microenvironment are evident among these cancers.

Conclusion

The adoption of spatial proteomics and computational techniques has positioned us at the forefront of deciphering the intricacies of CNS tumors. This study serves as a steppingstone for further exploration and development of novel immunotherapeutic strategies, holding promise for improved outcomes in the clinical management of gliomas.

Mild and deep hypothermia differentially affect cerebral neuroinflammatory and cold shock response following cardiopulmonary bypass in rat

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Introduction

Neuroinflammation is considered to play role in the pathogenesis of neurocognitive complications after cardiac surgery, particularly in cardiopulmonary bypass (CPB) assisted procedures. Targeted temperature management (TTM) serves as a neuroprotective strategy during cardiac surgery, possibly through the activation of cold shock proteins, but data on its effectiveness in mitigating neuroinflammation is lacking. We therefore investigated the effects of mild compared with deep hypothermia on the neuroinflammatory response and cold shock protein expression after CPB in rats.

Method & Materials

Rats were subjected to 1 hr of mild (33oC) or deep (18oC) hypothermia during CPB or sham procedure. PET scan analyses using TSPO ligand [11C]PBR28 were performed on day 1 (short-term) or day 3 and 7 post-procedure (long-term) to assess neuroinflammation. Hippocampal and cortical samples were obtained at day 1 in the short-term group and at day 7 in the long-term group. mRNA expression of M1 and M2 microglia associated cytokines was analysed with RT-PCR. Cold shock protein RNA-binding motive 3 (RBM3) and tyrosine receptor kinase B (TrkB) receptor protein expression were determined with Western Blot.

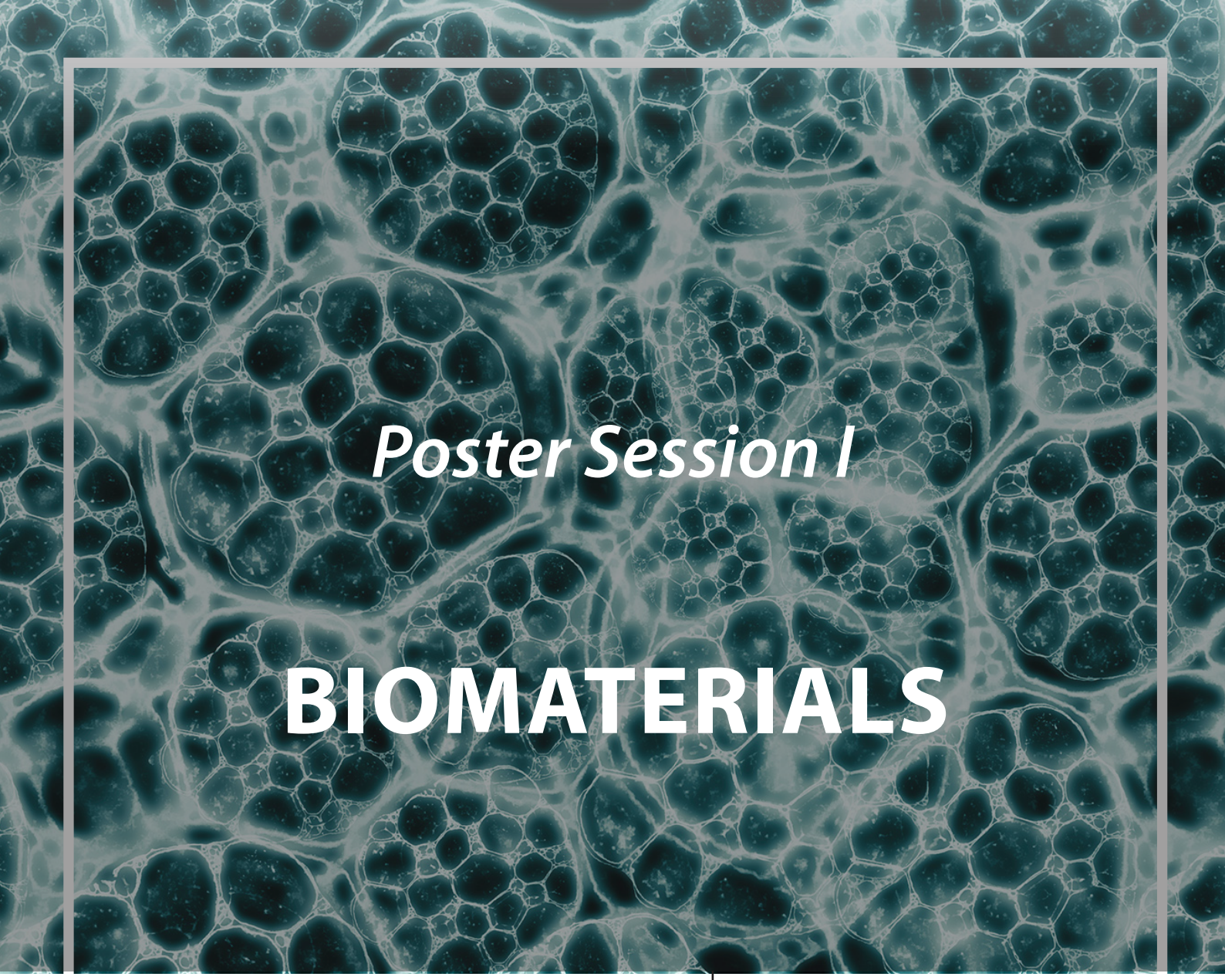
Results

Standard uptake values (SUV) of [11C]PBR28 in CPB rats at 1 day and 3 days were similar to that of sham animals. At 7 days after CPB the SUV was significantly higher in amygdala and hippocampal regions of the CPB 18oC group as compared to the CPB 33oC group. No differences were observed in the expression of M1 and M2 microglia-related cytokines between TTM 18oC and 33oC. RBM3 protein levels in cortex and hippocampus were significantly higher in CPB 33oC compared to CPB 18oC and sham 33oC, at day 1 and day 7, respectively.

Conclusion

TTM at 18oC increased the neuroinflammatory response in amygdala and hippocampus compared to TTM at 33oC in rats undergoing a CPB procedure. Additionally, TTM at 33oC induced increased expression of TrkB and RBM3 in cortex and hippocampus of rats on CPB compared to TTM at 18oC. Together, these data indicate that neuroinflammation is alleviated by TTM at 33oC, possibly by recruiting protective mechanisms through cold shock protein induction.

POSTER SESSIONS



Poster Session I

BIOMATERIALS

Presenters:

- Seyedehsepideh Ghadirnezhadshiadeh
- Henrike Sofie Schulze
- Bruno Terada
- Cristian Urrea Tavera
- Paula Andrea Vasco Galvis

Protective effect of chrysin nanoparticle on hepatotoxicity of acetaminophen in lab rats

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Introduction

Acetaminophen is the most widely used pain reliever-antipyretic drug, acetaminophen overdose is one of the main causes of acute liver failure. Chrysin is an important flavonoid compound of the passifloura plant family, which has a wide range of anti-cancer, antioxidant and anti-inflammatory activities. In the present study, the protective effect of chrysin nanoparticles on acute liver toxicity of acetaminophen in high doses has been investigated.

Method & Materials

In this study, chrysin nanoparticles were first prepared and the size of the nanoparticles was determined with the help of scanning electron microscope (SEM). In the following, 42 male and adult large white laboratory mice were divided into 7 groups of 6 and received a single dose of acetaminophen before treatment in all groups except the control groups (1000 mg/kg) orally on two occasions. One of the groups was treated with intraperitoneal injection daily for 14 days. On the first and fifteenth day, blood was taken from the mice and the factors of alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) and inflammatory factors TNF -a and IL2 by ELISA method, as well as Total Antioxidant activity by FRAP method, and finally, the liver was separated and placed in 10% formalin for histopathological examination. The data were analyzed using one-way analysis of variance.

Results

Chrysin nanoparticles reduced the activity of liver enzymes (AST, ALT and ALP) with a statistically significant relationship ($p=0.01$) with the untreated group. The total antioxidant capacity increased in a dose-dependent manner compared to the untreated group ($p=0.01$). Also, the effect of chrysin nanoparticle in both doses of 5 and 10 was greater than the effect of silymarin ($p=0.01$). TNF-a changes had a significant relationship ($p=0.03$) in groups 3, 4 and 7 showed to the group receiving acetaminophen without treatment. Also, chrysin nanoparticle did not have a significant reducing effect on IL2 compared to silymarin and the untreated group. According to the histopathological results, chrysin nanoparticle is able to reduce tissue damage by inhibiting oxidative stress parameters, which is probably The effect is due to the potential of chrysin nanoparticles in increasing the total antioxidant capacity and increasing the body's response to oxidants.

Conclusion

chrysin nanoparticles prevent hepatotoxicity by acetaminophen by reducing liver enzymes and TNF-a and increasing total antioxidant capacity and protecting liver tissue from necrosis.

Advancing Food Allergen Sensitization Research: The Promise of Immunocompetent Intestine-on-a-Chip Models

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Introduction

Food allergies have emerged as a significant public health concern. With the growing need for sustainable food and, therefore the transition from animals towards more plant derived protein use, novel allergens may be introduced in the diet. To address this challenge, there is a need for innovative models capable of accurately simulating the complex sensitization process underlying food allergies. These models hold the potential to assess the allergenicity of known and novel food proteins and advance the development of new therapeutics.

Method & Materials

This study combined fused filament fabrication and melt electrowriting (MEW) to create an Intestine-on-a-Chip model (IoC), in which human intestinal epithelial cells (Caco-2) were cultivated on novel U-shaped MEW scaffolds. We assessed biocompatibility and immunogenicity of all utilized materials by studding their effect on the monocyte derived dendritic cells (moDCs) phenotype and compared IoC functionality with a standard Transwell model, by examining intestinal barrier integrity (transepithelial electrical resistance), barrier permeability (FITC-dextran diffusion), cell viability (lactate dehydrogenase leakage (LDH)), metabolic activity (PrestoBlue assay), brush border maturation (alkaline phosphatase activity), cell morphology, and coverage (confocal microscopy).

Results

All materials used exhibited excellent biocompatibility and did not enhance moDC costimulatory molecule expression. After a three-week culture period, the IoC exhibited leak-tightness for up to four hours mirroring the performance of a conventional Transwell moldel. It displayed higher metabolic activity (p Û 0.05) and LDH activity (p Û 0.05) compared to the traditional Transwell model. Initial findings indicated enhanced brush border enzyme activity, a functional characteristic of enterocytes. However, the application of fluid flow in the IoC did not significantly modify the measured parameters compared to static conditions.

Conclusion

Our study represents a significant step towards the creation of an immunocompetent IoCs. The IoC's performance parallels, and in some aspects, could possibly surpass that of conventional Transwell models. Future phases will encompass fine-tuning fluid dynamics and incorporating an artificial mucus layer and immune cells, starting with moDCs followed by T cells, transforming the IoC into a functional immunocompetent model, enabling comprehensive investigations into the development of type 2 immune responses in food allergy.

Fat Graft Retention Rate: Fat graft enriched by Adipocyte Stem Cells and Nanofat

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Introduction

Fat grafting (FG) finds widespread application in plastic surgery, serving both cosmetic and reconstructive purposes. However, the FG retention rates exhibit significant variability, ranging from 20% to 80% over a two-year period. Several therapeutic strategies analyzed the fat graft retention rate (FGRR). Recently, FG enrichment has emerged as a promising alternative. This study aims to compare the retention rates between isolated FG and its enriched form by adipocyte stem cells and Nanofat.

Method & Materials

We analyzed 58 male Wistar rats. Three animals were designated for fat harvesting Nanofat or the adipocyte stem cell (ASC) preparation. The rest of the rats received autologous fat graft (by inguinal region). The rats were divided into three groups: the control group (1mL fat injection), ASC group (0.7 mL fat + 0.3 mL ASC (1x106 cells)), and Nanofat group (0.7 mL + 0.3 mL Nanofat). Then, each group was subdivided into three time periods: four, eight, and twelve-month follow-ups. We performed macroscopic analysis (ultrasound volume measurements and direct observation of the 12 weeks of fat graft dissection). The histologic analysis (vascular density, inflammatory cell counting and fibrosis). Also, we analyzed the level of gene expression of IL1-rap, IL-10, CD68, TNF, MMP-3, and MMP-9.

Results

Macroscopic examination showed an increase in FG volume in both the ASC and Nanofat groups compared to the control group across all timepoints. The microscopical analysis showed no difference in inflammatory cell count among the groups ($p = 0.3$). The number of arterioles in the graft was three times greater in the ASC and Nanofat groups ($p = 0.05$) versus the control group, while more cysts and fibrous tissue were exhibited in the control group. Furthermore, the ASC group showed a decrease in IL-10 ($p = 0.035$) and CD-68 ($p = 0.026$) levels compared to the control group.

Conclusion

Our study suggests that enriching FG with ASC and Nanofat enhances its retention rate.

Nanobioconjugates for Targeted Delivery of Antigenic and Therapeutic Peptides in Colorectal Cancer

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Introduction

Colorectal cancer (CRC) is a significant global health challenge, ranking third in cancer-related mortality. To address this, nanobioconjugates, specifically poly(lactic-co-glycolic acid) (PLGA) nanoparticles (NPs), with unique nanoscale physicochemical characteristics, have emerged as versatile platforms for advanced drug delivery in CRC treatment. Peptides, known for potent chemotherapeutic and vaccine antigen capabilities, play a vital role in CRC therapy. This study employs peptide-loaded PLGA NPs to confront current CRC therapy challenges. Through nano-level encapsulation, exploring the physicochemical properties of peptides and PLGA, the research aims for enhanced stability and precise controlled release. Surface modification of PLGA NPs enhances therapeutic efficacy while minimizing side effects, promising to reshape CRC therapy by leveraging nanobioconjugate attributes and the synergistic potential of peptide therapeutics.

Method & Materials

In this study, two strategies are employed for potential CRC approaches. Firstly, CDC25B-II peptide, inhibiting CRC tumor growth via CD8+ T-cell activation, is encapsulated in PLGA-COOH. Surface modification with D-mannosamine targets antigen-presenting cells for a specific immune response against CRC cells. Secondly, the GILGFVFTL peptide, inhibiting CRC cell proliferation, is encapsulated in PLGA-PEG-Mal NPs. Functionalized with the G3 peptide, specific to CRC cells, these NPs are designed for targeted delivery to the CRC tumor microenvironment. Both strategies use D-_-Tocopherol as surfactant and are achieved through the emulsion-evaporation method.

Results

The PLGA-CDC25B-II-loaded NPs exhibited a mean particle size of 240 Ò nm, a polydispersity index of 0.24 Ò 0.02, and a _-potential of -61.6 Ò 1.2 mV. Quantification of CDC25B-II involved constructing a calibration curve with an R2 value of 0.9905. The encapsulation efficiency was 26.3 Ò 15.7%, and the drug-loading capacity was 0.24 Ò 0.14%.

Conclusion

Encapsulation of CDC25B-II in PLGA NPs was successful, as indicated by the observed mean particle size, polydispersity index, and _-potential. The encapsulation efficiency and drug-loading capacity fall within the reported range for peptide encapsulation in PLGA NPs, affirming the effectiveness of the chosen formulation. The interplay between physicochemical properties of PLGA and CDC25B-II is evident in the particle size, suggesting a balanced influence of molecular weight and lactic acid:glycolic acid ratio, and the strong negative _-potential indicates the stability of the NPs.

Biopolymer-based drug delivery nanosystems for parasporin transport and release at colon tumoral microenvironment

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Introduction

Colorectal cancer (CRC) is a widespread disease ranking third among the most common cancers worldwide. Parasporins derived from Bacillus thuringiensis, such as Parasporin 2 (PS2), have demonstrated cytotoxic effects on CRC cells. Oral administration faces challenges due to gastrointestinal pH and stomach enzymatic action affecting their activity. Drug delivery systems (DDSs) based on chitosan nanoparticles (CS-NP) loaded with parasporins are proposed to overcome this issue. This study focused on producing recombinant parasporins in Escherichia coli (E. coli) and developing chitosan-based DDSs loaded with parasporins as a therapeutic alternative with improved specificity, efficacy, and release profile for CRC treatment.

Method & Materials

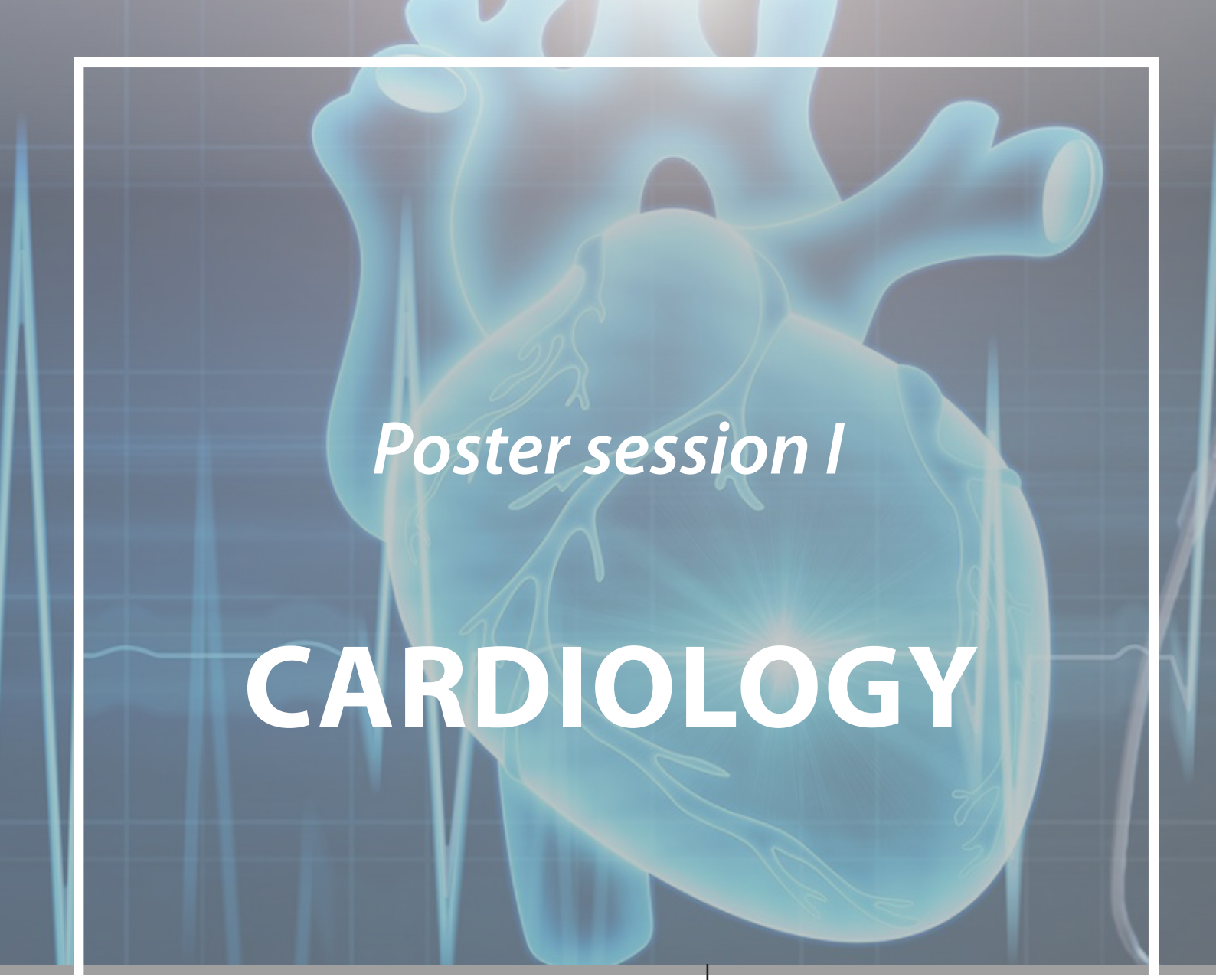
Chitosan (medium molecular weight), pentasodium tripolyphosphate (TPP), acetic acid, sodium chloride, and isopropyl-_-D-thiogalactopyranoside (IPTG) were obtained from Sigma Aldrich. Milli-Q quality water (18.2 MÍ˙cm) was obtained from Millipore (Bedford, MD, USA). All chemicals used were of analytical grade and used as received. Method The cDNA of PS2 was cloned into the pET-30a(+) vector, transforming the E. coli BL21 (DE3) strain and inducing expression with IPTG. PS2, found as inclusion bodies, was solubilized in sodium carbonate and purified through immobilized metal affinity chromatography (IMAC). Parasporin-loaded CS-NPs were prepared via ionic gelation. Chitosan was dissolved in acetic acid at 60 ¯C adjusting the pH to 6.3 with NaOH. PS2 and TPP was added to the chitosan solution under agitation, at room temperature. The particles were collected by centrifugation at 8000 rpm for 20 minutes at 4 ßC.

Results

PS2 was efficiently expressed in the E. coli expression system with a high degree of purity. The physical characteristics of the CS-NPs exhibited optimal size (188.5 Ò 0.5 nm), _ (0.2 Ò 0.0), and _ potential (+8.04 Ò 0.6 mV), with an encapsulation efficiency of 41.7 Ò 1.2 and a loading content of 1.0 Ò 0.9. The encapsulated NPs maintained antiproliferative activity when treating SW480 and SW620 cancer cell lines.

Conclusion

PS2 was produced in the E. coli expression system and successfully encapsulated in CS-NP, obtaining stable and moderately dispersed nanosystems with suitable size, EE (41.7%), DLC (1.0%), and SW480 and SW620 antiproliferative activity. The results are promising for implementing CS-NP as a therapeutic alternative for CRC treatment.



Poster session I

CARDIOLOGY

Presenters:

- Behzad Ensan
- Diba Haghian
- Teodora Milojević
- Hamza Saad
- Patricija Vanckavičiūtė
- Alicia del Carmen Yika
- Mei You
- Kimmia Azampanah

ISCOMS 2024 SCIENCE BEYOND BORDERS

Lipid variability in Drug-Na'Ive individuals affected with Major Depressive Disorder: A Systematic Review and Meta-Analysis

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Introduction

Major depressive disorder (MDD) is a common, chronic, recurrent, and multifactorial disorder, which is accompanied by psychological, physical, and biochemical disturbances. Although growing evidence shows that lipid profile is associated with disease severity and attempting suicide in MDD patients, controversies remain unresolved. Therefore, this study aimed to provide a comprehensive synthesis of the evidence examining lipid profiles in drug-naãve MDD patients

Method & Materials

We searched PubMed, Scopus, and ISI Web of Science up to August 2023. The primary outcomes were total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, and triglyceride levels in drug-naãve MDD patients. We performed meta-analyses and meta-regression using a random-effects model based on heterogeneity among studies and generated pooled standardized mean differences (SMDs).

Results

: A total of 17 articles comprising 2174 individuals including drug-naãve MDD subjects and controls- free of metabolic diseases- were included. Our results showed that concentrations of total cholesterol were lower in drug-naãve MDD patients than in healthy controls (SMD -0.49, 95% CI -0.881 to -0.105; P=0.015; I2 = 90.6%). However, the comparison of other lipid levels including LDL, VLDL, HDL, and TG between MDD patients and healthy controls demonstrated no significant difference. Subgroup analysis restricted reduced cholesterol levels to male-dominant investigations. This finding should be interpreted cautiously due to limited number of publications. In addition, the association of total cholesterol level with MDD is more prominent in male-dominant studies (SMD -1.20, 95% CI -2.23 to -0.18, I2=87.9%) than in female-dominant studies (SMD -0.25, 95% CI -0.63-0.13, I2=89.0%). In meta-regression, none of the factors including year of publication, NOS score, sample size, BMI, and mean age of participants had a remarkable influence on the relationship between cholesterol level and MDD. No obvious publication bias was reported.

Conclusion

Lower levels of total cholesterol are associated with MDD; so early lipid monitoring as a simple and available method and targeted interventions might be necessary. However, more investigations are required to elucidate any possible causality relationship between depression and lipid profile alterations.

Analyzing the diagnostic potential of diastolic echocardiography parameters in heart failure patients with preserved ejection fraction

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Introduction

Heart failure preserved ejection fraction (HFpEF) is growing worldwide. It is defined as LVEF >45% with HF clinical symptoms. Tissue Doppler imaging echocardiography (TDI) is an excellent tool for evaluating the diagnosis and prognosis of HFpEF. More data on the role of TDI parameters in evaluating HFpEF prognosis is needed. Our study aims to investigate the association between some echocardiography parameters and short-term clinical outcomes in patients with HFpEF.

Method & Materials

Between 2019 and 2021, a hundred sinus rhythm patients were enrolled based on Framingham criteria, diastolic dysfunction, ejection fraction (EF) of more than 45%, and amino-terminal pro-brain natriuretic peptide (pro-BNP) of more than 500 Pg/dL. TDI parameters, including E/EM and deceleration time, were measured. After six months of follow-up, patients were classified into two groups (with or without morbidity).

Results

At the end of our follow-up, 22 cases had morbidities. None of the patients died during our study period. Higher mean values of E/Em and E/A correlated with higher incidence of morbidities ($p<0.003$). Furthermore, shorter mean DTs showed a considerable association with morbidities ($p<0.004$). Covariance analyses indicated that E/Em and DT were independent determinants of HFpEF prognosis. In addition, at the cut-off of 13.5, E/Em was 96.8% sensitive and 54.1% specific for predicting comorbidity in HFpEF patients.

Conclusion

E/Em and DT parameters can be used as accurate and beneficial tools for prognosis in HFpEF patients.

Predictors of outcome in patients with transmural infarction

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Introduction

Transmural myocardial infarction is accompanied by high in-hospital mortality and is associated with the development of life-threatening complications. Determining the predictors of in-hospital mortality could significantly contribute to the understanding of pathophysiological mechanisms, and improvement of therapeutic strategies.

Method & Materials

The retrospective study included patients with a diagnosis of transmural infarction, who were hospitalized at the Cardiology Clinic of the University Clinical Center Kragujevac in the period from January to June 2022. Comorbidities, laboratory analyses, angiographic and echocardiographic characteristics were used as unchangeable variables. Primary events of interest were cardiogenic shock, cardiac arrest, and in-hospital mortality. Data from the Hospital Information System (Com Trade, Kragujevac, Serbia) were used.

Results

The research included 76 patients with diagnosed transmural infarction. Cohort consisted predominantly of male patients (76.3%), and average age was 64.9 years (SD 11.1). The most common comorbidities were arterial hypertension (72.4%), diabetes (42.2%) and dyslipidemia (21.1%). More than half of patients (59.2%) were previously hospitalized due to acute coronary syndrome, while 90.8% of patients previously underwent percutaneous myocardial revascularization. During hospital treatment, cardiogenic shock was recorded in 2.6% of patients, cardiac arrest in 9.2% of patients, while 6.6% of patients required (non)invasive ventilatory support. The overall mortality in cohort was 7.9%. Patients who did not survive had statistically significantly higher values of pro-forma brain natriuretic peptide (proBNP) (p 0.004; 29406 pg/mL (SD5593.5) - 3594.7 pg/mL (SD 858.4)) and lower left ventricular ejection fraction values (LVEF) (p 0.023; 27.5% (SD 2.5) - 42.8% (SD 1.04)) on hospital admission.

Conclusion

In-hospital mortality of patients with transmural myocardial infarction was significantly influenced by pro-forma values of brain natriuretic peptide and left ventricular ejection fraction.

Transthoracic Impedance Cardiography versus other non-invasive tests in Chronic Heart Failure Patients

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Introduction

Chronic heart failure (CHF) necessitates accurate, timely diagnosis for effective treatment. Current non-invasive methods including echocardiography, N-terminal pro-B type natriuretic peptide (NT-proBNP), and the 6-Minute Walk Test (6MWT) have limitations [1]. Transthoracic impedance cardiography (ICG) offers a promising, cost-effective alternative for cardiac function assessment in CHF patients, with benefits like continuous monitoring and reduced operator dependency [2]. Our study compares the diagnostic and prognostic accuracy of ICG with these methods in evaluating cardiac function, aiming to uncover benefits, limitations, and future research opportunities.

Method & Materials

In this retrospective study, data from 52 chronic heart failure patients diagnosed according to European Society of Cardiology (ESC) guidelines in power at that time were analyzed with a median follow-up time of 23 months. Based on their distribution continuous and categorical data were treated with appropriate statistical tests. Survival and hazard analysis utilized Kaplan-Meier estimates and Cox proportional hazards models, respectively.

Results

Moderate correlations were found between ICG and non-invasive diagnostic methods. Negative correlations with left ventricular ejection fraction (LVEF) were detected for ICG parameters pre-ejection period (PEP) ($r=-0.548$, $P<0.001$) and systolic time ratio (STR) ($r=-0.616$, $P<0.001$), while positive correlations with left atrial dimension (LAD) was seen for PEP ($r=0.510$, $P<0.001$), STR ($r=0.660$, $P<0.001$), and negative with stroke index (SI) ($r=-0.524$, $P<0.001$) and stroke volume (SV) ($r=-0.687$, $P<0.001$). NT-proBNP negatively correlated with cardiac CO and SV ($r=-0.393$, $P=0.004$). 6MWT demonstrated correlations with PEP ($r=0.673$, $P<0.001$) and left cardiac work index (LCWI) ($r=0.618$, $P<0.001$). By multivariate Cox proportional analysis, the following parameters were independently associated with cardiac death: thoracic cardiac fluid index (TFCI) Ú20.05/kÍ/m2 Hazards ratio (HR) 3.442, 95% confidence interval (CI) 1.192-9.938), NT-proBNP Ú332 pmol/L (HR 4.141, 95% CI 1.074-15.960), and LVEF Ú 28.5% (HR 3.902, 95% CI 1.006-15.125).

Conclusion

The combination of non-invasively measured TFCI, LVEF, and NT-proBNP showed great prognostic value for predicting death in patients with HF.

Validation of the Four-State Mathematical Model for Simulating Kinetic and Steady-State Voltage-Dependent Gating of Cardiac and Neural Gap Junctions

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Introduction

Gap junction (GJ) channels, composed of connexin (Cx) proteins, provide direct metabolic and electrical communication between cells. These specialized channels have been shown to gate robustly in response to transjunctional voltage, Vj. Voltage gating of GJs could play a physiological role, particularly in excitable cells, which can generate large transients in membrane potential during the propagation of action potentials. Mathematical models describing biophysical properties of gap junction channels are valuable, serving as tools for studying GJ channel gating and simulating cell clusters resembling cardiac or nervous tissue. Here, we demonstrate the validation of such a mathematical model and several variants of its applicability.

Method & Materials

For validation of mathematical model, we used electrophysiological measurements in HeLa cell pairs exogenously expressing Cx45 and in Novikoff cell pairs, which endogenously expresses Cx43. Junctional conductance was measured in selected cell pairs using a dual whole-cell patch-clamp system. Vj was induced by stepping the voltage in one cell while maintaining a constant voltage in the other. Junctional current (Ij) was measured as the change in the current of a neighboring cell, and conductance (gj) was estimated from the relationship gj = -Ij/Vj.

Results

From electrophysiological recordings in cell cultures expressing Cx43 or Cx45, the principal isoforms expressed in cardiac tissue, various data sets were fitted simultaneously using global optimization. Model-fitting results showed good correspondence with both kinetic and steady-state data. Our data demonstrate the (4SM) model reproducing a range of experimentally observed GJ behaviors, not achievable through modeling steady-state data alone. Additionally, mathematical analyses showed that the current model can be approximated by a reversible two-state system and solved analytically using a rapid equilibrium assumption (REA), often applied in modeling enzyme kinetics. This model property allows for a substantial reduction in computation time and could be efficiently applied when simulating large clusters of cells.

Conclusion

The 4SM model serves as a tool for studying GJ channel gating and its effects on excitation spread in networks of electrically coupled cells.

Clinical characteristics and long-term outcomes of patients with heart failure with supra-normal LVEF . First Polish experience from LECRA-HF registry

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Introduction

Heart failure with supra-normal left ventricular ejection fraction (HFsnEF) is a new category of HF introduced in 2019 by the European Heart Journal, with the main purpose of promoting research on this new category. Clinical characteristics and long-term outcomes of HFsnEF patients remain insufficiently elucidated. We sought to characterize Polish HFsnEF patients and to provide their long-term mortality in comparison to HFpEF.

Method & Materials

Of 1186 patients enrolled in the single-center Lesser Poland Cracovian Heart Failure (LECRA-HF) Registry between 2009 and 2019 and hospitalized due to HF decompensation. Based on echocardiography, 261 (22%) of them were those with HF with normal LV ejection fraction (LVEF; Ú50 percent). 40 (15,3%) of them were classified as HFsnEF and the remaining 221 (84.7%) as HFpEF.

Results

HFsnEF patients were less frequently hypertensive (P=0.026) and had higher baseline left ventricular ejection fraction (LVEF, P<0.001) than HFpEF subjects. Furthermore, HFsnEF patients presented lower INR (p=0.027) and total protein level (p=0.008) on admission. The Kaplan-Meier analysis showed that all-cause mortality is higher in HFsnEF than in HFpEF (65.0% vs 55.2%, p=0.044).

Conclusion

Our findings indicate that every seventh Polish patient admitted with HFpEF could be classified as HFsnEF. Baseline characteristics of HFsnEF patients are different than HFpEF. Simultaneously, the HFsnEF diagnosis is associated with lower long-term survival.

SIRT3 represses vascular remodeling via reducing mitochondrial acetyl-CoA accumulation in vascular smooth muscle cells

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Introduction

Phenotype switching of vascular smooth muscle cells (VSMCs) from a contractile phenotype to a synthetic one is fundamental to vascular remodeling. As the only deacetylase localized in mitochondria, SIRT3 displays a strong protective effect in the cardiovascular system. However, the regulatory role of SIRT3 in local vessels on vascular remodeling and its underlying mechanism remain unclear.

Method & Materials

We established a VSMC-specific SIRT3 knockout mice (SV-KO mice) and a VSMC-specific SIRT3 overexpression mice (SV-iOE mice). Mice were infused with Ang _ for 28 days to establish the conventional abdominal aortic aneurysm (AAA) model and to investigate the role of SIRT3 in vascular remodeling. In vitro, quiescent-state human aortic VSMCs were stimulated with platelet-derived growth factor type BB (PDGF-BB) to investigate the detailed mechanisms underlying the role of SIRT3 in VSMC phenotypic switching.

Results

We observed a decline of SIRT3 expression and activity during AAA formation. Compared with WT mice, the incidence of AAA and mortality were significantly higher in Ang II-treated SV-KO mice. Meanwhile, the maximal abdominal aortic diameter and the elastin degradation score were remarkably higher in Ang II-treated SV-KO mice. Moreover, knockout of SIRT3 resulted in a much higher and inflammation in abdominal aortas. In contrast, vascular remodeling induced by Ang _ was suppressed in SV-iOE mice. In VSMCs, the proliferation, migration and synthetic markers expression were increased, and the contractile markers and SIRT3 expression was decreased by stimulating with PDGF-BB. Adenovirus-mediated SIRT3 overexpression significantly erased PDGF-BB-induced phenotypic switching of VSMCs, accompanied with decreased level of mitochondrial acetyl-CoA (Ac-CoA). Adenovirus-mediated SIRT3 knockdown exacerbated the effect of PDGF-BB and increased mitochondrial Ac-CoA accumulation in VSMCs, but the phenomena could be reversed by knockdown of ATP Citrate Lyase (ACLY), a key enzyme for Ac-CoA transport from mitochondria to cytoplasm, but not Acyl-CoA Synthetase 2 (ACSS2), the enzyme for Ac-CoA transport in cytoplasm, suggesting that the inhibitory effect of SIRT3 on VSMC phenotypic switching depends on the inhibition of Ac-CoA transport from mitochondria to cytoplasm.

Conclusion

The study indicates a protective role of SIRT3 in vascular remodeling. Mechanistically, SIRT3 acted as a critical repressor of vascular remodeling via reducing mitochondrial Ac-CoA accumulation in VSMCs.

Continuous cardiac monitoring in VA ECMO patients using a digital twin

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Introduction

Patients with cardiogenic shock who do not respond to conventional therapies could benefit from venoarterial extracorporeal membrane oxygenation (VA ECMO). VA ECMO is used to restore systemic circulation while cardiac function recovers, or other treatment options are considered. VA ECMO is a complex therapy that is difficult to manage on a daily basis and quality of management depends strongly on the experience of health-care providers. To improve decision-making, a bedside tool to continuously monitor the cardiac function would be a valuable addition to daily care. A patient-specific cardiovascular computational simulation, or digital twin, could be used to individually monitor cardiac function continuously.

Method & Materials

For a period of 6 months, relevant hemodynamic parameters were registered from patients receiving VA ECMO therapy. These data were used to estimate computational model parameters and tune a cardiovascular simulator to a patient-specific digital twin. This twin was used to estimate the Left ventricular end-systolic elastance (Ees) and ventricular-arterial coupling (Ea/EEs) to provide insight into the cardiac function of the real patient.

Results

Six patients were included and fourteen registrations were performed. Preliminary results, of one patient and two registrations, show that the cardiovascular simulator can be used to model a digital twin successfully. The cardiovascular simulator produced the desired hemodynamic parameter values with an error of <10%. In the resulting digital twins, Ees remained stable around 0.4 mmHg/ml and Ea/Ees ratio increased from 4.08 and 4.48 between the two registrations.

Conclusion

Preliminary results of this explorative study show that a cardiovascular computational simulator can be used to create a digital twin for patients receiving VA ECMO therapy. The preliminary results are in accordance with the clinical outcome of the simulated patient. A digital twin of VA ECMO patients shows promise in becoming a very useful clinical decision tool for clinicians evaluating cardiac function.

Poster session I

GASTRO-INTESTINAL MEDICINE

Presenters:

- Varsha Coimbatore Sathyabal
- Mohammad Golzaresfahani
- Kexi Liao
- Samar Nobavar
- Shimolee Patel
- Aalesh Shah

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Development and Validation of a Risk Prediction Model for Gastroesophageal Reflux Disease (GERD) Using a Risk Factor-Based Questionnaire - GRSS

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Introduction

The steady rise in the prevalence of gastroesophageal reflux disease (GERD) has been attributed to the globalization process. GERD poses a significant global health burden, impacting the quality of life and leading to severe complications. However, this can be prevented if the lifestyle of the individual can be modified before the disease develops. Our literature review unveiled the deficiency in existing risk prediction models to assess an individual?s susceptibility to GERD. To address this void, we introduce a novel model ? the GERD Risk Scoring Scale (GRSS), which emphasizes primary prevention strategies over traditional secondary prevention.

Method & Materials

After obtaining ethical approval and informed consent, patients were recruited from the Out-Patient Department of our institution. Individuals diagnosed with GERD according to the American College of Gastroenterology guidelines constituted the case group, while subjects in the control group were recruited from the general population and comprised of healthy volunteers. We excluded minors and individuals diagnosed with peptic ulcer or hiatal hernia. We designed a 45-question questionnaire covering proven key risk factors for GERD and administered it to the participants. LASSO regression models using continuous and categorical variables were employed to develop a sophisticated equation and a user-friendly scoring scale. Validation was performed on an additional 355-patient cohort to assess discriminative accuracy, calibration, and reliability.

Results

We found strong associations between GERD and key risk factors that were used to develop the GRSS. The regression models demonstrated excellent predictive accuracy as assessed by the C-index. Both models displayed high sensitivity, specificity, and discriminative power. The internal consistency was assessed by Cronbach's alpha and was found to be excellent.

Conclusion

The GRSS presents a pioneering approach to GERD risk prediction, offering a sophisticated equation for computational applications and a practical scoring scale for clinical use. Its effectiveness in identifying high-risk individuals for targeted preventive interventions signifies a shift toward primary prevention. The substantial prevalence of GERD highlights the public health relevance of GRSS and marks an advancement in promoting overall health and well-being. Future research should focus on multicentric validation and regional˘modifications.

Examining the precision of sonographic diagnosis in the identification of intestinal malrotation

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Iran

Introduction

In pediatrics, malrotation is a congenital disorder that occurs primarily in neonates and rarely in older children. Sonography and upper gastrointestinal (GI) studies are both useful diagnostic methods for this condition. However, their diagnostic value remains unknown. The purpose of this study is to assess the diagnostic accuracy of sonography in the diagnosis of intestinal malrotation.

Method & Materials

Patients with abdominal pain and obstruction symptoms suspected to be caused by malrotation were evaluated using sonography at Mofid Children's Hospital in 2021 and 2022. With parental consent and suspicion of mesenteric disorders, sonography was performed. In addition to lack of parental consent, previous malrotations, volvuluses, or Ladd bands were excluded. Three sonographic findings were used to assess malrotation, including whirlpool sign, inversion of the superior mesenteric artery (SMA) and superior mesenteric vein (SMV), and abnormal pathology of the mesenteric vessels. In addition, the patients underwent an upper GI study with a barium swallow. The data were entered into SPSS as a final step. Using sonography and upper GI examination findings, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated.

Results

In total, 160 patients with mesenteric artery disorder were enrolled, including 84 males and 76 females. The average age of the patients was 23 months. Malrotation accounted for 112 cases (70%), and other diseases accounted for 45 cases (28.2%). Sonography had 75.0% sensitivity and 66.6% PPV. Furthermore, the SMA/SMV inversion has a sensitivity of 58.0%, a specificity of 35.0%, a PPV of 68.1%, and an NPV of 25.8%, respectively. Additionally, the sensitivity, specificity, PPV, and NPVs were calculated at 50%, 77.2%, 72.2%, and 56.6%, respectively. In the case of an abnormal mesenteric vessel route, the sensitivity was 90%, specificity was 17.0%, PPV was 64.5%, and NPV was 50.0%. Likewise, the upper GI study had 83.1% sensitivity, 100% specificity, 100% PPV, and 50% NPV.

Conclusion

Both sonography and upper gastrointestinal studies were found to have an acceptable diagnostic value. Since sonography is less prone to radiation-related harm, it should be chosen as the first method of diagnosis.

Protein arginine methyltransferase 3 (PRMT3) improves metabolic dysfunction-associated steatotic liver disease (MASLD) via enhancing NLRP6

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Introduction

Metabolic dysfunction-associated steatotic liver disease (MASLD) refers to a clinical pathological syndrome characterized by diffuse hepatic bullous steatosis caused by excluding alcohol and other clear liver injury factors.The mechanism of NAFLD is extremely complicated, which involves in many systems, such as immune, oxidative and antioxidative, and inflammatory response system, etc. PRMT3 is the main arginine methylase that mediates symmetric bimethylation of protein substrates through arginine. More and more studies have shown that it has important functions in a wide range of cellular biological processes. NLRP6 is important in host defense by inducing functional outcomes including inflammasome activation and interferon production. Previous reports have showed that NLRP6 inflammasomes could negatively regulate MASLD progression e via modulation of the gut microbiota. But there is still relatively little research on the relationship between PRMT3 protein and MASLD, how PRMT3 regulates MASLD was unknown.

Method & Materials

High-fat diet (HFD) and mixture of oleic acid and palmitic acid (FFA) were used to establish MASLD in vivo and in vitro. Proteomics, immunoprecipitation, molecular docking techniques, and protein arginine methyltransferase 3 (PRMT3) knockout (KO) mice and PRMT3 silence (PRMT3 siRNA) and PRMT3 inhibitor SGC707-treated primary hepatocytes (PHC) were used to search for the biomarkers and possible treatment targets and treatment measures for MASLD.

Results

PRMT3 in different subtypes (1-9) was significantly decreased in the serum of NAFLD patients. PRMT3 directly activates the NLRP6 gene expression via NLRP6 gene promoter. PRMT3 also physically interacts with the NLRP6 nucleotide-binding domain and promotes NLRP6 inflammasome assembly. PRMT3 KO, PRMT3 siRNA and SGC707 significantly exacerbated the above changes. Further, salvianolic acid B (SaB), was found to be a natural agonist of PRMT3 in this study, which could improve MASLD through PRMT3/NLRP6 signal pathway.

Conclusion

PRMT3 was significantly down-regulated in MASLD, which may be potential targets for MASLD PRMT3 could promote MASLD progression via NLRP6 signal pathway. Of course, the precise mechanism of PRMT3 on MASLD needs to be further studied.

Exploring the Therapeutic Potential of Rosemary Supplementation for Symptom Management in Irritable Bowel Syndrome Patients

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Introduction

There has been an increase in irritable bowel syndrome (IBS) and its symptoms include recurrent abdominal pain. IBS symptoms are improved by prebiotics, probiotics, and dietary polyphenols, according to recent studies. Rosemary contains antioxidants and anti-inflammatory compounds. Aim of this study is to determine whether the use of Rosemary supplements alleviates gastrointestinal symptoms, improves dietary intake, reduces anxiety, and enhances quality of life in IBS patients.

Method & Materials

Rosemary supplementation was evaluated in a double-blind, placebo-controlled study in Iran. In a six-week study, participants who met Rome IV criteria for IBS were given either Rosemary or placebos. IBS symptom severity, assessed with the IBS symptom severity scale, was used as the primary outcome measure. Additionally, IBS-QoL, anxiety, BMI, and waist circumference were evaluated as secondary outcomes. Moreover, dietary intake and physical activity were assessed during the evaluation. For the interpretation of the data, ANCOVA was used. Patients with IBS were evaluated for the efficacy of Rosemary in relieving symptoms and improving quality of life.

Results

There was a significant improvement in IBS symptoms, including abdominal pain severity, among 51 participants in the Rosemary group who completed the trial. An adjusted odds ratio of 6.22 for Rosemary significantly improved the grade of IBS as compared to placebo. Overall, Rosemary did not significantly affect the quality of life of subjects with IBS, but it significantly reduced anxiety levels compared to the placebo group. There was no difference in compliance rates between the Rosemary and placebo groups.

Conclusion

Patients with IBS reduced abdominal pain, bowel unsatisfaction, and anxiety by taking 850 mg of Rosemary three times daily. This study suggests that Rosemary could be used as an adjunctive therapy for managing IBS symptoms, despite its inability to affect IBS-related quality of life and dietary factors. The role of Rosemary in the gut microbiome of IBS patients? needs to be explored further in randomized controlled trials.

Diagnostic accuracy of CEUS in identifying Solid Pancreatic Lesions:- A Meta-Analysis

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Introduction

Solid pancreatic lesions are crucial to identify because of their high incidence rate and their poor survival rate. Surgical biopsy, ultrasonography, computed tomography, MRI, and PET-CT are examples of diagnostic tools. Although common, endoscopic ultrasonography-guided biopsy carries a risk of needle-track seeding. A more effective and affordable method for determining the differential diagnosis of solid pancreatic lesions is contrast-enhanced ultrasonography (CEUS). CEUS is a less nephrotoxic method that uses a contrast chemical to distinguish between teratomas, benign tumors, and neuroendocrine tumors. The goal of this meta-analysis is to evaluate how well CEUS can identify solid pancreatic lesions for use in clinical diagnostic procedures.

Method & Materials

Medical literature is comprehensively searched and reviewed without restrictions to particular study designs, or publication dates using PubMed, Cochrane Library, and Google Scholar databases for all relevant literature. The extraction of necessary data proceeded after specific inclusion and exclusion criteria were applied. The meta-analysis included 27 RCTs and 3061 patients and was analyzed using the QualSyst tool. The risk of bias was evaluated by using QUADAS-2 analysis. The statistical software packages MetaDiSc 1.4, RevMan (Review Manager, version 5.3), SPSS (Statistical Package for the Social Sciences, version 20), and Excel in Stata 14 were used to perform the statistical analyses.

Results

According to the findings of four studies, CEUS demonstrates high sensitivity, with values equal to or above 95%, and one study indicates specificity above 95%. True Positive (TP) and True Negative (TN) values are reported as 2080 and 621, respectively, while False Positive (FP) and False Negative (FN) values are noted as 124 and 236. With a 95% confidence interval, CEUS sensitivity is calculated as 0.90 (range: 0.89 to 0.91) and specificity as 0.83 (range: 0.80 to 0.86). The positive predictive value (PPV) of CEUS is estimated at approximately 94.3%. These results highlight CEUS as a promising tool for diagnosing pancreatic lesions.

Conclusion

The study concluded that CEUS (Contrast-Enhanced Ultrasound) is an important diagnostic test for pancreatic lesions. This is due to their high sensitivity and specificity, along with other aspects like enhanced visualization, real-time imaging, and safety benefits. Additionally, CEUS is cost-effective, making it a practical choice in healthcare settings with budget constraints. Thus, CEUS remains a valuable asset for healthcare professionals in their efforts to accurately diagnose pancreatic lesions.

Diagnostic Accuracy of Vibration Controlled Transient Elastography (VCTE) in patients of Non-Alcoholic Fatty Liver Disease (NAFLD) : A Meta-Analysis

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Co-authors: Desai D. (Dev)

Introduction

Non Alcoholic Fatty Liver Disease (NAFLD) has a prevalence of around 25% worldwide and is emerging as a leading cause of cirrhosis and hepatocellular carcinoma. NAFLD encompasses a spectrum of conditions form simple steatosis to steatohepatitis. Liver fibrosis is a key prognostic indicator of overall mortality in NAFLD and has been classified as per NASH CRN criteria into F0,F1,F2,F3 and F4. The gold standard test for classifying fibrosis is a liver biopsy which is invasive, resource intensive and time consuming. The purpose of this meta-analysis was to assess the accuracy of VCTE in classifying the grade of fibrosis in patients of NAFLD.

Method & Materials

We searched the Medline, Embase, and Cochrane Library databases, and performed a metaanalysis on the diagnostic accuracy of VCTE in patients of NAFLD. Published clinical trials using VCTE for the classification of fibrosis in NAFLD have been included in the meta-analysis.. After study selection, data and quality assessment, the Sensitivity, Specificity, PPV, DOR and DAC were calculated separately for the three groups of significant fibrosis (F2+F3+F4), advanced fibrosis (F3+F4) and cirrhosis (F4).

Results

A total of twelve studies including 740 patients with significant fibrosis , ten studies including 949 patients with advanced fibrosis and five studies including 600 patients with cirrhosis were available for the meta-analysis. The pooled sensitivity and specificity of VCTE were 70.7%/72.35%, 82.4%/72.1% and 90.4%/76.7% respectively for the three classifications of fibrosis in NAFLD. The PPV values are 0.66, 0.58 and 0.39 respectively. The DOR for each of the groups was 6.35, 12.36 and 31.46 respectively. DAC for the groups was calculated to be 0.71, 0.76 and 0.78 respectively. Some between-study heterogeneity was found in the meta-analyses. However, there was no evidence of a threshold effect.

Conclusion

Our meta-analysis of published studies demonstrates that VCTE has a high diagnostic accuracy especially for the advanced fibrosis and cirrhosis and plays an important role in the classification of fibrosis in NAFLD.

Poster session I

GENERAL SURGERY

Presenters:

- Larisa Dascau
- Felipe Gonçalves
- Tingna Luo
- Hamidreza Mosleh
- Manav Patel
- Sepideh Roshanchartagh
- Abdulmalek Alhithool
- Parnian Arghash

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Possible Association between Diabetes Mellitus and Early Metastasis in Pancreatic Ductal Adenocarcinoma Patients: A Cross-Sectional Study

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Introduction

Pancreatic cancer has a very high mortality rate. This is because of the lack of early symptoms and the speed at which surrounding tissues are invaded. Unlike type 1, caused by insulin insufficiency, or type 2, caused by insulin resistance, Diabetes Mellitus type 3c (DM3c) is caused by the pathogenesis of exocrine pancreas diseases. The second most common trigger of DM3c is pancreatic ductal adenocarcinoma (PDAC). PDAC and DM3c influence the development of each other. However, it is not known what effect DM3c has on the relapse rates of pancreatic cancer and whether the speed at which relapses occur is affected. If tumour aggressiveness is increased by insulin resistance and/or beta-cell dysfunction, counteracting the effects of the latter could lead to a less aggressive tumour and consequently, to a slower disease progression. The present study aims to establish whether DM3c is associated with early relapse of metastases in patients with PDAC.

Method & Materials

This was a retrospective cohort study which included 158 patients. The patients included in this study were diagnosed with primary pancreatic cancer between January 2018 and January 2023 at the University Medical Center Groningen. Only patients with PDAC who underwent tumour resecting surgery were considered. DM3c was defined as diabetes mellitus (DM) diagnosed with a maximum of 6 months prior to PDAC diagnosis. Data was retrieved from patient files.

Results

Of the 158 patients, 90 had no DM, 21 had a history of long-standing DM, 22 were diagnosed with DM3c, and 25 developed post-operative DM. When comparing patients without diabetes and those with diabetes (long-standing and type 3c) versus postoperative diabetes, the second category exhibited a significant association with cancer relapse, as evidenced by a p-value below 0.05 in univariate analysis. Furthermore, preliminary results indicate a significant association between DM3c patients and cancer relapse, when compared to the other diabetes categories.

Conclusion

These preliminary findings suggest that addressing specific diabetes subtypes may hold promise in potentially slowing the course of PDAC relapse. Further research of the relationship between pancreatic cancer relapse and DM3c is crucial for the development of targeted interventions and improving outcomes for affected individuals.

GreenLight Photoselective Laser Vaporisation versus Transurethral Resection of The Prostate for Large Prostates: Sytematic Review and Meta-Analysis

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Introduction

Transurethral resection of prostate (TURP) stands as a primary surgical intervention for benign prostatic hyperplasia (BPH), although laser techniques, notably photoselective vaporization of prostate (PVP), are gaining traction. Previous studies have already assessed the efficacy of TURP and PVP, although with small prostates (<70ml). Thus, this meta-analysis aims to assess the efficacy of PVP compared to TURP in the male BPH population with large prostates (>70ml).

Method & Materials

A comprehensive systematic review was conducted across MEDLINE, Embase, Scopus, Web of Science, and Google Scholar. Studies comparing PVP to TURP in male BPH patients were included. Our primary outcome was the International Prostate Sympton Score (IPSS). Secondary outcomes encompassed urinary peak flow rate (Qmax), postvoid residual volume (Vres), operative time, catheterization time, postoperative hospital stay and complications.

Results

Three articles encompassing 159 patients in each of the PVP and TURP groups were included. Our analysis revealed no statistically significant difference in IPSS score between PVP and TURP (MD 1.56; CI95 0.52, 3.64; $p = 0.14$; $I2 = 85\%$). TURP demonstrated a reduced operative time (MD 30.35; CI95 11.26, 49.44; $p = 0.002$; $I2 = 96\%$), whereas PVP exhibited shorter catheterization time (MD -2.22; CI95 -2.44, -1.99; $p < 0.00001$; $I2 = 1\%$) and postoperative hospital stay (MD -2.20 ;CI95 -2.69, -1.72; $p < 0.00001$; $I2 = 75\%$). No significant differences were observed in other outcomes assessed.

Conclusion

This meta-analysis suggests that PVP is non-inferior to TURP concerning IPSS, Qmax, Vres and complications, albeit with a longer operative time. PVP showed a reduced catheterization and postoperative hospital stay.

Using Anatomical 3D Printed Model for Genuvarum cases

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Introduction

Recent developments in 3D printing have given orthopedic surgeons a novel technology that has the ability to revolutionize preoperative planning. The appearance of three-dimensional (3D) printing technology enables the digital preoperative plan and simulation to move from the virtual phase to the reality phase. Varum disorders are recurrent lower limb malformations associated with many anatomical changes in the knee joint and adjacent segment. High Tibial osteotomy is one of the best treatment options in genu varus deformity. This study aimed to evaluate using 3D-printed model for pre-planning HTO.

Method & Materials

Thirty patients with genu varum were selected and divided into two groups. A standing alignment radiograph was taken from all patients to measure mMPTA, mLDFA, CA, and mFTA. CT scan was taken from eight patients in the model group. Mimics software was used to build the 3D model. Then, we had to prepare the model made for printing by a 3D printer. So, the surgeon operated on half of the patients with the help of a printed 3D model. An orthopedic surgeon performed an osteotomy on the printed model that was exactly the same as the actual surgery After the surgery, we once again took radiography (all patients) and a CT scan (main study group). The aim was to see if the angles have been corrected after surgery. Finally, a comparison was made between these two surgical procedures.

Results

The 3D models have great accuracy in comparison to real bone. Using 3D printed model had reduced costs of hospitalization, anesthesia, duration of surgery, and the number of fluoroscopies. Also, angles had a better correction in the model group.

Conclusion

Using 3d model has lots of benefits. An orthopedic surgeon can use it for preplanning of surgery and finally it has many fine outcomes for patients.

Basic and clinical research on in situ induction of self-organizing Autologous engineered skin

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Introduction

In the realm of burn treatment, where bringing both physical and psychological damage to patients, it?s vitally important to explore innovative avenues. In the past, skin substitutes like fish and pig skin have achieved significance success, offering promise with their rich sources but leaving unavoidable issue such as immune rejection. However, propelled by the evolution of stem cell technologies, we present a paradigm-shifting strategy: the in situ induction of human epidermal cells. This not only tackles the perennial challenge of immune rejection in allogeneic skin grafting but also presents a transformative approach to the limitations of autologous skin transplantation.

Method & Materials

To overcome these challenges, our study introduces a groundbreaking method for CEA construction. Skin cells are combined with GelMA hydrogel. The skin cells self-organize through in-situ induction, leading to the formation of autologous skin tissue engineered with remarkable efficiency.

Results

Our innovative approach outperforms traditional methods. Rapid epidermal stem cell expansion technology reduces the in vitro cycle by 5-20 days, achieving full coverage in 45 days. We rigorously assess the safety of P1-P8 expanded cells, addressing tumorigenicity and microbial concerns. The GelMA composite hydrogel with reparative properties for skin and other tissues, enhances the success of our strategy. Clinical trials confirm comparable epithelialization rates in cell membrane wounds to blade thickness grafts, with superior wound repair quality. To address autologous skin transplantation challenges, we proposal a low-temperature sample transportation box and a national research center with fast logistics.

Conclusion

Our innovative technology offers a promising alternative to traditional skin grafting and wound repair strategies for burn patients. This breakthrough not only addresses the challenges of burn treatment but also provides a novel approach for the wound repair of war burn patients, heralding a new era in burn medicine.

The Usefulness of Magnetic Resonance Imaging(MRI) for Detection of Appendicitis - A Diagnostic Test Accuracy Meta-Analysis

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Co-authors: Andharia D. (Dev), Shah A. (Abhijay), Patel D. (Dev), Shah H. (Hetvi)

Introduction

Appendicitis is a common cause of emergency department visits and appendectomies in the US, with 250,000 appendectomies performed annually. Current diagnostic methods, such as clinical findings, lead to inaccuracies and missed diagnoses, increasing morbidity and mortality. The only solution is surgery, but current hematological tests are not reliable and may lead to unnecessary surgery if the underlying etiology is self-limiting or requires medical treatment. This study explores the role of MRI as a diagnostic modality that can replace US/CT and supplement traditional clinical diagnostic signs while avoiding ionizing radiation and intravenous contrast medium. The purpose of this meta-analysis is to determine the accuracy of MRI as a diagnostic modality in diagnosing appendicitis, addressing concerns about diagnostic modalities and their adverse effects, and addressing the necessity and success of relevant interventions.

Method & Materials

Medical literature was comprehensively searched and reviewed without restrictions to particular study designs, or publication dates using PubMed, Cochrane Library, and Google Scholar databases for all relevant literature formulated in English. The extraction of necessary data proceeded after specific inclusion and exclusion criteria were applied. Meta Analysis was performed for 5206 patients, with 35 RCTs being selected. Analysis was done using the QualSyst tool, wherein two writers independently assessed the caliber of each study as well as the use of the Cochrane tool for bias risk apprehension. The statistical software packages RevMan (Review Manager, version 5.3), SPSS (Statistical Package for the Social Sciences, version 20), and Excel in Stata 14 were used to perform the statistical analyses along with other analytical software.

Results

MRI had an overall sensitivity of over 95%, an overall specificity of 94.2% with a PPV of 0.875 in comparison to CT scan in the diagnosis and intervention regarding appendicitis.

Conclusion

These findings strongly suggest that MRI is a reasonable alternative to CT for the diagnosis of appendicitis in hospitals with appropriate access to this technology for reasons about accuracy, reliability, and reproducibility as well as addressing safety concerns.

An investigation of vitamin D levels in patients who have undergone bariatric surgery and liver stiffness

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Introduction

Obesity is a growing problem in various communities. Several complications are associated with this condition, especially in the cardiovascular system. Moreover, obesity can result in heterogeneous body system involvement, termed metabolic syndrome. Obesity poses a problem not confined to a few body systems. Our study aimed to evaluate the relationship of different vitamin D levels with liver stiffness laboratory indices and elastography findings in obese patients who were candidates for bariatric surgery.

Method & Materials

This cross-sectional study was conducted on bariatric surgery candidates aged 18 and 60 between 2020 and 2022. Patients with contraindications for bariatric surgery were excluded. A pre-designed questionnaire was used to extract the needed data. These included demographic and anthropometric data such as age, gender, height, weight, and body mass index. Different laboratory indices and elastography were employed for liver stiffness measurements. These included the AST to ALT ratio and AST to platelet ratio index.

Results

851 patients who met the criteria were enrolled in the study. The median age of the cases was 37.00 years old, and 655 cases (77.05%) were female. Among the included cases, 451 (53.05%) had vitamin D deficiency, 190 (22.35%) had insufficiency, and 210 (24.70%) had sufficiency. Total bilirubin ($p=0.012$), ALP ($p<0.001$), FIB-4 ($p<0.001$), and NFS ($p=0.025$) showed significant differences between the three study groups.

Conclusion

In conclusion, our study revealed a notable prevalence of vitamin D deficiency. It also revealed a significant association with liver health parameters. The findings emphasize the complex interconnections between obesity, vitamin D status, and liver complications. Recognizing these relationships is crucial for informed clinical management and highlights the need for further research to refine therapeutic strategies in this population.

Predictive Potency of Artificial Intelligence and Machine Learning Algorithms in Post-Abdominal Wall Reconstruction Complications: A Systematic Review and Meta-Analysis

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Introduction

Background: Abdominal wall reconstruction (AWR) is a sophisticated surgical procedure associated with potential complications. Both artificial intelligence (AI) and machine learning (ML) have demonstrated potential in forecasting these complications. This study offers a systematic review and synthesis of the current evidence regarding the predictive accuracy of AI and ML models in AWR, with an emphasis on mesh infection and pulmonary failure.

Method & Materials

We conducted an exhaustive search across five databases to pinpoint studies focusing on AI's role in predicting complications following abdominal reconstruction. Inclusion was based on specific criteria, and study quality was gauged using the NIH Quality Assessment Tool. We employed random-effects meta-analyses, and heterogeneity was evaluated using the Q statistic, REML estimator for tau^2, and I^2 statistic. A p-value below 0.05 was deemed statistically significant.

Results

Results: Our review incorporated four studies (n=149,818) that utilized diverse AI and ML methodologies to forecast complications post-abdominal reconstruction. AI algorithms either matched or surpassed the performance of traditional models or expert surgical opinions. In terms of predicting pulmonary failure, a random-effects model (k=2) yielded an overall AUC of 0.5491 (95% CI: 0.5019 -0.5963), with negligible heterogeneity. Regarding mesh infection, a random-effects meta-analysis (k=2) indicated significant heterogeneity (I^2 = 99.39%) and an overall AUC of 0.7535 (95% CI: 0.4712 -1.0357).

Conclusion

Our analysis underscores the potential of AI and ML algorithms in forecasting complications subsequent to abdominal wall reconstruction. These algorithms typically surpassed traditional models and expert evaluations. Nonetheless, their efficacy varied depending on the type of complication. Upcoming research should delve into the integration of AI within clinical settings to enhance patient outcomes and refine surgical decision-making processes.

Comparative Analysis of Immediate Cord Clamping and Cord Milking in the Management of Preterm Labor

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Iran

Introduction

The present study focuses on managing preterm labor, with a specific emphasis on the method of umbilical cord management, comparing immediate cord clamping with cord milking for preterm neonates. The objective is to evaluate and compare the complications associated with these two approaches.

Method & Materials

Conducted as a randomized clinical trial in 2021 in east Iran, preterm neonates without certain complications were enrolled. Exclusions were made based on criteria like umbilical cord length, meconium concentration, true knot, and major cord anomalies. Participants were divided into control (immediate cord clamp) and intervention (cord milking) groups. Maternal and neonatal factors were recorded, and complications were assessed during the first 120 hours in the neonatal intensive care unit (NICU).

Results

Out of 100 participants, the intervention group (cord milking) demonstrated significantly lower rates of intubation, resuscitation, and blood transfusion compared to the control group ($P=0.012$). The incidence of intraventricular hemorrhage grade 3 (IVH3) was significantly lower in the intervention group ($P=0.042$), but the frequency of icterus was higher ($P=0.021$). Furthermore, the intervention group exhibited lower chances of resuscitation, intubation, and IVH, while having higher chances of icterus ($P<0.05$).

Conclusion

The study concludes that cord milking proves notably superior to immediate cord clamping in managing preterm labor neonates. These findings emphasize the potential benefits of cord milking in reducing certain complications associated with preterm birth.

Poster session I

GENETICS

Presenters:

- Sara Fernanda Arechavala Lopez
- Theo Marchant
- Grace-Thandekire Sibande

ISCOMS 2024 SCIENCE BEYOND BORDERS

Identification of rare single-nucleotide variants associated with extreme phenotypes of type 2 diabetes in Mexican population.

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Introduction

Introduction: Type 2 diabetes (T2D) comprises a group of common metabolic disorders characterized by hyperglycemia. In Mexico, it is the leading cause of permanent premature disability and the second-most cause of mortality. Recently, efforts have been made to characterize the genetic basis of T2D in the Mexican population, revealing the existence of alleles typical of this population. We aimed to identify rare single nucleotide variants associated with extreme phenotypes of T2D and thus be able to distinguish monogenic forms of T2D from polygenic ones.

Method & Materials

Materials & Methods: In a sample of 996 exomes from patients with T2D, individuals with fasting blood glucose ≥ 250 mg/dL and carried pathogenic SNVs according to Annovar annotation were identified, the presence of MODY diabetes was ruled out. Finally, the clinical and biochemical characteristics between pathogenic SNV carriers vs non-carriers were analyzed.

Results

Results: We identified 50 unrelated individuals who presented extreme T2D phenotypes and who carried pathogenic SNVs according to the in-silico prediction. The mean age diagnosis was 50 years ($p < 0.05$, 95% CI), correspondingly, there was a significant increase in the values of glucose, total body fat, visceral fat, HbA1c, and triglycerides ($p < 0.05$, 95% CI); as well as a decrease in insulin values in carriers compared to non-carriers ($p < 0.05$, 95% CI). These SNVs were found in 529 genes, mainly expressed in endocrine tissues, liver, adipocytes, and skeletal muscle. Endocrine gland-related genes in carrier patients showed elevated levels of cholesterol, HbA1c, insulin, and triglycerides ($p < 0.05$, 95% CI), while genes related to ATP-binding sites showed high values of total body fat, visceral fat, BMI, and waist circumference ($p < 0.05$, 95% CI), genes from both pathways showed elevated glucose levels compared to non-carriers ($p < 0.05$, 95% CI).

Conclusion

Conclusions: Patients carrying genetic variants presented characteristics of the extreme T2D phenotype. With more studies, these variants could help to differentiate the monogenic forms of T2D from the polygenic allowing identifying susceptible genetic relatives, providing genetic advice, and contributing to the development of precision medicine.

Crossover hotspots are characterized by a specific enrichment of histone modifications in the genome of mouse germ cells

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Introduction

Meiotic crossovers (CO) are essential for reproduction and evolution. They ensure the proper chromosome segregation into gametes and promote genetic diversity. Defective CO formation leads to aneuploidy and infertility; hence, learning how CO are regulated is key to understand reproductive health and inheritance. In mammals, what defines the CO localization is still unknown. Here we explore if COs hotspots in mouse are patterned by a special epigenetic arrange composed by active chromatin marks such as H3K4me3 and H3K9ac.

Method & Materials

ChIP and Tiled qPCR were performed on spermatocytes from C57Bl6 mice. We analyzed 3 genomic regions: i) the CO hotspot of the X chromosome ii) a region of DNA double strand breaks (DSB) formation but no CO production, iii) a region with no DSBs nor COs formation. Data analyses were performed using Delta Delta Ct (method to calculate relative gene expression levels) and statistical analyses were performed by t-student and ANOVA.

Results

We found that specific histone modification array shape the different genomic regions analyzed. We found different H3K9ac and H3K4me3 occupancy in the DNA DSB, no-CO nor DSB and CO regions as well as the enrichment of nucleosomes that exhibited these histone marks. H3K4me3 was present as few peaks in the DSB, high peaks in the no CO region and in very low levels in the CO region. Contrarily, this region was fully occupied in nucleosomes with H3K9ac in low enrichment levels as compared with the other genomic regions. Thus, a particular landscape of active histone modification marks in the CO region that is different than other genomic sites.

Conclusion

Our data show a specific epigenetic landscape in CO regions in the mouse genome. Moreover, suggest potential mechanisms by which histones regulates chromatin configuration and modulate the homeostasis of CO, which are crucial for the correct achievement of gametogenesis and for the maintenance of genome stability in germ cells.

Genetic Epidemiology and Antimicrobial Resistance Profile of Shigella isolated from Diarrhoea diseases from under-five children in Blantyre, Malawi

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Introduction

Shigella is the leading bacterial cause of moderate-to-severe diarrhoea in under-five children in resource-poor settings. However, antimicrobial resistance (AMR) is increasing in Shigella bacteria globally, complicating shigellosis management. While Whole Genome Sequence Analysis (WGSA) has been effectively used to broaden our understanding of shigellosis epidemiology, AMR, and transmission, it has been under-utilised in sub-Saharan Africa. In this study, multiple Shigella isolates from the 2022-2023 Malawi Shigella surveillance study were characterised using WGSA.

Method & Materials

Stool samples collected from under-five children were processed using a well-validated microbiological workflow. Serotyping was done using latex agglutination followed by automated sequence testing using Kirby Bauer to a panel of antibiotics to determine antibiotic susceptibility. 44 phenotypically confirmed Shigella isolates were subjected to DNA extraction and then Whole Genome Sequencing on the Illumina Miseq. Data was stored and analysed on the Centre for Genomic Research University of Liverpool server. Isolates were serotyped in silico with ShigEifinder, taxonomic classified with Kraken 2, and genotypic AMR and Virulence profiles for each isolate was done using AMRfinder and Virulencefinder. Only 27/44 genotypically confirmed as Shigella were included in this study. A maximum-likelihood phylogenetic tree was generated from a core single nucleotide polymorphism alignment (40075 SNPs) using quality trimmed reads mapped against the complete S. flexneri 2a strain 301 genome.

Results

From the 27 isolates 10 were identified as S.Sonnei (8 form I, 2 form II), 9 as S.Flexneri (5 SfXv, 4 Sf6) and 8 as S.Boydii (6 serotype 11, 2 serotype). Each serotype was found to be epidemiologically distinct in terms of geographical distributions, AMR, and virulence profiles. 15 genes encoded resistance to ten antimicrobial classes and mobile genetic elements were identified.

Conclusion

The results provide important baseline information for public health interventions including antibiotic treatment and deployment of the appropriate Shigella vaccine, the development of which is a World Health Organisation priority, currently underway in Malawi.

Poster session I

IMMUNOLOGY & ONCOLOGY

Presenters:

- Sawssen Bouali
- Adithya Chandran
- Sagar Goyal
- Milad Mashinchian
- Mahnaz Mohammadi Kian
- Yuqing Wang

Regulation of RKIP through Site-Specific Phosphorylation by Cdk1/Cyclin Complexes

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Introduction

Raf kinase inhibitor protein (RKIP) is a pivotal regulator of intracellular signaling pathways involved in numerous processes, including cancer progression and metastasis. We have been investigating the role of RKIP in cell cycle regulation. Phosphorylation of RKIP on threonine 42 (T42) appears to play a role in mitotic checkpoint control. Phosphorylation of this residue affects the structure and function of RKIP, resulting in its dissociation from Raf-1 kinase and thus activation of the Raf/MEK/ERK pathway. We are delving into the regulation and function of this specific post-translational modification of RKIP and its possible therapeutic implications.

Method & Materials

We looked at whether Cdk1/cyclin complexes can directly phosphorylate RKIP, particularly Cdk1/cyclin A2 and Cdk1/cyclin B1, whose activity windows correlate with T42 phosphorylation in cells. We thus performed kinases assays with RKIP as a possible substrate, alongside histone H1 as a positive control. Tandem mass spectrometry was employed to determine whether the Cdk1/cyclin complexes are active toward RKIP and, if so, identify the specific phosphorylation site(s) following kinase assays, PAGE and in-gel tryptic digestion.

Results

We found that both Cdk1/cyclin complexes can directly phosphorylate RKIP. This phosphorylation in both cases is absolutely specific to T42, with no other site of modification by either kinase complex detected. Furthermore, the level of phosphorylation was almost ten times greater at steady state with Cdk1/cyclin B1 than with Cdk1/cyclin A2.

Conclusion

Our findings demonstrate that RKIP is a direct substrate of Cdk1/cyclin complexes, with phosphorylation exclusively on T42 of RKIP. Cdk1/cyclin B1 is far more efficient at phosphorylation of RKIP than Cdk1/cyclin A2. These results suggest the possibility that RKIP may be regulated directly by Cdk1/cyclin complexes in mitotic checkpoint control, which we are now investigating, along with the downstream functions of this process. This work may help guide future efforts toward therapeutic modulation and control of RKIP-regulated pathways implicated in disease.

Beyond The Flakes - Unraveling Patterns of Complementary and Alternative Medicine (CAM) use among Psoriasis patients in South India

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Introduction

Complementary and alternative medicine (CAM) refers to medical practices that are not part of conventional medicine. Reports in literature suggest prevalence of CAM use ranges from 37% to 87%. There is no data on frequency of CAM use in Indian Patients with psoriasis. Therefore, this novel study was designed to fill the significant gap in existing literature. Our primary objective was to analyze the pattern of CAM used among psoriatic patients. Our secondary objectives were to estimate the prevalence of CAM use among psoriatic patients, finding the relationship between socio-economic status of an individual and CAM use, analyzing the influence of CAM use on quality of life of psoriatic patients using Dermatology Life Quality Index (DLQI) and analyzing the predisposing factors for CAM use among psoriatic patients

Method & Materials

The method used was a descriptive study, designed to look at frequency of CAM use in psoriasis patients attending the DVL OPD of a tertiary care hospital in South India. The clinico-epidemiological details and details of CAM use were entered into a predesigned proforma.

Results

Results of ninety-six psoriasis patients included in the study showed CAM use among thirty (31.58%) psoriasis patients with Siddha treatment being the most common CAM used. Statistical analysis showed significant association of gender (M>F), time since diagnosis, alcohol use, PASI score with use of CAM. Logistic regression analysis found age, education, socioeconomic status, alcohol use, time since diagnosis, presence of concomitant disease, affordability of medication and PASI score to be independent predictors of CAM use.

Conclusion

In conclusion, CAM is used by approximately 30% of psoriasis patients in South India and the most common therapy used is Siddha. Knowledge of evidence regarding CAM therapies will help the dermatologist offer a balanced view of risks and benefits of indigenous CAM practices to our patients.

Comparative Evaluation of Liver Function Tests in Psoriasis Patients Treated with Tofacitinib and Apremilast

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Introduction

This study compares liver function test results in psoriasis patients undergoing treatment with two prominent medications, tofacitinib and apremilast. Psoriasis, a chronic autoimmune skin disorder, often necessitates long-term therapeutic interventions. Tofacitinib, a Janus kinase (JAK) inhibitor, and apremilast, a phosphodiesterase-4 inhibitor, have emerged as effective options. However, concerns regarding their impact on liver function warrant a detailed comparative evaluation.

Method & Materials

A prospective cohort study was conducted involving 316 psoriasis patients, randomly assigned either to tofacitinib or apremilast treatment groups. Baseline liver function tests, including serum alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP), and total bilirubin, were assessed. Patients were monitored regularly over 12 months, with liver function tests performed before starting the treatment and next at 3rd month of treatment, 6th month from the last Liver function test last one at the end of the treatment. The paired t-test was done to analyze the liver function test results among the psoriasis patients.

Results

The analysis revealed notable liver function test outcome differences between the tofacitinib and apremilast groups. While both treatments demonstrated efficacy in managing psoriasis symptoms, tofacitinib slightly increased ALT and AST levels, suggesting a potential mild hepatocellular effect. In contrast, apremilast demonstrated a more favorable liver safety profile, with minimal changes in liver function markers. ALP and total bilirubin levels remained within normal ranges for both groups throughout the study. Tofacitinib's impact on liver enzymes appeared more pronounced in older patients, and those with a history of liver disease, emphasizing the need for personalized treatment considerations.

Conclusion

In conclusion, this comparative evaluation sheds light on the nuanced effects of tofacitinib and apremilast on liver function in psoriasis patients. While both medications effectively manage skin symptoms, clinicians should be mindful of the distinct hepatic profiles associated with each. Tofacitinib users may require closer monitoring of liver enzymes, especially in older individuals or those with preexisting liver conditions. Apremilast emerges as a safer option regarding liver function, providing an alternative for patients with underlying hepatic concerns.

Ketone Body -Hydroxybutyrate Enhances Mammary Cancer Cells Resistance Against Chemotherapy

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Introduction

A ketogenic diet and ketone supplementation have been identified as potential cancer therapeutics. However, there is no conclusive evidence that ketogenic diets reduce mammary cancers. More research is needed to understand how ketogenic diets impact metastasis. The primary characteristic of ketogenic diets can be recapitulated by _-hydroxybutyrate (BHB), which maintains intestinal stemness by regulating the Notch pathway. Using 2D and 3D cultures, we studied the effects of BHB on mammary gland cancer cells (CF41.Mg) before and after chemotherapy.

Method & Materials

Our study focused on examining CF41.Mg cells in vitro. Cells were pre- or post-treated with BHB and 5-Fluorouracil (5-FU). Using the MTT test, BHB therapy was examined for cytotoxicity. Next, we determined cell migration capacity in 2D. We evaluated the size, shape, and proliferation rate of the 3D-spheroid culture by employing Ki-67 microscopic labeling. Finally, the spheroids apoptosis rate of 3D-spheroids using flow cytometry and mucin-1 (MUC-1) expression profile.

Results

BHB administration, both before and after 5-FU treatment, decreased the cytotoxic effects of 5-FU in vitro which is consistent in multiple media with varying glucose concentrations that mimicked ketogenic and high-glucose diets. Cell migration was enhanced by 120.8 % for 48 hours and 144% for 72 hours in our wound healing assay, which aligns with MTT results. According to the results of the Ki-67 microscopy, the number of proliferating cells increased by 55.8% after BHB pretreatment of 3D spheroids. Mammary gland tumorigenesis and axillary node metastases are strongly associated with high MUC-1 expression. Using confocal microscopy, pre-treatment with BHB increases MUC-1 expression. Finally, flow cytometry analysis revealed a lower number of apoptotic populations in spheroids treated with BHB.

Conclusion

Our findings show that in vitro administration of BHB, particularly as a pre-treatment prior to 5-FU, can enhance cancer cell survival. Furthermore, the cell migration experiment confirmed that BHB treatment causes cancer cells to grow faster. BHB pre-treatment significantly increased the number of proliferating (Ki-67+) cells and MUC-1 expression in 3D culture. According to our study, supplemental ketone body BHB is not effective in vitro against mammary tumorigenesis. Further research should be conducted using animal models to explore its potential and mechanism as an adjuvant therapy.

Curcumin and Thalidomide Synergy Against Leukemia Cell Lines KG-1 and U937: An Invitro Study

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Introduction

Leukemias are widely recognized as the most common types of cancer in children. The Phosphatidylinositol 3-kinase (PI3-K)/Akt signaling pathway plays a crucial role in promoting cell growth and survival by inhibiting apoptosis in various human cancers. The survival and potential recurrence of leukemia are primarily attributed to two key mechanisms: the continuous activation of the PI3/AKT kinase and the NF-_B signaling pathway. To explore potential therapeutic options, this research study aimed to investigate the inhibitory effects of Curcumin and Thalidomide on myelogenous leukemia cell lines (U937 and KG-1).

Method & Materials

U937 and KG-1 cell lines were subjected to various concentrations of Curcumin, Thalidomide, and a combination of both compounds for a duration of 48 hours. The MTT test was employed to assess cell growth inhibition and cell proliferation status, while Annexin V-FITC/PI staining was utilized to measure the level of apoptosis, which was subsequently analyzed using flow cytometry. Additionally, real-time PCR was conducted to evaluate the mRNA expression of PTEN, IL-6, and the Akt/PI3K/mTOR pathway

Results

Our findings demonstrated that CUR effectively inhibited cell proliferation in both U937 and KG-1 cell lines, with an IC50 value of 40 _M. Similarly, THAL also exhibited inhibitory effects on cell proliferation, with an IC50 value of 60 _M for U937 cells and 80 _M for KG-1 cells. These results clearly indicate that CUR possesses significant cytotoxic properties against both cell lines in a dose-dependent manner. Furthermore, we investigated the potential synergistic effects of combining CUR with THAL by assessing the viability of treated cells at different time points. Interestingly, we observed that the viability of treated cells remained consistent at 72 hours compared to 48 hours post-treatment. In U937 cell lines, the expression levels of PTEN, IL-6, Akt, PI3K, and mTOR mRNA were significantly upregulated in cells treated with CUR and THAL, suggesting the activation of both cell survival and autophagy pathways. Conversely, in the KG-1 cell line, the mRNA expression of Akt and IL-6 increased upon CUR treatment, while the expressions of PI3K, mTOR, and PTEN were significantly elevated in the CUR-40 ÊM + THAL-80 _M combination as well as THAL-80 _M treatment. These findings shed light on the potential mechanisms underlying the cytotoxic effects of CUR and its combination with THAL in different cell lines.

Conclusion

To summarize, the potential of inhibiting PI3K/Akt/mTOR in laboratory settings holds great promise for advancing the field of novel strategies and anticancer therapies. Additionally, this approach paves the way for the creation of innovative drugs that target the PI3K/Akt pathway.

The single-cell landscape exploring abnormal t cell states and developmental trajectories in heterogeneous non-hodgkin lymphoma

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Introduction

According to the data published by WHO in 2023, the mobility of lymphoma is six point six-one hundred thousands. Lymphoma has the highest morbidity among hematological malignancies in Eastern Morocco, Korea and China. Non-Hodgkin lymphoma is not a single disease, but a group of diverse subtypes that have different molecular drivers, clinical outcomes, and therapeutic options. The mortality of T cell lymphoma is high and the molecular classification is unclear. Cutaneous T cell lymphoma (CTCL) is one of common types of T cell lymphoma. Currently, the advancement of single cell RNA sequencing (scRNA-seq) enables us to gain deeper insights into global patterns of transcriptomic changes at a single-cell resolution, which helps us to catch possible driver pathogenic molecules and find novel therapeutic target. However, most of scRNA-seq data focuses on B cells in non-Hodgkin lymphoma, rather than T cells.

Method & Materials

We integrated all of public scRNA-seq databases on non-Hodgkin lymphoma. We made quality control and integrated the datasets from 10 publications via Seurat. We did pseudotime analysis through Monocle 2 and Monocle 3. pySCENIC was used to do transcriptional factor enrichment analysis and Cell Chat was used for cell-cell communication analysis.

Results

We integrated 10 public datasets of non-Hodgkin lymphoma. Eleven types of cells were identified. Among these datasets, cells from CTCL are most. In order to clear out T cell states in the development of CTCL. Four development trajectories were simulated. For CD4 single positive (SP) T cells, Trajectory 1 is central memory T (Tcm)-1 to regular T cell (Treg), and Trajectory 2 is Tcm-2 ? resident memory T cell (Trm) ? CD7 loss T cell. For CD8 SP T cells, one trajectory is Tcm-1 ? Tcm-2 ? effector T cell (Teff)-2, and another trajectory is Tcm-1 ? Tcm-2 ? effector T cell (Teff)-2. Through four developmental trajectories, active signals and exhaustive signals simultaneously upregulated, leading to dysfunctional immune responses. Finally, IRF8, SPI1 and EZH2 were identified to play a significant role during T cell state transition and may be novel target for CTCL.

Conclusion

Both CD4 and CD8 T cells from malignant tissues exhibited the characteristics of high proliferation and high exhaustion, which may cause T cell dysfunction and lead to tumorigenesis. IRF8, SPI1 and EZH2 may be driver molecules in CTCL, which are potentially novel targets for therapy.

Poster session I

INFECTIOUS DISEASE

Presenters:

- Mohammad Ghasemian
- Arash Mohammadi Matak
- Mobina Sadat Zarabadi
- Seyedeh Mahdiye Mohati
- Tadala Mzengo
- Vishaal P.

A reduction in inflammation and fibrosis endpoints in HIV patients using losartan

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Introduction

Among people living with HIV (PHIV), persistent inflammation and incomplete immune recovery are associated with an increased risk of contracting a disease. As a result of its anti-inflammatory properties and ability to disrupt nuclear factor-beta (NFB)/fibrotic response, losartan was hypothesized to reduce inflammation by inhibiting nuclear factor-beta (NFB) reactions.

Method & Materials

The effect of losartan (100 mg) versus placebo over 12 months has been evaluated in a randomized controlled trial (1 : 1) involving PHIV patients aged at least 50 years who were receiving antiretroviral therapy (ART), with HIV RNA less than 200 copies/ml and CD4+ cell count of at least 600 cells/l or less. As part of this study, biomarkers of inflammation, fibrosis, and myocardial damage were assessed in blood using ELISA, electrochemiluminescence, and immunoturbidimetric methods, and T-cell and monocyte phenotypes were assessed using flow cytometry in a subset of participants. We compared the changes in biomarkers, as well as cell phenotypes, over a follow-up period, between the losartan and placebo arms using linear mixed models with a log-2 transformation.

Results

A month 12 visit was achieved by 96% of 89 PHIV patients (n = 39 to losartan; n = 4+ to placebo). There was a median age of 58 years and a baseline CD4+ cell count of 408 cells/_l. The treatment with losartan did not improve interleukin-6 levels, or other blood measures of inflammation, immune activation, fibrosis activity, or myocardial function. Both CD4+ and CD8+ T cells did not differ by treatment group. A reduction of 6 and 5mmHg in HBP and SBP was observed with losartan.

Conclusion

It did not improve blood measures of inflammation or T-cell immune recovery among older PHIV patients with viral suppression when losartan was administered. There is little evidence that losartan treatment reduces inflammation-associated comorbidities to a clinically meaningful extent, outside of lowering blood pressure.

Investigation of the Specificity and Sensitivity of an Optical Isothermal Technique for the Detection of a Bacterial Respiratory Infection Agent

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Co-authors: Mohati S. (Seyedeh Mahdiye)

Introduction

Klebsiella aerogenes is a bacterium commonly found in the human digestive system and can opportunistically cause infections. Identifying this pathogen in clinical samples is crucial due to the illnesses it can cause and the time-consuming diagnostic methods. It is essential to diagnose a condition to manage it effectively and quickly. In this study, a colorimetric method was developed to identify Klebsiella aerogenes.

Method & Materials

Isothermal amplification was performed using K. aerogenes and thirteen related bacteria. To perform sensitivity analysis, the nucleic acid solution of K. aerogenes was diluted to 10-4 before amplification. Hydroxy naphthol blue (HNB) was added to the reaction mixture for colorimetric detection of products immediately after the amplification. A spectrophotometric analysis was conducted to measure the turbidity of each assay. The absorbance of each measurement was scanned between 300-700 nm, and wavelengths were selected for maximum differentiation.

Results

When the target sequence was present in the samples, a color change from pink to sky blue was observed, indicating a positive result. On the other hand, the samples changed to dark blue or purple for the remaining twelve samples with non-complementary DNA sequences as negative results. After spectrometric analysis, two absorption peaks were identified at 640 and 580 nm. The ratio of absorption at 680 nm to 580 nm was also calculated. The positive sample had a ratio of 1.19, while the negative samples had ratios ranging from 0.76 to 0.96. As a result, the presence of K. aerogenes was successfully detected at dilutions as low as 10-3 among the other tested bacteria.

Conclusion

This method can be achieved visually or with a plate reader device and is fast, low-cost, and user-friendly.

Comparison between a newly developed isothermal method and a conventional PCR for detecting Serratia marcescens

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Co-authors: Mohammadi Matak A. (Arash)

Introduction

The quick identification of pathogens is crucial for managing the spread and mitigating their impact on public health. Serratia marcescens is an opportunistic bacterium that has been frequently associated with nosocomial outbreaks. Molecular detection methods, such as PCR and nucleic acid isothermal amplification, are commonly used to detect bacteria. The time-consuming PCR requires expensive equipment and trained personnel to operate. Isothermal techniques are fast, reliable, without the requirement of complex device. In this study, an isothermal amplification method was developed and compared with conventional PCR to detect S. marcescens.

Method & Materials

Specific primers were designed to detect S. marcescens. The boiling method was used to extract the nucleic acid content. The reaction condition for the PCR method was optimized. The specificity of both methods was measured using eleven other related bacteria. Gel electrophoresis was utilized to monitor the products; however, because of low resolution, hydroxy naphthol blue (HNB) was added to visualize the isothermal amplification products. The sensitivity of both methods was compared using samples that contained different dilutions of the nucleic acid of S. marcescens.

Results

Gel electrophoresis was used to monitor the PCR products and a clear band was observed only in the sample with S. marcescens. No band was visible in the other bacterial samples. The sample with S. marcescens showed a distinct sky-blue color change, while the negative samples with DNA from other bacteria changed to purple and dark blue. As a result, the new isothermal method can detect the presence of S. marcescens within only twenty minutes at a temperature of 65¯C. The isothermal method demonstrated a high level of accuracy with a specificity of 91%, while the PCR method had a lower specificity of 75%. Furthermore, the sensitivity of the isothermal method was measured at 94_10^-3 ng/mL, whereas the sensitivity of PCR was 94_10^-9 ng/mL.

Conclusion

In summary, although the sensitivity of PCR was 10^6 times greater than that of the developed isothermal amplification, the isothermal method had the advantage of being quicker, making it a promising tool for point-of-care detection. This early detection and control of outbreaks of pathogens can be achieved with this method.

Risk Factors for Klebsiella pneumoniae Infection in Infants less than 3 months of age at Queen Elizabeth Central Hospital (QECH).

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Introduction

Sepsis is one of the leading causes of neonatal death in Malawi. Beta lactams are crucial for treating neonatal infections. However, cephalosporin-resistant extended-spectrum beta-lactamase Enterobacteriaceae (ESBL-E) infections are increasing. Klebsiella pneumoniae has become the dominant neonatal pathogen in these settings, serving as the primary cause of neonatal infection at Queen Elizabeth Central Hospital (QECH). Risk factors for K. pneumoniae infection in infants need further investigation to identify those at risk, who would benefit from targeted antibiotic therapy, ultimately reducing drug-resistant infection mortality.

Method & Materials

A prospective case-control study was conducted to investigate risk factors for K. pneumoniae infection. Controls, were sepsis-free, and selected with a 2:1 ward-based matching ratio. Risk factors likely to impact K. pneumoniae exposure and guide antimicrobial therapy were included e.g Birthweight, prematurity, age(days), maternal status, delivery mode. Missing data was dealt with using multiple imputation. A Logistic regression was performed with the exposures of interest to determine the odds ratio (OR) for these risk factors.

Results

The study included 37 cases and 74 controls. 16% of cases were born in QECH rather than outside QECH. Compared to controls, cases were on average born, 2.69 weeks earlier, 483g [95% CI (185-781)] lower birthweight, 7 days older. In a multivariate logistic regression model increasing birthweight was protective against K. Pneumoniae infection (OR 0.13 [95% CI 0.027-0.53], p = 0.006), age (an indicator for ward time) was associated with an increased risk of K. Pneumoniae infection (OR 1.03 [95% CI 1.01 ? 1.06, p=0.01]. Other variables were not significantly associated with K. Pneumoniae infection

Conclusion

Low birthweight and age in days are risk factors for K. pneumoniae infection. Low birthweight infants may be inherently more vulnerable to infection and may receive more invasive interventions. Age in days is likely a proxy measure for time in hospital (most neonates had been admitted since birth), and longer time in hospital gives more exposure to hospital-acquired K. pneumoniae.

Prevalence of Gram-negative bacteria on the cell phones of health-care workers - A systematic review and meta-analysis

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Introduction

The use of mobile phones has become an essential part of daily life for a majority of the population, including healthcare workers (HCWs). Numerous studies have shown that healthcare workers? mobile phones can be colonized with gram-negative bacteria, and that these bacteria can potentially spread to patients, leading to healthcare-associated infections (HAIs) such as antibiotic resistance pneumonia, bloodstream infections, and urinary tract infections, among others. This Meta-analysis can help provide the prevalence of gram-negative bacteria (GNB) on the cell phones of health care workers and to identify the factors that may be associated with the high prevalence rates.

Method & Materials

A comprehensive literature search was conducted, including PUBMED, WOS, Scopus, Embase, and Cochrane. The search was conducted systematically to ensure that all relevant articles were identified from 2001-2022. R version 4.0.4, was used for the data analysis. PROSPERO registration was done to validate the methodology (ID ? CRD42023409080)

Results

Sixty-five studies were qualified for analysis. The overall prevalence of GNB on the cell phones of HCWs was 80.57% (95% CI: 77.57-84.76, I2: 96%). Maximum cases were reported in Iran. More recent studies show an increased prevalence of GNB. Moreover, the prevalence increases marginally as large sample studies are conducted.

Conclusion

A significant presence of GNB emphasizes the potential for mobile phones to serve as a source of transmission for GNB in healthcare settings. The findings also highlight the importance of implementing stringent hygiene practices among healthcare workers to minimize the risk of GNB transmission and associated infections. This study attempts to address the potential implications of gram-negative bacteria on the cell phones of healthcare workers. As these devices frequently come into contact with various clinical settings, understanding the prevalence of such bacteria can provide valuable insights into infection control measures and the broader issue of nosocomial infections.

Evaluation of Nystatin Chewing Gum Versus Suspension in Oral Candidiasis: A Randomized Clinical Trial

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Introduction

Oral candidiasis, a fungal infection caused by Candida species, is a common condition that can significantly compromise oral health and quality of life. Nystatin, an anti fungal medication, has long been utilized for the treatment of oral candidiasis; Particularly, in the form of oral suspension. However, it is known to be associated with some drawbacks such as unpleasant taste and potential gastrointestinal side effects. In recent years, the development of nystatin chewing gum formulations has offered a promising alternative for the treatment of oral candidiasis. This study aimed to assess the effectiveness of two routes of administration, nystatin gum and suspension in the treatment of oral candidiasis.

Method & Materials

Sixty participants with oral candidiasis were enrolled in this clinical trial and were randomly assigned into two groups. The first group received nystatin gum for 2 weeks, 5 times a day chewing for 20 minutes .while the second, received nystatin suspension at a dosage of 100,000 IU for 2 weeks, 5 times a day. After two weeks, a follow-up appointment was conducted to assess the response to treatment. Data analysis was performed using SPSS 21 software, and a chi-square test was employed to compare the treatment outcomes between two mentioned groups.

Results

After two weeks, 7 (23.3%) and 5 (16.7%) patients were fully recovered in the chewing gum and suspension group respectively. Improvement of candidiasis was noted in 12 patients (40%) in the chewing gum group and 8 patients (26.7%) in the suspension group. Meanwhile, no change in the condition was seen in 11 patients (36.7%) from the chewing gum group and 16 patients (53.3%) from the suspension group. It was noted that the symptoms of one person in suspension group, were exacerbated. Statistical analysis revealed no significant difference in the success rate among the two groups (P value=0.29).

Conclusion

This study demonstrated that both routs of administration, nystatin chewing gum and oral suspension, were efficient in the management of oral candidiasis and based on the results, chewing gum was as effective as the suspension. The superior acceptability, ease of administration, and improved taste of nystatin gum make it a suitable alternative to nystatin oral suspension. However, various studies with higher participants are required for a definite decision.

Poster session I

MEDICAL BIOCHEMISTRY

Presenters:

- Sem Geertsema
- Ursula Zuñiga
- Joyce Hamann
- Anna Tabor

ISCOMS 2024 SCIENCE BEYOND BORDERS

What determines female predominance in Desmoplakin (DSP)-related cardiomyopathy?

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Introduction

Desmoplakin (DSP), encoded by the DSP gene, is a structural protein that links the cardiac desmosome and intermediate filaments, thereby playing a crucial role in maintaining the integrity of force transmission within the myocardium. (Likely) pathogenic ((L)P) DSP variants can cause cardiomyopathies (CM), most commonly arrhythmogenic cardiomyopathy (ACM) or dilated cardiomyopathy (DCM). Arrhythmias and sudden cardiac death (SCD) are an intrinsic part of DSP-related CM. Interestingly, the prevalence of CM is higher in males than females. Various studies consistently report a 3:1 female-to-male ratio in DSP-related CM. The reason for this skewed ratio is unclear; nearly all inherited CMs show a male predominance in disease expression. We aim to assess the potential causes of this female overrepresentation in DSP-related CMs.

Method & Materials

Clinical and genetic data were collected on 13 families (32 individuals) with 11 different LP/P DSP variants. Multiple parameters were being studied as potential contributors, including number of pregnancies, male SCD, and non-cardiac comorbidity.

Results

Of the 32 carriers, 20 were female (63%). Five females (mean age 38.7 years) were nulligravida, and 15 females (mean age 59.1 years) were primi/multigravida (range 1-3). The mean age at pregnancy was 30.2 years (range: 23-44). CM was diagnosed in 60% (3/5) nulligravida and 73% (11/15) primi/multigravida females. The mean age at CM diagnosis was 52.3 years (range 47-55) and 55.6 years (range: 48-71), in nulligravida and primi/multigravida females respectively ($t=0.5394$, $p=0.2780$). Three females had died (mean age 56.3 years (range: 52-57)). Of whom two multigravida (2 and 3 pregnancies) due to SCD (52 and 57 years). Only one male experienced SCD (72 years). Four carriers had non-cardiac comorbidity, of which three were potentially immune-related (hypothyroidism, hyperthyroidism, type 1 diabetes).

Conclusion

In this preliminary study, we confirm the female predominance in DSP-related cardiac disease. No overrepresentation of male SCD cases could explain female predominance. The prevalence of CM was (statistically non-significant) higher in primi/multigravida compared to nulligravida female carriers. Three affected individuals had potential autoimmune disease-related comorbidities. To further investigate sex differences in DSP-related CM, we aim to expand this study to reach meaningful numbers and draw more definite conclusions.

Liposomes for intracellular delivery of monoclonal antibodies - novel approach in modern anti-cancer therapy

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Introduction

According to the World Health Organization, cancer is the leading cause of death worldwide. The overexpression of oncogenic intracellular proteins plays a crucial role in the development of many types of cancer. However, direct targeting of these proteins poses a challenge, making them "undruggable" targets. The size of small-molecule drugs is insufficient to disrupt protein-protein interactions, while therapeutic proteins cannot penetrate the cell membrane. The proposed solution to this problem is our novel therapeutic approach involving the use of liposomes to deliver monoclonal antibodies (mAb) to cells. The mAb transported to the cytoplasm bind specifically to the target proteins and are recognized by the recently discovered intracellular antibody Fc receptor TRIM-21 (Tripartite motif family protein), which is expressed in every tissue. Subsequently the antibody-antigen-TRIM21 complex undergoes proteasomal degradation. This phenomenon is called Antibody dependent intracellular neutralization (ADIN).

Method & Materials

Our team has developed a system ensuring the transport of mAb into the cell based on the liposomes grafted with polyethylene glycol. In the initial stage, we produced the mAb using the hybridoma technology which were encapsulated inside liposomes using the freeze-thaw method. The obtained liposomes undergo purification to remove free antibodies. We use purified liposome fractions with encapsulated mAb for cellular tests, investigating changes in TRIM21 protein levels and its colocalization with mAb.

Results

Our liposome preparations do not reduce viability or induce a proinflammatory response in RAW 264.7 monocyte-macrophage cells. We also used the HEK-Blue™ cell line overexpressing the human Toll-like receptors (hTLR) provided by InvivoGen to evaluate the presence of pyrogens in the produced mAb and liposomes. No lipopolysaccharide (LPS) contamination was detected in the tests. Additionally, we checked the presence of mAb inside cells, either added directly to the medium or delivered using liposomes.

Conclusion

Targeting the "undruggable" proteins represents the drug discovery frontier. Our team has developed a promising strategy for using liposomes to transport Ab into the cells, which in the future may be further developed into a modern anti-cancer therapy.

Systemic free thiols associate with clinical and biochemical disease activity in Inflammatory Bowel Disease: a prospective diagnostic validation study

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Introduction

In the pathophysiology of inflammatory bowel diseases (IBD), oxidative stress plays an important role. Lower levels of plasma free thiols (FT) reflect a higher oxidative stress burden and correlate with IBD disease activity. However, their clinical significance as biomarker for disease activity remains unclear. This study aimed to prospectively validate the utility of plasma FT levels as biomarker for clinical, biochemical, and endoscopic disease activity in patients with IBD.

Method & Materials

In an ongoing prospective diagnostic trial, we conducted an interim analysis of plasma FT levels in 52 patients with IBD (24 Crohn's disease [CD], 21 ulcerative colitis [UC], and 7 patients with undetermined IBD). Clinical disease activity was quantified by the Harvey-Bradshaw Index (HBI) for CD and Simple Clinical Colitis Activity Index (SCCAI) for UC. Biochemical disease activity was determined by measuring blood C-reactive protein [CRP] and faecal calprotectin [fCal]). Endoscopic disease activity was quantified with the Mayo endoscopic subscore for UC and the Simple Endoscopic Score (SES-CD) for CD. Plasma FT levels were assessed for correlations with disease activity parameters using linear and logistic regressions models. Discriminative capacity of biomarkers was evaluated through calculating receiver operating characteristics (ROC) statistics.

Results

Plasma FT levels were significantly negatively correlated in clinical parameters, like HBI ($r=-0.53$, $p<0.05$) (Fig. 1A). Other inflammatory biomarkers, like CRP, were also negatively correlated with plasma FT levels and were reduced in patients with active IBD ($r=-0.43$, $p<0.05$) (Fig. 1B). Plasma FT levels accurately discriminated between CD patients with clinically quiescent (HBI<5) and active disease (HBIÚ5) (AUC=0.80, p=0.02, Fig. 1C), better than fCal (AUC=0.55, p=0.83). Plasma FT were not significantly different for biochemically quiescent (CRP<5mg/l) and active (CRPÚ5mg/l) disease (AUC=0.69, p=0.20, Fig. 1D). Both Mayo and SES-CD scores, after adjusting for confounders, also exhibited a trend towards negative association with plasma FT levels (Fig. 1E).

Conclusion

Further completion of the trial will reveal whether systemic FT levels will reflect endoscopically observed disease activity, and this interim analysis shows strong correlations FT levels and parameters of clinically and biochemically active disease. Measuring systemic FTs in IBD may be a promising, minimally invasive strategy to monitor IBD disease activity.

Potential anti-inflammatory effect of endothelial small extracellular vesicles

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Introduction

Endothelial cells produce small extracellular vesicles (sEVs) that contribute to both physiological and pathophysiological processes. It?s been described that these sEVs have cardioprotective properties but, whether these sEVs wield specifically anti-inflammatory effects or if this can be exogenously modulated remains unknown.

Method & Materials

We isolated sEVs from Human umbilical cord vein endothelial cells (HUVEC) treated with or without 20 ng/ ml of Interleukin-10 (IL-10), using size exclusion chromatography. To determine size and concentration of sEVs, we used Nanoparticle Tracking Analysis. Expression of sEVs markers was evaluated using immunofluorescence and ELISA assays. Visualization of sEVs was achieved using Electronic Microscopy. The effect of sEVs was tested in two in vitro models, both treated with 108 particles/mL of sEVs from HUVECs treated with or without IL-10. 1) HUVECs undergoing replicative senescence, whereby expression of pro-inflammatory markers Interleukin-6 (IL-6) and p65 was evaluated by qRT-PCR. The senescent phenotype was assessed by -Galactosidase staining, Western Blot of p16 and p21, and measurement of area and perimeter using fluorescence microscopy. 2) Vascular Smooth Muscle Cells (VSCM) A7r5, treated with TNF- (10 ng/mL) where migration was assessed using a wound healing assay.

Results

The results show that IL-10 does not affect the size, concentration, morphology, or expression of surface markers of sEVs. Furthermore, 108 particles/mL of sEVs from HUVECs treated with or without IL-10 did not affect senescence-induced expression of IL-6 or p65. However, both types of sEVs reduced migration of VSMC elicited by TNF-.

Conclusion

sEVs derived from endothelial cells treated with or without IL-10 do not reverse the expression of pro-inflammatory markers in senescent HUVECs but do reduce migration of VSMC induced by TNF-, thus pitching these sEVs as potential therapeutic agents in cardiovascular inflammatory contexts.

Poster session I

NEUROLOGY

Presenters:

- Giorgi Amiridze
- Mohsen Chamanara
- Vasiliki Georgia Paplou
- Aynaz Mohammadi
- Susana Montoya Jaramillo
- Perminder Singh
- Mohammed Mohammadi

Cholinergic and GABAergic neurons from the basal forebrain modulate memory function and neurotransmitter markers in the prefrontal cortex and hippocampus

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Introduction

Most hypotheses regarding psychiatric disorders, including Alzheimer's disease, propose that the dysregulation of ascending neuromodulatory systems leads to abnormal Prefrontal Cortex function. The present research aimed to investigate the effects of selective immunolesions on cholinergic (choline acetyltransferase immunoreactive ? ChAT-ir) or gamma-aminobutyric acid (GABA) ergic (parvalbumine immunoreactive ? PV-ir) neurons in the nucleus basalis magnocellularis (NBM) on memory function. Additionally, the study assessed cholinergic activity and the expression level of glutamatergic receptors [specifically the NR2B subunit of N-methyl-D-aspartate (NMDA) receptors] in the medial prefrontal cortex (mPFC) and hippocampus of behaviorally characterized NBM immunolesioned rats.

Method & Materials

Behavioral experiments involved the assessment of working memory through a spatial alternation testing procedure in a plus-maze, while the acquisition and retention of spatial memory were evaluated in a Morris water maze. The rats were categorized into three groups: the NBM cholinergic or GABAergic immunolesioned groups, along with the normal control group. ChAT or PV staining of the NBM and acetylcholinesterase immunoreactive (AChE-ir) staining of the mPFC and hippocampal sections were conducted to visualize the impacts of immunotoxins. Additionally, electrophoresis and immunoblotting were performed to assess the influence of NBM lesions on the quantity of the NR2B subunit of NMDA receptors.

Results

The findings suggest that immunolesions targeting cholinergic neurons in the NBM result in impaired spatial working memory and long-term spatial memory. These impairments are associated with significant alterations in glutamatergic markers in the mPFC and cholinergic markers in the mPFC and hippocampus. Immunolesions targeting GABAergic NBM neurons do lead to working memory impairment, accompanied by a reduction in NMDA NR2B receptor signaling in the mPFC; no significant reduction of cholinergic markers was observed in GABAergic immunolesioned group. Thus, impairment of working memory as a result of cholinergic or GABAergic NBM lesions may be associated with an alteration in glutamatergic transmission in the mPFC, in particular, with a significant decrease in NR2B protein levels.

Conclusion

The current findings illustrate that the cholinergic and GABAergic NBM cell groups exhibit diverse and complementary functions, forming integrated networks within distinct NBM-mPFC circuits. These networks may serve varying roles in the memory function of the mPFC.

Pharmacological evidence for the possible involvement of the NMDA receptor pathway in the anticonvulsant effect of tramadol in mice

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Introduction

Previous studies have shown controversial results regarding the pro- or anticonvulsant effects of tramadol. Additionally, the underlying mechanism of seizure induction or alleviation by tramadol has not been fully understood. In the current study, the effects of tramadol on pentylenetetrazole (PTZ)-induced seizure and the possible involvement of the N-methyl-D-aspartate (NMDA) pathway were assessed in mice.

Method & Materials

Male Naval Medical Research Institute (NMRI) mice were treated with intravenous infusion of PTZ in order to induce clonic seizures and determine seizure threshold. Tramadol was injected intraperitoneally (0.1?150 mg/kg) 30 minutes prior to elicitation of seizures. The possible effects of intraperitoneal injections of NMDA receptor antagonists, ketamine (0.5 mg/kg) and MK-801 (0.5 mg/kg) on the anticonvulsant property of tramadol were investigated subsequently.

Results

Tramadol (1?100 mg/kg) increased PTZ-induced seizure threshold in a dose-dependent, time-independent manner, with optimal anticonvulsant effect at a dose of 100 mg/kg. Acute administration of either ketamine (0.5 mg/kg) or MK-801 (0.5 mg/kg) potentiated the anticonvulsant effect of a subeffective dose of tramadol (0.3 mg/kg).

Conclusion

These results suggest a possible role of the NMDA pathway in the anticonvulsant effect of tramadol.

Neuroprotective Effects of Metformin in Stroke Patients: A Systematic Review and Meta-analysis

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Introduction

People with diabetes are 1.5 times more likely to experience strokes than those without diabetes. Metformin is often the initial medication chosen to manage type 2 diabetes mellitus (T2DM). Many recent studies revealed different neuroprotective effects of metformin. The purpose of our systematic review and meta-analysis is to explore the potential neuroprotective effects of metformin in individuals who have received it prior to stroke.

Method & Materials

We systematically conducted an exhaustive online inquiry using Medline, Scopus, EMBASE, and Web of Science databases. Our study encompassed cohort studies that drew a comparison between the severity and diverse outcomes of stroke among individuals with diabetes mellitus (DM) who were administered metformin prior to the stroke event and those with DM who did not receive the treatment.

Results

Eight studies met the eligibility criteria. Four studies reported the initial National Institutes of Health Stroke Scale (NIHSS) score, which represents the severity of the stroke. As a control group, all four studies included diabetic patients not taking metformin (either not using drug for diabetes or using other drugs for diabetes). Metformin use for diabetes management was associated with a lower NIHSS score just after stroke (standardized mean difference (SMD) = -0.29, 95% confidence interval (CI) -0.67 to 0.09; I2 =94%). Three studies looked at the effect of metformin pretreatment on the modified Rankin Scale (mRS) score at 90 days after stroke, which represents neurological function recovery after a stroke. A pooled analysis showed that metformin pretreatment was associated with an increased score of mRS at 90 days (odds ratio (OR) = 1.85, 95% CI 1.40 to 2.44; I2 =59%).

Conclusion

Our meta-analysis has shown that administering metformin to stroke patients has neuroprotective effects. Stroke patients with DM who were treated with metformin before stroke developed less severe stroke and had a better 90-day functional outcome. The potential advantages of metformin for stroke patients with DM suggest its viability as a viable treatment strategy for limiting brain damage after a stroke. To further validate the effectiveness of metformin, clinical trials are required to definitively evaluate the metformin effect and to compare the efficacy and dosage of individuals.

“NEUROTANGO as a non-pharmacological therapy to improve motor symptoms, and quality of life in patients with Parkinson’s disease

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Introduction

Parkinson’s disease is a neurodegenerative, progressive disorder characterized by the presence of bradykinesia, rigidity, resting tremor, and difficulty in performing manual tasks. Individuals with Parkinson’s disease experience limitations at both somatic and psychological levels. Numerous studies have shown that activities such as dance bring benefits in mobility, coordination,balance, and quality of life; our aim is to conduct a single group (arm) trial to evaluate the impact of the intervention on motor, emotional, and quality of life levels in patients with the disease.

Method & Materials

The study involves 13 patients with Parkinson’s disease who participate in tango classes for 12 months, once a week for 120 minutes. Outcome parameters are collected at three points in time (first month, sixth month, and twelfth month of intervention) and assess motor, emotional symptoms, and quality of life using standardized instruments: Parkinson’s Disease Questionnaire-39 (PDQ-39), Beck Depression Inventory-II (BDI-II), Berg Balance Scale, and Timed Up and Go test. A T-test was employed to assess statistical differences at different time points in each patient.All participants provided a written informed consent before the participation.

Results

The study includes 9 women and 4 men with an average age of 64 Ò 10 years, currently in the 8th month of the intervention. No improvements were found during the first two data collections for all outcomes, with the exception of the Timed Up and Go test (p=0.020), with an average time of 12.54 Ò 2.99 Seconds (S) and 10.41 Ò 1.31 S at the first and second time points, respectively, representing an improvement of 2,13 Ò 1,68 S in the performance of the test.

Conclusion

Before heading into final conclusions data must be collected at the third point in time, considering that half of the tango classes are still pending, and prior studies have shown that the benefit has been greater with prolonged interventions. However, we believe that other studies with larger populations, or randomization could improve our study limitations ,and be beneficial in determining the influence of neurotango as a non-pharmacological therapy in this patients.

Functional, Morphological and Molecular Changes Reveal the Mechanisms Associated with Age-Related Vestibular Loss

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Introduction

The inner ear shows functional and morphological changes that contribute to both age-related loss of vestibular function (ARVL) and hearing (ARHL). Both ARVL and ARHL are prevalent disorders that compromise the ability to perform daily tasks and diminish quality of life. Detecting and treating ARVL and ARHL remains challenging because of the lack of insight into the underlying pathophysiological mechanisms. Therefore, our study examined young (1.5-month-old) and old (24-month-old) C57BL/6 mice, utilizing physiological, histological, and transcriptomic methods.

Method & Materials

We used a variety of methods, including 1) measurement of vestibular sensory evoked potentials (VsEPs) in young (1.5-month) and old (20-24-month old) C57BL/6 mice; 2) isolation and immunofluorescent staining of vestibular sensory evoked epithelia followed by confocal microscopy and quantitative image analysis of the vestibular sensory epithelia; 3) inner ear (vestibule) isolation, RNA extraction, and RNA sequencing; and 4) differential expression analysis and gene ontology enrichment analysis.

Results

Vestibular sensory-evoked potentials revealed that older mice had reduced wave I amplitudes and delayed wave I latencies, indicating reduced vestibular function. Immunofluorescence and image analysis revealed that older mice exhibited a significant decline in type I sensory hair cell density, particularly in hair cells connected to dimorphic vestibular afferents. An analysis of gene expression in the isolated vestibule revealed the upregulation of immune-related genes and the downregulation of genes associated with ossification and nervous system development. A comparison with the isolated cochlear sensorineural structures showed similar changes in genes related to immune response, chondrocyte differentiation, and myelin formation.

Conclusion

These findings suggest that age-related vestibular hypofunction is linked to diminished peripheral vestibular responses, likely due to the loss of a specific subpopulation of hair cells and calyceal afferents. The upregulation of immune- and inflammation-related genes implies that inflammation contributes to these functional and structural changes. Furthermore, the comparison of gene expression between the vestibule and cochlea indicates both shared and distinct mechanisms contributing to age-related vestibular and hearing impairments. Further research is necessary to understand the mechanistic connection between inflammation and age-related balance and hearing disorders and to translate these findings into clinical treatment strategies.

Chronic intrathecal co-administration of morphine and NPY diminishes morphine-induced tolerance

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Introduction

Opioids like morphine are the mainstay in the treatment of pain. However, development of tolerance to its antinociceptive effect limits its use clinically. The mechanisms underlying development of tolerance are not fully understood. Pain signals at the level of the spinal cord, modulates the release of different neurotransmitters and neuropeptides. Also, previous studies in our laboratory have shown that co-administration of calcium channel blockers attenuate morphine tolerance. Neuropeptide Y (NPY) is abundantly expressed in the dorsal horn of the spinal cord and has been reported to have anti-nociceptive effect. Consequently, the effect of NPY on morphine-induced tolerance was investigated in rats.

Method & Materials

Male Sprague Dawley rats (275-325g) were implanted with intrathecal catheters (ReCath Co, USA). These were divided randomly into groups and administered the following drugs: Saline, Morphine (10Êg), NPY (10Êg) and NPY+ morphine. Behavioural assessment of anti-nociception was performed by hot-plate test daily for 9 days. Expression of NPY in the spinal cord was observed by immunohistochemistry and RT-PCR in morphine treated rats.

Results

Repeated intrathecal administration of morphine produced tolerance in the hot-plate test. Administration of NPY alone produced an antinociceptive effect which was less than morphine. However, combined administration of NPY and morphine led to a significantly higher antinociceptive effect with delayed onset of tolerance. Expression of NPY in the spinal cord not significantly altered.

Conclusion

Co-administration of NPY persistently enhanced antinociceptive effect with attenuation of tolerance. However, the expression of NPY was not significantly altered in tolerant rats in the current study. The mechanism of this effect is being analyzed currently

The association between multiple sclerosis and migraine: a meta-analysis

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Co-authos: Berchi Kankam S. (Samuel), Mohammadi A. (Aynaz), Mirmosayyeb O. (Omid), Shaygannejad V. (Vahid)

Introduction

Multiple sclerosis (MS) is a chronic progressive condition marked by the deterioration of myelin and impairment of neurological function. The global prevalence of MS is approximately 2.2 million. Migraine is common in MS patients, with inconclusive data on their relationship. Our systematic review aimed to assess the prevalence and odds of migraine in patients with MS (pwMS) and investigate the potential factors that may influence these associations.

Method & Materials

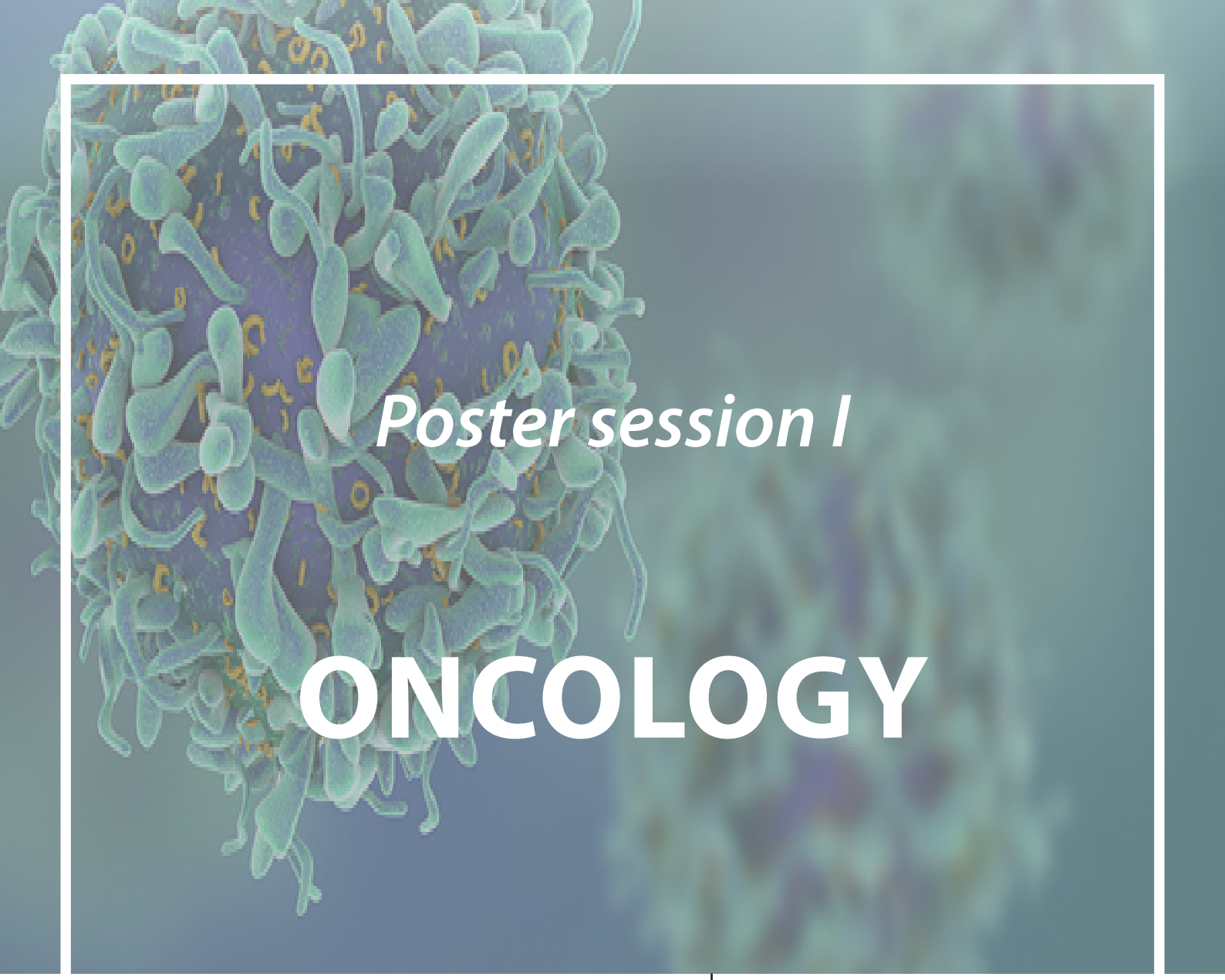
Through an extensive search and study selection, we identified pertinent literature investigating the occurrence and odds of migraines among pwMS. Additionally, we explored the comparative risk of migraines in MS patients compared to healthy controls. Data were extracted, including publication details, diagnostic criteria, and migraine prevalence in MS patients.

Results

A total of 35 studies were included, involving 279,620 pwMS and 279,603 healthy controls. The overall prevalence of migraine in pwMS was 0.24 (95% CI: 0.21–0.28). The analysis revealed that the prevalence of migraine with aura was approximately 7%, while the prevalence of migraine without aura was relatively higher at 18%. The meta-analysis indicated that pwMS had significantly increased odds of having migraine compared to healthy controls (OR = 1.96, 95% CI: 1.20–3.20). The findings indicated that the odds of experiencing migraine with aura were 0.8, suggesting a slightly reduced likelihood compared to the healthy controls. Conversely, the odds of migraine without aura were notably higher at 2.25 when compared to the healthy controls. Sensitivity analyses supported the robustness of our findings. Also, in the meta-regression analysis of the odds ratio, several parameters significantly influenced our results including: 1) age 45 and above 2) study type of cohort 3) MS duration of under 10 years 4) continent of Europe 5) publication year after 2010.

Conclusion

Our study highlights that approximately 24% of pwMS experience migraine. The method of diagnosis significantly affects the reported prevalence, with questionnaires yielding higher rates. Furthermore, pwMS have a 1.96-fold increased odds of having migraine compared to healthy individuals. These findings emphasize the importance of further research and interventions to address the significant burden of migraine in the MS population.



Poster session I

ONCOLOGY

Presenters:

- Saber Bakhtiaryfar
- Punya Gupta
- Lia Medina Montalvo
- Ali Mollahassani
- María Sánchez-Blázquez
- Pablo Siliceo

Impact of Allopurinol on Prostate Cancer Progression and Biomarker Modulation in a Phase II Clinical Trial

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Introduction

The prevalence of prostate cancer remains a significant public health issue, necessitating the development of novel therapeutic approaches to improve patient outcomes. Preclinical studies have demonstrated promising anticancer properties for allopurinol, a xanthine oxidase inhibitor used for taste. The Phase II clinical trial aims to assess allopurinol's safety and efficacy in prostate cancer patients.

Method & Materials

It involves 200 participants with localized prostate cancer under active surveillance who are randomized, double-blind and placebo-controlled. Each patient is randomly assigned to receive either allopurinol (300 mg/day) or a placebo for 12 months. By analyzing prostate-specific antigen (PSA) kinetics, magnetic resonance imaging (MRI), and biopsy results, the primary endpoint is to determine the rate at which the disease progresses. Biomarkers such as oxidative stress markers, inflammatory cytokines, and others may be used as secondary endpoints.

Results

Allopurinol appears to be well-tolerated in the trial, with no significant adverse reactions reported. According to preliminary data, the allopurinol group showed lower PSA velocities than the placebo group. Allopurinol administration was associated with the modulation of oxidative stress markers and with a potential anti-inflammatory effect as determined by biomarker analysis.

Conclusion

A Phase II clinical trial investigating allopurinol's potential as an adjunctive therapy for prostate cancer is currently in progress. Based on preliminary findings, the drug appears to have a favorable safety profile and early indications of efficacy. Allopurinol's role in treating prostate cancer will be better understood by further analysis of biomarker modulation and disease progression.

Brain metastasis: incidence, trend analysis, and impact on survival using SEER database (2010-2020)

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Introduction

Brain metastasis has a poor prognosis in cancer patients with high morbidity and mortality rates. An updated comprehensive analysis of patients with brain metastasis across all primary cancer sites is lacking. So, the study aims to provide the literature with updated evidence about recent trends and survival analysis of brain metastasis.

Method & Materials

Data of 75,797 patients with brain metastasis, diagnosed in 2010-2020, were extracted using the Surveillance, Epidemiology, and End Results (SEER) software. We used a rate session to calculate the incidence, percent change (PC), and annual percentage change (APC). Rates are per 100,000 and age-adjusted to the 2000 US Std population. Confidence intervals (CI) are 95% per rate with statistical significance at $P>0.05$. We used SPSS version 23 for data analysis and Kaplan Meier Curve and log-rank test for survival analysis.

Results

Brain metastasis represented 1.9% of all cancer cases with a mean age of 64.4 (Sd=11.2). The age-adjusted incidence rate of brain metastasis was 7.1 with a PC of -9.6 from 2010 to 2020 (APC= -0.60; 95% CI: -1.2-0.001, $P<0.05$). The APC was significantly declining in Caucasians (-0.70; $P>0.05$) and African Americans (-1.2; $P<0.05$) with a significant decrease in males (-1, $P<0.05$) while the Asian or Pacific islanders (API) race had PC of 11.7 and APC of 1.30 ($P<0.05$). Lung, breast, skin melanoma, and kidneys were the most common primary sites for brain metastasis (78.5%, 3.8%, 3.7%, and 3.2%). The 5-year relative survival of patients with brain metastasis was 6.1% compared to the non-metastatic group 71.5%. The 5-year age standardized relative survival was 5.7% for the metastatic group. The 5-year relative survival of brain metastasis was higher in the API race compared to Caucasians and African Americans (10.1%, 5.9%, and 5.3%).

Conclusion

The results of this study show a very poor survival outcome for brain metastasis. However, there was a significant decline in brain metastasis trends over the years, which highlights promising improvements in the early detection of primary cancers. Further stratifications showed disparities according to race and primary cancer site. These data may have clinical-directed variations in screening and counseling for subpopulations with cancer.

Characterization of C1q+ Macrophages in Pancreatic Ductal Adenocarcinoma

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Introduction

Pancreatic ductal adenocarcinoma (PDAC) is the most widespread subtype of pancreatic cancer with a five year survival rate of about 12%. Late diagnosis and therapeutic resistance make PDAC one of the most lethal cancers. The pancreatic tumor is difficult to target largely due to its heterogeneity and dense stromal makeup. Up to 90% of PDAC tumor mass can be attributed to non-cancerous cells consisting of macrophages, fibroblasts, and extracellular matrix components. Prior studies have hypothesized that the C1q+ subset of macrophages contribute to creating a pro-tumorigenic environment and suppress anti-tumor immune responses. However, a precise mechanism by which the C1q protein complex and the macrophage subset contribute to PDAC tumor progression is unknown. Here, we aim to characterize the prevalence of C1q+ macrophages and determine their functional role in PDAC tumorigenesis.

Method & Materials

We utilized orthotopic pancreas injections of KP (KrasLSL-G12D/+; Trp53fl/fl) cells to generate tumors in C57BL/6. Flow cytometry and immunohistochemical analysis will elucidate the distribution of C1q+ macrophages in PDAC when compared with control wildtype mice. Single-cell RNA sequencing data analysis will additionally reveal aspects of the mechanistic role of C1q+ macrophages in human PDAC.

Results

Single-cell RNA sequencing data analysis of Peng et al. 2019 revealed high expression of C1q genes including C1q A, C1q B, and C1q C in macrophages from PDAC patient samples. To further investigate the functional role of C1q+ macrophages, we generated C1q A knockout mouse embryonic stem cells (mESCs) using CRISPR-Cas9 mediated gene editing. Through blastocyst injections of the edited mESCs, we are developing a chimeric mouse to elucidate changes in tumorigenesis upon deletion of the C1q A gene. Initial immunohistological analysis of murine PDAC tumors demonstrates the prevalence of C1q, indicating the importance of C1q as a possible therapeutic target.

Conclusion

C1q+ macrophages have been implicated in pancreatic tumor development and correlate with poor prognosis for PDAC patients. Our data analysis demonstrated the prevalence of C1q in human PDAC samples, and our in vitro experiments reveal its importance as a potential prognostic marker. This research is pivotal to deeply understanding the therapeutic implications of C1q+ macrophages on pancreatic tumorigenesis.

An overview of phenotypic plasticity in pancreatic cancer stem cells

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Introduction

Pancreatic ductal adenocarcinoma (PDAC), the most common histologic subtype of pancreatic cancer (PC), exhibits high lethality with a 5-year survival rate of 2-8%, thoroughly due to late diagnosis, therapeutic resistance, high tumoral heterogeneity, and cancer stem cells. Phenotypic plasticity is the ability of cells to adopt different identities along a phenotypic spectrum. This event observed in embryonic differentiation, in terminally differentiated cells and in cancer cells, notably in cancer stem cells (CSCs), plays a crucial role in PDAC?s aggressive clinical features such as chemotherapy resistance and recurrence. To study phenotypic plasticity in PCSCs, we used a lentiviral reporter system based on GFP expression.

Method & Materials

Pancreatic adenocarcinoma ASPC-1 cells underwent lentiviral infection with the stem cell GFP-based reporter SORE6, designed to identify the activity of master transcription factors, OCT4 and SOX2. Post-infection, cells were sorted into GFP+ and GFP- subsets through fluorescence-activated cell sorting (FACS). These subsets were then seeded and cultured to assess differentiation and spheroid formation in a time series, with evaluations performed every 48 hours using an epifluorescence microscope and a 20x objective lens. Real-time polymerase chain reactions (qPCR) assessed phenotypic plasticity within each subset through the measurement of stem cells genetic markers expression.

Results

These preliminary experiments highlight two key features of CSCs: differentiation and self-renewal. Differentiation was measured by the decreasing GFP signal percentage, from the beginning of the experiment (T0) to the end (T240). Meanwhile, the GFP- subset demonstrated phenotypic plasticity by regenerating a small percentage of the GFP+ population by 96 hours post-sorting. Spheroid formation assay showed that GFP+ cells had a higher self-renewal ability of the CSCs, as per literature. Initial qPCR experiments also showed phenotypic plasticity in the GFP- subset with increased gene expression of CSC markers such as EpCAM, NANOG, and GATA6.

Conclusion

In conclusion, this study provides evidence of the role of PCSCs in determining tumor cell fate through asymmetric division, as well as in the formation of spheroids and possibly other cellular units. Insight into CSCs is vital for the future of Personalized Medicine because targeting these cells for eradication or localizing their biomarkers holds promise for therapeutic, diagnostic, and prognostic approaches.

Cisplatin is enhanced by Akkermansia muciniphila in Lewis lung cancer mice

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Introduction

Recently, there has been an increase in awareness that intestinal flora plays a crucial role in the development and occurrence of tumors, including Akkermansia muciniphila (Akk), which has been linked to cancer immunotherapy. However, it has not been established whether Akk will be effective in treating lung cancer. Therefore, this study aims to investigate the antitumor effects of cisplatin (CDDP) in combination with Akk on lung cancer as an antitumor treatment

Method & Materials

This study was conducted using the murine lung cancer model by subcutaneously inoculating the Lewis lung cancer model into 50 mice. The mice were divided into five groups based on their responses: normal, model, CDDP, CDDP+Akk, and CDDP+antibiotic. The administered group improved the changes in the pathomorphology of the tumor within 5 weeks after treatment, compared with the model group after treatment. Compared to the CDDP group, CDDP combined with Akk slowed down the growth of tumor volume, downregulated the levels of ki-67, p53, factor-associated suicide (Fas) ligand proteins, upregulated Fas proteins, and increased interferon, interleukin-6, and tumor necrosis factor levels, while suppressing CD4+CD25+Foxp3+ Treg in mouse peripheral blood and spleen.

Results

As a result of transcriptome analysis, Akk combined with CDDP increased levels of IFI272 and IGFBP7, which are related to cytokine-cytokine receptor interaction, Th17 cell differentiation, FOXO, JAK-STAT, and PI3K-Akt signaling pathways.

Conclusion

According to these findings, combined AKK and CDDP treatment improved immune regulation and could treat lung cancer.

Role of vitamin D in multiple myeloma: preclinical study of its antitumor and immunomodulatory effects

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Introduction

Multiple myeloma (MM) comprises 10% of all hematological malignancies. Monoclonal antibodies (mAbs), such as daratumumab, has become a promising treatment option for MM. mAbs have the potential to stimulate the immune system through mechanisms like antibody dependent cellular phagocytosis (ADCP) exerted by macrophages. Calcitriol, the active form of vitamin D, appears to be effective in preventing the malignant transformation and the progression of various types of human tumors. This research explores the direct impact of calcitriol on MM as well as its indirect immunomodulatory effect via ADCP mediated by daratumumab.

Method & Materials

Seven MM cell lines (MM.1S, NCI-H929, RPMI-8226, U266, JJN3, OPM2, and MOLP-8) were assessed for calcitriol sensitivity at different timepoints. Basal levels of the vitamin D receptor (VDR) were determined using Western Blot (WB) and qPCR analyses. WB was used to examine dose and time-dependent VDR expression upon presence of calcitriol. MM.1S, NCI-H929, and RPMI-8226 underwent MTT viability assays, cell cycle and apoptosis analysis through flow cytometry. Calcitriol's impact on immunotherapy was investigated through in vitro differentiation of healthy donor monocytes in its presence, followed by co-culturing resulting macrophages with MOLP-8 cells treated with daratumumab. ADCP was measured through flow cytometry, with individualized analysis accounting for donor variability.

Results

MM.1S, NCI-H929 and OPM2 showed the highest VDR expression in qPCR and WB. RPMI-8226 and NCI-H929, showed greater viability reduction following exposure to calcitriol (IC30: NCI-H929 = 0,002_M; RPMI-8226 = 0,087_M; and MM.1S = 0,238_M). Viability reduction was time and dose-dependent. All cell lines presented 10% apoptotic increase when exposed to calcitriol compared to the control . RPMI-8226 and NCI-H929 exhibited a slight rise in G0-G1 phases with a subsequent decrease in S and G2-M phases at 24 hours . VDR expression increased dose-dependently in RPMI-8226 after treatment. Daratumumab, as expected, increased macrophage phagocytic capacity over myeloma cells in donor samples. Calcitriol enhanced ADCP in 66% of donors.

Conclusion

This study provides evidence supporting the antitumor effects of calcitriol on various MM cell lines as well as its stimulatory ADCP capacity when combined with daratumumab. The findings suggest that vitamin D supplementation may yield positive anticancer effects in MM treatment, especially in conjunction with immunotherapy.

Exhausted T cells and M2 macrophages form progression-related spatial arrangements in tumors of patients with cancer-prone syndrome Fanconi Anemia

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Introduction

Fanconi anemia (FA) is a chromosome instability syndrome characterized by increased cancer predisposition, particularly to the development of aggressive squamous cell carcinomas (SCC) at a very early age. New methodological avenues in the study of cancer, like the implementation of spatial proteomics with single-cell resolution using formalin-fixed and paraffin-embedded samples (FFPEs) of solid tumors, are paving the way for exciting new therapeutic insights targeting the tumor/immune landscape.

Method & Materials

We performed single-cell spatial profiling of the tumor-immune microenvironment of FA tumors using highly multiplexed tissue cyclic immunofluorescence (t-CyCIF) in 11 SCC FFPE tumor samples from patients with FA. A certified pathologist annotated H&E slides of the specimens to identify the carcinogenic progression of the tumors in low-grade dysplasia, high-grade dysplasia, and invasive carcinoma. FFPE blocks were deparaffinized, dehydrated and rehydrated in citrate buffer. Slides underwent multiple staining cycles with a panel of >20 fluorochrome-tagged antibodies and were later imaged in each staining cycle with a Nikon Ni-E scanner. The resulting whole-slide multidimensional images were analyzed in the context of protein expression, cancer stage, immune microenvironment, and spatial tissue architecture using computational analyses based in artificial intelligence and machine learning (SCIMAP, Napari, StarDist, MCMICRO).

Results

We identified phenotypical heterogeneity among the annotated tumor regions, showing specific immune, tumor and stromal cell compositions. Cellular distribution showed unique spatial arrangements between cell types that correlated with carcinogenic progression, like an increased infiltration of T cells* at the invasive carcinoma compared with low- and high-grade dysplasia, as well as the formation of immune cell belts at tumor transition zones. Cellular neighborhood analysis, accounting for recurrent cell-to-cell interactions, showed that at the invasive carcinoma stage there is increased co-localization of exhausted T cells (TIM3+) with pro-tumoral M2 macrophages*, and loss of PD1 expression*, *($p<0.001$).

Conclusion

We found progression-related spatial arrangements of cells in the tumors, with a predominant cellular neighborhood composed of exhausted T cells and pro-tumoral M2 macrophages at the invasive carcinoma. Further identification of functional tumor-immune interactions among cell types could later be translated into potential actionable targets and biomarkers for immunotherapy and precision oncology for patients with rare cancer-prone syndromes.

Poster session I

PAEDIATRICS

Presenters:

- Ágnes Ábrahám
- Austeja Kairiukstyte
- Roya Kazemi
- Saskia Julie Kovács
- Tina Mehdipour Amjad
- Reza Mirzaei Ebrahimabadi
- Gillian Mwale

Changes in bone metabolism parameters and body composition in children with spinal muscular atrophy

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Introduction

Spinal muscular atrophy (SMA) is a progressive neuromuscular disease with autosomal recessive inheritance. Individuals with SMA typically have lower bone mineral content than those with other neuromuscular diseases, which increases the risk of developing pathological fractures. Since 2018, genetic-based disease-modifying treatments have been available in Hungary, and their efficacy in improving mobility performance has been demonstrated in a broad population. The objective of this study is to track changes in bone metabolism parameters, anthropometric data, and body composition data in SMA patients undergoing disease-modifying therapy.

Method & Materials

The study collected data from children with SMA who received nusinersen/risdiplam/onasemnogene abeparvovec therapy between 2018 and 2023. The following parameters were studied annually before and after treatment: osteodensitometry (ODM) scores, body measurements, mineral content measured by Inbody assay, muscle mass, BMI, vitamin D, and bone markers. The data were aggregated and statistically processed.

Results

During the study period, 57 patients diagnosed with SMA commenced treatment. Out of these, data from 39 patients (21 boys and 18 girls) were processed. The mean age at diagnosis was 4.1 (Ò4.68) years. The lumbar spine ODM Z-score value was -1.84 (Ò2.47) before treatment, -1.30 (Ò1.53) in the first year after treatment, -1.5 (Ò1.45) in the second year, -1.09 (Ò1.46) in the third year and -1.68 (Ò1.64) in the fourth year. The Z-score values remained unchanged during the treatment period compared to the initial value. The body mineral content, as measured by Inbody, increased by an average of 0.11 (Ò0.11) kg after one year of treatment, 0.15 (Ò0.22) kg in year two, 0.28 (Ò0.35) kg in year three, 0.5 (Ò0.44) kg in year four, and 0.55 (Ò0.47) kg in year five. Three children developed pathological bone fractures during the follow-up period.

Conclusion

In treated SMA patients, the absolute body mineral content increases. However, the bone mineral content measured by ODM relative to age is below average and remains unchanged by treatment. To ensure patients' quality of life is not affected by secondary abnormalities such as bone fractures, it is crucial to monitor bone metabolism parameters in addition to exercise capacity. Collecting data can help in developing therapeutic protocols.

Factors associated with hospitalization of febrile pediatric patients from PED

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Introduction

Various methods are being adapted to assess which patients require hospitalization from the pediatric emergency department (PED), especially in settings without the possibility of short observation. Therefore, clear pathways should exist in PEDs to avoid patient overload and unnecessary hospitalization. Our study aim: to analyze factors linked to the decision to hospitalize patients between 2019 June 29th and 2019 December 9th in the PED of Lithuanian University of Health Sciences Hospital Kauno Klinikos.

Method & Materials

Retrospective analysis from an electronic record data system was conducted including randomly selected data of children aged 0-5y. The following data were collected: demographics, triage category, physician's ?sense? (looks sick/doesn?t look sick); chief complaints, clinical findings; investigations, diagnosis, and treatment. Data were divided according to age (<1y/Ú1y), diagnosis (viral/bacterial), and physician?s ?sense? (looks sick/doesn?t look sick). Statistical analysis was done with SPSS 29.0; $p<0.05$ was considered significant.

Results

Data from 507 patients were collected; mean age-2.17y (1.03-3.16). Majority (55.2%) were male; 22.7%-younger than 1y. According to the physician, 66.3% of children looked sick. Older patients were considered sick (69.9%). ?Higher?(red/orange) triaged were assigned as sicker compared to those in the green/blue category (100% vs.60.6% respectively, p=0.001). 86 children were hospitalized. Hospitalization did not differ between age groups, triage category or time of referral. Initial evaluation ?looking sick?, as well as none of the complaints or clinical signs were associated with hospitalization. More children received CBC (89.5% for hospitalized vs.78.6% for discharged, p=0.02). CBC results nor CRP levels were linked to hospitalization, and neither did blood or urine cultures. Children who received chest X-rays were 2.3 times more likely to be hospitalized (OR 2.3, CI95% (1.2-4.3), p=0.014). X-ray result was not associated with the hospitalization rate.

Conclusion

We found that higher rates of hospitalization were not related to the triage category, patient?s age, time of referral, complaints, clinical signs, physician?s ?sense? or blood or urine cultures performed. Children who received CBC or Chest X-rays were admitted to the hospital more frequently. We suspect other factors, such as socioeconomic (lack of further safe-guarding, suspicion of not using antibiotics or other medicine), and parental (fair) to play significant roles in the decision to hospitalize.

Vitamin D Injections at Birth, Their Effect on Respiratory Problems in Newborns

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Introduction

Infants and mothers may suffer from vitamin D deficiencies, potentially affecting their lives. A study was conducted to investigate whether vitamin D supplementation affected the respiratory health of newborns.

Method & Materials

This double-blind clinical trial, conducted between 2020 and 2021, included 150 premature babies with a gestational age of less than 30 weeks who were admitted to the neonatal intensive care unit of Ghaim (AJ) Hospital in Mashhad, Iran. Infants were randomly divided into two groups, including infants receiving 10,000 units of vitamin D intramuscularly (intervention group) or not receiving vitamin D at birth (control group). The infants in the two groups were compared based on the need for oxygen therapy, nasal intermittent positive pressure ventilation (NIPPV), surfactant, and mechanical ventilation.

Results

The Mean Ò SD of birth weight was 1534.80 Ò 472.12 and 1622.950 Ò 505.0 (P= 0.691), the vitamin D level 25.26 Ò 11.58 and 25.47 Ò 11.14 (P= 0.892), Gestational age 30.27 Ò 2.72 and 30.22 Ò 2.45 (P= 0.614) for intervention and control groups, respectively. Ventilation needs were 42% in the control group and 24% in the intervention (P=0.02). The need for NIPPV was 95% in the control group and 93% in the intervention (P=0.500). The surfactant administration was 51% in the control group and 31% in the intervention (P=0.007).

Conclusion

Vitamin D intake at birth reduces non-invasive and mechanical ventilation and lessens surfactant administration. Premature infants with respiratory complications seem to benefit from it.

Constitutive activation of STING negatively affects T-cell development and function in murine SAVI

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Introduction

Gain-of-function mutations in the STING1 gene, which encodes the STING protein (stimulator of interferon genes protein), lead to its constitutive activation and the autoinflammatory paediatric disease SAVI (STING associated vasculopathy with onset in infancy). The chronic activation of STING provokes a massive production of inflammatory components through two main components: the IFN and the NF-_B pathways. SAVI leads to vascular inflammation in the skin and to inflammatory lung infiltrates. T-cell deficiency can be observed in SAVI patients as well as in established SAVI mouse models.

Method & Materials

We study SAVI using the STING knock-in (ki) mouse model (N153S/WT), which represents one of the most common human mutations in STING1 (p.N154S). To assess the effects on the IFN and the NF_B STING signalling pathways, we genetically developed two additional knock-out mouse models: Ifnar1-/- and Tnfr1-/-. All experiments were performed by comparing the same genotype (BL6, Ifnar1-/- or Tnfr1-/-) in STING ki and STING WT mice. To investigate T-cell function and development, we used FACS analysis, cell culture studies, ELISA and Western blot techniques, and histological methods.

Results

Phenotypic similarities of all STING ki genotypes are growth retardation and lymphopenia compared to the respective STING WT mice. We observed thymic atrophy, splenomegaly, and a massive loss of T-cells in spleen and blood. T-cells are restricted in their development and function. In the periphery we found mainly effector T-cells and rarely naive T-cells. Cell culture studies with splenocytes show a reduced IL-2 production in response to specific CD3/CD28 stimulation as well as to non-specific stimulation with Concanavalin A and PMA/Ionomycin.

Conclusion

Our group observed a relevant impact of the constitutive activation of STING on T-cell development and function in murine SAVI. As our mouse models showed phenotypic similarities to clinically described patients, we are confident that our investigations will lead to a better understanding of the pathophysiology of SAVI and will contribute to improved treatment options.

Genetic evaluation of patients suspected of immunodeficiency referred to the immunodeficiency clinic of Akbar Hospital in Mashhad, Iran

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Introduction

This study aimed to evaluate the genetics of patients suspected of immunodeficiency, without a definitive diagnosis, referred to Akbar Hospital's Immunodeficiency Clinic in 2020-2022.

Method & Materials

In this study, patients suspected of immunodeficiency, without a definitive diagnosis, referred to an immunodeficiency clinic were included. Expert specialists and clinical geneticists conducted a complete clinical and paraclinical examination. Blood samples were taken for genetic analysis using the Exome Sequencing technique and comprehensive bioinformatics analysis. Parents and healthy offspring were assessed for candidate gene variants.

Results

In this study, 185 patients were included; 51.35% were male. The average age of the participants was 9.43Ò4.40 years. Pneumonia, at 37.83%, was the most common clinical manifestation in patients with suspected immunodeficiency. In total, 44.86% of patients suffered from combined immunodeficiency. 18.91% had phagocyte number, function, or both defects and 24.32% had predominantly antibody deficiencies. Hyper IgE syndrome was detected in 16.21% of patients. In 36.75% of the identified genes, there was a discrepancy between clinical and genetic diagnosis in patients.

Conclusion

The most common clinical manifestation of primary immunodeficiency is pneumonia; therefore, patients suffering from recurrent respiratory infections should be checked for genetic immunodeficiency. Most patients in this study had multiple cell types of immunodeficiency, defects in phagocyte number, function, or both, and predominantly antibody deficiencies. The most common diseases diagnosed were: Hyper IgE syndrome, SCID and CGD, CVID, and LAD.

Investigating the Incidence of Thrombocytopenia and Associated Factors Among Inpatients at Akbar Hospital's Pediatric Intensive Care Unit in 2020

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China

Introduction

Several hematologic disorders lead to children being admitted to pediatric intensive care units (PICUs), but the most common one is thrombocytopenia. This study was conducted to evaluate the prevalence of thrombocytopenia and its related factors among the patients admitted to the PICU and the associated risk factors.

Method & Materials

260 patients were included in the cross-sectional study at the PICU of Akbar Hospital in Mashhad in 2020. A number of patients were excluded from the study due to their illness, including patients with malignancies, those who had undergone chemotherapy or radiotherapy in the previous month, and those receiving high blood volumes. A checklist containing demographic information, thrombocytopenic severity, bleeding, and other variables was completed for the participating patients during their hospitalization. A statistical analysis of the data was conducted using SPSS software.

Results

In total, 260 patients were included in the study (mean age was 51.03 months), of whom 142 (54.62%) were males and 118 (45.38%) were females. In total, 42.2% of patients suffered from thrombocytopenia of various severity levels. The results of the comparison showed that the severity of thrombocytopenia was significantly associated with bleeding ($p = 0.019$), coagulopathy ($p< 0.001$), and short-term outcomes (death or survival) ($p< 0.001$). There was, however, no significant association between the sex of patients and the presence of thrombocytopenia or between sepsis and thrombocytopenia ($p < 0.05$).

Conclusion

As a result of this study, more than 40% of patients admitted to PICUs experience thrombocytopenia. As a result of this study and other similar studies, it appears that thrombocytopenia significantly affects a patient's prognosis. Therefore, paying more attention to treating thrombocytopenia in these patients is important.

Effectiveness of a Locally-Made Eye Protector For Neonates Treated With Phototherapy at Queen Elizabeth Central Hospital (QECH), Malawi

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Malawi

Introduction

Uncorrected hyperbilirubinaemia in the newborn is known to progress to neurological sequelae, thus necessitating phototherapy treatment. Nonetheless, the high-frequency blue light in phototherapy can potentially cause retinal damage, prompting the routine use of eye protection for neonates undergoing this treatment. Various improvised materials are used at the Queen Elizabeth Central Hospital (QECH) to shield the jaundiced neonate?s eyes. However, it is unknown if these improvised methods are effective in their function. Furthermore, these improvised materials are not designed to act as eye shields for neonates, leading to neonatal discomfort and increased hospital waste. This study aims to develop a reusable eye protector and evaluate the effectiveness of the different eye protectors used for neonates undergoing phototherapy at QECH.

Method & Materials

The calculated sample size was 20 for each type of material. The materials used as improvised eye shields at QECH were collected and tested. A light metre was placed directly under each material to measure the amount of blue light radiating through it from distances of 35cm, 25cm, 15cm, and 10cm. A reusable cotton shield was developed with guidance from previous studies and tested similarly. Finally, the two groups of eye shields were compared using a gold standard: a commercially available eye shield.

Results

The lack of proper eye shields forced nurses at QECH to improvise with materials ranging from folded gauze and plaster to surgical masks. Surgical masks provided the least protection, with an average light radiance of 12.78 uW/cm2/nm at the longest distance. The amount of light blocked from gauze and plaster shields relied on the amount of gauze used, which, in turn, depended on the amount of resources available in the ward. The thickest shield had a light radiance of 2.0 uW/cm2/nm with an overall average of 5.96 uW/cm2/nm. On the other hand, the reusable cotton shield blocked all light at all distances, as did the gold standard eye shield.

Conclusion

In low-resource settings such as QECH, where formal eye shields are not available for phototherapy-treated neonates, the reusable cotton eye shield could be a comparable replacement as opposed to current improvised materials.

Poster session I

PHARMACOLOGY

Presenters:

- Eldar Bakhshaliyev
- Raha Kaviani
- Aleksandra Opęchowska
- Maryam Safaei
- Farida Aghayarli
- Sara Shokooh Saremi

Changes on sex hormones in the blood of white rats against the background of chronic clozapine intake

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Introduction

According to WHO, one in four people worldwide suffers from psychological and neurological disorders at some point in their lives. There is little and conflicting information about the changes in the concentration of sex hormones in men and women who suffer from mental illness and take antipsychotic drugs, and on the other hand, how these drugs will affect the fetus during pregnancy. Considering what I mentioned above in this research we studied effects of clozapine on changes in the amount of sex hormones in experimental white rats.

Method & Materials

The research was conducted on 30 white rats of both gender weighing 170-190 g. The rats were divided into 6 groups, 3 males and 3 females. First groups of both gender were control groups and nothing was done to them. The other two groups of both gender were injected with different doses of clozapine (10 mg/kg, 20 mg/kg) intraperitonally and chronically. Then, the concentration of sex hormones were measured in the blood taken from tail vein. We used Wilcoxon-Mann-Whitney test and Student?s t-test to quantify the experimental data.

Results

The concentrations of TTST, FRTST, FSH, LH, P, E3, E2 hormones in the blood of male rats injected with clozapine(10mg/kg) were significantly decreased. The hormone TTST decreased by 6.4%, the hormone FRTST decreased by 5%, and FSH decreased by 31.1%. This decrease was also observed in concentrations of LH, P, E3, E2 hormones. According to percentage indicators, the change was like this: -44,5%; -45,5%; -65,8%; and -96,3%. All the sex hormones decreased except for PRL (+14,2%). The concentrations of TTST, FRTST, FSH, LH, P, E3, E2 hormones in the blood of female rats injected with clozapine(10mg/kg) changed like this compared the control group: -14,3%; -14%; -22,2%; -62,8%; +11,3%; -42,2%; -40,5%; -28,2%. Injection of 20mg/kg dose of clozapine deepened same effects.

Conclusion

Chronic intake of antipsychotic drugs caused not only a decrease in the concentration of LH, but also a decrease in the concentration of all sex hormones except PRL.

Chiral resolution of ofloxacin via diastereomeric cocrystal formation with L-glutamic acid

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Iran
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Introduction

Resolution of chiral pharmaceuticals into their enantiopure form is an objective for the pharmaceutical industry due to their superior therapeutic efficacy. Ofloxacin (OFX) is a prominent fluoroquinolone antibiotic, and the S-enantiomer (levofloxacin) has a pharmacological activity 8-128 times that of the R-enantiomer. This research aims to discover novel cocrystals of ofloxacin with various amino acids as coformers that can be used in a chiral resolution process.

Method & Materials

The solvent evaporation method was used to screen OFX cocrystal formation with four amino acids (L-glutamic acid, L-glutamine, L-proline, and L-serine) from a 1:1 stoichiometric ratio of RS-OFX and coformers. DSC, FTIR, and PXRD data indicated the best coformer. The recrystallization of diastereomeric cocrystals from supersaturated solutions was tested in water, methanol, chloroform, ethyl acetate, acetone, and their different fractions. For chiral resolution, the most suitable solvent mixture was chosen using capillary electrophoresis (CE) analysis of the samples.

Results

Cocrystal screening tests of RS-OFX with four coformers revealed that only a diastereomeric cocrystal pair was formed when using L-Glutamic acid as coformer, as evidenced by new peaks in PXRD and FTIR spectra, as well as differences in DSC data between starting materials and products. The novel solid-state molecule was a diastereomeric cocrystal composed of S-OFX.L-Glutamic acid and R-OFX.L-Glutamic acid. Based on the CE analysis results, a methanol/chloroform (1:1/v:v) combination was selected for recrystallization of the diastereomeric cocrystals due to the maximum differences in solubility between the diastereomeric cocrystal pairs. Following two steps of recrystallization of the cocrystal in the mentioned solvent combination, the CE analysis of the final sample revealed an enantiomeric excess (ee) of 61.8% for the S-Ofloxacin cocrystal.

Conclusion

We report the chiral separation of racemic OFX by cocrystal formation with L-Glutamic acid. The resultant diastereomeric cocrystal was separated with 61.8% ee, yielding 80.9% levofloxacin using a simple, cost-effective crystal engineering process that might be regarded as an alternate option for chiral resolution, since it would only need one reaction pathway.

Assessment of Lipid Peroxidation Product Variations in Various Brain structures of Male White Rats Following Prolonged Haloperidol Administration

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Introduction

Haloperidol is one of the most commonly used drugs for treatment-resistant mental illnesses in modern times. Long-term use of haloperidol by patients leads to the development of serious disorders at the brain level. Although some scientists attribute this to the pro-oxidant effect of haloperidol, some scientists deny this. The association between haloperidol and lipid peroxidation (LPO) remains controversial. We studied how long-term haloperidol intake affects the amount of LPO (lipid peroxidation) products in brain structures.

Method & Materials

Our study involved 15 white rats, categorized into control and two haloperidol-treated groups receiving doses of 0.5 mg/kg and 3 mg/kg respectively. Following chronic haloperidol administration, brain structures were examined for LPO products using established methodologies.

Results

As a result of our study, it was found that haloperidol at a dose of 0,5; 3 mg/kg changed the amount of in LPO products different structures of the brain (hypothalamus, frontal cortex, striatum). At 0.5 mg/kg, LPO products increased by 28.5%, 23.1%, and 32.1% respectively, compared to control group. At 3 mg/kg, the increase was more pronounced (1.4–2.5 times). Similar trends were observed in the frontal cortex and striatum

Conclusion

Our findings suggest that haloperidol-induced LPO may stem from enhanced calcium influx and dopamine metabolism, ultimately leading to heightened free radical generation. This underscores the potential contribution of oxidative stress to haloperidol-associated brain pathology. Further research is needed to explore therapeutic interventions targeting oxidative stress in haloperidol-treated patients

Evaluation of metformin potential as anti-cancer drug against non-small cell lung cancer (NSCLC) in vitro model

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Introduction

Biguanide family drug metformin is a first-line anti-hyperglycaemic therapy for type 2 diabetes patients. Besides its main metabolic effect, novel immunomodulatory properties are being revealed in many research areas, especially in cancer-related studies. Non-small cell lung cancer (NSCLC) is an aggressive tumor with mostly unsuccessful treatment outcomes due to high resistance levels to classical chemotherapy or radiation. Therefore, it is of great importance to investigate new potential options for the treatment improvement. Recently, some studies presented increased overall survival in lung cancer patients for whom metformin was implemented as part of the therapy. Here, we verified the properties of metformin testing in vitro its effects on non-small cell lung cancer cell lines.

Method & Materials

NSCLC cell lines - A549 and H2030 were cultured with metformin at increasing concentrations for 24, 48, and 72 hours. Subsequently, the proliferation and viability of cancer cells were evaluated using flow cytometry. Cancer cells- structure (TEER analysis) and secretion of inflammatory cytokine assessment (ELISA) were also performed. We additionally analysed the immunomodulatory properties of metformin. Viability and proliferation rate were also determined within healthy immune cells, together with their activation status.

Results

Metformin caused a significant reduction in the proliferation rate of both studied NSCLC cell lines. Moreover, the observed effect was related to the applied drug concentration. It seemed that pro-apoptotic effects accompanied the decreased proliferation rate, with increased values of late-apoptotic and necrotic cells. Although both assessed cell lines responded to the applied treatment, metformin was most effective towards A549 cells. Metformin was found to modulate immune cells? function slightly, especially those of innate immunity. Additionally, we observed a reduction in the level of lymphocyte activation and then reduced their proliferation. Nevertheless, those effects were considerably lower compared to cancer cells.

Conclusion

Metformin was discovered to have anti-cancer properties in the NSCLC in vitro model. That effect could also be supported by the immunomodulatory effects of that drug in immune cells. Further research is required to establish specific molecular mechanisms responsible for the observed results of metformin action on cancer and immune cells.

Treatment Efficacy of Insulin, Rosiglitazone, Liraglutide, and Pioglitazone in Mild to Moderate Alzheimers: Systematic Review and Meta-Analysis

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Introduction

Alzheimer's disease is the global leading cause of disability and the most complex form of dementia. Despite scientific advancements, effective therapies to halt disease progression are still lacking. Hence, researching on disease-modifying therapies is a priority.

Method & Materials

The systematic literature search identified 19 studies comprising 3599 patients Central Register of Controlled Trials from inception to 10 Jan 2024 fulfilled the eligibility criteria. A literature search was performed using the electronic databases including PubMed, clinicaltrial.gov, Google Scholar, and Scopus. Eligible studies were randomized controlled trials excluded Phase I, II studies and observational studies. The pooled incidence, risk ratio (RR), and 95% confidence interval (CI) of Alzheimer?s disease (AD) and cognitive improvement, were calculated using the random-effect model. We utilized the random-effect model rather than the fixed-effect model using a Comprehensive Meta-Analysis program software 3.3 version and PRISMA 2020 for the systematic review. The quality of studies was evaluated using the Cochrane Risk of Bias 2.0 tool.

Results

In the study of 19 eligible RCTs (pooled N =3599) where patients treated with insulin (N= 535), Rosiglitazone (N= 1173), Liraglutide (N=296) and Pioglitazone (N=1595) compared to placebo, for a minimum duration of 6 months. Accordingly, patients treated with Liraglutide were more likely to show reduction in amyloid deposition and neuroinflammation, improves brain glucose metabolism and cognitive outcomes, and increases the proliferation of neuronal progenitor cells. On the other hand, no significant clinical effect was shown with insulin (both intranasally and regular), Rosiglitazone and Pioglitazone. Among studies with healthy individuals and other patient populations, no significant effects were found.

Conclusion

Liraglutide, the novel GLP-1 analogue has shown promising neuroprotective effect in slowing the advancement of Alzheimer?s Disease and improve cognitive ability in AD patients.

Developing a high loaded liposomal formulation of lapatinib with enhanced therapeutic effects on breast cancer cells

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Iran

Introduction

lapatinib is a tyrosine kinase inhibitor possessing lipophilic molecular structure. It inhibits both EGFR and her2 receptors and can serve as a suitable candidate to treat her2 positive cancers such as breast cancer. The low water solubility can restrict the clinical effect of the drug due to poor and incomplete absorption from the gastrointestinal tract. Patients should administer high doses and therefore severe side effects appear. By incorporating such small molecules in drug delivery systems, therapeutic effects can be enhanced and adverse effects can be diminished. Liposomes are versatile lipid bilayers which can surround various drug molecules and enhance their effects. In this study, by using remote loading method, high loaded liposomal lapatinib was developed and its therapeutic effects on her2 positive breast cell line was evaluated.

Method & Materials

First, empty liposomes consisting of HSPC, DPPG, mPEG and cholesterol were formed and the drug was loaded into inner aquatic phase by means of remote loading method. After purification steps, the final liposomal formulations were evaluated and liposome size, charge, poly dispersity index and encapsulation efficacy were recorded. The formulation cytotoxicity on TUBO cell line was tested by means of MTT assay. Therapeutic effects was assessed through monitoring the tumor size and body weight of mice inoculated with TUBO tumors.

Results

The final liposomal formulation was negatively charged and its particle size was about 128 nm. The poly dispersity index was 0.142, which confirms the homogeneity and 90% of the total drug was loaded into liposomes. According to the MTT test results, the formulation was able to inhibit TUBO cell growth successfully. Tumor growth study indicated that the liposomal formulation was able to hinder the tumor growth, especially in comparison to oral lapatinib.

Conclusion

Liposomal formulation of lapatinib is able to inhibit tumor growth and have shown promising effects on disease regression.

Poster session I

PSYCHIATRY

Presenters:

- Abdulelah Alkadi
- Mohammad Ayoob Ione
- Parnia Kamyab
- Abdulrahman Krayim
- Laura Valentina Orozco Betancourt
- Deeksha Sharma

Factors Associated with the Prevalence of Depression and Anxiety among Parents of Children with Neurodevelopmental Disorders in Saudi Arabia

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Introduction

Neurodevelopmental disorders (NDDs) are a group of conditions that include attention-deficit/hyperactivity disorders, autism spectrum disorder, and other disorders. Raising a child who suffers from an NDD can be challenging for parents, as it might affect their relationships, social lives and require a different set of parenting skills compared with raising a typically developed child. Therefore, the study aimed to to measure the prevalence rates of depression and anxiety among parents of children with different NDDs, compare the rates between mothers and fathers, and measure the relevant associated factors.

Method & Materials

This study was a cross-sectional, questionnaire-based study. The participants were 416 parents of children with NDDs in Saudi Arabia. The sample size was determined using the Richard Geiger equation with a 5% margin of error and a 95% confidence level. The screening was performed using a validated Arabic version of the Patient Health Questionnaire-9 (PHQ-9) and Generalized Anxiety Disorder-7 (GAD-7). Data were collected, reviewed, and then entered into SPSS ver. 21 (IBM); the Pearson chi-square test for significance and the exact probability test for small frequency distributions were used.

Results

In total,416 parents of children with NDDs participated in the study with a mean age of 29.2 Ò 13.9 years. We demonstrated that 85.1% of parents of children with NDDs had depression and 85.8% had anxiety. Mothers and fathers had similar rates of depression (83.5% vs 89.1%) and anxiety (85.2% vs 87.4%). No significant difference was found between the type of NDD and rates of depression and anxiety. We discovered that chronic illnesses, (P=0.028), having more than one child with an NDD (P=0.03), and the child's age at diagnosis(P=0.009) affect the severity of depression and anxiety.

Conclusion

We found that parents of children with NDDs had significantly higher degrees of depression and anxiety. Moreover, we discovered that several factors, such as having chronic illnesses, more than one child with an NDD, and children diagnosed at the age of 6?10, contribute to the severity of depression and anxiety. To ensure that appropriate interventions are included for parents, healthcare professionals should measure parental mental health and seek an early diagnosis of mental illness.

Association Between Big Five Personality Traits and Hypertension in Saudi Patients: A Case Control Study

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Introduction

Hypertension is a well-known risk factor for cardiovascular disease, and it has been considered as a global disease burden and public health concern.The association between personality traits and hypertension is complex and has so far not been studied in depth.The present study aims to explore the connection between the Big Five personality traits and hypertension.

Method & Materials

This case control study includes 310 participants, and the relationship between personality traits and hypertension was investigated in normotensive and hypertensive patients by the Big Five Inventory-10. We examined the association of each of the Big Five personality traits in hypertensive patients and a control group using binary logistic regression analysis.

Results

The findings of the study revealed that amongst the Big Five personality factors, low conscientiousness (OR: 1.09, 95% CI: 0.92?1.29, P<0.005) and high neuroticism (OR: 0.54, 95% CI: 0.45?0.66, P<0.001) were related with high risk of hypertension. Male, older people, and physically inactive individuals have been found to be at a higher risk of hypertension. No significant relationship was found between hypertension and marital status, education, or smoking habits.

Conclusion

These results suggested that a low score in conscientiousness trait and a high neuroticism score may be an additional risk factor of hypertension. Thus, it may be worthy to investigate further in order to identify patients at risk and develop a more individual treatment strategy. Cognitive behavioral therapy and pharmacological options can be used preemptively in high-risk patients.

Investigating the Prevalence of Irritable Bowel Syndrome and its Associated Demographic Factors among Patients with Obsessive-Compulsive Disorder

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Introduction

The co-occurrence of gastrointestinal diseases with mood disorders and anxiety has been extensively documented. Specifically, individuals with irritable bowel syndrome (IBS) often experience heightened levels of anxiety and depression compared to the general population. Numerous studies have highlighted the association between IBS and anxiety disorders. However, the extent to which this correlation extends to Obsessive-Compulsive Disorder (OCD) remains unclear, despite anxiety being a prominent symptom of OCD. To fill this gap, the present study aims to ascertain the prevalence of IBS in a diverse group of OCD patients and explore its relationship with sociodemographic characteristics.

Method & Materials

The patients with OCD, based on the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5), were recruited from three main psychiatric centers in Shiraz, Iran and randomly included in this cross-sectional study. Alongside comprehensive psychiatric evaluations, participants provided self-reported demographic data and severity ratings of their gastrointestinal symptoms. The diagnosis of IBS was made based on the Rome IV criteria. Chi-square and Independent t tests were used to analyze the obtained data in SPSS software version 27, and a P value <_0.05 was considered statistically significant.

Results

A total of 226 OCD patients were enrolled in this study, and among them, 55 individuals (24.3%) met the criteria for IBS (known as OCD-IBS). Within the IBS-OCD group, the most prevalent symptom was a change in stool form, observed in 96.4% of patients, followed by relief of abdominal pain after defecation (89.1%). A comparison of OCD patients based on IBS status revealed higher education levels ($p = 0.005$) among those with IBS. Furthermore, more than half of the OCD-non-IBS participants were single (51.4%), representing a larger proportion compared to singles in the OCD-IBS population (38.1%) ($p = 0.014$). Regarding age, however, no significant difference was found between the two groups.

Conclusion

The high prevalence of IBS and the severity of gastrointestinal symptoms in OCD patients should be a key consideration in clinical treatment, particularly when exploring pharmacotherapeutic options for them. Also, demographic differences between OCD patients with and without IBS suggest multifactorial presentations of IBS in the presence of OCD, warranting further investigation in future research.

Efficacy of Cognitive Behavioral Therapy for Anxiety and Depression in Parkinson's Disease: A Systematic Review and Meta-analysis

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Introduction

Parkinson's disease (PD) patients often suffer from non-motor symptoms like depression and anxiety, which significantly impact their quality of life. With the limitations of pharmacological treatments, there is a growing need for effective non-pharmacological interventions. This systematic review and meta-analysis aimed to evaluate cognitive-behavioral therapy's (CBT) efficacy in mitigating depression and anxiety symptoms in PD patients.

Method & Materials

We included Randomized controlled trials (RCTs) exploring CBT's effectiveness for depression and anxiety, published until April 2023, were identified from databases of PubMed, Web of Science, and Scopus. Methodological quality was assessed using the Risk of Bias-2 (ROB-2) tool. Independent data collection was performed by two reviewers using the Rayyan.io platform. Statistical analysis involved calculating effect sizes and the corresponding 95% confidence intervals (CIs) using Review Manager 5.4.1._

Results

This systematic review encompassed 12 studies that involved a total of 241 patients with Parkinson's disease (PD). CBT resulted in a substantial reduction in anxiety (SMD -0.95, 95% CI [-1.15 to -0.74], P<0.00001) and depression (SMD -1.02, 95% CI [-1.39 to -0.65], P<0.0001). The findings showed that cognitive behavioral therapy administered over the phone (tele-CBT) as well as regular CBT were beneficial for treating depression and anxiety. Traditional CBT (SMD_-1.16, 95% CI [-1.83 to -0.49], P < 0.00001) and Tele-CBT (SMD_-0.90, 95% CI [-1.31 to -0.48], P<0.00001) Both Traditional CBT (SMD_-0.94, 95% CI [-1.25 to -0.63], P<0.00001) and tele-CBT (SMD_-0.95, 95% CI [-1.22 to _ -0.67], P<0.00001) significantly reduced anxiety.

Conclusion

The results of this systematic review and meta-analysis demonstrated the efficacy of CBT in reducing depression and anxiety among individuals diagnosed with PD. Healthcare providers are encouraged to integrate CBT into their daily treatment protocols for PD patients. However, it is important to note that additional studies of superior quality and longer-term follow-up assessments are still needed to enhance our understanding of this topic further. _

Cannabis Use During Pregnancy: Comparative Analysis of Sociodemographic and Mental Health Outcomes in Users vs. Non-Users

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Introduction

Cannabis is a commonly used psychoactive during pregnancy, and its reported use is increasing in legalized countries. The safety of cannabis for offspring neurodevelopment and gestation in humans remains undetermined, with literature indicating potential risks. In addition, there has been evidence of underreporting of consumption possibly associated with stigmatization. Therefore, an observational study was conducted to compare the sociodemographic and mood profile of non-cannabis consumers vs. consumers before, during and after pregnancy. We also characterized maternal substance use in the consumer group.

Method & Materials

The database from the ongoing study "Prenatal cannabis: A fetal neuroimaging study of neurodevelopment" in Quebec, Canada was utilized. Information for the analyses was collected via self-report questionnaires covering sociodemographics, monthly drug use, the Patient Health Questionnaire-9 (PHQ-9) and the Generalized Anxiety Disorder-7 (GAD-7). Results are presented using descriptive statistics such as means, medians and standard deviations. Some inferential analyses were conducted using z-tests, reporting p-values and confidence intervals.

Results

Out of the 68 total participants included in this analysis (44 consumers and 24 non-consumers): Consumers were less likely to have planned pregnancies than non-consumers (p=0.028, 95% CI: 0.094 - 0.61). Fewer consumers completed higher education than non-consumers (20.5% vs 54.2%, p=0.01, 95% CI: 0.07 - 0.60). More consumers earned under $50,000/year than non-consumers (72.5% vs 41.7%, p=0.029, 95% CI: 0.03 - 0.57). Consumers had shorter relationship lengths than non-consumers prior to pregnancy (medians 4 vs 6 years). Fewer consumers owned homes than non-consumers (27.3% vs 75%). More consumers drank alcohol (20.5% vs 4.2%) and smoked (13.6% vs 4.2%) during pregnancy than non-consumers. Consumers had higher PHQ-9 and GAD-7 scores than non-consumers, indicating more severe depression and anxiety symptoms.

Conclusion

Female cannabis consumers had more unplanned pregnancies, less education, unstable housing, shorter relationships, lower income, more drinking/smoking during pregnancy, and worse mental health than non-consumers. Although sample size is a limitation, these initial results identify a high-risk profile to inform public health measures and education about potential consumption risks.

Effect of antidepressants on neurodegeneration and neuroplasticity in patients with depression: A comparison between SSRI and SNRI

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Introduction

Depression, a widely prevalent mental health disorder (57 million people) in India is inadequately addressed and commonly associated with neurodegeneration (10-90% of the time). This prospective observational study aims to compare the effect of SSRI and SNRI monotherapy on neurodegeneration, neuroplasticity and social cognition-related changes.

Method & Materials

Treatment naãve patients of unipolar depression were evaluated for depression treatment response [using Hamilton Depression Rating Scale (HDRS)] and neurodegeneration related parameters at enrolment and 6 weeks after antidepressants treatment. Neurodegenerative serum biomarkers [indoleamine-2,3-dioxygenase (IDO), neurofilament light chain protein (NLCP), brain derived neurotrophic factor (BDNF)] were assessed using ELISA. Social cognition was assessed using Social Cognition Rating tools in Indian setting (SOCRATIS). Neuroplasticity was assessed by resting state MRI.

Results

A total of 150 patients of unipolar depression were enrolled, out of these n=126 patients were prescribed SSRI and 24 patients were prescribed SNRI. Both SSRI and SNRI group have significant reduction in HDRS score at 6-week compared to baseline (both $p<0.001$), but no intergroup difference. Overall treatment responder rate (HDRS score reduction >50%) was 11.33%, but SSRI group has more responder (12.69%) compared to SNRI (4.16%). After 6 weeks of follow-up, serum IDO in SSRI group and NLCP levels in both groups were significantly decreased when compared to baseline ($p<0.001$) and BDNF levels were significantly increased in SSRI group when compared to baseline ($p<0.01$). As per SOCRATIS, after 6 weeks treatment, SSRI and SNRI didn?t show any significant difference. However, compared to baseline, there is improvement in different domains of SOCRATIS as follows: first order theory of mind (FOT) index in SSRI group ($p<0.001$), second order theory of mind (SOT) index and Faux Pas Composite Index (FPCI) in both SSRI and SNRI ($p<0.001$, for both), personalizing bias in SNRI ($p<0.05$), externalizing bias in both SSRI and SNRI groups ($p<0.001$, $p<0.05$ respectively), and Social Perception Index (SPI)-concrete and abstract in SSRI group ($p<0.05$, for both). Depression patients revealed significant decrease in cortical thickness of inferiortemporal, parsopercularis and precuneus regions of brain ($p<0.05$) in comparison with healthy controls. But there was no significant difference/increase in cortical thickness after 6 weeks of follow-up when compared to baseline

Conclusion

After 6 weeks of antidepressant treatment, HDRS score was less in both SSRI and SNRI groups. However, significant improvement in social cognition, reduced neurodegeneration related biomarkers (IDO, NLCP) and increase BDNF level were found in SSRI vs SNRI group.

Poster session I

PUBLIC HEALTH

Presenters:

- Vansh
- Zeeshan Ali
- Abdulelah Alshebly
- Shubhangi Arohee
- Shaza Babikir
- Samson Ojedokun
- Aparna Parashar

Assessing ChatGPT's Comparability to 1st year MBBS Students of India in Medical Physiology Examination Knowledge and Interpretative Ability.

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Introduction

ChatGPT is a chatbot that uses natural language processing and large language models (LLMs) to simulate human communication. Since its founding, it has had a tremendous influence on the world scene overall, but particularly in areas like banking and finance, e-commerce, education, law, human resources (HR), and hiring. The smooth integration of ChatGPT with the healthcare system has been the subject of numerous ongoing debates due to a number of issues, including factual correctness, lack of experience, lack of clarity, lack of knowledge, and, most importantly, lack of empathy. Our study aims to compare the medical physiology knowledge and interpretive skills of ChatGPT with those of first-year medical students in India.

Method & Materials

In the this study, during second term examination of first year medical students, a total of 65 questions covering medical human physiology were assigned (40 multiple-choice questions and 25 subjective short answer questions). Chat GPT started the class as the 121st student. The queries were input into the ChatGPT interface, and the answers were recorded. Additionally, the time taken to answer the multiple-choice questions (MCQs) was recorded. Two subject teacher reviewed the answers provided by ChatGPT and the 120 MBBS students in the class of Kalpana Chawla Government Medical College, Karnal Haryana, and grades were assigned based on the caliber of the responses. The grades that the AI chatbot and the pupils received were compared.

Results

ChatGPT fared better than practically every other student in the class, finishing sixth overall with a score of 154 out of 200. It fared poorly on descriptive clinical scenario-based questions (48%) but excellently on answering multiple-choice questions (95%) and descriptive logical reasoning (78%). Logical reasoning multiple-choice questions (MCQs) required a substantially longer time to answer than basic information-based MCQs (4.10Ò0.882 sec vs. 2.02Ò0.477 sec, $p<0.005$).

Conclusion

In the field of human physiology, ChatGPT was able to perform better than nearly majority of first-year students. These large language models offer a great deal of promise for successfully utilizing modern medicine teaching and learning techniques for students, provided that ethical difficulties are resolved.

Comprehensive Quality Improvement Training for Doctors and Nurses: A Catalyst for Reducing Medical Errors in a Tertiary Care Hospital

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Pakistan

Introduction

This study objective was to evaluate the medical errors i.e., documentation errors, medication errors, discharge summary errors, readmission rates and noncompliance of surgical safety checklist in a tertiary care hospital and to find out significance of quality improvement training of doctors and nurses on prevention and reduction of these errors.

Method & Materials

It is a retrospective and prospective observational study in a tertiary care hospital. The retrospective patients medical record was reviewed as pre training assessment for the month of January to March 2021. The Prospective data was reviewed as post training assessment for the month of April 2021 to June 2021. Three quality improvement training sessions on clinical documentations and prevention of medical errors were conducted after the pre training assessment. A total of 700 medical records were reviewed 350 during pre-training assessment and 350 after the training of doctors ands nurses.

Results

Five categories of medical record were reviewed: medical documentation errors, discharge summary errors, medication errors, noncompliance of WHO safety checklist and readmission rates. 66 out of 68 KPIs of clinical documentation showed a statistically significant improvement in clinical documentation after the quality improvement training. There was significant improvement in medical documentation errors and medication errors, after the training the p-value was less than 0.0001 in all the key performance indicators (KPI) of medical documentation and medication errors. Readmission rates among medicine patients were decreased from 14.7% to 9.1% and 15.9% to 5.5% in surgery patients. A significant improvement in discharge summary errors was also seen after the training except for the KPI follow-up instruction which was non-significant after training with p-value 0.0955. The compliance of WHO safety checklist was also significantly improved in all KPI?s with p-value less than 0.001 except for antibiotic prophylaxis information which was non-significant with p-value 0.230.

Conclusion

The study demonstrated that medical errors can be prevented with comprehensive and continuous quality improvement team trainings of doctors and nurses.

Elderly awareness on healthy lifestyle during aging in Al-Ahsa -population, Saudi Arabia: a cross-sectional study

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Introduction

The research explores healthy aging among elderly individuals globally and in Saudi Arabia. _Factors like health services, lifestyle, and chronic diseases affecting seniors are examined. _However, there?s a gap in culturally relevant research, particularly in Arabic-speaking countries. _This study aims to understand elderly individuals? knowledge, attitude, and practice regarding _healthy lifestyles for effective functional preservation in aging._ Specific lifestyle recommendations could be made to certain older persons at risk of functional _decline. The goal of extending healthy years of life will be helped enormously by this research._

Method & Materials

A cross-sectional study was conducted in Alhasa of Saudi Arabia, _from February to May 2023. People from Alhasa who were 60 years old or older were eligible to participate. People from _cities other than Alhasa and those under the age of __60__ were excluded. _The Raosoft calculator was employed to determine the sample size. The data was analyzed using SPSS._

Results

Regarding the associations between knowledge levels and demographics. Education significantly _impacts knowledge (p=0.003). Retired respondents exhibit higher knowledge (50.4%) compared _to those with jobs (10.4%) (p=0.002). Smoking has a significant impact on knowledge __(p=0.012). Regarding the opinions on elderly care, respondents agree on the importance of fresh _fruits and vegetables (52.2%), increased protein intake (64.3%), less fat (83.5%), and regular _exercise (44.3%). Supplements? necessity is disagreed upon (95.7%). Living with family is _favored (67.8%), and elderly self-management is recognized (60.9%). Significant differences are _seen in fruit and vegetable consumption (p=0.001), less fat usage (p=0.000), exercise habits __(p=0.000), smoking (p=0.000), and using just salt in cooking (p=0.000)._

Conclusion

Study findings underscore the importance of education in influencing healthy behaviors and _informed choices, with education levels significantly impacting knowledge levels. Respondents? _preferences for balanced diets, exercise, and self-management reflect a positive trend towards _embracing healthy aging principles. Notably, the study identifies disparities between knowledge _groups in various lifestyle factors, highlighting the potential of education to drive positive _changes in behaviors._

Male Partner Involvement In Birth Preparedness, Complication Readiness And Obstetric Emergencies In Central Rural India

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Co-authors: Dhatrak A. (Amey), Shyam Sundar R. (R Naveen)

Introduction

Worldwide, 2.8 million pregnant women and newborns die each year from preventable causes of delivery problems. This can be prevented by making a birth plan that constitutes birth preparedness and complication readiness (BPCR) for pregnant women and their family. AIMS/ OBJECTIVES- The study aims- 1.To assess the male involvement in birth preparedness and complication readiness during antenatal and postnatal period. 2. Accessibility to health-care services in rural populations. 3. Knowledge of the Husband regarding danger signs in Pregnancy.

Method & Materials

A cross sectional study conducted in two settings; a rural tertiary care hospital in India and few field practice villages on the basis of random sampling after IEC approval. The study constituted 350 husbands with expecting wives (last trimester) or men with a child under 20 weeks of age to avoid recall bias; they were interviewed on the basis of a structured questionnaire after taking an informed consent (95% confidence interval, 10% precision, 80% power and design effect as 1). Data was collected from the husbands accompanying their wives to the Obstetrics OPD and by visiting their houses in villages. Collection was done using Kobotoolbox and analysis using Excel and Epi info; later scored accordingly between 0-10 (scale adapted from a study from Bangladesh).

Results

Out of 350 males, it was observed that only 28% were well involved in BPCR whereas 56% were moderately involved and the rest showed poor involvement. Involvement was directly proportional to the socio-demographic status, family type, distance from the nearest health-care centre and knowledge about danger signs. Data showed that more than 50% of the rural population lived within 5km radius of the hospital; rest had to travel long distances hence had saved more money for emergencies. Knowledge about danger signs was poor with only 35% subjects knowing atleast one danger sign attributing the poor interaction between ASHA worker and husbands in relation to RMNCH+A topics.

Conclusion

Male involvement in birth preparation is poor rural areas. ASHA/ healthcare staff should educate men about BPCR components. The study can help increase awareness, develop better policies, and train healthcare staff to be more sensitive towards male participation.

Malaria Treatment-seeking Behavior, Awareness and Preventive practices among People Living in a Rural Area in Gezira State, Sudan, 2022

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Introduction

Malaria poses a significant health threat globally, with Sudan accounting for a substantial proportion of cases and deaths in the Eastern Mediterranean Region. Sudan malaria strategic plan 2021-2025 aims to reduce morbidity and mortality by 30%. To achieve this population at risk should be aware of malaria and its prevention. Assessment of their attitude towards malaria prevention is key for program implementation. The aim of this study is to investigate malaria prevention and treatment seeking behavior among Om Shanig rural residents.

Method & Materials

This descriptive cross-sectional study was conducted in Omshanig village, Gezira state, Sudan. A probability-clustered sampling technique was used to select 289 households. Data were collected using a modified interviewer-administered questionnaire on malaria knowledge, treatment-seeking behavior, and preventive practices. Statistical analysis was performed using SPSS version 24.

Results

A total of 289 household heads were interviewed indicating a response rate of 89.8%. Eighty-five percent of them reported having malaria among the members of the household within the past 12 months. Fever was the most reported symptom (87.0%). Eleven percent of household heads denied knowledge of any method to prevent malaria and 10.4% didn?t use any preventive method. 65.7% of household have mosquito nets for all the members of household. Among them 40.9% don?t use them mainly due to laziness (21.8%) or considering it unimportant (19.8%). Lack of use of preventive measures was weakly correlated with malaria cases ($r = 0.128$, $p = 0.02$).

Conclusion

In spite of decades of malaria control programs, it remains a prevalent issue in Om Shanig rural area. The use of preventing methods is not universal in the society. Even among those who have mosquito nets more than third are not using them. Qualitative studies to further investigate the issue are needed.

Perceptions of Medical professionals on Artificial Intelligence in optimizing Healthcare Sector in Nigeria

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Introduction

The deployment of artificial intelligence (AI) in the healthcare sector in Nigeria is in an evolving state. Its use in the medical industry promises many benefits to all, however, its adoption in medical practice is primarily in developed countries. The rollout of AI in Nigeria depends on the level of acceptability of medical/health professionals, public opinion, and government readiness to integrate the technology. This study aimed to assess the awareness, level of perception, and opinion on AI among medical professionals

Method & Materials

The study was a cross-sectional design conducted among medical professionals (medical students, medical interns, medical officers, Residents, and consultants) across various geopolitical zones using an online Google survey form prepared from a validated questionnaire adapted from a previous study. It comprises 3 sections, Section 1: the consent page and biodata, section 2: 15 questions on perceptions on AI, and Section 3: assesses the opinions on AI using a three-point Likert scale assessment tool consisting of 7 variables. Data entry, coding, and analysis were done using Statistical Package for Social Sciences (SPSS) Version 25

Results

A total of two hundred and fourteen responses were received with a male-to-female ratio of 1.35:1, and the majority were medical students and interns between the 18?30year age group. Almost all respondents are aware of AI however only 11.2% had some theoretical training on AI. The most common combined sources of AI awareness were the internet source 87.4% and social media platforms 86.9%. Overall, 160(75%) medical professionals have good perceptions and opinions on AI. There is a significant correlation between the medical cadre and opinion. Practitioners in the lower cadre have better opinions on AI compared to their seniors and those working in private hospitals have better opinions compared to state and government hospital workers ($p < 0.05$)

Conclusion

The advent of AI is welcoming among medical professionals of their good level of awareness, perception, and opinion which implies their readiness to accept or adopt the technological change in the medical sphere. More effort is required from the government to vest resources in this direction to actualize this to upgrade the healthcare sector to international standards

Wellness unveiled: examining synergy of self-care, motivation and self efficacy among hypertensive rural elderly

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Introduction

India needs preparedness to address the challenges of demographic and epidemiological transition, with 21% of the older population affected by chronic illnesses. Elderly hypertensive individuals need lifestyle adjustments alongside therapeutics for better management of hypertension. Self-care embodies the actions that people take to live a healthy lifestyle, care for chronic illnesses, and prevent further illness. Lack of motivation to modify behaviour has been recognized as one of the obstacles to self-care. Individuals with higher perceived self-efficacy can encourage themselves to engage in self-care activity on a regular basis and overcome difficulties that impede them from doing so.

Method & Materials

A cross sectional study was conducted in the nearby villages of a tertiary care medical college hospital of central India, including 123 individuals above the age of 60 years with hypertension. Their self care behaviour(SCB), motivation and self efficacy(SE) was analysed using the hypertension self care profile questionnaire(HBP-SCP); medication adherence was analysed using the Morisky medication adherence scale (MMAS-8). Data was analysed in jamovi using Pearson?s correlation and multiple linear regression.

Results

The HBP-SCP scale revealed mean scores of 0.55Ò0.08, 0.63Ò0.14, and 0.66Ò0.12 for SCB, Motivation , and SE, respectively. The mean MMAS-8 score was 0.63Ò0.19. Furthermore, SCB score demonstrated a positive correlation with Motivation score (r=0.542) and SE score (r=0.649), while Motivation and SE scores exhibited a positive correlation as well (r=0.622).

Conclusion

The escalating prevalence of hypertension in India demands a paradigm shift with a greater emphasis on cultivating self care behaviours. The observed levels of SCB scores among study participants indicate their capacity to sustain and enhance their well-being. Noteworthy is the finding that individuals with hypertension who had higher SCB scores also demonstrated elevated scores for Motivation and SE. As we progress, it becomes imperative to explore and implement effective strategies ensuring sustained motivation and fostering self-efficacy beliefs among individuals with hypertension, thereby aiding in the improvement of their self care behaviours. Furthermore, these findings may extend to the prevention of hypertension and other lifestyle disorders at the community level.

Poster session II

ENDOCRINOLOGY

Presenters:

- Saeed Al Beshi
- Seyyed Mohammad Reza Azimi
- Reza Heidari
- Mahsa Heidari Foroozan
- Nadyatul Husna
- Erik Lopez-Gallardo
- Julia Wykrota
- Yuxian Zheng

ISCOMS 2024 SCIENCE BEYOND BORDERS

Exploring the Relationship Between Vitamin D Deficiency and Osteoporosis in Geriatric Patients With Chronic Kidney Disease

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Introduction

Vitamin D deficiency presents a significant public health concern, particularly among the geriatric population. This deficiency is exacerbated by age-related factors impacting vitamin D production and metabolism, including reduced sun exposure, limited dietary intake, and decreased skin capacity for vitamin D synthesis.

Method & Materials

A cross-sectional study design was employed to efficiently collect data on vitamin D levels, bone mineral density, and fracture history in geriatric patients with chronic kidney disease (CKD). Participants with diagnosed CKD were recruited from healthcare facilities. Data encompassed demographic information, medical history, laboratory results, vitamin D levels, bone mineral density measurements, and fracture history. The analysis involved correlation analysis to explore the relationship between vitamin D levels and bone mineral density, regression analysis to evaluate the impact of vitamin D deficiency on fracture risk, and chi-square tests to assess the association between vitamin D deficiency and fractures. Ethical considerations were upheld, with approval from the research ethics committee and informed consent from participants.

Results

In our study, a substantial 67.3% of geriatric patients with CKD were diagnosed with vitamin D deficiency. Osteoporosis was found in 30.2% of participants, and fractures following low-impact injuries were reported by 79.9% of those with vitamin D deficiency. These findings underscore the critical role of vitamin D in maintaining bone health and preventing fractures.

Conclusion

Vitamin D deficiency appears to be highly prevalent among geriatric CKD patients and is significantly associated with poorer bone health outcomes, like lower bone mineral density and increased fracture risk. Routine screening and management of vitamin D levels may help mitigate bone-related complications in this high-risk group. Further research is warranted to establish causality and inform targeted interventions.

Mitigating gestational diabetes risk: A clinical trial of omega-3 supplementation in high diabetes risk pregnancy

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Iran

Introduction

Gestational diabetes mellitus (GDM) is a common pregnancy complication that poses risks to both mother and child. This study aimed to investigate the effects of omega-3 supplements on the emergence of GDM in high-risk pregnant patients.

Method & Materials

A randomized double-blind clinical trial was conducted, involving 50 pregnant mothers with high-risk criteria for diabetes. They were divided into two groups: a drug group receiving omega-3 supplements and a placebo group. Various clinical and biochemical parameters were measured before and after a 6-week intervention.

Results

The placebo group showed significant increases in serum low-density lipoprotein (LDL) levels ($P = 0.02$) and the homeostatic model assessment of insulin resistance (HOMA-IR) index ($P = 0.008$). Conversely, the drug group demonstrated a statistically significant increase in high-density lipoprotein (HDL) levels ($P = 0.007$). However, no statistically significant differences were observed in the development of GDM between the two groups ($P = 0.25$).

Conclusion

This study suggests that omega-3 supplements may positively influence specific metabolic parameters, such as serum LDL levels and the HOMA-IR index, in high-risk pregnant patients in terms of diabetes. However, no significant differences were observed in the development of gestational diabetes mellitus between the two groups. Further randomized controlled trials with larger sample sizes are recommended for more conclusive results.

Mitigating Hemoglobin Glycation in Diabetic Conditions: Investigating the Therapeutic Potential of Aspirin through Comprehensive Analysis and Mechanistic Insights

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Introduction

Various complications can result from diabetes, a widespread medical condition characterized by hyperglycemia and increased protein glycation. In this study, the impact of aspirin on human hemoglobin during the process of glycation in diabetic conditions is investigated in more detail.

Method & Materials

In order to conduct a comprehensive analysis, hemoglobin extracted from the blood of non-diabetic individuals was incubated for a period of five weeks. A variety of conditions were manipulated during this incubation, including the presence and absence of glucose and aspirin. As part of the assessment of heme glycation, the hem degradation products were examined, band-shifting analysis was performed, and the appearance of febrile states was monitored. A rigorous statistical analysis, including a One-Way Analysis of Variance and Tukey's test, was performed in order to discern any discernible patterns or trends.

Results

A reduction of 50% in glycation levels was observed in the presence of aspirin. Further, band-shift sorting and assessment of febrile states were employed to reveal a significant reduction in protein glycation when aspirin was introduced into the experimental conditions. According to these findings, aspirin may have a potential role in reducing the adverse effects of glycation on hemoglobin. An examination of the mechanistic mechanisms by which aspirin exerts its influence on hemoglobin exposed to glucose is prompted by the observed reduction in glycation levels. It is likely that aspirin's effect is mediated by the acetylation of amine groups within proteins, highlighting a possible avenue for further research and understanding.

Conclusion

The study confirms that aspirin is effective in diminishing the extent of glycation when hemoglobin is exposed to glucose. A compelling area for future research is the intricate interaction between aspirin and protein glycation. Developing targeted therapeutic interventions for individuals suffering from diabetes-related complications may be possible with the use of this technique.

Investigating the causal relationship between type 2 diabetes and grave's disease: a bidirectional mendelian randomization study

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Introduction

Numerous observational studies have suggested a potential association between Graves? disease (GD) and the vulnerability to Type 2 diabetes (T2D). This study aimed to investigate the potential causal connection between GD and T2D using bidirectional Mendelian randomization (MR) analysis.

Method & Materials

MR analysis utilized summary-level data from genome-wide association studies (GWAS) for GD and T2D. GD-related single-nucleotide polymorphisms (SNPs) were extracted from 458,620 Europeans, and T2D summary-level data came from the DIAGRAM consortium.

Results

Initial analysis showed no significant causal relationship (OR = 1.019, 95% CI 0.997-1.042, P = 0.373), but after sensitivity analyses and SNP removal, a significant causal relationship emerged (ORIVW = 1.017, 95% CI 1.002-1.033, P = 0.03).

Conclusion

The study reveals a causal link between GD and an elevated risk of T2D, emphasizing the importance of monitoring blood sugar and providing specialized care for GD patients. Further research into GD-T2D mechanisms is crucial for preventive strategies and interventions

Central Obesity Risk Factors and their Association with Cardiovascular Diseases among Adults in Indonesia

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Introduction

Central obesity is emerging as a major contributor to the worsening of non-communicable diseases. Various risk factors contribute to the development of central obesity, further exacerbating the overall impact on health. The research aims to analyze risk factors for central obesity and their correlation with cardiovascular diseases among Indonesian adults men.

Method & Materials

This cross-sectional study utilized secondary data from household questionnaires in a nationwide longitudinal study, specifically drawing from 4953 male participants in the RAND Indonesian Family Life Survey 5 (IFLS 5) who met predefined inclusion and exclusion criteria. Collected data encompassed sociodemographic characteristics, lifestyle risk factors, smoking status, the Brickman Index for smoking grade, physical activity, BMI, hypertension, diabetes, and waist circumference. Bivariate logistic regression analysis identified candidate variables at $p < 0.25$, and subsequent multiple logistic regression analysis estimated odds ratios with a 95% confidence interval to discern factors associated with central obesity.

Results

The analysis revealed associations between age, education, smoking status, smoking grade, BMI, physical activity, economic status, hypertension, stress physiology status, diabetes, fast food consumption, meal patterns, dyslipidemia, and the incidence of central obesity ($p<0.001$). Associated factors of central obesity were age [AOR = 1.6, 95% CI (1.40, 1,96)], BMI (obesity) [AOR = 37.2, 95% CI: (30.1, 45.3)], physical activity [AOR = 0.084, 95% CI: (0.74, 0.94)], hypertension [AOR = 0.48, 95% CI: (0.32, 0.72)], and dylipidemia [AOR = 0.76, 95% CI: (0.63, 0.91)].

Conclusion

Central obesity demonstrated a strong association with an increased incidence of risk factors related to cardiovascular diseases. This study underscores the importance of incorporating the central obesity index into clinical assessments. Moreover, it recommends educational interventions to manage risk factors associated with central obesity, with potential implications for the prevention and control of cardiovascular diseases.

Insulin regulates MUL1 expression in cultured skeletal and cardiac muscle cells

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Introduction

Insulin regulates mitochondrial dynamics and function by Akt, generating an elongated mitochondrial phenotype and stimulating mitochondrial oxidative metabolism. ˇMUL1, a mitochondrial E3 ligase, ubiquitinates Akt and Mfn2, targeting proteasomal degradation. MUL1 also increases Drp1-induced mitochondrial fragmentation and decreases insulin-induced mitochondrial metabolism. Furthermore, MUL1 expression significantly increases under insulin resistance conditions. Thus, MUL1 can potentially regulate insulin sensitivity. However, the role of MUL1 on the insulin signaling pathway is poorly explored. We aimed to evaluate the effect of insulin on MUL1 expression in cultured skeletal and cardiac cells. We aimed to evaluate the effect of insulin on MUL1 expression in cultured skeletal and cardiac cells.

Method & Materials

We investigated the effect of insulin (10 nM) on MUL1 expression at mRNA and protein levels by RT-qPCR and Western bot, respectively, in cultured rat L6 myoblasts at different times. Also, we determined the MUL1 protein level in cultured mouse C2C12 myoblasts and neonatal rat cardiomyocytes (NVRM) under insulin stimulation. Then, to evaluate the effect of insulin on MUL1 activity, we quantified the Drp1 and Mfn2 protein levels in cultured skeletal and cardiac muscle cells.

Results

The results showed that the MUL1 expression level did not change in L6 myoblasts under insulin stimulation until 4 hours post-stimulation, but increases Mfn2 and Drp1 protein level. Also, no changes in MUL1 protein level were observed in cardiomyocytes under insulin stimulation. But, MUL1 protein level decreased in C2C12 myoblasts 4 hours post-stimulation with insulin. However, we observed that insulin did not alter the Drp1 and Mfn2 protein expression in C2C12 and NVRM cells

Conclusion

Our findings suggest that insulin could regulate the MUL1 expression or activity in cultured skeletal cells, but no in cardiomyocytes. Also, insulin could induce mitochondrial fusion and oxidative metabolism by MUL1-dependent NF-_B activation, which increases the Opa1 expression, and maintains the Drp1 and Mfn2 protein levels unaltered. Thus, MUL1 could be a novel component of the insulin signaling pathway in skeletal and cardiac muscle, but further studies are required to test this hypothesis.

T1Drink study - alcohol-related glycemic variability in people with type 1 diabetes supported by continuous glucose monitoring technology

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Introduction

People with type 1 diabetes (T1D) are affected by their disease in almost every aspect of their lives. Insulin treatment and strict monitoring are crucial for ensuring proper diabetes management. One of the factors, that can hinder it is alcohol consumption. As advice to refrain from alcohol is rarely heeded, data on its effects and improvement in patients? education are needed.

Method & Materials

Anonymous online questionnaires from 216 participants regarding alcohol consumption in young adults with T1D (16-35 years old) were obtained. 58 episodes of alcohol consumption (from 36 participants) together with a reference non-drinking day (the day before alcohol consumption) for each episode were retrieved from Continuous Glucose Monitoring (CGM) in the csv. format and analysed using Glyculator 3.0 and Statistica 13.3. The study was international (12 languages) and answers were received from 23 countries. Study design available at https://t1drink.umed.pl/en.

Results

137 (63.4%) respondents were female, 78 (36.1%) male and 1 (0.5%) did not want to specify their gender. Their age ranged from 16 to 26 years. 207 (95.8%) had time of duration of diabetes >1 year. The main method of glycemic control was CGM, used by 88.9% (192) participants. Method of insulin therapy varied ? 99 (45.8%) were on insulin pump therapy, 78 (36.1%) on multiple daily injections, 39 (18.1%) were using hybrid closed-loop insulin delivery systems. 20 (9.3%) experienced hypoglycemia and 31 (14.4%) ketoacidosis related to alcohol consumption. 48,15% (N=104) described effect of alcohol consumption on their blood glucose as unpredictable and 35.2% (N=76) did not feel safe in terms of diabetes management while consuming alcohol. Days on which alcohol was consumed did not differ significantly from the preceding ones in terms of mean sensor glucose (165.21Ò49.35 vs 161.27 Ò 49.35, p=0.5798), glucose variability (coefficient of variation 34.5Ò20.5% vs 34.1Ò16.0%, p=0.8897) or time spent in target range 70-180mg/dl (65.0Ò23.7% vs 66.2Ò22.5%, p=0.5869) or hypoglycemia (<70mg/dl: 2.8Ò4.7% 3.3Ò5.4%, p=0,5394).

Conclusion

Alcohol consumption can have various issues on glucose variability and safety of people with type 1 diabetes and almost half of participants consider it unpredictable. CGM data did not reveal a clear tendency to hyper- or hyperglycemia, necessitating more individualized and short-term analyses.

Identification of different groups among diabetic patients with distinct comorbidity patterns: a retrospective study

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Introduction

With the rising prevalence of diabetes, it is imperative to understand the patterns of co-morbidities in diabetic patients to facilitate prevention and treatment. This study aimed to investigate the comorbidity profiles of diabetic patients using public datasets.

Method & Materials

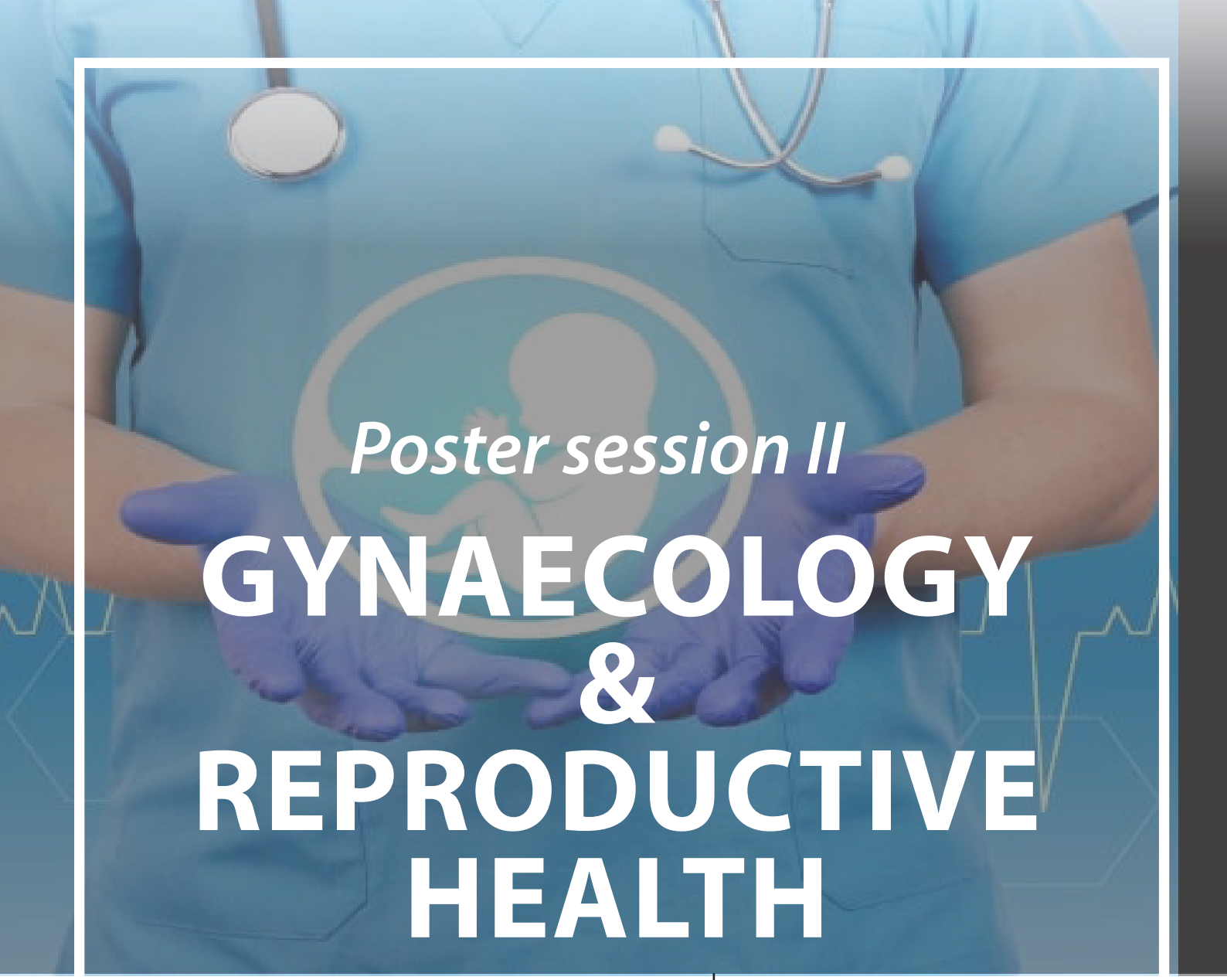
Diabetes Complications Data Set (DCDS), a thematic dataset of diabetic patients in China, were retrieved and K-Means clustering, and consensus analysis were deployed to identify patterns of comorbidities and categorize patients into distinct groups. Random forest models were deployed for each comorbidity and the importance along with contribution of variables were determined. Decision tree to classify patients with intuitive nodal information was constructed and applied for diabetic population in the National Health and Nutrition Examination Survey (NHANES), and thus the comorbidity patterns between groups were assessed.

Results

2321 cases with 58 variables in DCDS were recruited. Through clustering, two heterogenous patient groups were identified, and three distinct comorbidity patterns, crudely microvascular diseases, macrovascular diseases, and other diseases were revealed. Patients in Group 2 were slightly younger, more hypertensive. but less overweight and showed a higher prevalence rate in Comorbidity Cluster 1 compared to Group 1, while the trend was reverse for Comorbidity Cluster 2 and a non-uniform pattern was observed in Comorbidity Cluster 3. Through random forest models, the intergroup distinction was further disclosed by the discrepancy about the rank and contributory trend of variables for different comorbidities between groups. The decision tree for group assignment demonstrated the impacts of SCR, ALB, HCT, IBILI and BU. Similar comorbidity patterns were uncovered in the NHANES dataset (n= 2643).

Conclusion

Through clustering and characterizing, we observed variances of comorbidity susceptibility in different diabetic subgroups. Such discrepancy might indicate different pathophysiological processes and this robust clustering algorithm might provide framework for patient stratification and personalized management of diabetic patients.



Poster session II

GYNAECOLOGY & REPRODUCTIVE HEALTH

Presenters:

- Joni Koerts
- Diba Haghian
- Ekram Shoa Jemal
- Jamileh Sadat Mirsanei
- Hamidreza Mosleh

The impact of corpus luteum number on adverse pregnancy outcomes: The Rotterdam Periconception Cohort

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Introduction

Pregnancies conceived through assisted reproductive technology (ART) techniques are associated with increased risk of adverse obstetric and perinatal outcomes. Recent studies suggest differences in pregnancy outcomes among the various ART treatment protocols. This could be explained by the artificially induced perinatal hormonal environment, physiologically regulated by the corpus luteum (CL). ART protocols affect the quantity of CL at conception, resulting in CL absence or a supraphysiological number of CL. The aim of this study is to investigate the association between ART-induced alterations in CL physiology, by using CL number around conception, and maternal and neonatal pregnancy outcomes.

Method & Materials

The Rotterdam Periconceptional Cohort is an ongoing tertiary center prospective cohort study at the Erasmus Medical Centre, Rotterdam. Patients were grouped by number of CL, based on mode of conception: 0 CL (artificial cycle frozen embryo transfer (AC-FET), n=72); 1 CL (natural cycle frozen embryo transfer (NC-FET) and spontaneous conceptions, n=1414); and >1 CL (ovarian stimulated fresh embryo transfer, n=462). Hypertensive disorders of pregnancy, gestational diabetes, gestational age at birth and birth weight were derived from medical records.

Results

From all pregnancies included in the Rotterdam Periconceptional Cohort between 2010 and 2022, 1948 pregnancies were included in this study. The results were adjusted for maternal age, maternal body mass index, nulliparity and obstetric history. In pregnancies with >1 CL, preeclampsia rates were significantly lower compared to the physiological situation of 1 CL (aOR 0.37 [95% CI 0.18; 0.74]). CL absence (0 CL) was associated with higher rates of preeclampsia, albeit non-significantly (aOR 2.08 [95% CI 0.93; 4.62]), as well as higher rates of gestational diabetes (aOR 2.56 [95% CI 1.30; 5.06]). In males, >1 CL was associated with a lower birthweight percentile (aβ -6.40 [95% CI -11.26; -1.54]). In contrast, females showed no effect of >1 CL, whereas CL absence was associated with a higher birthweight percentile (aβ 12.82 [95% CI 2.41; 23.23]).

Conclusion

Rates of hypertensive pregnancy disorders, gestational diabetes and birthweight percentiles differ between CL groups. Both CL absence and the presence of multiple CL might have a profound impact on maternal and neonatal health.

Prediction of preeclampsia using support vector machine data mining approach

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Introduction

Pre-eclampsia is diagnosed as blood pressure of at least 140/90 mmHg in two separate stages at least 4 hours apart, along with proteinuria of at least 30 grams in urine collected within 24 hours. So far, no suitable clinical screening test has been known to diagnose this disorder, so in this study, we tried to present a model based on the data mining approach of Support Vector Machine (SVM) as a screening tool.

Method & Materials

The data used to conduct this case-control study were extracted from the records of 726 mothers with preeclampsia and 726 mothers without preeclampsia who visited Fatemieh Hospital in Hamedan during 2018-2023. After collecting information, approximately 70% of the total sample (1016 people) was used for training and the remaining 30% (436 people) was used for model testing. SVM was fitted on the training data and its performance was evaluated using the criteria of accuracy, sensitivity and specificity on the test set. The data were processed in the R3.2.2 software environment.

Results

The average age for people with preeclampsia (7.91Ò35.41) was higher than people without preeclampsia (6.72Ò34.53), but this difference was not statistically significant (p=0.22). The age distribution of the mothers was not the same in the two groups, and most people are diagnosed with this disease at an older age (40-39 years). Most of the mothers in the preeclampsia group had blood type O (63.4%). Meanwhile, in the group without preeclampsia, most people had blood type A (58.7%). 68.7% of mothers with preeclampsia had a male baby, but this percentage was 58.9% for mothers without the disorder, which is a statistically significant difference (p=0.001). The highest frequency of preeclampsia was observed in March and the lowest in July, and there was a significant relationship between hot and cold months with the occurrence of preeclampsia (p=0.001). For the SVM method, accuracy 0.891, sensitivity 0.86 and specificity 0.87 were obtained.

Conclusion

Based on the results of this study, it can be concluded that SVM has performed well in predicting preeclampsia. Therefore, this model can be considered as a screening tool to diagnose this disorder.

Enhancing cervical cancer screening for dutch women over 60: evaluating the need for regular screening at age 65

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Introduction

Cervical cancer is the 4th most common cause of cancer in women worldwide. Early detection by screening and early treatment of precancerous lesions named Cervical Intraepithelial Neoplasia (CIN) will prevent most cancer cases and deaths. Recent studies in the Netherlands indicate an increase in overall incidence, with a notable increase among women aged 60 and above. In the Netherlands, women are offered regular screening until the age of 60, with recent changes in 2017, as women at age 65 are also invited if they tested positive for HPV at 60 and were not referred for cytology. This study assessed which women would benefit from regular screening at the age of 65. To do this, we analyzed the association between the last screening round participation around age 60 and diagnosis of cervical (pre) cancer in women above age 60 years, where we adjusted for several confounders.

Method & Materials

Cervical cancer is the 4th most common cause of cancer in women worldwide. Early detection by screening and early treatment of precancerous lesions named Cervical Intraepithelial Neoplasia (CIN) will prevent most cancer cases and deaths. Recent studies in the Netherlands indicate an increase in overall incidence, with a notable increase among women aged 60 and above. In the Netherlands, women are offered regular screening until the age of 60, with recent changes in 2017, as women at age 65 are also invited if they tested positive for HPV at 60 and were not referred for cytology. This study assessed which women would benefit from regular screening at the age of 65. In order to do this, we analyzed the association between the last screening round participation around age 60 and diagnosis of cervical (pre) cancer in women above age 60 years, where we adjusted for several confounders.

Results

Between 2006 and 2021, we identified 91 women diagnosed with CIN2+ and 273 matched controls after applying inclusion and exclusion criteria. The median age of cases and controls at the time of inclusion to Lifelines was 62.0(48-86). The median age of diagnosis was 68 (60-89). There were significant differences in the last screening attendance around age 60 between cases and controls. While 57.9% of controls attended, a higher proportion (75.8%) of cases had participated in the last screening around that age.

Conclusion

The analysis will be finished in March 2024.

Mesenchymal stem cells and Extracellular vesicles, a major revolution in the treatment of male infertility

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Introduction

Infertility is a global reproductive disorder that has caused disappointment among young couples. Almost half of this is due to the male factor. In recent years, studies on stem cell-based therapies in the treatment of numerous diseases have been the focus of attention. Due to their ability to self-renew, differentiate, and produce a variety of paracrine factors including extracellular vesicles (EVs), mesenchymal stem cells have been introduced as a promising replacement approach for the treatment of several diseases, including infertility. Extracellular vesicles (EVs) contain biological molecules such as proteins, lipids, and nucleic acids. EVs are secreted in various physiological and pathological processes. The review aims to not only raise readers' awareness of this fascinating but little-known topic but also to provide them with a deeper understanding of the latest stem cell-based therapy options.

Method & Materials

This search was done in PubMed, Scopus, Google scholar, and Science Direct databases using keywords infertility, therapy, male infertility, and mesenchymal stem cell(MSCs), extracellular vesicles (EVs).

Results

The results of studies confirmed the successful regenerative effect of stem cell therapy in male infertility disorders such as azoospermia, oligospermia, erectile dysfunction and varicocele. In addition, it has been reported that factors secreted by MSCs including EVs can induce the process of spermatogenesis in infertile animal models. The important point is that despite significant advances in the use of MSCs and their secretion factors, no clinical trial has been completed to treat infertile men.

Conclusion

The successful treatment of mesenchymal stem cells and their secretion factors can lead to a revolution in the field of infertility and increasing population rates. This reduces negative physical, psychological, social, and economic consequences for the individual, family, and society.

The effect of alginate-chitosan scaffold containing graphene-oxide nanocomposite on neonatal spermatogonia stem cell differentiation

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Introduction

Boys who survived childhood cancer are at risk of azoospermia, a condition characterized by the absence of sperm in the semen. To address this issue, the isolation and purification of spermatogonial stem cells (SSCs) are crucial. Creating scaffolds that mimic the natural environment for these cells is essential for promoting their differentiation. A study aimed to assess the effectiveness of nanocomposite scaffolds made of alginate, chitosan, and graphene oxide (GO) in aiding SSCs differentiation.

Method & Materials

The scaffolds were tested for cytotoxicity using an MTT assay, and the sample containing 30 Êg/mL of GO (ALGCS/GO30) showed the most promising results. Flow cytometry confirmed the identity of the cells using C-Kit and GFR_1 markers. Various analyses, including FTIR, XRD, and SEM, were conducted to evaluate the scaffolds' properties. The differentiation of SSCs was assessed using qRT-PCR

Results

The results demonstrated that the ALGCS/GO30 nanocomposite scaffold was biocompatible, supported cell attachment, and promoted SSC differentiation. The scaffold showed a significant increase in differentiation markers compared to the control group. Immunocytochemistry confirmed higher levels of Sycp3 and Tekt1 protein expression in the nanocomposite scaffolds compared to those without GO.

Conclusion

In conclusion, the biocompatible ALGCS/GO30 scaffold shows promise for promoting SSC differentiation in in vitro applications.

Poster session II

IMMUNOLOGY

Presenters:

- Abdulrahman El Edreiss
- Felipe Galvez-Jiron
- LinKang Hsu
- Zahra Mansourabadi
- Katharina Menzel
- Mariana Peláez Muñoz
- Mohammadreza Rajabi
- Roberto Souza

Quantitative assessment of inflammatory markers (IL-6 & Ferritin) and transferrin in hospitalized patients with pneumonia

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Introduction

Pneumonia, a global health threat, necessitates precise assessment of systemic inflammation in hospitalized patients through specific markers like IL-6 and ferritin. The study aims to illuminate the intricate interplay of these markers, particularly IL-6, a proinflammatory cytokine, and ferritin, an iron storage indicator, in understanding pneumonia's inflammatory response. By quantitatively evaluating IL-6, ferritin, and transferrin, the research anticipates refining diagnostics, monitoring disease progression, and improving therapeutic interventions in pneumonia management

Method & Materials

cross-sectional study investigates the inflammatory markers interleukin-6 (IL-6), ferritin, and transferrin in 118 hospitalized pneumonia patients. Samples were analyzed for IL-6, ferritin, transferrin, iron, unsaturated iron-binding capacity (UIBC), and total iron-binding capacity (TIBC). Diverse blood parameters, including transferrin, TIBC, UIBC, iron, and IL-6, were assessed during hospitalization using the Mindray CL900i and analyzed with the ERBA 200XL instrument. Exclusion criteria ensured a focused study on pneumonia patients, excluding those with anemia, acute myocardial infarction, diabetes mellitus with acute complications, acute pancreatitis, and chronic kidney disease. Sample size calculations determined a required sample size of 66. Following data collection, and analyses were performed using the (SPSS) (version 28)

Results

Results reveal a nuanced gender distribution (52.5% males, _47.5% females), emphasizing age-specific considerations, particularly in the 2-12 years age group. IL-6, ferritin, transferrin, iron, UIBC, and TIBC levels exhibit considerable variability with age-specific patterns. Correlation analyses illuminate significant relationships among these markers, highlighting IL-6 and ferritin as pivotal indicators of inflammation crucial for gauging the body's response to infection. In the context of COVID-19, the study reports a high prevalence of IgG antibodies (86.4%), indicative of a substantial infection history. Correlation analyses, especially regarding IL-6 levels, reveal intriguing associations, where high IL-6 correlates with altered transferrin and iron levels, emphasizing inflammation's potential impact on iron metabolism. Acknowledging study limitations, including the cross-sectional design's constraints and sensitivity-specificity issues in COVID-19 antibody tests, future research should explore additional inflammatory markers and immune-related variables.

Conclusion

conclusion, this study provides valuable insights into age, gender, and biochemical variations in pneumonia patients, contributing to a broader understanding of immune responses and potentially refining diagnostic approaches and therapeutic interventions. Further longitudinal research is imperative for validation and a more comprehensive exploration of these intricate relationships.

Chitosan/Lemon Pectin capsule systems and their beneficial impact on intestinal barrier function

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Introduction

Intestinal epithelial barrier disruption is a hallmark of mucosal inflammation and a common feature of several systemic inflammatory disorders. Dietary fibers such as pectins, which have proven health benefits, exert immunomodulatory effects through different mechanisms (strengthening the mucus layer, enhancing epithelial integrity, cell modulation). Therefore, pectins may be an effective strategy to prevent intestinal barrier disruption. However, the protective role of pectin-based capsule systems have not been studied.

Method & Materials

Chitosan/lemon pectin DM18 and chitosan/lemon pectin DM88, and alginate/lemon pectin DM18 and alginate/lemon pectin DM88 empty capsules were obtained using chitosan 2.7% w/v, alginate 1.9% w/v, lemon pectin DM18 1.5% w/v and lemon pectin DM88 2.7% by electrodripping, using extrusion method. To study the protective role of pectin-based capsule systems, T84 cells were pre-incubated for 24 hours with 6, 8 or 10 capsules of both chitosan or alginate pectin empty capsules. Then A23187 disruptor was added and the AUC of TEER for a 24 hrs time after A23187 was calculated and compared to visualize and compare the effects of the empty capsules. The percentage of the AUC of untreated controls was set to 100%. The empty pectin-based capsules system as such did not affect gut epithelial barrier integrity in unstressed T84 epithelial cells

Results

After 24 hrs of A23187 disruptor challenge, empty capsules in either amounts pre-treatment, did not produce a protective role against A23187 disruptor. Alginate/lemon pectin and chitosan/lemon pectin DM18 in either amounts pre-treatment, did not produce a protective role against A23187 disruptor. However, chitosan/lemon pectin DM88 empty capsules produced differences in barrier protective effects and a delay in the effect of A23187 was observed in a dose-dependent manner. 6 and 8 C/LPDM88 capsules did not have a very strong effect and AUCs of 51.50 Ò 1.2% and 59.76 Ò 3.2%, meanwhile, 10 C/LPDM88 capsules was produced a strong effect and delay in the effect of the disruptor with an AUC of 71.70 Ò 3.7% ($p < 0.0079$), respectively. Genes related to tight junctions and cytokines release will be analyzed to confirm the protective role of the capsules.

Conclusion

Chitosan/lemon pectin-based capsule systems by reducing barrier disruption in a dose- and DM-dependent manner might ameliorate mucosal inflammation and other associated gastrointestinal and systemic immunological disorders.

Role of pancreatic peptidylarginine deiminases-4 (PAD4) enzyme in the streptozotocin (STZ)-induced diabetes of rats

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Introduction

Peptidylarginine deiminases (PADs) have an important role in the pathogenesis of generating citrullinated proteins which is one type of protein posttranslation modifications (PTMs). Additionally, peptidylarginine deiminases 4 (PAD4) is a component of neutrophil extracellular traps (NET) that leads to autoimmune disease during NETosis. Increased levels of PAD4 in neutrophils of individuals with type 1 diabetes (T1D) have been reported. Our aim was to check the PAD4 enzyme expression at level of gene and protein expression in streptozotocin (STZ) induced diabetic rat pancreas.

Method & Materials

Wistar rats were divided into two groups: control group and diabetic STZ group. STZ was administered by intraperitoneally (60 mg/kg/ body weight). Rats were caged for six weeks and then terminated. Pancreatic tissue was harvested for measurement of PAD4 protein expression, PAD4 mRNA, citrullinated histone-3 protein (CITH3) and Ca2+ content.

Results

PAD4 protein concentration (0.374±0.047 vs. 0.509±0.145 PAD4/ beta actin), PAD4 mRNA expression (2-ΔΔCT :0.952±0.282 vs. 3.170±1.394), CITH3(0.264±0.039 vs. 1.24±0.835 intensity/mm2) and Ca2+content (52.118±4.56 vs. 35.766±8.873µg/µL), were significantly increased compared to control. In addition, our data showed that PAD4 gene profile was correlated with PAD4 protein concentration (R2 =0.9395), CITH3 (R2 =0.923) and Ca2+ volume (R2 =0.8012)

Conclusion

PAD4 expression in STZ-induced diabetic rat pancreas is significantly increased compared to the control group to suggest that PAD4 may play a critical role in citrullinated pancreatic tissue.

Memory CD8+ T cell subsets in tumor draining lymph nodes of patients with bladder cancer

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Introduction

Crucial role of memory T-cells in mediating recall responses to previously encountered tumoral antigens is well documented. Frequency of different memory T-cell subsets in tumor draining lymph nodes may affect further immune responses toward tumor cells. We proposed to evaluate the frequency and prognostic relevance of memory T-cell subsets in tumor draining lymph nodes of patients with bladder cancer (BC) and their association with clinicopathologic characteristics.

Method & Materials

Mononuclear cells were isolated from 50 tumor draining lymph node of untreated patients with BC using Ficoll gradient centrifugation. Cells were stained with appropriate fluorescent conjugated antibodies specific for CD8, CD95, CD45RO and CCR7 markers. Cells were read on four-color FACSCalibur cytometer. Data were analyzed using FlowJo software package. Frequency of different subsets was determined among CD8+ lymphocyte.

Results

On average, 8% (2.67-15.50) of the mononuclear cells in draining lymph nodes were positive for CD8. The CD8+ memory cells accounted for 49.32Ò20.15 (1.62-87.20) percent of these cells. TCM cells had the highest frequency (34.71Ò17.04), whilst TSCM cells (7.51Ò8.53) were the lowest memory cell subset. Statistical analysis revealed that total memory T-cells tended to increase in patients with positive muscle invasion (P=0.052) and patients with stage III (P=0.042) compared to those without invasion and those with stage I, respectively. TSCM subset had significantly higher frequency in patients with N2 (more than one regional lymph node metastasis in the true pelvis) compared to free nodes (N0; P=0.042). TCM cells were significantly more frequent in patients with positive necrosis in comparison to those without (P=0.048). Total memory T-cells (P=0.027) and TCM subsets (P=0.001) were significantly higher in elder patients (>60 years), while naãve cells were more frequent in patients with age lower than 60 years (P=0.008).

Conclusion

Our data collectively suggest that with tumor progression (Invasion to muscle, higher stages, and node positivity) the frequency of memory T-cells and their subsets (TSCM and TCM) increased. This elevation might be due to frequent exposure of T cells to the tumor antigens and their attempts to provide an efficient anti-tumor immune responses. However, more functional and phenotypic analysis is needed to reveal the exact role of memory T-cells in BC.

Investigation of induced cytokine responses in patients with autoinflammation and autoimmunity

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Introduction

During the diagnostic work-up of patients with autoinflammatory and autoimmune diseases, basal cytokine levels often provide only limited insight into the altered signaling pathways underlying immune dysregulation. We therefore aimed to establish a functional assay to investigate induced cytokine responses upon stimulation of different nucleic acid-sensing pathways.

Method & Materials

To quantitatively assess cytokine responses to a variety of DNA and RNA ligands, we stimulated heparin blood samples from a cohort of healthy individuals. For each agonist, different doses and stimulation times were tested. Following stimulation, simultaneous analysis of 13 cytokines was carried out with a bead-based flow cytometry immunoassay. Based on these data, we set-up optimal conditions to analyze induced cytokine responses in patients with immune dysregulation.

Results

We first optimized the whole blood assay in healthy individuals (n = 6) by testing the immunostimulatory effects of specific ligands in a dose and time-dependent manner to better understand the dynamics of immune activation. We next investigated the immune response in three patients with early-onset SLE carrying heterozygous mutations in the UNC93B1 gene. UNC93B1 is critical for trafficking and function of nucleic acid-sensing Toll-like receptors (TLR), which are essential for antiviral immunity. We employed optimized doses of agonists targeting UNC93B1-dependent TLR7, TLR8 and TLR9. Stimulation of whole blood with the TLR7 agonist, R837, and the TLR8 agonist, TL8-506, revealed a significantly stronger proinflammatory response in patients compared to healthy controls. Interestingly, the cytokine response to the TLR9 agonist, ODN2216, did not differ between patients and controls. Thus, our findings indicate a selective hyperactivation in signaling pathways associated with TLR7 and TLR8 in patients with early-onset SLE due to UNC93B1 mutations.

Conclusion

Our functional assay represents a useful tool to investigate patients with immune dysregulation of unknown cause. Using this assay provided valuable insights into the immune dysregulation of patients with monogenic SLE due to UNC93B1 mutations. Noteworthy, our assay not only enables a better understanding of the mechanisms driving autoinflammation and autoimmunity but can also help to devise personalized therapeutic approaches.

Immune response to Monkeypox virus in infected individuals with or without HIV and in individuals vaccinated against the smallpox virus

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Introduction

The Monkeypox virus (MPXV), confined to African regions and linked to rodent contact, showed an epidemiological shift during the 2022 multinational outbreak. Now associated with sexual transmission, particularly among men who have sex with men, approximately 40% of cases are coinfected with HIV. In Colombia, 4059 cases were registered in 2022, 64 in 2023 and 5 cases until January 2024, exposing a similar behavior as shown globally. The extent and dynamics of the immune response to the virus remain unknown, even in those infected with HIV, who may be more vulnerable. It?s unclear if prior vaccination against the Variola virus (VARV), causing smallpox, confers protection against MPXV. We aim to characterize the magnitude and duration of the immune response to MPXV in individuals naturally infected, with and without HIV, and in those previously vaccinated against VARV.

Method & Materials

This observational study comprises: Group 1 (MPXV-HIV coinfection, n=5), Group 2 (MPXV infection without HIV, n=5) sampled in the acute phase and 1 year postinfection, and Group 3 (VARV-previously vaccinated individuals, n=20). Immune profiling in response to MPXV peptide stimulus will be evaluated through plaque reduction neutralization assays (PRNT), T cells memory profiling (CD45RA, CCR7), activation-induced marker assays (AIM) (CD137, CD25, CD69, CD134), molecules associated with cytotoxicity (Granzyme B, perforin) and intracellular cytokines (IL-2, IL-10, TNF-a, IFN-g) through flow cytometry. Cytokine production will also be assessed extracellularly, via capture beads assay (CBA). RNASeq will also be performed.

Results

Virus isolation in 2022 was confirmed through samples from a suspected Monkeypox patient. Sixty-five peptides shared for Vaccinia virus, MPXV and VARV, and most prevalent HLA-I and II in Colombia were selected. There are 25 collected samples, 5 from group 1, 4 from group 2, which are men, with a meanÒSD age of 35Ò12 and diversity of lesions location. Group 3 (n=16), vaccinated against Smallpox are 63Ò8 years old. The samples will be processed together once all of them have been collected.

Conclusion

Looking ahead, our research holds critical implications within the comprehensive immune profiling and development of future Monkeypox management and outbreak response strategies.

C4d Factor Evaluation in the Diagnosis of Antibody Mediated Rejection in Biopsies Following Liver Transplant

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Introduction

Attendance of C4d in renal and cardiac allografts is a symptom of Antibody-Mediated Rejection (AMR) and is related with worse results. But, it is still remained unknown regarding the significance of C4d and its staining pattern in LT (liver transplantation) rejection. Therefore, the aim of this study was to investigate the role of C4d in the diagnosis of antibody mediated rejection in post liver transplant biopsies.

Method & Materials

In this retrospective study, all patients who received ABO-compatible LT in Namazi and Abu-Ali-Sina hospital, affiliated to Shiraz University of Medical Sciences, between March 2015 and March 2019 with varying degrees of liver allograft rejection included. This cohort was assessed for the presence of AMR. So, the intensity and diffuseness of C4d positivity by IHC as well as DSAs result and clinical, histological and outlook data were obtained. We performed C4d IHC on paraffin embedded tissues. As a preliminary goal, we were expected to find at least 15 cases in each groups of mild, moderate and severe acute rejection to assess the correlation between C4d positivity and histopathologic findings. The patients who had received MTP pulse therapy prior to biopsy were excluded. Statistical analysis was carried out using SPSS Version 26.

Results

A total of 90 ABO compatible transplanted subjects were entered into analysis. Data of C4d was available for 47 subjects, which C4d was positive in 12 (25.5%) of them according to BANFF criteria. C4d positivity was not associated with mortality rate, rejection rate, mean AST, mean ALT, mean ALK, mean number of rejection and mean transplantation-rejection interval. Also, the survival distributions for C4d+ and C4d- groups were not statistically significantly different (_2: 1.599, P=0.21). In our combined dataset, 12 subjects (13.3%) had concomitant DSA and C4d results and all of them were negative for C4d.

Conclusion

We might confirm that using single ancillary tools (sole C4d or DSAs) are insufficient to diagnose AMR in ABO-C LT which is an infrequent type. It is not enough to recommend diagnostic criteria such as the Banff Working Group. More prospective large-scale studies are necessary to correlate DSAs and C4d with histology and outcome of ABO-C LT.

Longitudinal SARS-CoV-2 Antibody and T-Cell Immune Responses in Vaccinated Kidney Transplant Recipients and Patients on Dialysis

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Introduction

Kidney transplant recipients (KTRs) have an inferior immune response to vaccination due to chronic immunosuppression compared to dialysis patients (DPs). This study aims to measure the effect of de novo immunosuppression on long-term humoral and cellular immune response in CKD patients submitted to kidney transplant.

Method & Materials

This is a prospective interventional study comparing the post-vaccination humoral and cellular response in de novo KTRs and DPs. All patients received at least two doses of a COVID-19 vaccine, and none had previous disease. Blood samples were collected on inclusion, and after 1-, 3-, and 6 months and tested for anti-SARS-CoV-2 IgG, neutralization antibody activity, and IFN-_ activity. The primary outcome was sororreversion at month 6. Patients with anti-SARS-CoV-2 IgG negative at inclusion were excluded. All patients received additional doses of COVID-19 vaccine during this study, according to the governmental recommendations.

Results

There was no sororreversion during the period of follow-up. The anti-SARS-CoV-2 IgG titers were similar at Screening, 1 and 3 months and lower in KTRs at 6 months [KTR 5,529.8 (IQR 2,514.2-19,337.4); DP 14,427.9 (IQR 6,605.5-35,285.2); p<0.001). The neutralizing antibody activity was similar at Screening, 1, 3, and 6 months (p=0.938). The IFN-_ activity was lower in KTRs at screening (7.1% vs. 24.7%; p<0.001) and similar between the groups during the follow-up. After the first month, the cell-T immune response decreased within each group: KTR (M1 19.6%; M3 11.0%; M6 4.1%; p<0.001) and DP (M1 22.1%; M3 6.8%; M6 2.2%; p<0.001).

Conclusion

The sororreversion of anti-SARS-CoV-2 IgG was absent in both KTRs and DPs during 6 months of follow-up. Compared to DPs, KTRs had lower anti-SARS-CoV-2 IgG titers, but similar neutralizing antibody activity and T-cell immune response at month 6.

Poster session II

MEDICAL MICROBIOLOGY

Presenters:

- Camila Cabrera Ampuero
- Shuai Yue
- Italo Güinno Lorandi Camacho
- Nur Aina Yasmin Mat Saat
- Melita Janice Miss Rodrigues
- Tarun Kumar Suvvari
- Ramses Valenzuela
- Atieh Yaghoubi

Comparison of different techniques for detecting Helicobacter pylori infection in children and adolescents.

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Introduction

Helicobacter pylori is the most prevalent chronic infection worldwide. It can be acquired in childhood and promote the development of inflammation and eventually gastric cancer. Due to the difficulties in routinely culturing H. pylori, it has been difficult to find a reference standard for diagnosis. The most accepted practice is to use the combination of ≥2 non-culture-based assays from gastric biopsies. There is little literature comparing the performance of these techniques and other based on plasma analytes in children. Therefore, the objective of this study is to compare the proportion of positive samples by different techniques, their agreement and the performance of different test combinations, including serological detection.

Method & Materials

Analytical observational study that included patients aged 8 to 20 years who underwent upper endoscopy for abdominal pain study. The presence of H. pylori was determined using five tests: 1) Urease test; 2) Histology with Giemsa stain; 3) Amplification of ureA by real-time PCR; 4) Microbiome study; 5) IgG antibodies against H. pylori. Kappa index, positive percent agreement (PPA) and negative percent agreement (NPA) were calculated using histology as a reference technique.

Results

Samples from 118 patients aged 8-20 years were analyzed (average= 13.4). Of these, 29 were positive by urease test, 41 by histology, 37 by ureA PCR, 37 by microbiome analysis and 21 by IgG against H. pylori. The histology-ureA PCR combination did show the best detection agreement (PPA= 95,1%; NPA= 98,7%; kappa index= 0.944). There were 2 positive samples by histology, with a moderate amount of Helicobacter-type bacilli, which did not amplify by ureaA PCR and no H. pylori was identified in the microbiota study.

Conclusion

Although there is no complete agreement between the diagnostic methods evaluated, the histology-UreA PCR combination achieved the highest frequency of detection with the best agreement. Discordance between gastric biopsy-based methods could be explained in some cases because were taken from different areas of the gastric mucosa. Detection of bacilli by histology could correspond to other bacterial species. In this context, serology was not an appropriate diagnostic method.

Streptomyces translocates the immunodominant APA glycoprotein through the Tat pathway, and APA mutant can be targeted to the Sec pathway

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Introduction

The dominant immunogenic effect of APA, a native Mycobacterium tuberculosis glycoprotein heterologously expressed in Streptomyces, has been demonstrated, and it has been proposed as a potential vaccine for tuberculosis. Likewise, the APA signal peptide is used to facilitate the purification of antigenic lipoglycoproteins, by mediating their secretion. The Sec system and Tat system are candidate pathways that could secrete APA. However, the pathway by which APA is secreted in Streptomyces is still unknown. We aimed to determine which secretion system recognizes and translocates the APA glycoprotein, in Streptomyces.

Method & Materials

A bioinformatics approach was used to analyze the signal peptide motif of APA. Directed mutagenesis (Quikchange) was employed to obtain APA mutants designed to be specifically substrates of the Tat or Sec pathways, (APA-TAT and APA-SEC, respectively). The wild-type APA and the mutants were expressed in wild-type Streptomyces, in a mutant unable to glycosylate (_pmt) and in a mutant unable to translocate through the TAT pathway (_tatAC), derived of Streptomyces. Immunodetection by anti-APA antibodies in supernatants was performed, and glycosylation was detected by ConA assays.

Results

The wild-type APA was detected in the supernatant of the wild-type strains cultures. Otherwise, APA was absent from the supernatant of the _tatAC mutant culture. Therefore, the secretion of APA does not occur when the Tat pathway is defective. APA-TAT mutant was not detected in this mutant supernatant either. While the APA-SEC mutant was the only variant detected in the _tatAC mutant supernatant. Glycosylation was detected regardless of the pathway by which APA was translocated.

Conclusion

Through the Tat pathway, Streptomyces recognizes, secretes, and glycosylates the APA glycoprotein of M. tuberculosis. Our work presents one of the few reported cases where a secreted glycoprotein goes through the Tat pathway but not the Sec pathway. Also, we show that the conservation of the two arginines motif in signal peptide is essential for Tat machinery recognition. Finally, two original signal peptides which direct the secretion towards Sec or Tat pathway exclusively in Streptomyces were presented. These signal peptides could be used to facilitate the purification of antigens anchored to the cell membrane.

Targeting Tumor Cells Toward the Antigenic Specificity of Bystander T Cells in Tumor Microenvironment Potentiates Cancer Immunotherapy

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Introduction

Tumor-specific T cells are crucial in anti-tumor immunity and act as targets for cancer immunotherapies. However, these cells are numerically scarce and functionally exhausted in tumor microenvironment (TME), leading to the inefficacious immunotherapies in most cancer patients. In contrast, emerging evidence suggested that tumor-irrelevant bystander T (TBYS) cells are abundant and preserve functional memory properties in TME.

Method & Materials

We developed an oncolytic virus-based immunotherapy that delivers TBYS cell epitopes (OV-BYTE) into tumor cells, which efficiently redirects the antigen specificity of tumor cells to preexisting TBYS cells and effectively retards tumor growth in multiple preclinical models.

Results

In this study, we provide a proof-of-concept that redirecting the antigen specificity of tumor cells to tumor-infiltrating TBYS cells effectively controls tumor progression. This strategy, called OV-BYTE, was proven to curtail tumor growth and show synergistic effects with PD-L1 ICB therapy in multiple preclinical tumor models. Most studies thus far focused on CD8+ TBYS cells, leaving CD4+ TBYS cells being less investigated. Herein, we found that in TME, CD4+ TBYS cells adopt TH1-like differentiation.These TH1-fated CD4+ TBYS cells retain functional memory phenotypes.Such characteristics entail CD4+ TBYS cells with a dramatic memory-to-effector transition with massive cell expansion and enhanced cytotoxicity upon OV-BYTE treatment. Due to the prolonged pandemic, a tremendous population in the globe has been infected by SARS-CoV-2 and/or immunized with COVID-19 vaccines.We provided key proof-of-concept data illustrating that OV-BYTE strategy can effectively harnesses SARS-CoV-2-specific T cell memory derived from either infection or vaccination to treat cancers in preclinical models.

Conclusion

We revealed that OV-BYTE immunotherapy redirects the cytotoxicity of functional TBYS cells toward tumor cells for improved tumor control and has synergistic effects with PD-L1 ICB. Hence, the combination of OV-BYTE and PD-1/PD-L1 ICB might expand the toolkits for cancer immunotherapy.

Isolation and Screening of the Sirih Soil Bacterial Microorganism to be an Antimicrobial agent against ESKAPE Pathogen

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Introduction

The microorganisms in soil could be beneficial to the ecosystem or pathogenic to crop plants. Sirih plant or betel plant is chosen as it is one of the most important medicinal plants closely associated with the Southeast-Asian culture. Studies shows that Sirih leaves has antimicrobial potential in treating and preventing from certain diseases. However, there is no data available on identification of bacterial microorganism in sirih soil as an antimicrobial agent. Hence, this study initiated to isolate and screen the potential of soil microorganism in sirih soil to be an antimicrobial agent against ESKAPE pathogens (Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacteriaceae).

Method & Materials

Sirih soil has been collected from Forest Research Institute Malaysia garden (FRIM) & Chubadak Village garden in Kuala Lumpur, Malaysia. The sample preparation and isolation of soil bacterial microorganism was done using nutrient, water and TSA agars. The standard serial dilution of 101 - 106 technique was used for the isolation of bacteria from the soil samples. Then, the individual colonies were picked using sterile toothpicks and streaked onto fresh Muller Hilton (MH) agar plates to get pure cultures. The pure culture was incubated and used for testing antimicrobial activity against the ESKAPE pathogenic bacteria. Then, primary screening was done on the potential sirih soil bacteria for antagonistic activity in an in-vitro condition against the ESKAPE pathogenic bacteria.

Results

All 144 sample of sirih soil bacteria microorganisms have been successfully isolated with ESKAPE pathogen on MH agar. Among the 144 MH culture plates, 6 culture plates showed inhibition zone in varies range of diameter under primary screening. Each 3 samples from Chubadak Village and 3 samples from FRIM. Therefore, increase the possibilities of sirih soil bacterial microorganisms to be an antimicrobial agent against the ESKAPE pathogen.

Conclusion

The preliminary results shows that sirih soil bacterial microorganism to be an antimicrobial agent against the ESKAPE pathogen by showing an inhibition zone around the soil bacteria microorganisms isolated. Further experiments are needed to develop an alternative antimicrobial substances in sirih soil that can be used in human antibiotics treatment.

Antimicrobial Action of Liquids Treated by a Novel Multiunit Decontamination Module

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Introduction

The global issue of antibiotic resistance (AR) has reached alarming levels, with the emergence and spread of new resistance mechanisms posing a threat to our ability to treat common infectious diseases. Without immediate action, we risk entering a post-antibiotic era where previously manageable infections and minor injuries can once again become fatal. Therefore, it is evident that the research and development of a new generation of antimicrobials remains an urgent concern worldwide. (WHO 31.07.2020)

Method & Materials

Georgian scientists from I. Javakhishvili Tbilisi State University?s A. Natishvili Institute of Morphology have developed and tested a prototype (Georgian Patent P 5987) of liquids activated by a new, original, multiunit module (LAM). Microbiological studies are performed using the Quantitative Method for Evaluating Bactericidal Efficacy of Biocides Used on Hard Surfaces and Agar Disk-diffusion Method.

Results

Pilot studies conducted at Tbilisi State Medical University?s V. Bakhutashvili Institute of Medical Biotechnology and Institute of Morphology have shown that the module-treated liquids (normal saline, water) reveals pronounced and stable antistaphylococcal effect and prevents S. aureus growth. These results were confirmed by the studies carried out at the Lugar Center for Public Health Research. After 24h of incubation, a typical growth that is characteristic of B. anthracis was observed in the control dishes, with no growth in the LAM-treated dishes. When exposed to B. anthracis: after 30 minutes post-exposure, the growth of B. anthracis continued; however, a total biocidal effect was obtained after 45 minutes post-exposure.

Conclusion

The LAM developed possess notable biocidal properties, effectively preventing the growth of various bacteria and spores. These preliminary findings show potential in addressing the concerns over the growing risks of antibiotic resistance, and call for further research in this field to develop new strategies against this global issue.

Molecular Characterization of E. coli Causing UTI Through NGS: A Comprehensive Analysis of Serotypes, Sequence Types, Antimicrobial & Virulence Genes

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Introduction

In recent times, there is an enormous increase in antimicrobial resistance among bacteria isolated from human clinical specimens which has been contributing to treatment failures. Increased surveillance through next-generation sequencing (NGS) could facilitate the study of the epidemiology of drug resistant bacterial strains, the resistance genes, and other virulence determinants they are potentially carrying.

Method & Materials

This study included 30 Escherichia coli (E. coli) isolates obtained from patients suffering from urinary tract infections attending tertiary care teaching hospital from South India. All bacterial isolates were identified, and antimicrobial susceptibility patterns were determined through conventional microbiological techniques and confirmed by automated systems. Additionally, all the isolates were analyzed using NGS to identify the genes coding for resistance extended-sspectrum beta-lactamases (ESBLs) and metallo-beta lactamases, and virulence. Multilocus sequence typing (MLST) was used to understand the prevalent strain types and serotyping was carried out to evaluate the type of O and H serotypes carried by the isolates.

Results

The mean age of the patients was 46.96Ò20.18 years. Among the patients included 19 (63.33%) were males and 11 (36.66%) were females. Conventional antimicrobial susceptibility testing revealed that 15 (50%) isolates were resistant to imipenem, 10 (33.33%) were resistant to amikacin, 13 (43.33%) were resistant to piperacillin-tazobactam, 17 (56.66%) were resistant to cephalosporins, and 14 (46.66%) were resistant to nitrofurantoin. Among the isolates, 26 (86.66%) had revealed the presence of multiple antibiotic-resistant genes with evidence of at least one gene coding for beta-lactamase resistance. There was a high prevalence (19, 63.33%) of bla CTX-M , bla TEM , and bla OXA-1 [36.66% (11/30)] and bla NDM-5 was found in 3 isolates (10%). The E.coli serotype found predominantly belonged to O25:H4 (5, 16.66%) followed by O102:H6 (4,13.33%), O4:H1 (3, 10%), and O89:H9 (2, 6.66%), O1:H6 (2, 6.66%), O8:H21 (2, 6.66%),O101:H9 (1, 3.33%), O54:H28 (1, 3.33%), O199:H4 (1, 3.33%), O75:H5 (1, 3.33%), O101:H21(1, 3.33%), O11:H30 (1, 3.33%), O16:H5 (1, 3.33%), O4:H5 (1, 3.33%), and O9:H23 (1,3.33%). A total of 16 MLST variants were identified among the analyzed samples. Of the MLST-based sequence types (ST) identified, ST-131 (7, 23.33%) was the predominant one followed by ST-167 (3, 10%), ST-12 (3, 10%), ST-5954 (3, 10%), ST-648 (2, 6.66%), ST-410 (2, 6.66%), ST-156 (1, 3.33%), ST-448 (1, 3.33%), ST-14 (1, 3.33%), ST-1284 (1, 3.33%), ST-405 (1, 3.33%), ST-38 (1, 3.33%), ST-8881 (1, 3.33%), ST-2851, ST-827 (1, 3.33%), and ST-2006 (1,3.33%).

Conclusion

The study results demonstrated that the E.coli strains isolated from patients suffering from UTIs potentially carried antimicrobial resistance, and virulence genes and belonged to different strain types based on MLST. Careful evaluation of bacterial strains using molecular analyses like NGS could facilitate an improved understanding of bacterial antibiotic resistance and their virulence potential. This could enable physicians to choose appropriate antimicrobial agents and contribute to better patient management, thereby preventing the emergence and spread of resistant bacteria.

Role of DDX3X in human respiratory syncytial virus replication

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Introduction

The ATP-dependent DEAD-box helicase protein family plays a pivotal role in transcription and translation processes in eukaryotic cells, with DDX3X standing out. This protein has been described as an essential cellular factor in processes such as the replication of various viruses. However, its role during the replication of the respiratory syncytial virus (RSV), the main cause of acute lower respiratory infections (ALRI) like bronchiolitis and pneumonia in infants, remains unknown. During infection, RSV induces the assembly of inclusion bodies (IBs), large non-membranous viral ribonucleoprotein complex, where the synthesis of genomic RNA and viral mRNAs takes place. The preliminary results show that DDX3X colocalizes in IBs. However, the role of DDX3X in IB formation and viral RNA metabolism is still unknown. The objective we propose to this work is analyze how the pharmacological inhibition of catalytic activity of DDX3X using RK-33 affects the replication of viral genomic RNA, synthesis of viral proteins and conformation of IBs.

Method & Materials

A549 cells were treated with different concentrations of RK-33 and were infected with RSV for 24 hours. Viral RNA was amplified using RT-qPCR, and viral proteins were analyzed using Western blot. Additionally, IBs were analyzed through immunofluorescence and confocal microscopy.

Results

We observed that treatment with 5 and 8 ÊM of RK-33 significantly decreased the synthesis of genomic RNA, viral mRNA, and viral proteins. Moreover, there was up to a 7-fold increase in the number of IBs, accompanied by a reduction in size compared to the control.

Conclusion

The inhibition of DDX3X reduced gRNA synthesis, proteins, and affected the formation of IBs, suggesting DDX3X as an essential cellular protein acting as a pro-viral factor during RSV replication.

Differential Identification of Non-Tuberculous Mycobacteria Using Gene Sequencing Analysis

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Introduction

The role of non-tuberculous Mycobacteria (NTM) species in causing infections in human communities has become much more pronounced in recent years as compared to the past. Hence, hsp65 and ITS gene sequencing determination method were used in the present study to develop a valid method with high diagnostic value for the identification of clinical isolates of NTM in the Mashhad Tuberculosis Reference Laboratory.

Method & Materials

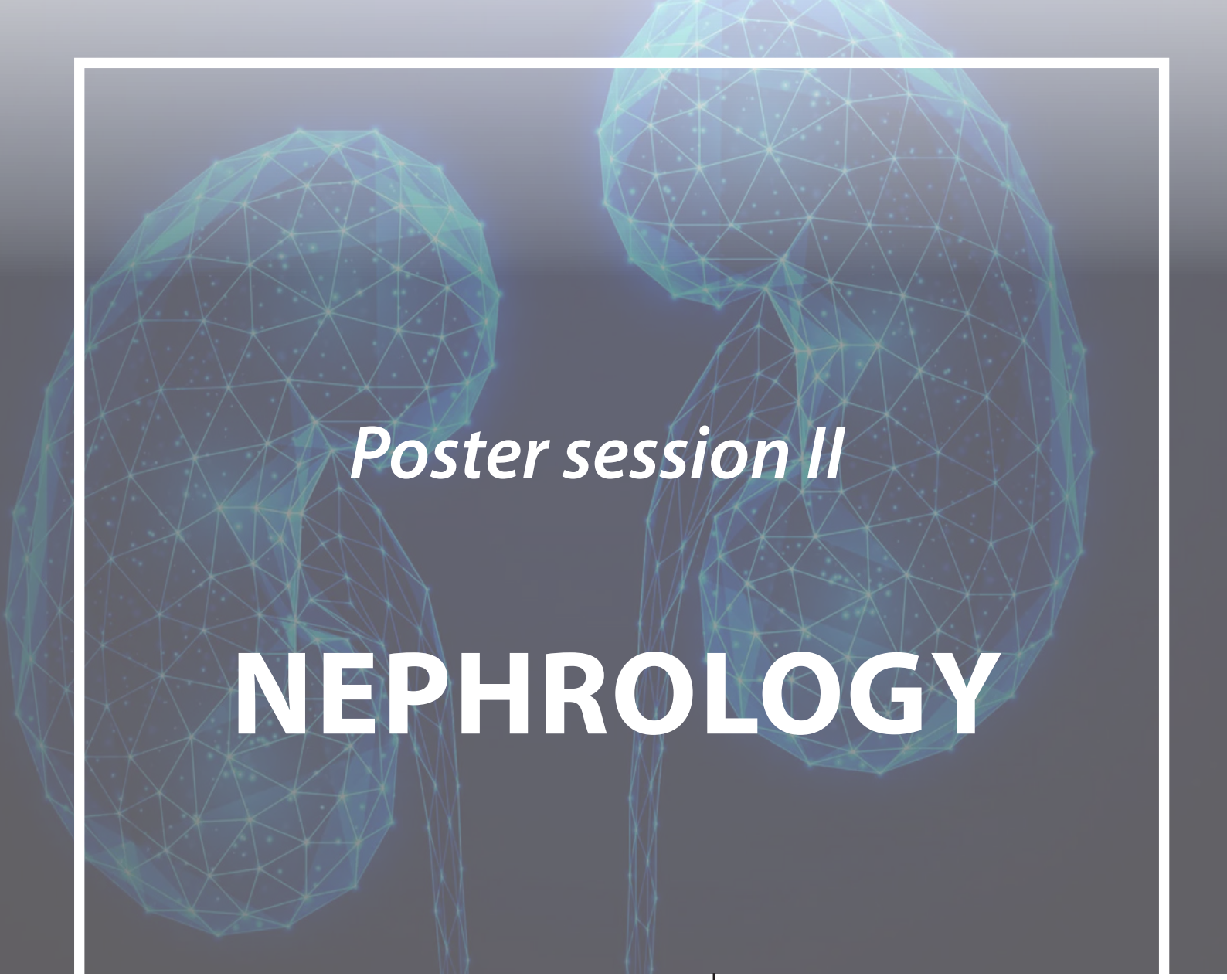
The required samples were collected in the period of April 2015 to March 2018. The patients with positive culture results, who had positive 16SrRNA-PCR and negative IS6110-PCR results were included in the study for further investigations and species identification. All the phenotypic species determination methods including analysis of the characterization of the colony, niacin, nitrate, catalase, aryl sulfatase, and tween 80 were performed for each of them. Subsequently, hsp65-PCR and ITS-PCR tests were done on the DNA of each sample. The PCR products were sent for sequencing determination.

Results

Out of 556 clinical isolates of Mycobacterium were isolated from 4503 suspected tuberculosis patients, the 48 (8.6%) samples were included in the study as the suspected NTM. The results of hsp65-sequencing and ITS-sequencing showed that out of 48 tested samples, 30 (62.5%) M. simiae, 3 (6.25%) M. abscessus, 3 (6.25%) M. fortuitum, 2 (16.4%) M. kansasii, 2 (4.16%) M. szulgai, 1 (2.08%) M. intracellulare, and also 1 (2.08%) was diagnosed as M. thermoresistibile .

Conclusion

All these findings showed that hsp65 and ITS genes can be used in identifying the most common species quickly and accurately in the country. The results also show a high prevalence of M. simiae in the northeast of the country.



Poster session II

NEPHROLOGY

Presenters:

- Larissa Silva
- Mohsen Chamanara
- Deea Deepanshi
- Rafaela Francisquetti Barnes
- Harshit Goyal
- Pedro Moretti-Pepato
- Samar Nobavar
- Shubhajeet Roy
- Beatrice Sato

ISCOMS 2024 SCIENCE BEYOND BORDERS

Potassium Citrate versus Lemonade for The Treatment of Hypocitraturic Nephrolithiasis: a Systematic Review of the Literature and Meta-Analysis

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Introduction

In the realm of nephrolithiasis, hypocitraturia stands out as the second most prevalent cause, prompting the need for effective interventions. Current recommendations emphasize increased fluid intake and reduced dietary sodium to alleviate this condition, with dietary supplementation of potassium citrate gaining prominence as a crucial strategy for managing lithogenesis. Building on this foundation, there is a hypothesis suggesting that lemonade supplementation might serve as a viable alternative to potassium citrate in treating hypocitraturia. Thus, this study aims to compare the efficacy of an intervention involving potassium citrate and the lemonade supplementation in patients with hypocitraturic nephrolithiasis.

Method & Materials

A systematic search was conducted in PubMed, Embase, Cochrane, LILACS, SciELO and Google Scholar. We included studies that compared patients who consumed lemonade and those who received potassium citrate supplementation for the treatment of hypocitraturic nephrolithiasis. Our primary outcome was the post-treatment urinary citrate concentration. Secondary outcomes encompassed other urinary parameters such as urate levels, pH, and urinary volume.

Results

We retrieved 3 articles, encompassing 42 patients in the lemonade group and 38 patients in the potassium citrate group. Overall, our analysis revealed no significant difference in post-treatment urinary citraturia between the two groups (MD -51.37; 95% CI -119.60, 16.85; $p = 0.14$; $I2 = 0\%$). Similarly, there were no notable distinctions in urate levels (MD -56.01; 95% CI -150.24, 38.22; $p = 0.24$; $I2 = 0\%$) and urinary volume (MD 140.53; 95% CI -151.03, 432.09; $p = 0.34$; $I2 = 0\%$). The potassium citrate group exhibited higher urinary pH values (MD -0.48; 95% CI -0.70, -0.27; $p < 0.0001$; $I2 = 40\%$).

Conclusion

In summary, our comprehensive meta-analysis provides evidence supporting lemonade as a viable alternative to potassium citrate for patients with hypocitraturic nephrolithiasis. Lemonade stands out as an economically accessible option, making it a practical choice for a wider range of patients. Additionally, its liquid form addresses the concerns faced by individuals who find capsules problematic, enhancing overall patient compliance and satisfaction.

Examining Functional Bladder Capacity Disparities in Pediatric Patients with Monosymptomatic and Non-Monosymptomatic Nocturnal Enuresis

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Introduction

As a common disorder, nocturnal enuresis is classified as either mono-symptomatic (MNE) or non-monosymptomatic (NMNE). The purpose of this study was to compare the functional bladder capacity of the two groups.

Method & Materials

During the period 2016-2021, a cross-sectional study was conducted at the Mofid Hospital's nephrology clinic. According to the International Children's Continence Society (ICCS), enuresis was defined and classified. This study excluded children with underlying neurologic diseases (such as myelodysplasia, spinal cord injuries, and brain injuries like cerebral palsy) and those with urologic disorders such as vesicoureteral reflux. A total of three methods were used to assess bladder capacity, including bladder ultrasound measurements at full capacity, frequency-volume charts (recorded over a period of two days), and uroflowmetry tests to determine maximum voided volume. Coffer's formula was used to determine bladder capacity as a function of age. The results of the MNE and NMNE groups were compared using SPSS software. The significance level was set at 0.05.

Results

A total of 122 children participated in the study, of which 58.7% were boys and 41.3% were girls. In 74.8% of cases, MNE was observed, and NMNE was diagnosed in 25.2% of patients. MNE and NMNE groups had an average age of 103.15 32.84 months and 93.44 32.21 months, respectively (P=0.129). Overall, 76.9% and 23.1% of participants had NMNE and MNE, respectively. In 52 (50%), 73 (70.2%), and 43 (41.3%) cases, functional bladder capacities were measured using bladder ultrasound, frequency volume chart, and uroflowmetry test, respectively. The bladder capacity measured by bladder ultrasound, frequency volume chart, and uroflowmetry test did not differ significantly between cases with NMNE versus MNE (P =0.973, 0.517, and 0.187, respectively). In addition, small bladder capacity was as common in MNE patients as in those with NMNE (P=0.37, 0.369, and 0.591 for bladder ultrasound, frequency volume chart, and uroflowmetry test, respectively).

Conclusion

In terms of bladder capacity, there is no significant difference between NMNE and MNE, and the prevalence of small bladder capacity is comparable in both groups.

Combination therapy with Lanreotide and Tolvaptan: Effect on kidney volume and kidney function in Autosomal Dominant Polycystic Kidney disease

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Introduction

Autosomal Dominant Polycystic Kidney disease(ADPKD) is a common inherited kidney disorder characterized by the growth of cysts in the kidneys leading to progressive kidney function decline and eventually kidney failure. Despite the substantial impact of ADPKD, the current treatment options have limitations. Vasopressin V2-receptor antagonists like Tolvaptan can mitigate cyst growth but come with side-effects. Somatostatin analogues like Lanreotide show promise for treating ADPKD-associated liver disease, but they are not highly effective as standalone treatments for improving kidney function in ADPKD. This underscores the need for more effective therapeutic approaches for ADPKD, potentially by targeting multiple mechanisms involved in cyst growth. Therefore, our aim was to investigate the effect of combination treatment with a vasopressin antagonist and a somatostatin analogue in ADPKD.

Method & Materials

This retrospective study examined the effects of Tolvaptan and Tolvaptan-Lanreotide therapy on estimated Glomerular Filtration Rate(eGFR) and Total Kidney Volume(TKV) slopes in adult ADPKD patients treated with Tolvaptan from DIPAK observational and OBSERVA cohorts. Baseline data, including demographics, medication history, and genetic information, were collected from 167 patients. The study employed Mann-Whitney tests and propensity score matching (1:1) to compare 'Tolvaptan only'(n=159) and 'Tolvaptan-Lanreotide'(n=8) groups.

Results

Patients receiving Tolvaptan and Lanreotide exhibited a significantly slower kidney volume expansion than those on Tolvaptan alone (TKV slope mean difference 1.44% per year, p=0.005). There were no significant differences in kidney function decline between the two patient cohorts (eGFR slope mean difference -0.22 mL/min/1.73 m2 per year, p=0.86).

Conclusion

Our retrospective analysis found that combined therapy with Tolvaptan and Lanreotide had a distinct impact on renal morphology, slowing the rate of total kidney volume expansion. While kidney function decline remained comparable, these findings suggest that the combination therapy may offer potential benefits in managing kidney volume expansion in ADPKD.

Impact of necroptosis on the outcome of Delayed Graft Function after kidney transplantation

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Introduction

Organ transplantation is an important renal replacement therapy for significant pathologies, such as Chronic Kidney Disease, which affects a considerable portion of patients across various groups. The course can lead to significant kidney injuries, which, like other pathologies, may require a kidney transplant. Various outcomes can be observed that directly impact the success or failure of the procedure, influencing the survival of both patients and the graft. Delayed Graft Function (DGF), is an outcome observed in a considerable range of transplants. This scenario can be associated with various external factors, such as cold ischemia time and ischemia-reperfusion injury, as well as molecular signaling pathways, like cell death by necroptosis.

Method & Materials

Understanding the impact of necroptosis on the occurrence of DGF after renal transplantation allows the identification of potential therapeutic targets. For this purpose, histological analysis of biopsies from deceased donors diagnosed with acute tubular necrosis with DGF will be performed, along with the analysis of proteins specifically involved in necroptosis (p-MLKL, p-RIPK1, and p-RIPK3) through immunohistochemistry assays. Initially, 40 biopsies with histological diagnosis of acute tubular necrosis will be analyzed divided into 20 cases with and without clinical criteria for DGF. We will also analyze data from deceased donors and recipients to identify health parameters and transplant conditions, as well as the evolution of patients afterwards. Statistical matters will be processed through the software SPSS.

Results

The results are ongoing. Patients already included in the research come from Hospital do Rim, S?o Paulo, Brazil, where approximately 1000 kidney transplants were performed, of which 75% were from a deceased donor. Among the expected results to be presented, scenarios and outcomes that can be used to identify the causes and associations between DGF and necroptosis after renal transplantation will be highlighted, as well as the relationship between late graft function and necroptosis, and therefore, biomarkers of this process, as previously indicated in scientific investigations.

Conclusion

The necroptosis pathway is characterized as emerging in the study of cell death. Gaining insight into the connection between this pathway and delayed graft function can pinpoint potential targets, paving the way for improving positive outcomes and advancing patient care.

Acute Kidney Injury (AKI): Correlating clinical features, urinalysis, and urine microscopy with short-term prognosis in patients requiring intensive care

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Introduction

Acute Kidney Injury (AKI) is a clinical syndrome of heterogeneous etiologies characterized by impairment of kidney?s excretory and filtration functions. KDIGO?s definition provides uniform criteria based on serum creatinine and urine output that reflect the dysfunction in glomerular filtration. AKI is common in ICU with an incidence of 30-60% and is associated with a mortality rate upto 51% This study was conducted to evaluate the contribution of urine analysis and microscopy to the diagnosis, management, and prognosis of AKI in patients admitted to our medical ICU.

Method & Materials

Study design cross-sectional study. Study period: 2 months. Adult patients (age Ú 18 years) admitted in ICU, and diagnosed to have AKI as per KIDGO guidelines were included. Patients not consenting, patients with chronic kidney disease, and hospital stays of less than 48 hours were excluded. Sample size was 132. Various clinical, outcome variables and relevant laboratory data were recorded. Urinalysis with dipstick and urine sediment microscopy were done. Statistical analysis was done using SPSS software, descriptive data in percentage, suitable correlation test (Pearson?s and Spearman?s correlation test) were used for parametric and non-parametric variables respectively. Chi-squared test was used where applicable to find an association between qualitative variables.

Results

Among admissions to MICU of 452, in the study period, 156 (34.51%) patients had AKI. 132(n) patients were enrolled after excluding 24 patients. 97 patients were from age groups 40-75 years with a male preponderance. Fever, oliguria, and pyuria were the most common clinical presentations of AKI. Stage III of AKI was seen in 49.24% of patients. Shock, congestive heart failure, and use of nephrotoxic drugs were the commonest causes of AKI inferred from working diagnoses made by physicians. AKI was complicated by acidosis, encephalopathy, hyperkalemia, and fluid overload. Urine microscopy examination finding of Renal tubular epithelial casts was associated with significant mortality. There was 17.42% mortality, 7 days of average ICU stay, and 12 days of average hospital stay. Almost half of the patients had persistent renal dysfunction after day 7. Dialysis was required in 41% of patients.

Conclusion

Around one-third of patients in the ICU had AKI, urinalysis, and microscopy proved to be an accurate diagnostic and prognostic modality. Our study showed that along with clinical assessment, urinalysis is an inexpensive, accurate, bedside modality that can be used as a marker for early detection of renal injury, helps in providing an insight into kidney damage, and also detects pathophysiological causes of acute kidney injury, and predicts the need for renal replacement therapy, dialysis, also have proven to be an early biomarker for predicting prognosis, severity, worsening and mortality. Urinalysis/ sediment microscopy as a biomarker has proven to be a window into kidneys? structural integrity and function.

The impact of diabetes among standard criteria donors on long-term outcomes for kidney transplant recipients: A propensity score-matched analysis

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Introduction

Given the scarcity of kidney donors, using diabetic donors is an option, yet their inclusion is not reflected in the UNOS criteria for expanded donors. Thus, we aimed to evaluate the long-term outcomes of kidney transplant recipients (KTRs) who received kidneys from diabetic donors but who met the standard UNOS criteria.

Method & Materials

This cohort study included KTRs who received kidneys from deceased donors meeting standard UNOS criteria between 2013 and 2017 at a Brazilian center. The last follow-up data was 2022. Outcomes: 5-year eGFR (mL/min/1.73m 2 , estimated by CKD-EPI and imputed using LOCF) and non-censored graft survival. The analysis compared KTRs from diabetic (DM+) and non-diabetic (DM-) donors, initially involving the entire cohort, followed by a 1:2 propensity score (PS) matched analysis (DM+:DM-).

Results

Out of 3,059 KTRs, 1,931 (63.1%) met the standard UNOS criteria, 73 being DM+ (3.8%). The DM+ donors were older (45.0 vs. 41.0 years; $p<0.001$), with a higher prevalence of hypertension (54.8 vs. 23.2%, $p<0.001$) and cerebrovascular brain death (63.0 vs. 46.5%, $p=0.005$), resulting in a higher KDPI (76 vs. 51%, $p<0.001$). There were no differences in the KTRs demographic characteristics in both groups. The incidence of DGF and 1-yr acute rejection (AR) was similar in both groups: 58.9 vs. 67.1% ($p=0.16$) and 17.9 vs. 19.2% ($p=0.77$), for recipients from DM+ and DM- groups, respectively. Considering the entire cohort, the 5-year eGFR was significantly lower for recipients from DM+ (29.5 vs. 41.8, $p<0.001$) but with no difference in graft survival (83.3 vs. 75.9, $p=0.28$). For matching, the following variables were controlled: donor age, hypertension, cause of brain death, and DR compatibility. After PS matching, there were no differences in baseline variables between both groups; the 5-year-eGFR was 35.2 vs. 29.5 for recipients from DM+ and DM-, respectively ($p=0.19$), and the 5-year graft survival was 83.3 vs. 71.9% ($p=0.09$).

Conclusion

Even in non-extended UNOS criteria donors, diabetic donors present several demographic differences that interfere with the KTR's long-term outcome. However, when matched for key characteristics using PS, the 5-year outcomes in recipients from diabetic and non-diabetic donors are comparable.

Assessment of Pediatric Kidney Transplantation Outcomes in Tehran, Iran: A Study on Transplant Survival in Children

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Introduction

Globally, chronic renal failure (CRF) affects over 400 million people, mainly in developing countries. CRF has become the 19th leading cause of death in recent years. Children with CRF may develop end-stage renal disease (ESRD), which is associated with increased mortality and morbidity. ESRD patients need renal replacement therapy, including transplantation. Despite the near-normal quality of life transplantation can provide, several concerns still exist, including graft dysfunction. This study aims to provide insight into critical aspects of pediatric kidney transplantation by studying kidney transplant survival among pediatric CRF patients.

Method & Materials

This retrospective cohort study examined pediatric patients under 18 with renal failure referred to Hashemi Nezhad Hospital, Tehran, Iran, between February 2017 and October 2018. Participants' demographics, underlying conditions, serum creatinine, donor type, and transplant complications were collected. Within 100 days of the transplant, acute complications were classified as acute, while chronic complications were classified as chronic. The patient's survival, kidney function, and complications were assessed after one year. Students' t-tests and Wilcoxon signed-rank tests were used to compare data, with significance set at $p<0.05$ for both tests.

Results

A total of 124 pediatric kidney transplant recipients were included in the study (78 females, mean age 11.9Ò12.4 years). The most common causes of CRF are congenital anomalies of the kidney and urinary tract (50%) and nephrotic syndrome (25%). Hemodialysis prevalence was 69% before transplantation. There were 25% of patients on peritoneal dialysis, and 8% had both. Previously, 15 recipients received kidney transplants. Ninety-six donors died (brain death), with a majority of males (67%) and a mean age of 7.64Ò 8.17 years. Ninety-one patients required dialysis due to graft failure. Graft survival at 1, 3, and 5 years was 78%, 72.9%, and 73.7%. Patient survival rates during these intervals were 91%, 88.7%, and 82.5%. Eighteen patients died due to infections.

Conclusion

To conclude, this study of pediatric kidney transplantation outcomes highlights the importance of properly managing CRF in children. Insights from this study are essential to future research and clinical improvements in pediatric renal transplantation. This publication urges efforts to improve transplant protocols and post-transplant care for healthcare practitioners and policymakers worldwide.

Long-Term Outcomes of ≥Grade 3 Renal Trauma: A Preliminary Observation from Northern India

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Introduction

Renal injuries, accounting for 1% of total trauma cases, have a significant impact. Despite this, there is a lack of research on the lasting effects on renal function post-trauma. We utilised the widely accepted AAST classification in our study and aim to fill this gap by investigating the long-term outcomes of Grade 3 and higher renal injuries.

Method & Materials

The study was conducted by following-up of retrospective data over a period of 3 months at a North Indian Tertiary Care Centre, which included patients of renal trauma with Grade 3 and more severe renal injuries that occurred at least 6 months prior (maximum: 5 years?age of our relatively new Trauma Surgery department). Exclusions comprised patients who had undergone nephrectomy or had coexisting conditions such as diabetes or hypertension. All participants who consented to follow-up and reported underwent tests including serum urea and creatinine, as well as DMSA (Diethylenetriamine penta-acetate), and DTPA (dimercaptosuccinic acid) scans. MS Excel v2019 was used to store the data, and SPSS v24.0 was used for the statistical analysis, including multivariate analysis. $p<0.05$ was considered significant.

Results

A total of 36 (n) patients (27 male, and 9 female) were enrolled in the study. The mean age of patients was 20.50Ò12.08 years. There were 9 patients each from grades 3, 4, and 5 (AAST). The split kidney function of the affected kidney was 31.83Ò12.69%, and the dye uptake for the affected side was 35.71Ò13.40%. In multivariate analysis, time at follow-up (p= 0.024* and 0.001*), and female gender, (p= 0.003* and 0.004*) were associated with higher differential-GFR and higher dye uptake by the affected kidney respectively, while Grade 5 (p= 0.0003* and 0.005*) was associated with lower differential-GFR and lower dye uptake by the affected kidney respectively.

Conclusion

A notable decline in the affected kidney?s function persisted in Grade 5 injuries, contrasting with Grade 3&4 injuries, which indicates an irreversible loss of renal function in Grade 5 injuries. Moreover, the length of the follow-up period showed a positive association with the affected kidney?s function, suggesting improvement in the affected kidney's function over time.

Clinical outcomes and graft function dynamics in kidney transplant recipients with sepsis admitted to an intensive care unit

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Introduction

Infection is a common occurrence among kidney transplant recipients (KTRs), carrying the risk of progressing into sepsis and increasing the risk of acute kidney injury (AKI). Thus, this study aimed to explore the dynamics of graft function in KTRs following a sepsis event and to identify the factors associated with severe AKI and mortality.

Method & Materials

Retrospective cohort study including 258 KTRs admitted to the intensive care (ICU) due to sepsis between 2016 and 2019. The last follow-up date was 90 days after ICU admission. The primary outcome was graft function (in ml/min/1.73m2, estimated by CKD-EPI, eGFR), and the secondary were AKI KDIGO 3 and death. The eGFR three months before the ICU admission was considered as the baseline. Logistic and Cox regression identified variables associated with AKI-3 and death, respectively.

Results

KTRs were 61 years old and had a long transplant vintage (84.3 months). The primary sites of sepsis were pulmonary (33.3%), abdominal (19.8%), or urinary (18.6%) infections. At ICU admission, the SOFA and SAPS3 scores were 5.0 and 54.0, respectively, with an eGFR of 20.9. During the ICU stay, 47.7% required vasoactive amine and 30.6% mechanical ventilation. The incidence of AKI-3 was 30.6%, and the associated variables were diabetes (RR=2.43, p=0.004), the baseline eGFR (RR=0.97, p=0.001), and SOFA (RR=1.21, p=<0.001). The 90-day mortality rate was 34.5%, which was associated with previous neoplasia (HR=1.63, p=0.034), age at ICU admission (HR=1.02, p=0.026), the site of infection (HR urinary vs. others=0.37, p=0.013), and the requirement for vasoactive amines (HR=5.11, p=<0.001) and dialysis (HR=1.81, p=0.01) during the ICU stay. Among the survivors (n=169), the baseline eGFR was 34.1, which decreased to 20.0 at ICU admission but improved to 32.6 three months later.

Conclusion

KTRs admitted to ICU due to sepsis experienced a significant decline in eGFR. While the requirement for dialysis during the ICU stay was associated with baseline eGFR and the severity of sepsis, mortality was associated with age, the site of infection, and the overall severity of sepsis. Among the survivors, there was a notable recovery in eGFR, returning to levels comparable to the baseline.

Poster session II

NEUROLOGY

Presenters:

- Mohammad T. Abuawwad
- Rohan Chouhan
- Makaya Claassen
- Ety Sari Handayani
- Mohammad Mohammadi
- Seyed Mohammadmisagh Moteshakereh
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Guillain-BarrÇ Syndrome After COVID-19 Vaccination: A Systematic Review and Analysis of Case Reports

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Introduction

Cases of Guillain-BarrÇ Syndrome (GBS) have been believed to be in association with the novel COVID-19 infection, and also with the following vaccines developed against the infection. Our work aims to investigate the incidence of GBS after COVID-19 vaccination, and to describe its clinical characteristics and potential confounders.

Method & Materials

An electronic search was conducted through four databases: PubMed, Scopus, medRxiv, and Google Scholar for all case reports and case series describing GBS manifestation in relation to COVID-19 vaccine administration. All published articles from inception until November 1st, 2022 were included. Differences between groups were assessed using Pearson chi-square test. Modified Erasmus GBS Outcome Score (mEGOS) for the ability to walk after GBS was calculated for all cases with sufficient clinical data, and Kaplan-Meier survival analysis were performed to study the effect of vaccine type on the relationship between vaccination time and complication of GBS.

Results

About 103 studies describing 175 cases of GBS following COVID-19 vaccination were included. The Acute Inflammatory Demyelinating Polyradiculoneuropathy subtype was the most reported subtype with 74 cases (42.29%), followed by Acute Motor Sensory Axonal Neuropathy and Acute motor axonal neuropathy 17 (9.71%) and 14 (8%), respectively. The affected age group averaged around 53.59 Ò18.83 years, with AMSAN occurring in a rather older group (63.88 Ò20.87 years, p=0.049). The AstraZeneca vaccine was associated with AIDP (n=38, 21.71%) more than other vaccines, followed by the Pfizer vaccine (n=23, 13.14%), p=0.02. The bilateral facial palsy subtype was mostly linked to adenoviral vector vaccinations, accounting for an average of 72% of the total BFP cases. Dysesthesias was the most reported sensory complication (60%, p=0.349). Most GBS patients survived (96%, p=0.036), however, despite the higher survival rate, most patients had low mEGOS scores (4 Ò3.57, p<0.01). On average, patients developed GBS at 13.43 Ò11.45 days from vaccination (p=0.73), and survival analysis for complication of GBS into mechanical ventilation or walking impairment yielded a severely increased probability of complication after 25 days (p<0.01). Intravenous immunoglobulins (p=0.03) along with rehabilitation (p=0.19). were the most commonly used treatment.

Conclusion

Although rare, GBS of all subtypes can manifest after COVID-19 vaccination. Most cases occurred after receiving the AstraZeneca vaccine, and despite low mortality rates, ambulation was compromised in most patients. A higher risk of GBS complication is associated with an onset later than 12-13 days, particularly with Pfizer, AstraZeneca, and Moderna vaccines.

Assessment Of Therapeutic Efficacy Of Cyclosporine A Against Stroke : A Meta Analysis

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Introduction

Cyclosporin A(CsA), a widely used immunosuppressant in transplantation and rheumatic medicine, has been recently shown to possess neuroprotective properties through its ability to block MPTP (Mitochondrial Permeability Transition Pore), which in turn inhibits neuronal damage. Extensive research has been aimed at studying cell death that accompany stroke and to use them as potential therapeutic targets for treating the disease like stroke, a leading cause of death and disability with limited treatment options. This Meta-Analysis is to assess the potential of CsA as a neuroprotective agent.

Method & Materials

Five Trials, involving 297 patients of 16-65 years age groups were included. The studies were single and double blind, randomized, and placebo-controlled clinical trials studying the effects of CsA on patients with stroke. The included patients suffered from stroke with a therapeutic window of 8-72 hours. The patients received either CsA in dose range of 0.625 to 5mg/kg of body weight or placebo in same dose range. The analyzed measures were Relative Risk (RR), Risk Difference (RD), and Odd's Ratio (OR). Efficacy analysis was done by using different methods like forest plots. All the calculations were compiled with the help of RevMan 5.4.1

Results

The pooled odd's ratio for 297 participants was 1.90(1.06,3.39) {fixed} and 2.06(0.54,7.85) {random} [95% confidence interval (CI) P=0.01]. The relative risk was 1.06(0.80,1.41) {random} and 1.15(1.00,1.33) {fixed} [95% confidence interval (CI) P=0.02]. The risk difference was 0.12 (-0.07,0.30) {random} and 0.07(-0.02,0.16) {fixed} [95% confidence interval (CI) P=0.02]. Across all data, we detected a slight advantage of CsA over Placebo treatment.

Conclusion

Meta Analysis of 5 trials involving 297 patients yielded Cyclosporine A to be slightly more efficacious than Placebo, with lesser mortality. Despite that the margin of benefit could not be considered to a conclusive significant level. Hence more trials are required, on a large number of patients before advising CsA to the patients diagnosed with stroke.

To Treat, or Not to Treat: The Identification of Predictors in Biopsy-Indicated High-Grade Glioma Patients to Prevent Overtreatment

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Introduction

The outcomes for high-grade glioma (HGG) patients remain largely unchanged, necessitating a reevaluation of treatment in radiological suspected HGG patients who are indicated for biopsy. This study addresses overtreatment concerns, aiming to identify predictors and develop a predictive model to decrease unnecessary treatment burden.

Method & Materials

A retrospective analysis was conducted on 132 HGG patients diagnosed via biopsy from 2016 to 2022. Overtreatment was defined as no treatment with survival < 3 months or treatment with survival < 3 months. Logistic regression with backward elimination (Premoval = 0.05), incorporating patient and tumor factors, was performed. Bootstrap was performed to internally validate the model.

Results

In total, 43.2% of the patients are overtreated. Logistic regression identified age at biopsy Ú 64.2 (OR 2.746; p = 0.006) and KPS pre-biopsy <70 (OR 3.805 p = 0.006) as significant predictors of overtreatment. The Nagelkerke R squared value was 0.140, the Hosmer and Lemeshow p-value was 0.998, and the AUC was 0.671.

Conclusion

Age at biopsy and KPS pre-biopsy were key predictors of overtreatment, indicating that an older age at biopsy (Ú 64.2 years) and a KPS pre-biopsy < 70 increase the probability of overtreatment. The model showed a good fit, though explanatory and discriminative power were moderate. Despite the small sample size and the limited discriminative power, the model could aid clinicians in decision-making and potentially alleviate patient and relatives? and healthcare system burdens. Recommendations include strengthening the model with additional variables, increasing the sample size, reaching consensus on overtreatment definition, and externally validate the model for broader applicability.

Impact of RAGE on Cortical Ischemia in Diabetic Rats Induced by Streptozotocin Nicotinamide and Transient BCCAO: A Post-Test Study

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Introduction

This study investigates the specific impact of the Advanced Glycation Endproducts-Receptor (AGEs-RAGE) axis on cortical ischemia in a diabetic rat model. AGEs, products of non-enzymatic reactions between carbohydrates and proteins, have been closely associated with the pathogenesis of diabetes, suggesting a potential contribution to cortical damage during ischemia. RAGE, as the primary receptor in the AGEs-RAGE axis, is considered a key mediator in the inflammatory response and oxidative stress associated with diabetes.

Method & Materials

The research employed a post-test only control group design, utilizing a diabetic rat model subjected to transient bilateral common carotid artery occlusion (BCCAO) to induce focal cortical ischemia. RAGE expression was meticulously evaluated in control groups without diabetes, diabetes groups with BCCAO, and control groups with BCCAO without diabetes. Statistical analysis utilized ANOVA, followed by post hoc tests to identify significant differences between groups.

Results

The study unveiled a significant increase in RAGE expression in the diabetes group with BCCAO compared to the control group without diabetes and the control group with BCCAO without diabetes. The impact on cortical ischemia was evident, emphasizing the potential contribution of RAGE in stimulating inflammatory responses and oxidative stress within the cortex during diabetes.

Conclusion

These findings underscore the critical role of the AGEs-RAGE axis in the pathology of cortical ischemia in diabetes, specifically affecting the cortex cerebri. The heightened expression of RAGE in diabetes indicates its significant impact on mechanisms exacerbating cell damage during cortical ischemia. This conclusion establishes a foundation for a deeper understanding of RAGE's specific contribution in the context of diabetes, emphasizing the implications for cortical ischemia. The study opens avenues for developing therapeutic strategies targeting the AGEs-RAGE axis to mitigate the negative impact on the cortex cerebri among individuals with diabetes, laying the groundwork for more effective and specific therapies.

Neutrophil to Lymphocyte Ratio in Alzheimer's Disease: A Systematic Review and Meta-Analysis

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Introduction

The Neutrophil-to-Lymphocyte Ratio (NLR), is a clinical indicator of peripheral inflammation that is easily accessible. It's worth noting that the formation of A_ plaques and neurofibrillary tangles has been linked to inflammation and immune dysregulation. The main objective of this systematic review and meta-analysis is to comprehensively evaluate the existing body of research concerning the NLR in the context of AD (Alzheimer?s disease) and MCI (mild cognitive impairment).

Method & Materials

We conducted a comprehensive online search via MEDLINE, Scopus, EMBASE, and Web of Science and included the studies that evaluated the NLR in 1) AD or MCI patients, and 2) HC (healthy control) participants.

Results

Ultimately, 12 studies encompassed 1,309 individuals diagnosed with AD with mean NLR levels of 2.68, 1,929 individuals with MCI with mean NLR levels of 2.42, and 2,064 HC with mean NLR levels of 2.06 were included in our systematic review and meta-analysis. NLR was notably higher in AD when compared to HC (MD= 0.59 [0.38; 0.80]). Likewise, NLR exhibited a higher level in AD when compared to MCI (MD= 0.23 [0.13; 0.33]). Furthermore, NLR was found to be elevated in MCI compared to HC (MD= 0.37 [0.22; 0.52]). In the subgroup meta-analysis based on MMSE, AD patients with lower MMSE scores (using a cutoff of 20) exhibited markedly higher NLR levels (3.10 vs. 2.70, with a p-value for subgroup differences < 0.01).

Conclusion

In summary, our research provides valuable insights into the association of NLR and the pathogenesis of AD. The NLR, which serves as a marker of peripheral inflammation, exhibits increased levels in individuals with both AD and MCI when compared to HCs. Additionally, our research reveals that NLR levels are significantly higher in AD compared to MCI. These findings form a hierarchy: NLR in AD > MCI > HC. Moreover, our novel finding suggests significantly higher NLR levels among AD patients with more severe cognitive decline. So, it can be concluded that the higher cognitive decline in humans is accompanied by higher NLR levels. Further longitudinal researches are needed to explore more details about the relationship between inflammation and dementia.

The stress-induced antinociceptive responses to the persistent inflammatory pain involve the orexin receptors in the nucleus accumbens

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Introduction

Stress-induced analgesia (SIA) is a well-documented physiological phenomenon where stress suppresses the perception of pain. Brain orexin peptides play a significant role in regulating various physiological functions, including wakefulness and nociception. However, the specific contribution of the orexinergic system within the nucleus accumbens (NAc) to the modulation of antinociception induced by forced swim stress (FSS) remains poorly understood.

Method & Materials

In this study, 106 adult male Wistar rats, weighing between 250?305 g, underwent unilateral stereotaxic surgery. Different doses (1, 3, 10, and 30 nmol/0.5 _l DMSO) of antagonists for orexin-1 receptors (OX1r) or orexin-2 receptors (OX2r), namely SB334867 and TCS OX2 29, were administered into the NAc five minutes prior to a 6-minute exposure to FSS. To evaluate antinociception, the formalin test was employed, involving the injection of formalin (50 _l; 2.5%) into the hind paw plantar surface of the rats. This test elicits biphasic pain-related responses, with the first phase commencing immediately after formalin infusion and lasting 3?5 minutes, followed by the late phase, which begins 15?20 minutes after formalin injection and lasts 20?40 minutes.

Results

The study revealed that the intra-accumbal microinjection of both SB334867 and TCS OX2 29 attenuated FSS-induced antinociception in both phases of the formalin test, with TCS OX2 29 exhibiting greater potency. Furthermore, the impact of TCS OX2 29 was more pronounced during the early phase of the formalin test.

Conclusion

These findings suggest that orexin receptors, OX1 and OX2, within the Nucleus Accumbens (NAc), may play a pivotal role in modulating the antinociceptive responses induced by forced swim stress. Specifically, the results highlight the potent influence of TCS OX2 29 during the early phase of the formalin test, shedding light on the potential for orexinergic systems to modulate stress-induced analgesia during persistent inflammatory pain models in rats.

Effect of add-on vitamin D supplementation on seizure control and epileptogenic biomarkers in drug-resistant epilepsy: A double-blind placebo-controlled trial

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Introduction

Drug-resistant epilepsy (DRE) is a major challenge in epilepsy treatment, as antiseizure medications (ASMs) only provide symptomatic relief without significant effects on disease progression. Vitamin D (Vit-D), has shown anticonvulsant potential in some . experimental studies and two pilot clinical studies. Some animal studies emphasized the possible role of vitamin D receptor (VDR) in epileptogenesis. Hence, our study aims to investigate the effect of Vit-D supplementation on seizure control, epileptogenic biomarkers, and vitamin-D receptor (VDR) expression in persons with DRE.

Method & Materials

This double-blind placebo-controlled trial randomized adult DRE subjects with serum vitamin-D3 <30 ng/ml into Vit-D group and matching placebo groups (CTRI registration no: CTRI/2020/12/029862). Vit-D group received recommended dose of vitamin-D3 orally 60,000 IU once weekly for 3 months, followed by once monthly for 3 months along with ongoing ASMs. Along with safety parameters, for efficacy, percentage changes in seizure frequency (primary outcome), drug-responder rate, serum vitamin-D3, PTH, calcium, VDR mRNA expression, epileptogenic biomarkers including high-mobility group-box protein-1 (HMGB1), neurotrophin-3], quality of life and sleep quality, psychiatric and behavioural adverse effects (PBAEs) were assessed.

Results

Out of 200 randomized subjects, 99 were on Vit-D group and 101 were on placebo. In both Vit-D group and placebo groups significant reduction in seizure frequency was found compared to baseline ($p<0.001$ and 0.014, respectively). However, there was no intergroup significant difference in percentage change in seizure frequency (33%. vs. 25%, $p=0.43$) and drug responder rate. After 6-months, serum vitamin-D3 level and VDR mRNA expression and protein were increased and neurotrphin-3 was decreased significantly in Vit-D group compared to placebo ($p= <0.001$, 0.044 and 0.02, respectively). Serum HMGB1 was significantly reduced in Vit-D group compared to placebo. Though no significant difference in PBAEs and safety findings, sleep quality significantly improved in Vit-D than placebo group ($p=0.034$).

Conclusion

: Compared to baseline, significant reduction in seizure frequency was found in both Vit-D and placebo group; however, no significant intergroup difference was noted despite the increased VDR mRNA and protein expression, and decreased epileptogenic markers in Vit-D group. Further study with long-term follow-up and higher dose of Vit-D supplementation is needed to establish the finding.

Poster session II

NEUROSURGERY

Presenters:

- Lina Albakri
- Yuequn Chen
- Yasmin Sa
- Djenghiz Samlal
- Tejas Shelar
- Ziyi Wang

ISCOMS 2024 SCIENCE BEYOND BORDERS

Occurrence of Hearing Loss and Tinnitus following Microvascular Decompression for Hemifacial Spasm

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Introduction

Hemifacial spasm (HFS) is a condition where the facial nerve is compressed, leading to debilitating, unilateral, involuntary contractions of facial muscles. The surgical treatment is microvascular decompression (MVD). Due to the proximity of the facial nerve to the auditory nerve, hearing loss (HL) and tinnitus are susceptible complications of MVD surgery. Intraoperative brainstem auditory evoked potentials (BAEP) could be used to prevent these complications. This study aims to identify the prevalence of HL and tinnitus following MVD for HFS, along with predictors for their development.

Method & Materials

A single-center cohort of 55 HFS patients who underwent MVD was sent a questionnaire about postoperative HL and tinnitus, median 5 years after surgery. Additional data was retrieved from medical charts. Data analysis was conducted using the statistical software R. Descriptive statistics and logistic regression analyses were employed.

Results

At the time of surgery, the median age of participants was 58 years. Duration of HFS symptoms ranged from 3 to 8 years, mostly affecting the left side (60%). Preoperative HL and tinnitus were reported by 18% and 16%, respectively. While postoperative HL was reported by 45%, and postoperative tinnitus by 36%. Almost half the patients with postoperative HL and tinnitus had those complaints on the surgical side, while the other half had them bilaterally. Roughly 70% of patients who had them bilaterally, already had that preoperatively, and around 30% developed them bilaterally only postoperatively. The onset of the new complaints was usually shortly after surgery. Significant predictors for postoperative HL included male sex, older age at the time of surgery, preoperative HL, and time elapsed since surgery. Preoperative tinnitus was the only significant predictor for postoperative tinnitus. Intraoperative BAEP did not significantly predict neither postoperative HL nor tinnitus.

Conclusion

HL and tinnitus are common complications of MVD surgery for HFS. BAEP may not predict all postoperative auditory outcomes. Clinicians should be aware of these complications and the need for long-term monitoring to ensure the best possible outcomes for HFS patients undergoing MVD surgery. Further research is needed to refine the risk prediction for these auditory complications and develop strategies for minimizing them in this patient population.

Serum osmolality as a biomarker in traumatic intracranial hemorrhage: exploring beyond single-factor analysis

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Introduction

Traumatic intracranial hemorrhage (TICH) leads to poor clinical outcomes, with the role of serum osmolality, an important biomarker reflecting the central nervous system's regulation of the internal environment, remaining unclear.

Method & Materials

TICH patients from the MIMIC-IV and EICU databases were recruited. After assessing the association between TICH outcomes and serum biomarkers, including sodium, glucose, and urea nitrogen, which contribute to serum osmolality, we evaluated the relationship between these outcomes and the calculated serum osmolality in the MIMIC-IV TICH cohort, comparing the results with the EICU database.

Results

In the MIMIC-IV dataset (n=2308), serum osmolality at admission independently associated with in-hospital mortality(HR: 1.048, 95% CI: 1.029?1.068) and in-ICU mortality (HR: 1.056, 95% CI: 1.032?1.080). Restricted cubic spline regression revealed non-linear relationships between serum osmolality, sodium levels, and critical care needs, with cutoffs at 288.19 mmol/L and 139.01 mmol/L, respectively. Slightly asynchronous trends were observed when deviating from their corresponding cutoff values. Remarkably different survival risks were noted between groups based on these cutoffs, with the high sodium but low osmolality group showing the best and the low sodium but high osmolality group the worst survival outcomes. To address that, the ratio of serum osmolality and sodium with exponential conversion, exp(Osmol/Na), were proposed and it was an independent risk factor for in-hospital mortality (HR: 2.027 , 95% CI: 1.353 ? 3.035) and better predictor of in-hospital mortality (AUC: 0.703) and in-ICU mortality (AUC: 0.672),compared to using osmolality alone. These results was corroborated by findings from the EICU TICH dataset (n= 1843).

Conclusion

This study highlights the significant impact of serum osmolality on TICH outcomes. The complex interplay between serum osmolality and sodium suggests the need for comprehensive evaluation and further pathophysiological research on TICH patients.

Evaluation of cerebral hemodynamics and its correlations with intracranial pressure variations in an animal model of cerebral rebleeding

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Introduction

Intracranial hemorrhage (ICH) poses a significant burden on clinical outcomes and financial resources. After initial bleeding, expansion of the hematoma is common and an important cause of death and disability after ICH. Although ICH effects on cerebral hemodynamics has been analyzed in multiple studies, its effects at rebleeding still not conclusive in literature. We aimed to compare the cerebral hemodymanics and intracranial pressure behaviors at a single large hemorrahge and at the rebleeding in a controlled experimental environment for ICH simulation by means of balloon inflation.

Method & Materials

It consisted of two groups in which intracranial balloons were inflated with 4+3 mL (A) and 7 mL (B) for controlled simulation of expansion and hemorrhage. The intracranial pressure and Transcranial Doppler parameters (systolic, diastolic, and mean cerebral blood flow velocities and pulsatility index) values were collected in 6 moments: baseline, pre-inflation, post-inflation, pre-infusion of hypertonic saline solution (HSS), post-infusion of HSS, pre-deflation and post-deflation. The parameters assessed were described according to summary measurements and compared between groups and times. The softwares IBM-SPSS for Windows version 22.0 and Microsoft Excel 2013 were used and the tests were carried out at a 5% significance level.

Results

The preliminary results showed an increase of pulsatility index in group B between pre-infusion of HSS and pre-deflation, while there was a reducement in group A. No major difference was observed for the other moments in both groups and, at post-deflation, the values came closer again. Only group B showed a mean increase in sistolic velocity from pre to post deflation ($p = 0{,}001$) and in mean velocity from post-deflation to post-inflation ($p = 0.001$). Parenchymal intracranial pressure showed a inverse correlation with systolic, diastolic and mean velocities and a direct correlation ($r = 0.595$ and $p = 0.003$) with the pulsatility index.

Conclusion

Re-bleeding in group A caused the same total volume of hematoma to be reached less acutely than in group B. The speed with which intracranial hypertension sets in seems to be an important factor in cerebral hemodynamics. It was also observed that the higher the parenchymal intracranial pressure, the lower the systolic, diastolic and mean velocities and the higher the pulsatility index.

Deskeletonizing the sigmoid sinus is noncompulsory in skull base surgery: 3D modeling of the translabyrinthine approach

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Introduction

The translabyrinthine approach (TL) is used for tumor resections near the brainstem. During this operation, the sigmoid sinus is compressed and could be injured, which is associated with various post-operative complications. This study quantifies the effect of the sigmoid sinus (SS) on the operative exposure during the TL. Leaving the SS skeletonized with bone would protect this vessel. It is hypnotized that in selected cases a posteriorly mobilized skeletonized SS will provide sufficient exposure to perform a TL resection of cerebellopontine angle tumors.

Method & Materials

Twelve translabyrinthine approaches were performed on cadaveric heads. The position of the sigmoid sinus was varied in three procedures: stationary skeletonized (TL-S), skeletonized posterior retraction (TL-R), and deskeletonized collapsing of the sinus (TL-C). Based on the post-operative CT-scans, a high-definition 3D reconstruction of the resection cavity was created. The primary outcome, ?surgical freedom? (mm2), was the area at the level of the craniotomy from which the internal acoustic porus could be reached in an obstructed straight line. Secondary outcomes include the ?exposure angle? (degrees), ?angle of attack? (degrees) and pre-sigmoid depth (mm).

Results

When retraction of the SS was performed during TL-R, surgical freedom increased by a mean of 41% (range: 9-92%, SD: 28) when compared to no retraction (TL-S). Collapsing the SS in TL-C provided a mean increase of 52% (range: 19-95%, SD: 22) compared to TL-S. In some specimens, the TL-R provided a greater surgical freedom than the TL-C; however, on average an increase of 10% (range: -10?30%, SD: 12) in favor of the TL-C is observed when compared to TL-R. In most cases the exposure is the greatest when the sigmoid sinus is collapsed. However, in 40% of the specimens the provided exposure, while retracting (TL-R) instead of collapsing (TL-S) the sinus, is equal or greater than 50% of other specimens in which the sinus is collapsed.

Conclusion

In cases with favorable anatomy, a translabyrinthine resection in which the skeletonized sigmoid sinus is retracted, provides sufficient exposure for adequate and safe tumor resection. However, further research is necessary to evaluate the translatability of this maneuver from cadaveric specimens to a clinical setting.

A novel approach to Spondylodiscitis - Full Endoscopic Debridement and Drainage (FEDD) with "Trocar Rotating Technique"

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Introduction

In recent years, full-endoscopic debridement and drainage (FEDD) is gaining popularity for treating spondylodiscitis. Compared to traditional open surgery, FEDD possess many advantages such as lower anesthesia risk and minimally invasiveness, amongst others. In this study, we report our surgical technique of FEDD with ?Trocar rotating technique? and preliminary clinical outcome in 23 consecutive patients with minimum 6 months? follow-up.

Method & Materials

23 patients including 8 males and 15 females with average age of 47 years (17 to 77 years old) who had sustained spine infection were treated by FEDD .

Results

Amongst these, 22 patients had lumbar spondylodiscitis while 1 patient had thoracic spondylodiscitis. Off these, 6 patients had involvement of multiple levels where as remaining 17 patients had a single level disease. Fusion was required in 1 patient only. _ 18 patients belong to primary spondylodiscitis with 14 patients among them had a concomitant psoas abscess _ 5 patients belonged to post-operative category _ FEDD was done in all patients with 2 patients requiring instrumentation for instability, 1 amongst them underwent Fusion _ Mean ESR for the study was 63.08 while it was 112.2 for only the post-operative discitis group _ Mean CRP for the study was 24.49 and for the only post-operative discitis group was 60.83 _ Procalcitonin levels were normal for all primary spondylodiscitis patients, while all patients with post-operative discitis had levels > 0.05 _ Positive culture was obtained in all 5 patients while gram-positive cocci (Staphylococci) being the most frequent pathogen (60%) _ Infection was controlled in 21 patients in the primary sitting _ 2 patients were defined as treatment failure with infection recurrence, they underwent open revision surgeries. There were no major intraoperative complications.

Conclusion

FEDD is a safe and effective procedure to that reduces hospital stay and patient morbidity while facilitating early mobilization and hastening recovery. FEDD surgery definitely has the potential to be the first-line surgery method to treat lumbar spine infection globally in the near future.

Prognostic Value of Complete Resection of the High Frequency Oscillations Area in Intracranial EEG: A Systematic Review and Meta-analysis

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Introduction

High-frequency oscillations (HFOs; ripples 80-250 Hz; fast ripples (FRs) 250-500 Hz) recorded with intracranial electrodes generated excitement and debate about their potential to localize epileptogenic foci. We performed a systematic review and meta-analysis on the prognostic value of complete resection of the HFOs-area (crHFOs-area) for epilepsy surgical outcome in intracranial EEG (iEEG) accessing multiple subgroups.

Method & Materials

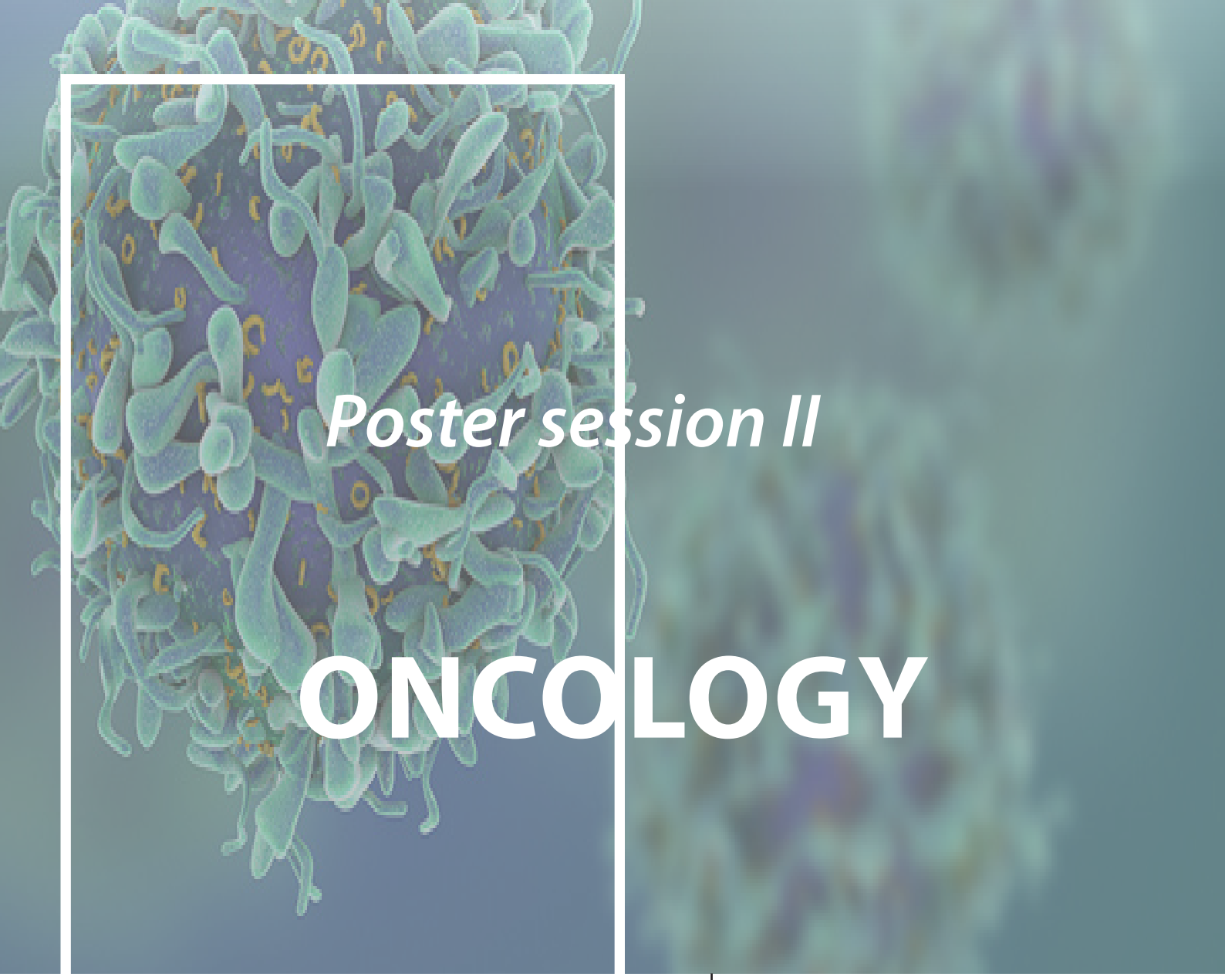
We searched Pubmed, Embase, and Web of Science for original research from inception to October 27th, 2022. We defined favorable surgical outcome (FSO) as Engel class I, ILAE class 1, or seizure-free status. The prognostic value of crHFOs-area for FSO was assessed by a) the pooled FSO proportion after crHFOs-area; b) FSO for crHFOs-area vs without crHFOs-area; c) the predictive performance. We defined high combined prognostic value as FSO proportion>80% + FSO crHFOs-area>without crHFOs-area + area under the curve (AUC)>0.75; and examined this for the clinical subgroups (study design, age, diagnostic type, HFOs-identification method, HFOs-rate thresholding, iEEG state). Temporal lobe epilepsy (TLE) was compared to extra-TLE via dichotomous variable analysis. Individual patient analysis was performed for sex, affected hemisphere, MRI-findings, surgery location, and pathology.

Results

Of 1387 studies screened, 31 studies (703 patients) met our eligibility criteria. 27 studies (602 patients) analyzed FRs and 20 studies (424 patients) ripples. Pooled FSO proportion after crHFOs-area was 81% (95% confidence interval 76-86%) for FRs and 82% (73-89%) for ripples. Patients with crHFOs-area achieved more often FSO than those without crHFOs-area (FRs odds ratio (OR) 6.38 (4.03?10.09), p<0.001; ripples 4.04 (2.32-7.04), p<0.001). The pooled AUCs were 0.81 (0.77-0.84) for FRs and 0.76 (0.72-0.79) for ripples. Combined prognostic value was high in ten subgroups: retrospective, children, long-term iEEG, threshold (FRs and ripples); automated detection and interictal (FRs). FSO after complete resection of FRs-area (crFRs-area) was achieved less often in people with TLE than extra-TLE (OR 0.37 (0.15?0.89), p=0.006). Individual patient analyses showed that crFRs-area was seen more in FSO patients with than without MRI-lesions (p=0.02 after multiple correction).

Conclusion

Complete resection of the brain area with HFOs is associated with good postsurgical outcome. Its prognostic value holds, especially for FRs, for various subgroups. The use of HFOs for extra-TLE patients requires further evidence.



Poster session II

ONCOLOGY

Presenters:

- Francis Adu-Amankwaah
- Atena Aghaee
- Zhimao Chen
- Tim Janik Froitzheim
- Teng Fu
- Eline Kormelink
- Sarah Mathilda Vincent

Cytotoxic properties and high-resolution respirometry mitochondrial activities of Eriocephalus racemosa against MDA-MB 231 triple-negative breast cancer

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South Africa

Introduction

Triple-negative breast cancer (TNBC) represents a significant global health crisis due to its resistance to conventional therapies and lack of specific molecular targets. This study explored the potential of Eriocephalus racemosa (E. racemosa), a fynbos plant, as an alternative treatment for TNBC. The cytotoxic properties and high-resolution respirometry mitochondrial activities of E. racemosa against the MDA-MB 231 TNBC cell line were evaluated.

Method & Materials

Hexane solvent extraction of E. racemosa was performed, while mass spectrometry-based metabolite profiling was used to identify the phytochemical constituents of the extracts. The crude extract was further tested against MDA-MB 231 cancer cells to determine its cytotoxicity. The mode of cell death was confirmed using flow cytometry, and we assessed the activities of caspases 3, 8, and 9 using a multiplex activity assay kit. High-resolution respirometry measurements of mitochondrial function in the MDA-MB 231 cell line were conducted using the Oroboros O2K.

Results

Metabolite profiling of E. racemosa extract identified the presence of quinolines and derivatives, stigmastanes and derivatives, triterpenoids, and four unknown compounds. The extract demonstrated promising cytotoxic activity, with a half maximal inhibitory concentration (IC50) of 12.84 Êg/mL. Further, the extract induced apoptosis in the MDA-MB-231 cancer cell line, similar to the reference drug cisplatin (17.44% and 20.25%, respectively) when compared with untreated cells. Caspase 3 activities confirmed the induction of the apoptosis pathway in both cisplatin and the crude plant extracts. Additionally, caspase 8 and 9 activities confirmed the activation of both the intrinsic and extrinsic apoptosis pathways in the plant crude extracts. High-resolution respiratory measurements showed elevated mitochondrial activities in all components examined except for complex-IV activities

Conclusion

: It was concluded these findings support further exploration of E. racemosa as a potential therapeutic agent for TNBC, offering a promising avenue for the development of targeted treatments with minimal adverse effects.

Comparison of treatment efficacy after thyroid remnant ablation with 1110 versus 5550_MBq of iodine-131 in intermediate-risk differentiated thyroid cancer

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Introduction

Radioiodine ablation may be associated with improved survival in patients with intermediate-risk follicular cell differentiated thyroid cancer (FCDTC). The aim of this study was to compare ablation efficacy of 1110 versus 5500_MBq of iodine-131 (131I) in FCDTC patients with intermediate risk.

Method & Materials

Thirty-nine patients with intermediate-risk FCDTC (T3N0, T1-2N1b and T1-3N1a) were treated with 1110_MBq of 131I and compared with 43 age-matched and sex-matched patients who received 5550_MBq of 131I. Patients with invasive histology, extensive lymph node involvement, and preablation thyroglobulin (Tg) of more than 100_ng/ml were excluded from the study. All patients underwent total or near total thyroidectomy with or without lymph node dissection. Response to treatment was evaluated 1 and 2 years after 131I treatment.

Results

We studied four male and 78 female patients, age range 21?69 years. Preablation Tg level was 12.7Ò17.8 and 15.8Ò22.6_ng/ml in patients in the low-dose and high-dose groups, respectively (P=0.48). Anti-Tg antibody level as well as T and N staging were not significantly different in the two groups (P>0.2). One and 2 years after treatment, an excellent response was noted in 19 and 22 patients in the low-dose group and in 16 and 23 patients in the high-dose group, respectively (P>0.3). Using logistic regression analysis, preablation Tg was the only significant factor in the prediction of an incomplete response 2 years after therapy.

Conclusion

1110_MBq of 131I was as effective as 5550_MBq of 131I in the treatment of FCDTC patients with intermediate risk 1 and 2 years after therapy.

The Double-Edged Sword Behavior of a-MSH/ MC1R pathway: Targeting Tumor Immune Microenvironment (TIME)

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Introduction

The melanocortin-1 receptor (MC1R) , activated by _-MSH, regulates melanin synthesis and exhibits protective functions against UV-induced DNA damage, which thus inhibit melanomagenesis. Normally, _-MSH activates MC1R to suppress proinflammatory cytokines, while upregulating immunosuppressive cytokines, thus inhibiting T cell and macrophage activation. The protection of _-MSH rely on the normal physiological interaction of melanocytes with neighboring cells and extracellular matrix, mitigating surge of inflammatory factors and immune overactivation in response to stress-induced cellular damage. However, the protective effect of _-MSH in physiological condition could change as an adverse effect when in melanoma, by turning an immunologically ?hot? cancer into an immunologically ?cold? cancer which may facilitate melanoma progression. This study investigates if long-term _-MSH application alters the tumor immune microenvironment, potentially enabling tumor cell evasion from anti-tumor immunity and immune surveillance, and contributing to resistance to immune therapy.

Method & Materials

The RNA sequencing profiles and corresponding clinical information related to the MC1R gene were downloaded from TCGA database. Comprehensive pan-cancer, survival analyses and the abundance scores of immune cells were analysed by R. In a melanoma study using HGF/SF transgenic mice, long-term MC1R activation with _-MSH was used to monitor tumor number and size biweekly.

Results

The expression of the MC1R gene was found to be considerably higher in melanoma tissues compared to their corresponding normal tissues. In the cohort with low MC1R expression, a significant increase was observed in the abundance of various immune cells, including CD8+ T cells, macrophages (particularly M1), and activated dendritic cells (aDCs). Intriguingly, a higher expression level of MC1R emerged as a negative prognostic indicator for both overall survival (OS) and disease-free survival (DFS) in melanoma patients. Additionally, administration of continuous MC1R activation led to an increase in both tumor burden and tumor number in vivo.

Conclusion

MC1R high expression is linked to a weakened anti-tumor immune microenvironment, which could be a reason for poorer survival in melanoma patients. MC1R constantly activated can stimulate melanoma growth and progression. Thereby, therapeutically targeting MC1R, possibly in combination with immunotherapy, could have potential therapeutic value for melanoma.

The role of PARP13 in stress-induced LINE1 retrotransposition

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Introduction

The long interspersed nuclear element 1 (LINE1), a mobile genetic element, possesses the capacity to self-replicate and integrate into the human genome, in a process known as retrotransposition, which introduces genomic instability and promotes mutagenesis. During retrotransposition, an accumulation of cytoplasmic LINE1 RNA copies activates a Type I Interferon response, purposed for eliminating the LINE1 overexpressing cell. Cells have evolved mechanisms to counteract the presumed infection, such as employing regulators to prevent excess RNA transcript accumulation. One such regulator, the anti-viral protein PARP13, is hypothesized to degrade LINE1 transcripts. We propose that PARP13-deficient cancer cells exhibit an increase in LINE1 copies, stimulating an amplified immune response and, thus, enhanced clearance by immune cells. This study was designed to determine whether PARP13 modulates LINE1 RNA stability and to elucidate the underlying mechanisms. Additionally, we aimed to understand the general role of PARP13 in cell death regulation.

Method & Materials

To test our hypothesis, we compared LINE1 expression between PARP13-deficient and wild-type Calu-6 cells via western blots as well as qRT-PCR and assessed RNA stability through an Actinomycin D assay. We then subjected cells to chemotherapy and examined the effect on LINE1 transcription. Lastly, we conducted cell death assays using a range of chemotherapeutic drugs.

Results

Our findings reveal elevated LINE1 levels in PARP13-deficient cells, coherent with increased post-transcriptional LINE1 RNA stability. Moreover, we found slightly increased LINE1 levels upon chemotherapeutic treatment. Intriguingly, we report increased cell death resistance of PARP13-deficient cells and elevated levels of Bax transcription in wild-type cells, indicating that PARP13 plays an interesting role in apoptosis.

Conclusion

We conclude that PARP13 post-transcriptionally modulates LINE1 RNA stability and that LINE1 activity can be elevated by chemotherapeutic stressors. Furthermore, our results underscore the role of PARP13 in the regulation of cell death and make it an intriguing target in pursuit of cancer treatment.

phosphorylation of ANLN-S792 residue regulates the cytokinesis in esophageal squamous cell carcinoma cells

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Introduction

Uncontrolled proliferation is a typical characteristic of tumor cells. Cytokinesis occurs during mitosis, starting at anaphase and ending at telophase. Although the basic mechanism of cytokinesis has been established, many problems still remain unclear. Anillin (ANLN) is a mitotic protein that promotes cytokinesis by recruiting contractile ring components. However, whether the phosphorylation of ANLN is involved in the regulation of cytokinesis still needs to be further revealed. The aim of this study was to identify the phosphorylated sites of ANLN in esophageal squamous cell carcinoma (ESCC) cells and to demonstrate that cytokinesis is regulated by the phosphorylation of ANLN.

Method & Materials

ANLN phosphorylation sites in ESCC cells were identified by protein mass spectrometry. Then, ESCC cell lines stably expressing ANLN phosphorylation site mutants were constructed using lentiviral infection methods. Furthermore, a cell cycle synchronization model was constructed using thymidine, and the localization of ANLN mutants was observed through immunofluorescence. Next, the effect of ANLN phosphorylation on RhoA recruitment was analyzed by immunofluorescence. In addition, the candidate kinases for ANLN phosphorylation were identified by immunoprecipitation.

Results

the eight phosphorylation sites (S72, S182, S323, T472, S485, S553, S661 and S792) of ANLN were identified by protein mass spectrometry. Mutating these sites to non-phosphorylatable residues did not affect the contractile ring localization of ANLN, but reintroduction of ANLN wild-type but not S792A mutant rescued the localization defect of F-actin induced by endogenous ANLN depletion. The amino acid sequence analysis revealed that the S792 site was located in the RhoA binding domain of ANLN. Consistently, immunofluorescence analysis revealed that the S792A mutant but not the S792D mutant prevented RhoA recruitment at the contractile rings. Immunoprecipitation assays found that several classical mitotic kinases interact with ANLN, including PLK1, CDK1, Aurora B, and PPP1CA.

Conclusion

The S792 phosphorylation site of ANLN is located in the RhoA binding domain, which mediates the recruitment of RhoA and F-actin to the contractile rings, and may regulate the cytokinesis and malignant progression of ESCC cells.

Optimization of RAS/MAPK pathway targeting in RAS-driven Low-Grade Serous Ovarian Carcinoma

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Introduction

Low-grade serous ovarian cancer is a rare subtype of epithelial ovarian cancer, often harbouring activating mutations in the mitogen-activated protein kinase (MAPK) pathway. With no approved effective treatment, a newly developed dual panRAF/MEKi clamp inhibitor (Avutometinib) is a promising new targeted therapy. This drug is currently being tested in phase 1 & 2 clinical trials in LGSOC together with FAK inhibitors (Defactinib). Historically, it has been shown that acquired and intrinsic resistance often prevent long-term benefits of targeted therapies. Therefore, this study aims to understand panRAF/MEK inhibitor (Avutometinib) resistance mechanisms and consequently identify rational drug combinations to suppress resistance. This will be tested in parallel in mucinous ovarian cancer (MOC) cell lines, as this is also MAPK driven in most patients.

Method & Materials

The CRISPR-CAS9 loss-of-function Avutometinib resistance screen is used to identify genes that are involved in the response of LGSOC to Avutometinib. Spontaneous resistant clones of LGSOC cell lines are generated in response to Avutometinib, to identify pathways involved in resistance.

Results

Previously, spontaneous resistant clones of MOC have shown EMT features, an upregulation of NGFR and inflammatory pathways. LGSOC is not characterized by a significant EMT, however LGSOC spontaneous resistance is characterized by NGFR, JNK pathway, and SOX10 (neural crest stem cell features). Furthermore, both MOC and LGSOC are characterized by a pre-existing NGFRhigh population. Based on the genetic loss-of-function resistance screen, EP300, CCDC101, and DOHH are possible genes driving resistance in both LGSOC and MOC. To target loss of EP300 and CCDC101, combinational therapy of HDAC inhibitors and Avutometinib provides synergistic effects. DOHH leads to a decrease in EIF5A-mediated apoptosis upon Avutometinib exposure, which can be synergistically targeted by SINE analogues in combination with Avutometinib.

Conclusion

Spontaneous resistance of LGSOC to Avutometinib is characterized by neural crest stem features. Pathways that mediate acquired resistance in LGSOC and MOC towards Avutometinib are loss of histone acetylation and reduced EIF5A-mediated apoptosis. The combination of HDAC inhibitors or SINE compounds with Avutometinib provide a promising combinational therapy.

Potential novel anti-cancer drug: Implication of a rhenium-based compound in the hypoxic response

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Introduction

Cancer is a major cause of death and its incidence is increasing worldwide. Moreover, a major burden is the development of drug resistance. One characteristic of solid tumours is their hypoxic core. Hypoxia, the decrease in oxygen level, stabilises the hypoxia-inducible transcription factor (HIF), with two main isoforms HIF-1_ and HIF-2_, which plays a crucial role in cellular adaptation and regulates multiple cancer hallmarks. In 2020, a study found strong evidence of the anti-cancer potential of a rhenium(I) tricarbonyl-based compound (Re) displaying an anti-angiogenic, anti-metastatic, and tumour growth inhibition in zebrafish-human HCT116 xenografts. The current study aimed to evaluate the impact of the compound in cancer progression and especially its HIF-dependent pathway regulation.

Method & Materials

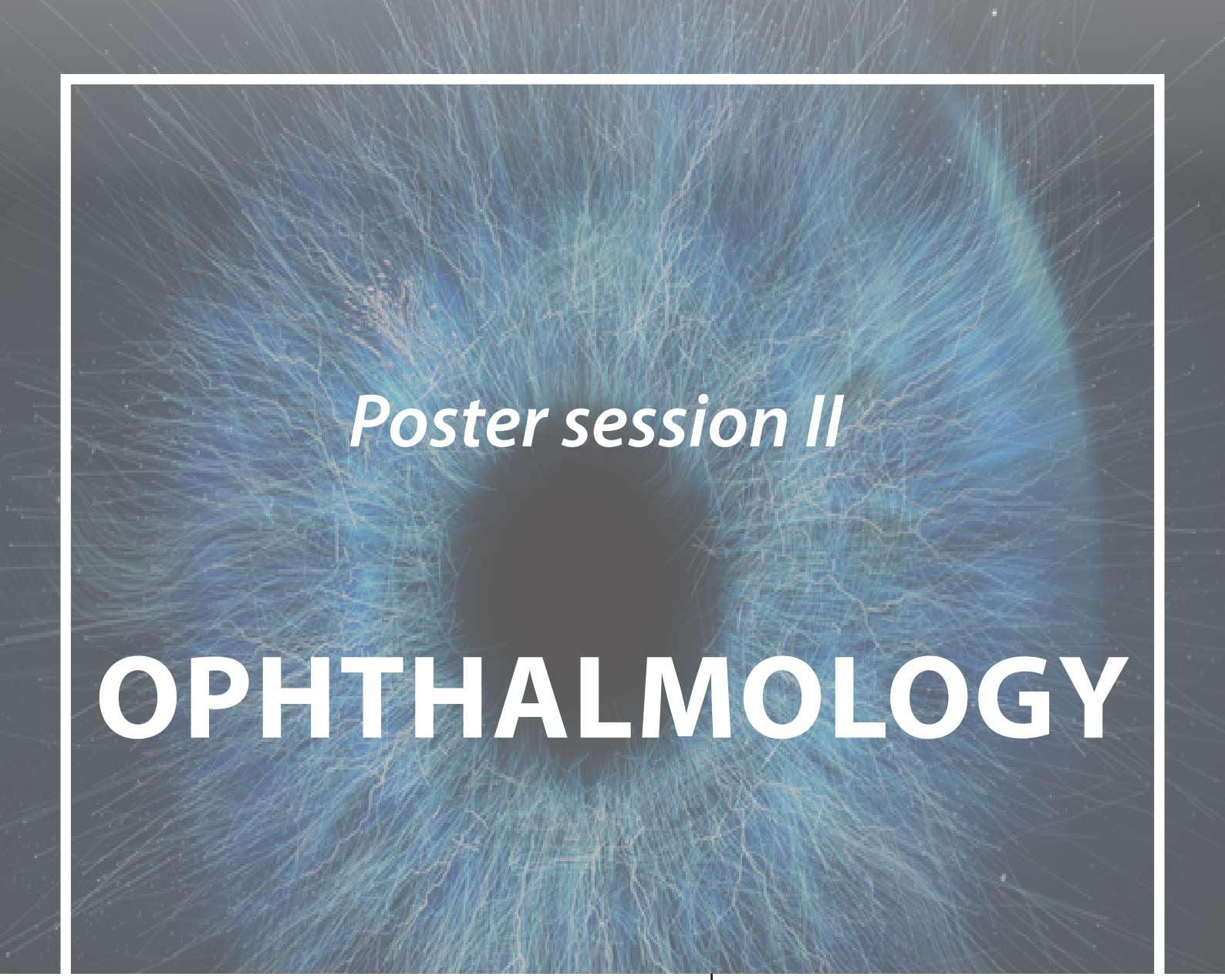
Hepatocellular and neuroblastoma cancer cell lines were treated with increasing doses of Re under normoxic (21% O2) and hypoxic (0.2% O2) conditions for 24 hours. RNA sequencing (RNA-seq) and GSEA analyses were conducted to generate a gene enrichment profile signature in treated and untreated cells. The expression of genes of interest was analysed at the mRNA and protein levels by qPCR and immunoblotting. Cell proliferation and motility were assessed using a non-invasive live-cell imaging technique. Cellular metabolism was measured using a Seahorse XF24 Analyser. Reactive oxygen species (ROS) were indirectly measured by antioxidant response element-driven luciferase reporter gene assays.

Results

Our results reveal that the compound exhibited an anti-angiogenic effect by reducing vascular endothelial growth factor (VEGF) expression under hypoxic conditions in a concentration-dependent manner. Simultaneously, cell proliferation and motility were negatively affected. Moreover, RNA-seq analysis suggests ROS generation, as reflected by modulation of mitochondrial metabolism and increased expression of antioxidant genes. Reporter gene assays and expression levels of redox-sensitive genes independently confirmed these observations. Additionally, the treatments induced morphological changes which correlate with apoptosis. Intriguingly, HIF-2_, but not HIF-1_, protein levels displayed a compound induced dose-dependent decrease. Consistently, expression levels of specific HIF-2 target genes were reduced accordingly. Lastly, our results display a compound-dependent reduction in transcriptomic cancer markers.

Conclusion

Our study demonstrates that Re exhibits anti-tumour efficacy and highlights a novel HIF-2_-dependent mechanism. These data strongly suggest its therapeutic potential as a novel treatment for hypoxic tumours.



Poster session II

OPHTHALMOLOGY

Presenters:

- Amnah Alkhawajah
- Abdulaziz Almutlaq
- Abdullah Afif Alshakhs
- Yuxiao Guo
- Sama Huseynli
- Tian Lin
- Mohamed Youssef
- Paola Danaeth Ramirez Moreno

Assessing Laser Therapy?s Impact on Ischemic Central Retinal Vein Occlusion: A Systematic Review and Analysis of Clinical Studies

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Introduction

A potentially blinding disorder known as ischemic central retinal vein occlusion (CRVO) is caused by blockage of the central retinal vein. This blockage can lead to swelling and damage to the retina, which can lead to vision loss. Many studies have evaluated the use of different treatments for ischemic ICRVO. Nevertheless, improvement and complication rates vary significantly. The objective of this systematic review was to evaluate the efficacy of laser therapy in treating ischemic CRVO compared with a control group using other treatments. The results of this assessment will help make decisions for patients and their healthcare providers.

Method & Materials

The databases of PubMed, Google Scholar, and ClinicalTrials.gov were searched using a variety of keywords, including ?ischemic central retinal vein occlusion,? ?CRVO,? ?laser,? and ?panretinal photocoagulation.? Following the extraction of data, each study?s quality was assessed using the methodological index for nonrandomized studies (MINORS) or grading of recommendations, assessment, development, and evaluation or GRADE standards. A sum of 195 abstracts were reviewed, and eventually, seven clinical trials were chosen. Of these, four were prospective studies, two were randomized control studies, and only one was a retrospective study.

Results

The assessment of potential biases in our included studies revealed that all of these studies demonstrated moderate or high quality. Two studies were selected for meta-analysis, and the results demonstrated that there was no significant difference in visual acuity (VA) outcomes between the treated group and the control group ($P = 0.17$). In the remaining five studies, laser therapy was found to be more effective at neovascular complications, with a higher rate of neovascular glaucoma (NVG), iris neovascularization (INV), neovascularization at disc (NVD), and retinal neovascularization (NVR) in the group without laser treatments.

Conclusion

This review suggests that laser therapy is effective in preventing neovascular complications such as NGV, NVI, NVD, and NVR rather than in improving VA. In addition, the combination of LPC and IVI did not improve VA, but further studies are required to confirm such finding.

Quality of Life in Dry Eye Disease (DED) Patients: King Abdul-Aziz Medical City, Riyadh, Saudi Arabia

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Introduction

Dry Eye Disease (DED) is one of a major public health concern that impairs Quality of Life (QoL). The aim of the study was to estimate the prevalence of DED, and to assess the impact of DED on patients? Eye-Related Quality of Life (ER-QoL) and Vision-Related Quality of Life (VR-QoL).

Method & Materials

An interview based survey was conducted in Ophthalmology outpatient clinics in King Abdul-Aziz Medical City, Riyadh. Saudi adults diagnosed with DED were invited to participate. The questionnaire consisted of demographic/ clinical data, and validated tools in Arabic; Ocular Surface Disease Index (OSDI) and Visual Functioning Questionnaire 25 (VFQ-25). The tools scored between 0-100; OSDI higher scores denotes poor QoL, while higher scores on VFQ-25 denotes good QoL. Wilcoxon rank sum test was used to compare OSDI and VFQ-25 scores by OSDI groups. Significance was declared using alpha less than 0.05.

Results

Out of total 401 participants, 246(61%) were females. 216(53%) had a co-morbidity, 43(10%) had an ocular co-morbidity. Duration of DED was 3.78Ò4.59 years. The overall prevalence of DED was [6.77% (95% CI; 6.16, 7.44)], higher in females [4.15% (95%CI, 3.64, 4.66)], and highest in the young age category 15-30 years [1.6% (95%CI,1.28,1.92)]. 35(8.7%) had mild DED, 56(14%) had moderate DED, and 285(71%) had severe DED. Participants who had severe DED had poor ER-QoL (p=<0.0001), as well VR-QoL (p=<0.0001). The common reported symptoms were watery eyes (71%), uncomfortable eyes in wind/dry area (70%), and blurred vision / photosensitivity (53%).

Conclusion

The DED was more prevalent in young age group and females. Watery eyes, blurred vision and photosensitivity were commonly reported symptoms. Participants with severe DED had poor ER-QoL and VR-QoL. The patients? daily activities were impacted by the severity of DED. It is essential to have DED screening, patient education, and to enhance awareness among patients.

The Progression of Myopia in school-aged children with prolonged screen time; a real-life sequel to the mandatory virtual learning

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Introduction

Myopia is the most common refractive-error, Recently, many studies have reported an extreme rise in the prevalence of myopia over the last few decades, It is thought to be influenced by hereditary and environmental factors, Extended outdoor activities have been associated with a lower incidence rate of myopia; however, a family history of myopia, and near-work activities, have been linked to myopia risk. between increased near work and restricted outdoor activities in myopic children. There are a few studies reported the effect of these risk factors on non-myopic children. This study was conducted to investigate the effects of prolonged screen-time on myopic progression among school-aged children during the COVID-19 pandemic, as well as other factors, such as home-confinement and decreased outdoor activities.

Method & Materials

A retrospective cohort study on children aged 6-12 years attending regular visits to the pediatric ophthalmology clinic was conducted in a tertiary eye hospital in Saudi Arabia. The cycloplegic refraction was determined from three visits at least six months apart; two visits before the start of the COVID-19 pandemic and one during the pandemic. Data were collected regarding myopia risk factors such as time spent at near-work and outdoor activities, devices used during virtual learning. Statistical-analysis was conducted to compare myopia progression before and during the pandemic, with a P-value of 0.05.

Results

In total, 160 eyes were studied, 18.1% of which had myopia, and 81.9% had hyperopia. Most eyes had a hyperopic-shift before the confinement; however, all eyes had a myopic-shift during the confinement. When comparing both eyes of the same patient, the more myopic or the less hyperopic eye in the same patient had significantly more myopic-shift than the other eye. Participants using tablets were found to have more myopic shifts (p=0.03) than those using personal computers (p=0.135). In addition, younger age, constricted living space, negative family history of myopia, and parents? education were positive-factors for myopic progression.

Conclusion

Myopia progression was accelerating in children during the COVID-19. Hours spent on digital screen devices at near distances is considered a significant environmental contributor to the myopic shift in children.

Mechanism of inhibition of corneal immune arms by BMP4-Smad signaling pathway

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Introduction

Corneal neovascularization (CNV) after corneal injury is directly proportional to the degree of corneal lymphangiogenesis (CL), which is driven by VEGF family. Both of them work together to form immune arms and break the immune privilege state. Studies have confirmed that BMP4 can inhibit CNV through Smad pathway, and enhancing BMP-Smad pathway can inhibit lymphatic neovascularization in vertebrates. This experiment aims to explore the effect of BMP4 Smad pathway on immune arms, To provide a theoretical basis for promoting the repair of corneal injury.

Method & Materials

Wistar rats were randomly divided into BMP4 group, suture control group, noggin group (BMP4 Smad pathway inhibitor)/noggin+BMP4 group. Rat corneal suture models were established at 3, 5 and 7 days. The corneas of the four groups were observed by slit lamp microscope, he staining, transmission electron microscope and PCR.BMP4 inhibits corneal immune double arm formation through Smad signaling pathway.

Results

1. slit lamp microscope: the length and area of CNV were noggin group>noggin group+bmp4 group Ú suture control group>bmp4 group, and increased with the modeling days. These results indicate that BMP4 can inhibit the formation of CMV, while noggin can increase the formation of CNV and counteract the effect of BMP4. 2. He section: in the suture control group, the corneal stromal structure was disordered, and the number of neovascularization and lymphatic lumen was large; In BMP4 group, corneal epithelial structure was relatively complete, the degree of edema was mild, and the number of lumen and inflammatory cells decreased. These results indicate that BMP4 can promote corneal healing and inhibit corneal immune function. 3. transmission electron microscope: CNV and CI exist in corneal stromal layer after suture modeling, and CNV grows faster. CNV has a complete basement membrane, the wall of the tube is mostly composed of multi-layered endothelial cells, and red blood cells can be seen in the lumen. The nuclei of CL cells protruded into the lumen, the basement membrane was incomplete, the lumen was large and the wall was thin. After BMP4 treatment, the proliferation and migration of vascular and lymphatic endothelial cells were improved. These results indicate that BMP4 has an inhibitory effect on both immune arms. 4. PCR detection: the expression of LYVE-1, VEGFR3 and VEGF-C in noggin group>noggin+bmp4 group Ú suture group>bmp4 group; The expression of Smad1/4/5 and BMP4 was BMP4 group>suture group Ú noggin+BMP4 group>noggin group. The inhibitory effect of BMP4 Smad signaling pathway on corneal immune function was verified at the molecular level.

Conclusion

BMP4 inhibits corneal immune two-arm formation through the Smad signaling pathway.

The Prevalence of Refractive errors and identifying factors associated with myopia among medical students at Azerbaijan Medical University

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Introduction

The second most common cause of blindness in the world is refractive error, and it is the most common visual impairment among students. The medical curriculum includes a lot of long-term, focused work, such as writing, reading, and utilising a microscope. Excessive use of mobile devices, computers, video games, reading in dim light, and spending more time indoors than outside are also aggravating factors that contribute to refractive errors. The purpose of the study is to examine the prevalence and contributing variables of visual impairments among undergraduate medical students.

Method & Materials

200 medical students in their first through final years were questioned for the study using a self-evaluation questionnaire between October and December 2023. Non-cycloplegic auto-refraction was used to determine refractive error. Refractive errors were measured for each student using an auto-refractometer. An ophthalmologist examined the students that were randomly chosen. The questionnaire, created and distributed through a Google Form.com account, IBM SPSS was employed for data analysis.

Results

Refractive error was observed in 141 students (70.5%). Simple myopia was the most common form (45.5%), followed by myopia with astigmatism (12.5%), only astigmatism (5.5%), and simple hyperopia (5%) followed by hyperopia and astigmatism (2%).Myopia, with or without astigmatism, was identified as the most prevalent type of refractive error among students, accounting for 58% of students. The most common kind of myopia was low myopia at 68.9%, followed by moderate at 29.3%, and severe myopia at 1.8%. Myopia was substantially more common in people who typically did not exercise their eyes, continuous studied without breaks, or slept after 00:00. The prevalence of myopia was higher among students with myopic parents (62.8%) than among those without myopic parents (36.2%). The prevalence of myopia with or without astigmatism was higher in female medical students than in male medical students (59.6% vs. 53.7%). Spectacles were the most commonly used visual correction device, with 44.7% of myopic students wearing glasses since middle school.

Conclusion

In this study, we focused on refractive errors among students of Azerbaijan Medical University, particularly the high prevalence of myopia and the various factors contributing to it, including genetic and environmental influences.

Clinician-driven Automated Label Noise Cleaning for Multimodal Retinal Images

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Introduction

The ophthalmic artificial intelligence has developed rapidly recently, while the accuracy of image labels directly impacts the model?s performance. In this study, we aimed to comprehensively assess the efficacy and potential risks of automated multi-iteration label cleaning in retinal images and its effect on the performance of multi-categories classification.

Method & Materials

Firstly, two datasets with 8 categories of Color Fundus Photographs and 7 categories of Optical Coherence Tomography were constructed. Subsequently, label noise was deliberately injected randomly and proportionally to establish multiple noisy gradients ranging from 0% to 70%. Then, Cleanlab, an open-source framework, was utilized to detect and rectify label errors without manual confirmation in multiple iteration. A foundation model, Retfound, was trained using the datasets before and after cleaning separately and their performances were compared.

Results

Repeated data cleaning improved the label accuracies by 3.4% to 62.9% and dataset quality scores by 5.1% to 74.4%, except in the original noise-free datasets. Most (86.6% to 97.5%) issue labels can be correctly identified and modified. Only few issue images were missed (0.5% to 2.8%) or mistakenly modified to incorrect categories (0.4% to 10.6%). Furthermore, label cleaning alone significantly improves classification accuracies by 0.9% to 37.7%. However, over-cleaning decreased the label accuracy in the datasets free of or with low proportion of noise. The dataset quality score has excellent correlation with label accuracy and the data cleaning process guided by dataset quality prevent the issue of over-cleaning.

Conclusion

Simple implementation of Cleanlab in fundus image datasets is a highly automated and effective method for rectifying label errors, increasing dataset quality and enhancing model performance of classification. Dataset quality can be used to prevent the risk of over-cleaning.

Efficacy of Repeated Low-Level Red Light (RLRL) therapy on myopia outcomes in children: A systematic review and meta-analysis

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Introduction

Myopia is the most prevalent form of refractive error that has a major negative impact on visual function and causes blurring of vision. We aimed to determine if Repeated Low-Level Red Light (RLRL) treatment is beneficial in treating childhood myopia in terms of axial length (AL), spherical equivalent refraction (SER), and sub foveal choroidal thickness (SFCT).

Method & Materials

This systematic review was performed on RLRL for treatment of myopia in children compared to single vision spectacles (SVS). We employed the search strategy with key terms myopia and low-level light therapy then we searched PubMed, Scopus, Cochrane, and Web of Science databases. The mean differences (MD) were used to evaluate the treatment effects. Heterogeneity was quantified using I2 statistics and explored by sensitivity analysis.

Results

Five randomized controlled trials (RCTs) were included in our meta-analysis with a total of 833 patients, 407 in treatment group and 426 in control group. At a 3 month follow up period, pooled studies show a statistical difference in AL between RLRL and SVS group (MD = -0.16; 95% CI [-0.19, -0.12], SER (MD = 0.33; 95% CI [0.27, 0.38]), and SFCT (MD = 43.65; 95% CI [23.72, 45.58]). At a 6 month follow up period, pooled studies show a statistical difference in AL between RLRL and SVS group (MD = -0.21; 95% CI [-0.28, -0.15]), SER (MD = 0.46; 95% CI [0.26, 0.65]), and SFCT (MD = 25.07; 95% CI [18.18, 31.95]). At a 12 month follow up period, pooled studies show a statistical difference in AL between RLRL and SVS group (MD = -0.31; 95% CI [-0.42, -0.19]) and SER (MD = 0.63; 95% CI [0.52, 0.73]).

Conclusion

This is the first systematic review and meta-analysis investigating evidence supporting the efficacy of 650 nm RLRL for myopia control in the short term of 3, 6, and 12 months follow up. The present review revealed the clinical significance of RLRL as a new alternative treatment for myopia control with good user acceptability and no documented functional or structural damage. However, the effect of long-term RLRL treatment and the rebound effect after cessation require further investigation.

Determination of local and systemic sensitization to aeroallergens in patients with Allergic Conjunctivitis

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Introduction

Allergic conjunctivitis (AC) is known as a chronic IgE-mediated inflammatory disease of the ocular surface, with a global prevalence of approximately 30-40%. The gold standard for diagnosis is Skin Prick Tests (SPT) as well as total and specific IgE serology, however SPT results are not always positive despite the presence of classical ocular symptoms, so in vitro testing to determine sensitization in other biologically representative samples of the affected tissues has been studied.

Method & Materials

21 individuals with AC have been recruited and serum, tear and nasal fluid were collected. Total IgE (tIgE) concentration of serum, tear and nasal fluid samples were measured with Fluoro-enzyme-immunoassay while specific IgE (sIgE) concentration of the same three samples were measured with Immunoblot for the 29 most prevalent allergens in our country.

Results

There were significant differences in tIgE mean concentration between serum, tear and nasal fluid samples. sIgE was measured in 12 of the 21 individuals. The percentage of detected sIgE was 91.6% regardless the type of sample. In most patients, there are differences in allergen sensitization profiles in serum, tear and nasal fluid. The allergen sensitization prevalence varies from sample to sample, such as Salsola kali in serum (66.7%), Chenopodium album in tear (41.67%), and Alternaria alternata, Ligustrum vulgare and Phleum pratense in nasal fluid (33.3% each).

Conclusion

It is possible to detect tIgE and also to determine the pattern of sensitization to allergens in other biological samples such as tears and nasal fluid. All individuals were polysensitized, showing differences in local and systemic sensitization with a higher prevalence in seasonal allergens. Further research is needed in this type of studies where the use of in vitro methods with other biological samples could be useful as diagnostic aids as well as a new open door in AC management.

Poster session II

PATHOLOGY

Presenters:

- Alejandra Hernández Villanueva
- Dev Patel
- Shaurya Sharma
- Wanqi Huang
- Laura Thessa Antonia Otten
- Seyedehsepideh Ghadirnezhadshiadeh

Role of fibroblast growth factor 15 in cardiovascular and liver disease in an experimental model of gallstone disease

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Introduction

Gallstone disease (GSD) is a multifactorial disease highly prevalent, and its cardiovascular and hepatic consequences are still poorly understood. Previously, preclinical studies have shown increased circulating levels of fibroblast growth factor 15 (FGF15) in GSD. To date, no preclinical studies have investigated the mechanism underlying GSD with cardiovascular and liver disease. Aim: To evaluate whether FGF15 levels correlate with myocardial dysfunction and hypertrophy, vascular remodeling and liver disease in an experimental model of GSD.

Method & Materials

All experiments were conducted according to the Bioethics Committee of Universidad de Chile (CICUA-CQyF2021-34). Eight-week-old female and male C57/BL6N mice were assigned into two groups: Chow diet (n=9) and lithogenic diet (GSD; n=7) to promote GSD. After 9 months, an echocardiography (ECO) was performed. After sacrifice, hearts, livers and plasma were collected. We used an in vitro model of neonatal rat ventricular myocytes (NRVM) to study the heart-specific mechanism of FGF15. Mann-Whitney test was used for statistical analysis.

Results

GSD decreased ejection fraction (83.8 Ò 4.7% vs 93.0 Ò 1.2%, p<0.001), increased cardiomyocyte cross-sectional area (525 Ò 55 vs 372 Ò 101 Êm, p<0.05), increased coronary artery thickness (14.0 Ò 1.9 vs 11.5 Ò 1.0 Êm, p<0.05), increased cardiac _-MHC mRNA levels (4.7 Ò 2.9 vs 1.2 Ò 0.6, p<0.05) and tended to increase FGF15 serum levels (64 Ò 29 vs 26 Ò 7 ng/ml, p=0.11). Interestingly, FGF15-treated NRVM increased hypertrophy-related genes significantly. Moreover, GSD increased liver weight (32 Ò 2 vs 76 Ò 12 mg/g, p<0.01), hepatic triglycerides (1687 Ò 371 vs 2909 Ò 216 ng/nmol, p<0.01) compared to controls. Liver hematoxylin-eosin staining showed diffuse inflammatory infiltrate and steatosis in GSD. NAFLD activity score (NAS) that evaluates ballooning, steatosis, inflammation and fibrosis, also increased in GSD (0.2 Ò 0.4 vs 11 Ò 1, p<0.01).

Conclusion

GSD alters cardiac function and promotes cardiac hypertrophy and vascular remodeling. Moreover, GSD promotes steatohepatitis. However, more research is required to analyze if FGF15 is involved in cardiovascular and liver function during GSD development.

Investigating the effect of nano curcumin on lung tissue oxidant toxicity in subacute toxicity with paraquat compared to curcumin

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Introduction

Paraquat are one of the most common herbicides used in agriculture, which can cause severe poisoning in humans and animals. The most important target tissue of paraquat is the lung. In this study, the effect of curcumin and nano curcumin on lung tissue oxidant toxicity in subacute toxicity with paraquat was compared.

Method & Materials

36 Wistar albino male rats 8-week-old were randomly divided into 6 groups (n=6) (one healthy control group, the second group poisoned with paraquat at a dose of 5mg/kg/day, the third group: treatment treated with curcumin at the rate of 30 mg/kg/day, the fourth group treated with nano curcumin at the rate of 30 mg/kg/day, the fifth group: poisoned with paraquat treated with curcumin, the sixth group poisoned with paraquat treated with nano curcumin.) This treatment It continued for 7 days. At the end of the treatment period, the lung tissue of all mice was collected. Total antioxidant capacity (TAC), lipid peroxidation (LPO), thiol groups (SH) of hydroxyproline, were evaluated in lung tissue by spectrophotometry and ELISA.

Results

In the groups poisoned with paraquat compared to the healthy control group, lipid peroxidation and hydroxyproline increased and total antioxidant capacity decreased significantly. In the groups treated with curcumin and nanocurcumin compared to the group poisoned with paraquat, lipid peroxidation, hydroxyproline and as a result lung tissue damage significantly decreased, showing that the simultaneous use of nanocurcumin and paraquat compared to the group of curcumin and paraquat, this decrease in damage was greater.

Conclusion

Nanocurcumin and curcumin can improve oxidative stress and lung tissue damage caused by paraquat herbicide.

Diagnostic Accuracy of Fine-needle Aspiration (FNA) in Comparison to Core Needle Biopsy (CNB) in Salivary Gland Lesion - A Meta-analysis

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Introduction

Salivary gland tumors comprise 6% of total head and neck tumors. Parotid, being the major gland involved forms 80% of the cases while submandibular gland tumors make up 10-15% of the cases. However, the histopathology and cytology of these tumors are complex due to diverse patterns of growth and morphology; making the diagnosis a challenge. Despite being widely used as a preoperative diagnostic tool, Fine Needle Aspiration yields results that are less than satisfactory, are time-consuming, and require local anesthesia. To overcome this, core needle biopsy using (Ultrasound) US guidance is used.

Method & Materials

A detailed search through the medical literature was done using PubMed, Google Scholar, and Cochrane Library databases for the collection of relevant data. A total of 16 RCTs with a total of 2068 patients were selected. Meta-analysis was done using the two writers who independently assessed the caliber of each included study. We have used the following statistical software for the analysis of the data and result creation;1.Rev-Man (Review Manager, version5.3),2.SPSS (Statistical Package for the Social Sciences, version 20), and 3.Excel in Stata 14.

Results

FNAC as a tool for preoperative diagnosis has a sensitivity of 93%, a specificity of 98.5%, and a positive predictive value of 0.972 in comparison to Core Needle Biopsy (CNB) in the diagnosis and intervention regarding Salivary gland tumours.

Conclusion

The results suggest Core Needle Biposy (CNB) as a superior modality in the preoperative diagnosis of salivary gland tumors as compared to FNAC. However, FNAC can be used as a preliminary step in the process of diagnosis. Nevertheless, CNB overcomes the shortcomings of FNAC, making it a better method.

Development of a scoring system to distinguish between benign and malignant effusions using a combination of biomarkers

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Co-authors: Gupta S. (Subodh)

Introduction

Effusions are abnormal fluid collections in body cavities which can be transudates or exudates. Malignant effusions are associated with spread of cancers indicating an advanced stage, impaired quality of life and shortened survival time. Although a variety of cytological and biochemical markers are in use to distinguish between benign and malignant effusions, they are limited by low sensitivity and specificity. The aim of our study was to develop a simple scoring system using a combination of routinely used biomarkers in blood and effusion fluids which will be useful to quickly select a therapeutic regime or predict prognosis.

Method & Materials

This cross-sectional laboratory-based diagnostic study was conducted at a tertiary care hospital. A total of 150 samples of pleural, peritoneal and pericardial effusions received in the Department of Pathology were worked up. Anonymized patient data was entered in MSExcel and analyzed using ?R software?. Logistic regression was done to identify factors favoring malignant effusions. These factors were tested for collinearity using variance inflation factors (VIF) and were adjusted to bring the VIF below 2.0 for all factors included in the model. Receiver operating characteristic curves were plotted for each factor thus identified and the best cut-off point was identified by Youden index. A scoring system was built for the individual factors to determine highest area under the curve.

Results

The scoring system for detection of malignant effusion included presence of malignant cells in effusion (5 points), neutrophil-lymphocyte ratio in effusion > 0.05 (4 points), serum albumin > 2.985 (4 points), effusion adenosine deaminase > 6.135 (3 points), and serum LDH > 435 (2 points). With a cut-off > 9 points, the area under the curve, specificity and sensitivity for identifying malignant effusion were 0.912 (CI:0.887-0.936), 71.9%, and 95.5% respectively.

Conclusion

This scoring system was developed from a retrospective study and exhibits good diagnostic performance with more than 95% sensitivity and more than 75% specificity. However, this needs to be validated on an independent sample. Following validation, it would serve as an important tool for suspecting malignant effusions.

CD3+/CD8+ Lymphocyte Intensity Score as Prognostic Predictor of Gastric Adenocarcinoma

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Introduction

Gastric adenocarcinoma is an aggressive cancer with poor prognosis. The role of tumor infiltrating lymphocytes as an anti-tumor response has become increasingly known. The Immunoscore System (IS) is a method based on the quantification of CD8+ and CD3+ T-cell densities. It demonstrates the prevalence of immune lymphocytic infiltrates in the center and margins of the tumor. In this study, we have used IS to evaluate the immune status and prognosis of patients with gastric adenocarcinoma.

Method & Materials

This retrospective study consisted of fifty histopathological samples of gastrectomies. T-cell densities in the center and invasive margins of the tumor were quantified by performing immunohistochemistry with CD3+ and CD8+ antibody markers. Ratio of CD3+/CD8+ was obtained and intensity score was calculated, which was correlated with several clinicopathological characteristics and survival time of patients.

Results

Out of 50 patients, 19 patients had an IS of 0&1, 15 had an IS of 2, and 16 had an IS of 3&4 (Where IS of 0 was associated with low lymphocyte density and IS of 4 was associated with high lymphocyte density). 20 patients had succumbed to death. An overall median survival time of 7 months was obtained amongst the surviving. A statistically significant co-relation between Immunoscore and histopathological characteristics of tumor and survival time was not obtained. This could be attributed to the higher stages of disease in our center and limited sample size. However, it was observed that patients with an IS of 3 and 4 had a higher survival time than patients with lower IS.

Conclusion

IS demonstrates prevalence of lymphocytic infiltrates in the tumor, which directly correlates with prognosis and survival. With a larger cohort study, more significance of IS in gastric cancers can be brought out. Fine tuning of the manual method devised in this study might prove to be a cost-effective method for assessment of tumor immune status in other organs and initial diagnostic biopsies of cancers, which could help in planning neoadjuvant therapies. The adjunct practice of immunoscoring is set to play a significant role in the context of individualized immune therapy, in the future.

Neutrophil Extracellular Trap Formation in Kidney Donors

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Introduction

Chronic kidney disease (CKD) affects ~10% of people, and left untreated, progresses to end-stage renal disease (ESRD), which carries high mortality rates despite dialysis. Kidney transplantation offers better outcomes, but only ~10% of patients have access to donor kidneys due to shortages. Neutrophil extracellular traps (NETs), structures made of DNA-complexes and proteins released by neutrophils, contribute to inflammation and thrombosis. NETs may worsen graft injury, leading to loss of graft function. Investigating NETs in kidneys can thus provide insights into the mechanisms underlying kidney injury; and into strategies to improve kidney quality, reduce graft failure, and rehabilitate otherwise discarded kidneys .

Method & Materials

NET formation, platelet infiltration, as well as endothelial activation and integrity in donor kidneys will be evaluated using immunohistochemistry (IHC) and immunofluorescence (IF). Analysis of perfusate and plasma will include ELISAs to assess local and systemic circulating NETs, and endothelial and platelet activation. NET formation and NET-related mRNA expression after neutrophil stimulation with PMA, TNF-α, C5a, and platelets will be investigated in-vitro through analyses of cell-free DNA in the supernatant, IHC, and qRT-PCR.

Results

Of the 13 biopsies, 2 had a Kidney Donor Profile Index (KDPI) between 35-59, 6 between 60-84, and 5 >85. A scoring method for pre-implantation biopsies was developed according to modified Banff criteria and demonstrated a positive correlation with KDPI. A preliminary IHC/IF experiment showed presence of NET in 33% of perfused kidney biopsies, specifically in the biopsy with the highest KDPI. C5a stimulation alone was inadequate for inducing NET formation in-vitro.

Conclusion

Following preliminary data, increased NET formation is expected in kidneys with high KDPI compared to those with low KDPI. However, the results are not yet sufficient to establish a direct correlation between KDPI and NET formation. Additionally, endothelial and platelet activation still need to be evaluated in all samples. Further investigation into kidney biopsies, perfusate, plasma, and in-vitro neutrophil stimulation can reveal whether a connection between NET formation and platelet and endothelial activation exists. Summarised, the analysis of NET formation in kidneys with varying KDPI may provide insights into the factors affecting kidney quality and the success of transplantation.

Electric field promotes dermal fibroblast transdifferentiation through activation of RhoA/ROCK1 pathway

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Introduction

Endogenous electric field (EF) is an important regulatory signal in wound healing microenvironment, which can accelerate wound healing by promoting the directional migration of keratinocytes. However, the significance of EF on early wound contraction where transdifferentiation of dermal fibroblasts into myofibroblasts plays an important role remains unknown. So we conducted this study to reveal the mechanism underlying early wound contraction and verify our hypothesis that EF promoted wound early contraction by promoting the transdifferentiation of dermal fibroblasts into myofibroblasts.

Method & Materials

A model of EF treatment in vitro was established, where cells were randomly divided into control and electrified groups. The changes of protein expression and distribution were detected under different conditions by Western Blot and immunofluorescence staining, along with Zeiss imaging system observing the response of cells.

Results

It was found that after applying 200mv/mm electric field for 3 hours, the fibroblasts were obviously arranged vertically and moved toward the anode at a faster speed, which proved that our electrification model worked successfully. Then Western Blot results showed that the expression of myofibroblast transdifferentiation marker protein (α-SMA) and collagens (Col-1 and Col-3) increased in a time-dependent manner under 200mv/mm EF for 1 h, 2 h and 3 h, so we speculated that EF promoted the transdifferentiation of fibroblasts into myofibroblasts. In addition, we also found that the expression of RhoA and ROCK1 increased in a time-dependent manner under EF, which was consistent with the increase of α-SMA, Col-1 and Col-3, so we supposed that the EF may promote the transdifferentiation of fibroblasts to myofibroblasts by activating RhoA/ROCK1 pathway. To test our hypothesis, we used RhoA inhibitor Y27632 to treat fibroblasts, and as our expectations, the use of RhoA inhibitors led to a decrease in the transdifferentiation of fibroblasts to myofibroblasts despite the addition of EF.

Conclusion

In general, our study found that EF promoted dermal fibroblast transdifferentiation via activating RhoA/ROCK1 pathway, offering an alternative explanation for how EF might speed up wound closure.

Poster session II

PHARMACOLOGY

Presenters:

- Ghazal Bagheri
- Rushduddin Al Jufri Bin Roosli
- Roya Kazemi
- Mehdi Kordjazy
- Nasim Sadat Saderi
- Bruno Terada
- Cassidy Wijmans

Machine learning approaches in predicting herbal compounds activity for atrial fibrillation management

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Introduction

Atrial fibrillation (AF), a prevalent cardiac arrhythmia, disrupts heart rhythm, leading to severe complications such as strokes. Targeting ion channels, specifically the Nav1.5 subtype, emerges as a promising avenue to restore normal heart function. Despite advancements, current AF treatments have limitations. A novel class, atrial-selective sodium channel blockers (ASNCBs), shows promising effects by selectively inhibiting atrial sodium channels, suppressing AF without affecting ventricular channels. The aim of this study is to Integrate machine learning with herbal compound exploration to offer innovative AF treatments.

Method & Materials

A dataset of 3950 molecules from Chembl and BindingDB databases were used in this study. Data were categorized based on pIC50 values into four classes: inactive (pIC50 < 6), intermediate (6<pIC50 < 7), active (7<pIC50 < 8), and potent (pIC50 > 8). Expanding our analysis, we predicted activity classes for herbal compounds: curcumin, crocin, lappaconitine, salvianolic acid B, rosemary, and Camellia sinensis. Padel software generated molecular fingerprints for machine learning classification, employing CatBoost and Optuna for accurate predictions. DataWarrior facilitated cliff analysis, revealing structural relationships between these herbal compounds and known molecules. Integration of structure-activity similarity (SAS) maps visualized molecular features alongside predicted activity classes.

Results

Our model showed a remarkable Matthews Correlation Coefficient (MCC) of 0.95 on the training set, indicating high performance in learning from the data. When evaluated on previous unseen data, the model maintained a strong MCC of 0.91, emphasizing its ability to generalize well to new instances. The predicted activity classes for the herbal compounds were aligned with established literature: Curcumin and Crocin were categorized as active, Lappaconitine as potent, Salvianolic acid B as intermediate, while Rosemary and Camellia sinensis were categorized as inactive. Moreover, our cliff analysis unveiled crucial structural insights, delineating similarities and differences between these herbal compounds and known molecules across distinct activity groups.

Conclusion

Our model accurately predicted activity classes for herbal compounds targeting the Nav1.5 channel. These compounds demonstrate potential in managing atrial fibrillation. This work marks a significant step toward treatments for atrial fibrillation, emphasizing on these compounds in future research and clinical applications.

Synergistic nephroprotective effects of Terminalia chebula and Annona muricata in mitigating renal toxicity in zebrafish

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Introduction

Annona muricata (AM) and Terminalia chebula (TC), two medicinal plants known for their diverse pharmacological properties have individually demonstrated promising health benefits but the potential synergies between their bioactive compounds, especially in the context of nephroprotection, remain an understudied area. The research was prompted by the rising concern over nephrotoxicity and the need for natural compounds with potential protective properties. The objective of the study was to evaluate the combined impacts of TC and AM extracts on kidney toxicity induced in zebrafish.

Method & Materials

The method involved exposing zebrafish to gentamicin, followed by the administration of either vehicle, TC, AM, or a combination of both extracts. Renal function parameters and histological analyses were employed to assess the protective effects.

Results

Results demonstrated a significant reduction in nephrotoxicity markers in zebrafish treated with the combined extracts compared to individual treatments or the control group. TC and AM exhibited synergistic effects in mitigating kidney damage, as evidenced by improved renal function and reduced histopathological alterations associated with nephrotoxicity.

Conclusion

In conclusion, the study highlights the synergistic nephroprotective potential of TC and AM in alleviating kidney toxicity in zebrafish. These findings underscore the significance of exploring natural compounds for their combined therapeutic effects, providing valuable insights for the development of potential interventions against nephrotoxicity. Further research is warranted to elucidate the underlying mechanisms and validate the translational relevance of these findings in higher vertebrates, including humans.

In vivo antidiabetetic effects of marrubium parviflorum L. extract on streptozotocin-induced diabetic mice

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Introduction

One of the largest worldwide epidemics, diabetes is currently regarded as a global public health concern. The use of herbal remedies is becoming more widespread. The genus Marrubium of the Lamiaceae family includes about 40 species and many of them have been used in traditional medicine to treat various diseases. Aerial parts of the plant include flavonoids, phenylethanoid glycosides, and phenylpropanoids. The aim of this study is to investigate the anti-diabetic effect of M. parviflorume on Streptozocin-diabetic male mice.

Method & Materials

Methanolic extract of the plant was extracted by Soxhlet method. Forty male Syrian mice were divided into 5 equal groups including; healthy control group, diabetic control group, healthy control group receiving the extract with a dose of 50 mg/kg, and diabetic group receiving extract with a dose of 50 mg/kg. DPPH test and Malondialdehyde (MDA) measurement were done to investigate the anti-oxidant effect of the extract. To induce diabetes, a single dose of 150 mg/kg streptozocin was injected. Then, daily extract administration followed for 21 days. Before the induction of diabetes and then every three days, blood sugar, and insulin concentration of the animals were measured by ELISA method, and two days before surgery, (oral glucose tolerance test) OGTT was performed. Moreover, Histopathological changes of liver samples was done to investigate the extracts effect on liver cells.

Results

The obtained IC50 from DPPH test on methanol extract of plant was 29.74 micro/ml. Also, a reduction in the amount of serum malondialdehyde after extract administration was observed ($P<0.05$) which shows the anti-oxidant ability of the extract. Moreover, administration of the extract resulted in lowering the blood sugar of diabetic mice and improvement in oral glucose tolerance (p-value<0.001). The hepatoprotective effects of the extract are demonstrated by an improvement in the structure of the liver tissues, and a decrease in dilation of central liver vein and expansion of liver sinusoidal area.

Conclusion

Due to the high prevalence of diabetes and a growing interest of patients to use herbal medicines, searching for new plants as therapeutic agents is important. Based on our analyzes, methanolic extract of M.parviflorum shows promising anti-diabetic effects which could be attributed to its antioxidant properties.

evidence for the involvement of nitric oxide in cholestasis-induced itch-associated response in mice

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Introduction

Cholestasis is a major systemic disorder that is associated with distressing pruritus. The pathogenesis of cholestasis-induced itch is not clear. Nitric oxide (NO) is a signaling molecule that is assumed to be involved in pruritus generation. Regarding the NO overproduction in cholestatic liver disease, we aimed to investigate the involvement of NO and the effectiveness of nitric oxide synthase (NOS) enzyme inhibitors in pruritus-associated behaviors due to cholestasis in mice.

Method & Materials

male mice were used during this study. The itch-associated response due to cholestasis was evaluated on days 0, 5, and 7 of the operation procedure, for the assessment of the utmost pruritus-induction effect of cholestasis. For bile duct ligation (BDL) the bile duct was identified and ligated in two places and sectioned between the ligatures. Scratching behavior was evaluated by measuring the number of bouts during 60 minutes after the procedures or injections. To determine the NO levels in serum, we measured nitrite levels as the NO end product in another group of animals by a colorimetric assay.

Results

Bile duct ligation in mice elicited significant scratching on the fifth and seventh day after the procedure ($P<0.05$ and $P<0.001$), but not on the day of surgery ($P>0.05$). This cholestasis-induced scratching was inhibited by intraperitoneal treatment of mice with non-selective NOS inhibitor L-NAME (3 mg/kg) ($P<0.001$) and iNOS inhibitor aminoguanidine (100 mg/kg) ($P<0.01$). The inhibitory effect of L-NAME and aminoguanidine was reversed by pretreatment with L-arginine (100 mg/kg) ($P<0.01$). On 7th day, serum NOx level in BDL group was significantly higher than control animals both in serum ($P<0.001$) and skin ($P<0.01$). L-NAME and AG significantly reversed the serum and cutaneous nitrite level elevation that had occurred after BDL ($P<0.01$ and $P<0.05$).

Conclusion

We have, for the first time, shown that BDL, as a model of acute cholestasis in rodents, by activating the NOS enzymes, especially iNOS, induces NO over-production which practically mediates itch sensation. Finally, we introduce NO and NOS might be possible targets for antipruritic agents for cholestasis-induced itch. Further studies on the role of NO and other mediators in cholestasis in experimental and clinical settings are valuable.

Evaluation of Gabapentin supplementation as an adjunct to standard (anticholinergic) treatment for stone patients after double-J stent placement

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Introduction

Various urological procedures are frequently performed using ureteral stents today. After ureteral stent implantation, patients experience multiple symptoms. The present study investigated the additive effect of gabapentin on controlling irritative symptoms after double-J stent implantation in ureteral stone patients.

Method & Materials

This research was conducted as a randomized clinical trial between 2020 and 2022 at Imam Reza Hospital, Mashhad. Adult patients who underwent ureteroscopy with a unilateral ureteral stone and were implanted with a double-J stent were included in the study. During this study, 220 people were examined in two treatment and control groups. The treatment group was treated with gabapentin 200 mg daily and Solifenacin 10 mg daily. The control group was treated with Solifenacin 10 mg daily and a placebo. All patients were examined two weeks after the surgical procedure regarding stent-related symptoms using the Persian version of the Ureteral Stent Symptom Questionnaire (USSQ).

Results

The two groups were not significantly different regarding gender distribution and average age. The results show that the total score of the USSQ questionnaire in the treatment and control groups was 70.75Ò11.35 and 84.48Ò16.54, respectively, significantly lower in the treatment group. Furthermore, the results showed that the scores of urinary symptoms index, pain symptom index, general health index, work performance index, and other problems in patients in the treatment group improved significantly compared to the control group.

Conclusion

Despite its tolerable side effects and effective use in treating pain and general health indicators, gabapentin is an effective drug when used following ureteral stent implantation. Its combination with solifenacin can manage patients well.

Unveiling the Impact of Opioid-Free Postoperative Regimens in Ureteroscopy: A Comprehensive Systematic Review and Meta-Analysis

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Introduction

Ureteroscopy (URS) and retrograde intrarenal surgery (RIRS) are minimally invasive urologic procedures that are commonly used to treat kidney stones. However, they often result in significant postoperative pain. Historically, like in many other medical procedures, patients undergoing these surgeries have predominantly been managed with opioids. This practice has contributed to the escalating global complications associated with these drugs, including abuse and addiction. As a result, over the recent years, many healthcare centers have made efforts to minimize opioid use, opting instead for safer alternative medications. In this study, we aim to compare the efficacy of both opioid and opioid-free pain management regimens following URS or RIRS procedures.

Method & Materials

A systematic search was conducted in MEDLINE, Embase, Scopus, Cochrane, LILACS, and Google Scholar. We included studies that compared opioid-based and opioid-free postoperative care for managing pain in patients who underwent URS or RIRS for lithotripsy. Our primary outcome of interest was the frequency of postoperative emergency department (ED) visits. Secondary outcomes included pain-related phone calls, postoperative unexpected encounters, the need for opioids at discharge, and patients with opioid refills.

Results

We retrieved 10 articles, encompassing 6,786 patients in the opioid group and 5,276 patients in the opioid-free group. Overall, our findings lean towards favoring the opioid-free regimen, revealing notable differences between the groups. Opioid-free regimen was associated with less ED visits (OR 0.67; 95% CI 0.58, 0.77; p=0.00001; I2=0%) and required less opioids at discharge (OR 0.11; 95% CI 0.02, 0.64; p=0.01; I2=89%).

Conclusion

Our meta-analysis suggests that an opioid-free regimen outperforms the use of opioids after URS or RIRS. It consistently demonstrates statistically superior results in terms of pain management, while it also effectively reduces the risks associated with opioid use for these patients, particularly concerning opioid abuse and dependence.

Precision-cut placenta slices as an ex vivo model for placental toxicity after maternal drug exposure: a viability study

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Introduction

To study fetal drug exposure after maternal drug intake, several in vivo, ex vivo and in vitro models have been developed. These all have their own limitations, and mostly limited focus on placental toxicity. One of the new approaches to examine the effect of chronic drug exposure on placental tissue is precision-cut slicing (PCS) technique. The aim of this study is to provide insights on the viability of precision-cut placental slices.

Method & Materials

Small strips of both the fetal and maternal side of eight placentas were excised and sliced using a Krumdieck tissue slicer. Slices were incubated with medium supplemented containing gentamicin and glucose. ATP/protein and morphology assessments were performed to assess tissue viability.

Results

Viability measured by the amount of ATP increased vastly following incubation with medium for 24 hours in both maternal ($p = .010$) and fetal ($p = .051$) tissue. The layer of syncytiotrophoblasts remained intact, but the incubated tissue presented a higher fraction of villous stroma cells with karyorrhexis compared to placenta slices without incubation. There was a decreasing trend in viability measured through ATP visible in tissue incubated with medium. The syncytiotrophoblast layer remained intact, and there was no higher fraction of villous stroma cells presenting with karyorrhexis compared to untreated placenta slices.

Conclusion

This study demonstrates that precision-cut placenta slices remain viable when incubated in medium, and implies that the precision-cut placenta slices can be used as an ex vivo model to study placental toxicity after maternal drug exposure.

Poster session II

PUBLIC HEALTH

Presenters:

- Jacek Burzyński
- Esther R. Evers
- Shrinivas Jiragal
- Kamila Kozmíková
- Denise Taner
- Chaitali Nath
- Hamrish Kumar Rajakumar

ISCOMS 2024 SCIENCE BEYOND BORDERS

Determinants of effective cardiopulmonary resuscitation performed by children after community-wide training

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Introduction

Early first aid performed by bystanders, including cardiopulmonary resuscitation (CPR) is crucial for survival in a sudden cardiac arrest. Current guidelines recommend starting CPR training at as early as 12 year olds, though this cut-off is still under debate. In view of changing guidelines regarding target chest compression (CC, currently minimum 50 mm, previously minimum 38mm), we aimed to evaluate the efficacy of CPR delivered by 11-14 year olds.

Method & Materials

We organized 1-hour workshop sessions on CPR for 11-14y.o. in volunteering schools, which covered theory as well as supervised training. After training, willing subjects performed 2 min of recorded continuous CCs by (Laerdal Resusci Anne? with CPRMeter2?), with visual feedback. Compression pace was given by metronome; instructors supervised the correct body position. Collected data included age, sex, as well as measured body weight and height.

Results

We analyzed CPR records from N=702 study participants (mean age: 12.76Ò1.02 years, 379 (51.63%) boys). Their mean median compression depth (MCD) was 46.70Ò7.74mm, and only 42.88% of children achieved at least 50% of compressions Ú50mm. Boys performed significantly deeper CCs than girls (49.34Ò7.05mm vs 45.97Ò8.07mm, p<0.0001). Two cutoffs were established: 12.1 for age (85% sensitivity and 41% specificity, AUC=0.69) and 44.8 for weight (77.4% sensitivity, 61.1% specificity, and AUC=0.74).

Conclusion

Sex, age and anthropometric factors are significant CC quality factors. Children with higher body weight are more likely to deliver CCs of target depth.

Empowering Healthcare: Unleashing the Potential of Artificial Intelligence for Cervical Cancer Screening in the Netherland

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Introduction

In the Netherlands, colposcopies are important in cervical cancer screening, despite being subject to observer bias (1,2,3). Artificial Intelligence (AI) decision support software, as seen in projects like PRESCRIP-TEC, has proven effective making lesion interpretation more reliable in low resource settings (4). This raises the question of whether AI can enhance the screening process in high income countries like the Netherlands, by reducing the time between an abnormal PAP smear and the colposcopy, when being used by other healthcare workers to perform colposcopies.

Method & Materials

We conducted interviews with gynecologists practicing in the Netherlands, who perform colposcopies on a regular basis and will continue working in the field for at least 5 further years. The data was coded and analyzed to sort out the potential role and effectiveness of AI in Dutch cervical cancer screening. Participants? opinions covered the reliability of (AI-assisted) colposcopies, their view on the total screening program, and as well as their current experiences and beliefs regarding AI assistance and its potential to allow other healthcare professionals to perform colposcopies. Lastly, we explore the feasibility of involving other healthcare workers in colposcopies, with or without AI assistance, which could optimize Dutch screening protocols and reduce waiting times.

Results

Gynecologists are anticipated to show interest in integrating AI into colposcopies. This pilot study holds significant potential for the RIVM to re-evaluate the cervical cancer screening pathway and methodology in the Netherlands. If AI proves beneficial, there is substantial scope for widespread innovation and transformation. This has the potential to enhance the health of approximately 8,759,554 women and could serve as a model for other high-income countries contemplating crucial transformations in their screening processes to meet the WHO's 90/70/90 goals.

Conclusion

To be finalized before presentation

Emotional Intelligence and its Influence on Medical Student Performance: A Cross-Sectional Analysis

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Introduction

Research has consistently demonstrated the significant influence of emotional intelligence (EI) on various aspects of individuals' lives, including their proclivity for prosocial behavior, academic achievement, and enhanced empathy, particularly in healthcare settings. In the context of medical education and clinical practice, a higher level of EI has been associated with superior academic performance and more effective physician-patient relationships. This study delves into the connection between emotional intelligence and the academic performance of medical students across their entire undergraduate journey, spanning from the first year to the sixth year, at the Mkhitar Gosh Armenian-Russian International University.

Method & Materials

Methods: Employing a cross-sectional research design, we utilized the Mayer-Salovey-Caruso Emotional Intelligence Test (MSCEIT) as an objective measure to assess emotional intelligence. The academic performance of medical students was evaluated through a combination of continuous assessment (CA) and final examination (FE) results. Participants from all academic years were invited to partake in the study during the second semester. Each student provided demographic information through a paper questionnaire and independently completed the MSCEIT. Multivariate analysis was employed to explore the relationship between the total MSCEIT score and academic achievement.

Results

Results: A total of 300 medical students participated in this study, representing a broad range of academic levels (45 first-year students and 86 sixth-year students), with a response rate of 66.0%. The gender and ethnic distribution of participants closely mirrored the student population. Among the participants, 30% hailed from Iran, while the remaining 70% came from India. The results revealed that the total EI score positively predicted better overall CA outcomes (OR 1.01) and good overall FE outcomes (OR 1.07), while negatively predicting poor CA outcomes (OR 0.97). Moreover, emotional intelligence was significantly associated with the final annual FE scores (adjusted $R2 = 0.43$).

Conclusion

Conclusions: This study demonstrates a compelling relationship between emotional intelligence and the academic performance of medical students. Those with higher levels of emotional intelligence exhibited superior performance in both continuous assessment and final professional examinations. This suggests that fostering emotional skills may hold the potential to enhance the academic success of medical students.

Walking habits in a European population and its association with socio-economic and health factors - a cross-sectional study

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Introduction

Regular physical activity can contribute to the prevention of a number of civilizational diseases. Our study was focused on walking, specifically in what quantity it is performed by a wider population and what are the associated socio-economic and health factors.

Method & Materials

We used data from the pan-European study European Health Interview Survey 2019 (EHIS), a representative epidemiological questionnaire study with stratified random sampling design. One of the questions was ?How much time do you spend in total walking from place to place in one typical day when you walk??. According to the answers, respondents were divided into three groups: Group I (GI) walking of less than 10 min, group II (GII) walking of 10-29 min and group III (GIII) walking at least 30 min daily. The separate multinominal logistic regression was used to estimate the odds ratio for set of variables.

Results

There were 7864 participants (3842 men and 4022 women) aged at least 15 years and older enrolled in the study with mean age 44.49 (CI95% 43.76?45.22), mean BMI 27.6 (CI95% 27.25?27.94). The analysis attributed 53.28% of the respondents to GIII, 36.17% to GII, and 10.55% to GI. Males were more likely to be assigned to GI (RRR (relative risk ratio) sex, male, (female = 1), 1.66, CI95% 1.379-1.998, p<0.001). We found an inverse relationship between education and income and the daily activity level. Respondents with primary education (RRR education, primary (tertiary = 1), 1.51, CI95% 1.057-2.144, p<0.023) and income of the fifth quintile (RRR income, 5th quintile (1st = 1), 1.72, CI95% 1.270-2.327, p<0.001) were most likely assigned to GI. Respondents attributed to GI subjectively rated their health as the worst (RRR self-rated health, bad and very bad (very good and good = 1), 5.20, CI95% 3.891-6.941, p<0.001). We did not find the differences in the BMI or diabetes between the groups.

Conclusion

People with the lowest amount of daily walking are those with the lowest income and education. Improving pupils' attitudes to various kinds of exercise within the framework of basic and secondary education should be stressed.

The Impact of Water Hardness on Kidney Stone Incidence in Varna City

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Introduction

This study delves into the potential correlation between water hardness and kidney stone incidence in Varna City. Despite assurances of water purity, anecdotal evidence suggests elevated water hardness. This research investigates whether increased water hardness is associated with heightened kidney stone occurrence, considering age and gender as potential influencing factors.

Method & Materials

Water samples were collected from various locations in Varna City, and water hardness was measured using a digital Total Dissolved Solids (TDS) meter. Additionally, a comprehensive water analytical test kit determined calcium and magnesium concentrations. Concurrently, data on kidney stone incidence over the past two years were obtained from the archive of St Anna Hospital in Varna City. Statistical analyses, including correlation tests and regression analysis, were conducted to evaluate the relationship between water hardness and kidney stone incidence.

Results

Analysis revealed that water hardness in Varna City exceeded recommended levels, particularly in calcium content. Both the digital TDS meter and the analytical test kit consistently revealed elevated water hardness. Statistical scrutiny demonstrated a significant positive correlation between water hardness and kidney stone incidence. These findings remained robust even after adjusting for potential confounding factors such as age and gender. Preliminary results indicate a noteworthy association between increased water hardness and elevated kidney stone prevalence, considering demographic variables.

Conclusion

This study presents compelling evidence supporting the hypothesis that heightened water hardness in Varna City, measured by both digital TDS meter and comprehensive water analytical test kit, is associated with an increased prevalence of kidney stones. These preliminary findings underscore the significance of considering water quality in public health assessments, especially concerning age and gender. Further research is imperative to confirm these associations, and public health initiatives, including heightened awareness and alternative drinking water sources, may be vital in mitigating the risk.

Development of a Comprehensive Scoring System for Esophageal Cancer Screening Using Multiple Indicators

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Introduction

Esophageal cancer remains a significant global health concern, with challenges in early detection and screening. This study addresses the existing gaps in esophageal cancer screening by developing a scoring system utilizing eight key indicators: acid reflux, gender, age, smoking (in pack years), alcohol consumption (beverages per week), location of residence, genetic predisposition, pre-existing gastroenterological conditions and obesity measured by BMI. The aim is to enhance the accuracy and efficiency of early detection through a multifaceted approach.

Method & Materials

Our methodology involved a rigorous meta-analysis of numerous studies published from 2013 to 2023 to identify the most reliable indicators for esophageal cancer risk. Data from diverse populations were synthesized, ensuring a comprehensive and representative analysis. The scoring system was developed through statistical modeling, assigning weights to each indicator based on their significance. The model's validity and reliability were assessed through cross-validation and comparison with existing screening methods.

Results

The key findings reveal a robust scoring system that effectively integrates the selected indicators, providing a nuanced and accurate assessment of esophageal cancer risk. Notably, indicators such as acid reflux, smoking history, and genetic predisposition emerged as strong predictors. The model demonstrated superior sensitivity and specificity compared to current screening methods. Subgroup analyses highlighted variations in risk patterns across different demographics and geographic locations.

Conclusion

In conclusion, our research establishes a novel scoring system for esophageal cancer screening, utilizing a combination of eight indicators. This approach offers a more nuanced and personalized risk assessment, potentially leading to earlier detection and improved outcomes. As we move forward, the integration of this scoring system into routine screening protocols holds promise for enhancing preventive strategies and reducing the burden of esophageal cancer. Future perspectives include prospective validation studies and continuous refinement of the scoring system based on emerging research and technological advancements.

Development and Validation of Betel-Year: A Clinical Tool for Quantifying Exposure to Betel Quid Chewing Utilizing Nuclear Morphometric Analysis

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Introduction

Betel quid chewing, prevalent in Southeast Asia and South Asia, involves components like betel leaf, areca nut, slaked lime, and sometimes tobacco. Despite the potential health benefits of betel leaf alone, the habit's combination with Areca nut and tobacco poses carcinogenic risks. Betel quid chewing has a global prevalence of 10?20%. This study aims to assess buccal mucosa changes in betel quid chewers using nuclear morphometry, develop a clinical tool for betel chewing exposure, and investigate its usability in predicting dysplasia. The lack of standardized assessment tools necessitates an approach to evaluate the lifetime betel exposure of an individual and its impact on oral health.

Method & Materials

After obtaining ethical approval and informed consent, patients were recruited from the Out-Patient Department of our institution. We recruited betel quid chewers, excluding those under 18, alcoholics, smokers, or those with oral infections. The data included the history of betel quid chewing, buccal mucosa cells obtained by oral cytology, and the severity of dysplasia of the slides assessed by pathologists. Nuclear morphometry of buccal mucosa cells was measured using Image J. We utilized principal component analysis and confirmatory factor analysis to validate a new outcome variable reflecting nuclear morphometric parameters. Multiplicative regression models were developed for betel years based on betel exposure and additives. Spearman correlation and ANOVA were used to check the association between betel years and dysplasia. Dwass-Steel-Critchlow-Fligner test highlighted significant differences in betel years among dysplasia categories.

Results

Significant differences in NMPs were observed among different betel chewing groups. We derived multiplicative regression models for betel years. In the logarithmic transformation approach, betel year = 0.05_betel-exposure_0.09_slaked-lime use_0.11_tobacco-use. In the original variable approach, betel year = 5.05_betel-exposure^0.00048_slaked-lime-use^0.18133_tobacco-use^1.47513. Spearman correlation and Kruskal?Wallis tests confirmed associations with dysplasia.

Conclusion

The introduced "betel year" is a pioneering clinical tool for assessing cumulative betel quid exposure, akin to pack years for smoking. It offers personalized risk stratification, aiding targeted interventions and shaping public health policies. Despite limitations, the betel year holds promise for revolutionizing oral health risk assessment, and future research can expand its scope globally, considering diverse betel quid compositions.

Poster session II

PUBLIC HEALTH & EPIDEMIOLOGY

Presenters:

- Amir Abderam
- Ramzi Faraj Mohammed Alhadi
- Muna F. Alnaim
- Varsha Coimbatore Sathyabal
- Byambazaya Dorjzodov
- Raidah R. Gangji
- Ana Beatriz Nasser
- Sywert Westerhof

Is there any association between social capital and sarcopenia among the elderly? Insights from a population-based study

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Introduction

Due to advancements in medicine and the subsequent increase in life expectancy, the proportion of the elderly population has risen significantly over the past decades. Advanced age is associated with a decrease in body mass attributed to muscle wasting. Therefore, exploring factors associated with sarcopenia is of paramount significance. Here, we report the impact of social capital on sarcopenia in a population of aged participants.

Method & Materials

The study utilized baseline data from the Birjand Longitudinal Aging Study (BLAS). Elderly participants (aged 60 years and above) were identified through stratified cluster sampling. Social capital was assessed using a previously validated questionnaire, which includes five domains: social network, social support, social coherence, and social collectivity. The subjects were classified into five groups according to the quintiles of social capital. Sarcopenia was evaluated using the European Working Group on Sarcopenia in Older People 2019 (EWGSOP2) criteria. Participants were categorized based on EWGSOP2-2019 into four classes: normal, presarcopenia, confirmed sarcopenia, and severe sarcopenia. Multivariable ordinal logistic regression was employed to determine the impact of social capital on sarcopenia.

Results

The study comprised 1348 participants, with 697 (51.7%) being female and a mean age of 69.7 (7.5). Findings revealed that the fifth quintile, compared to the first quintile of social capital, had a significant association with pre-sarcopenia (OR: 0.61, 95% CI: 0.40 to 0.92, p = 0.018) and confirmed sarcopenia (OR: 0.10, 95% CI: 0.01 to 0.67, p = 0.018). Specific domains of social capital, such as social coherence and social network, showed significant associations with pre-sarcopenia (Social coherence: OR: 0.57, 95% CI: 0.38 to 0.86, p = 0.007; Social network: OR: 0.52, 95% CI: 0.35 to 0.78, p = 0.002), and confirmed sarcopenia (Social network: OR: 0.13, 95% CI: 0.02 to 0.96, p = 0.046).

Conclusion

In conclusion, our study emphasizes the significant impact of social capital on sarcopenia in elderly individuals. The highest quintile of social capital revealed a significant decrease in the chance of having pre-sarcopenia and confirmed sarcopenia. Therefore, enhancing social capital, with specific attention to social coherence and network, could have a beneficial effect on the muscular status of the elderly.

Enhancing Safety and Competency in Disaster Response: A Study on the Effectiveness of a Novel Medical Application for Disaster Response

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Introduction

Responses to disasters must be swift and substantial. The backbone of disaster management is volunteers. With the lack of access to massive trained medical volunteers, a novel application was used to bridge the gap to overcome the needs of personnel and ensure their safety and effectiveness. As part of this innovation, volunteers can also receive guidelines and instructions for managing various scenarios during a natural disaster. In this study, we evaluate the effectiveness and impact of this application on volunteers managing disaster responses.

Method & Materials

This is a cross-sectional study to measure the application's effectiveness in real-world scenarios. A structured questionnaire was employed, encompassing sections on demographic data, previous experience with disaster response tools, self-assessment of operational efficiency post-application deployment, communication efficacy, and challenges encountered while using the application. Additionally, the questionnaire integrated scales to measure attitudes towards the technology.

Results

The study included 40 volunteers who used the app during the Derna floods, in 2023. They were predominantly male (96.30%), with an average age of 26.63 years Ò3.90. The findings showed that 55.6% of the volunteers have a positive attitude toward the application. Whereas, 46% of volunteers experienced increased time demands to take action. From the Application Operational data. Key safety features were highlighted, with 39.3% lowering and prevention of harmful interventions by volunteers and 22% more protection against electrical shocks. Additionally, data showed 70% effectiveness in guiding correct management for eye injuries and 55.5% successful management of ligament tear cases. Also, there was a moderate positive correlation (Correlation Coefficient: 0.46; p-value < 0.01) observed between the benefits gained from the app usage and the volunteers' experience.

Conclusion

The study gives us insights that the application is a promising tool for enhancing the efficacy and safety of non-medical volunteers in responding to disasters. This technology can be used as a solution for the lack of human resources during disasters. The findings encourage further exploration and development of the application to maximize its impact and utility in diverse disaster scenarios.

The Impact of Gender on a Patient's Choice of a Plastic Surgeon in Saudi Arabia

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Introduction

The competitive nature of plastic surgery requires a thorough understanding of patients' surgeon preferences. This information is crucial for plastic surgeons to create and implement effective marketing strategies. Patients' preferences for gender-specific doctors in medical fields other than plastic surgery have been studied. However, there is little empirical data on these preferences in plastic surgery patients, notably in Saudi Arabia. This study aimed to assess the impact of gender on patients' choice of plastic surgeons in Saudi Arabia and investigate the association between sociodemographic characteristics and surgeon preference.

Method & Materials

A quantitative cross-sectional study was conducted between January and July 2023 using a web-based survey distributed to the general public in Saudi Arabia. The survey included questions on sociodemographic characteristics, social media usage, and preferences for plastic surgeons' gender and other attributes. Data were analyzed using RStudio, and multivariable binary logistic regression was performed to assess the association between sociodemographic factors and preference for surgeon's gender.

Results

A total of 1,873 participants responded to the survey, with 59.8% preferring male plastic surgeons and 40.2% preferring female surgeons. Preference for surgeon's gender was significantly associated with participants' gender, marital status, educational level, region, and occupation. The most important factors considered when choosing a plastic surgeon were experience (97.6%), board certification (78.1%), and appointment time (64.5%). Social media influenced the decision to undergo plastic surgery for 28.9% of participants, with Snapchat being the most commonly used platform.

Conclusion

This study found substantial connections between sociodemographic factors and Saudi Arabian participants' preference for male plastic surgeons. Social media affected some participants' plastic surgery decisions, but the surgeon's experience, board qualification, and appointment availability were essential. These findings will help healthcare professionals and governments tailor services to population requirements.

Longitudinal Study Assessing Mean Platelet Volume as a Surrogate Marker for C-Reactive Protein in Monitoring Tuberculosis Treatment Progression and Severity

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Introduction

Tuberculosis, caused by Mycobacterium tuberculosis, remains a global burden affecting 10.6 million people worldwide. Adherence and regular monitoring during treatment are crucial to reduce the global burden. Conventionally treatment progress is assessed by chest X-rays, molecular tests, sputum microscopy, and clinical evaluation. Studies highlight the value of serial CRP values for assessing progress. However, repeated X-rays pose radiation risks and limited CRP measurement facilities in primary healthcare centers prompt the search for surrogate markers. Our study aims to propose an alternative, easily available, and cost-effective marker for treatment assessment.

Method & Materials

After obtaining ethical approval and informed consent, individuals diagnosed with pulmonary tuberculosis according to National Tuberculosis Elimination Programme (NTEP) guidelines were included, while those with familial platelet disorders, chronic infections, and minors were excluded. Participants were recruited for a 6-month longitudinal study, reporting at three key time points: initiation of Anti-Tubercular Treatment, conclusion of the Intensive Phase, and conclusion of the Continuation Phase. Venous blood and sputum samples were collected at each visit, and Complete Blood Count (CBC) and Serum CRP analyses were conducted using automated hematology and biochemical analyzers. Sputum smears were graded according to NTEP guidelines. Subsequently, data analysis aimed to determine the potential of MPV (Mean Platelet Volume) as a surrogate marker.

Results

150 individuals were recruited. The data did not follow a normal distribution. Strong correlations were observed among CRP, MPV, and sputum grade at each assessment using Spearman Correlation. Repeated Measures ANOVA demonstrated significant differences in MPV and CRP across repeated assessments. Scatter plots visually depicted the relationship between CRP and MPV. Concordance Correlation Coefficient analysis highlighted an excellent agreement between CRP and MPV measurements. Bland-Altman analysis indicated no systematic bias in the dataset. Employing Baron and Kenny's approach, CRP was eliminated as a mediator variable.

Conclusion

This study highlights the utility of serial MPV measurements as a surrogate biomarker to monitor TB severity and treatment progression. As per standard protocols, routine CBC investigations are regularly conducted to monitor potential drug side effects during treatment. Automated Hemoanalyzers now include MPV measurement within the CBC report, providing physicians with a parameter to evaluate treatment compliance and effectiveness.

Mongolian Serum Ferritin as a Key Contributor to HCV Susceptibility

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Introduction

This study explores the crucial role of Mongolian serum ferritin levels as a major risk factor for Hepatitis C Virus (HCV) infection. Serum ferritin, an iron overload indicator, is linked to chronic liver disease and cardiac dysfunction, heightening susceptibility to infections like HCV by increasing the activity of eukaryotic initiation factor 3 (eIF3), crucial for HCV translation. Given Mongolia's endemic HCV prevalence of around 140 cases annually, understanding specific risk factors for HCV susceptibility is paramount, with recent studies hinting at a potential correlation between serum ferritin levels and increased vulnerability among Mongolians.

Method & Materials

We conducted a comprehensive cross-sectional analytical study involving 552 randomly selected Mongolian individuals. Serum ferritin levels were measured, and HCV infection status was determined. Data were analyzed using the SPSS program, encompassing descriptive statistics, ANOVA, independent mean t-tests, and correlation analyses to elucidate relationships between variables.

Results

The study included 552 participants (296 males, 256 females), with mean ages of 40.09 for males and 41.69 for females. Significant positive correlations were found between ferritin levels and HCV ($r = 0.096$, $p = 0.024$) .Those with HCV had higher mean ferritin (330.14) compared to non-infected (242.94) ($t = 5.137$, $p = 0.024$). ANOVA confirmed differences in ferritin levels based on HCV ($F = 5.137$, $p = 0.024$). Ferritin was a significant predictor in the regression model ($F = 5.137$, $p = 0.024$). Ferritin demonstrated high diagnostic accuracy for HCV ($t = 6.649$, $p < 0.001$) .Results reveal a statistically significant positive correlation (Pearson coefficient = 0.096) between ferritin and HCV at the 0.05 significance level ($p = 0.024$).

Conclusion

This study highlights the vital connection between Mongolian serum ferritin levels and HCV infection, identifying elevated ferritin as a significant risk factor. These insights are pivotal for crafting targeted interventions in HCV prevention and management. Further studies are needed to uncover shared risk factors influencing Mongolian serum ferritin levels and their role in predisposing individuals to HCV infection.

Peer-Led Neonatal Resuscitation Training among Medical and Nursing Students: Experience of Hubert Kairuki Memorial University

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Introduction

The first 28 days of life continues to be a crucial period for newborn survival in Sub-Saharan Africa. Tanzania, like other Low-and-Middle-Income Countries (LMICs), has high Neonatal Mortality Rates largely driven by birth asphyxia. To address this challenging burden in resource-limited areas, the Helping Babies Breathe (HBB) initiative trains future and current Healthcare Professionals (HCPs) in neonatal resuscitation techniques. This retrospective study highlights the novel approach to peer-led neonatal resuscitation training among medical and nursing students at Hubert Kairuki Memorial University (HKMU).

Method & Materials

The HBB-HKMU initiative is a student-led program established in 2016. The training workshop includes both theoretical and practical components attended by future and current healthcare providers from a range of health disciplines. Pre- and post-training knowledge surveys and self-evaluation tests are routinely conducted to assess participants? knowledge and level of confidence. Test results of all workshop participants between November 2016 to November 2023 were analysed using the paired t-test to identify if participants demonstrate any significant improvement in knowledge after the HBB program training.

Results

The HBB-HKMU initiative successfully trained 1389 trainees. Majority of the participants were students, a total of 1243 (93.11%) were medical students, nursing students (bachelor?s degree and diploma), and other health and allied science students. Pre (10.63Ò2.53) and post (14.71Ò1.60) training knowledge test-scores demonstrated statistically significant ($P<0.01$) improvements within all participant subgroups: future and current HCPs. Confidence to conduct neonatal resuscitation was obtained through self-evaluation surveys. Prior to training, 15.97% Prior to training, 15.97% participants reported feeling ?very confident? however, following training, a substantial increase was noted reaching 56.03% demonstrating a marked difference of 40.06%.

Conclusion

The results indicate the HBB-HKMU initiative?s effectiveness in mitigating knowledge gaps and boosting confidence around neonatal resuscitation amongst workshop participants. Significant improvement in the pre-to-post knowledge tests illustrated the trainings? impact on participants? understanding. Notably, the increase in confidence post-training emphasizes the assurance in practical abilities among the trained. Utilizing students to teach and train peers and practicing HCPs may be an effective way to expand neonatal resuscitation training programs in settings where health educators are limited in number.

Affordable and adjustable prosthesis mainly focused for children in non-developed countries

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Introduction

In Brazil, more than 50 thousand people face amputation surgery annually, but there are not enough professionals working in the area of prosthetics to support this demand. Additionally, it is crucial that such technology fits impeccably in order to prevent harm and promote comfort. However, children grow fast; and prosthesis devices don?t grow. That means: disabled children who need prosthetics have to change their devices periodically and in Brazil, the waiting line ranges 1 year. Therefore, this project envisions that by design an adjustable and affordable, 3D printable, femoral socket and leg prosthesis, children could use their prosthesis longer and for being 3D printed instead of handmade, waiting lines would be faster.

Method & Materials

Following step by step of ?Designing Biomedical Products Reader?, from GJ Verkerke, this project contains an analysis phase, synthesis phase I, synthesis phase II, prototype and recommendations for the desired socked and leg.

Results

After analyzing the problem, brainstorming solutions and creating the mind and morphological map, we sketched some pre-concepts and selected the most probable of achieving all our desired requirements and wishes list. Then, during synthesis II phase, we detailed the concept, modeled the estimated dimensions and created technical drawings with Fusion 360 software. Later, we chose the ideal material to 3D print each part of the final product and made a risk plan and risk management of the product. Finally, we 3D printed the prototype of a lower leg that we redesigned, together with its feet and knee; and manually made the prototype of the adjustable socket?s as we idealized in the synthesis phase.

Conclusion

In conclusion, it is possible to design an above knee prosthesis that adapts to the human body as it naturally grows, and we believe that due to the fact that adults with amputation suffer from shrinking of their remaining limb, mainly due to atrophy, our model would be also useful to them by making it tighter instead of higher. The product still needs to be produced in the correct proposed material and be tested by humans, but it holds a high potential. Additionally, we believe our model could be easily adapted to fit other amputation levels, for example transtibial amputation level.

Understanding the impact of consent methods on participation bias in medical research at the emergency department – an Acutelines study

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Introduction

This study assessed the impact of different consent procedures on survival outcomes, patient characteristics, and ICU admissions in an Emergency Department (ED) setting, and if this leads to participation bias in the research population.

Method & Materials

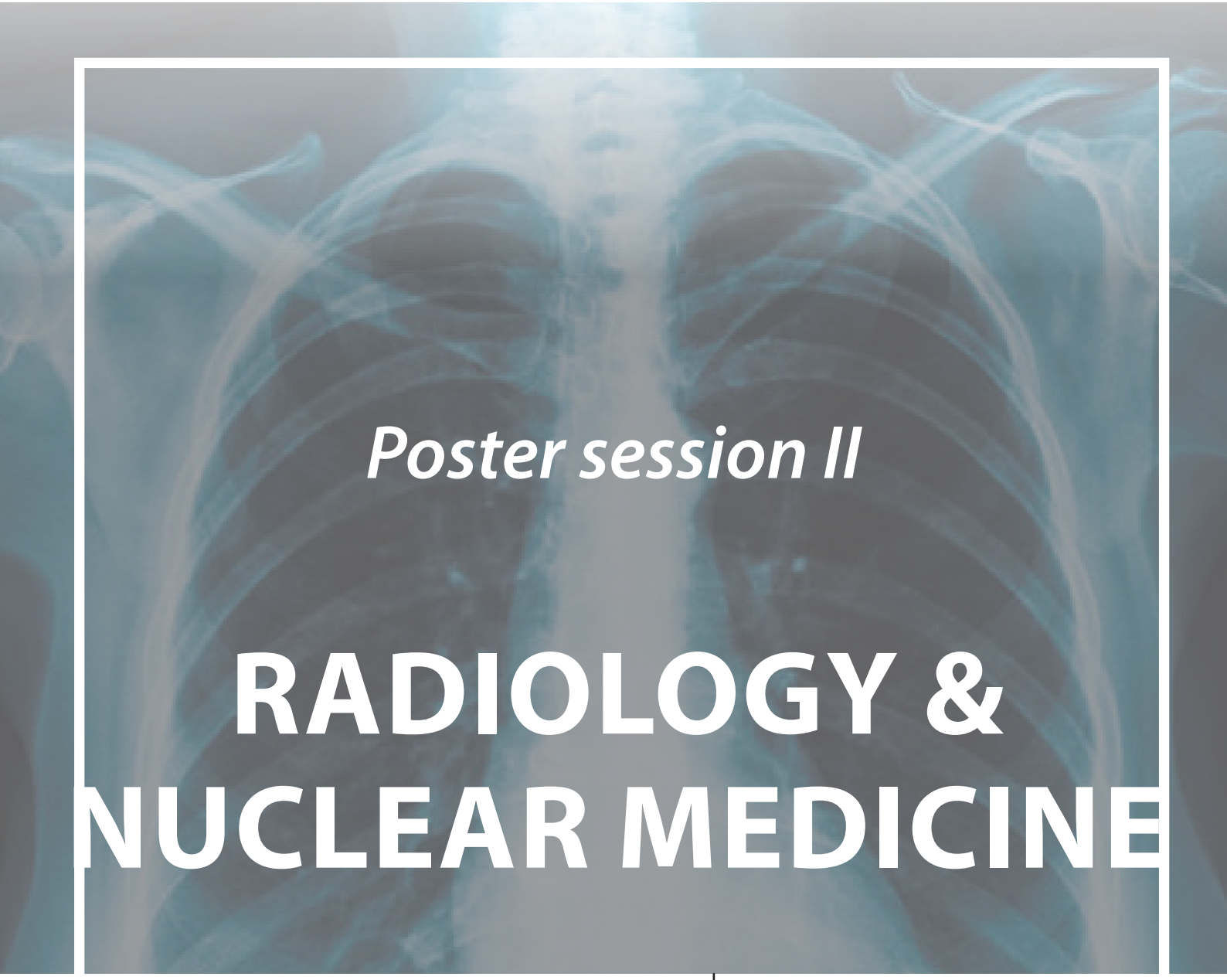
We performed a post-hoc analysis of prospectively collected data by the Acutelines biobank at a tertiary teaching hospital in the Netherlands, involving patients ≥18 years admitted through the ED. Four types of consent were analyzed: Direct Consent, Deferred Consent, Consent by Proxy, and opt-out. Mortality- and survival rates, ICU admissions, and clinical scores (MEWS, SOFA) and comorbidity (CCI) were examined using Kaplan-Meier graphs, Cox proportional hazards models, and Kruskal-Wallis and Chi-squared test.

Results

Among 1,860 patients, differences in survival and ICU admissions were noted across consent types. Consent by proxy had lowest survival ($p < 0.005$), when compared to direct consent, deferred consent and opt-out. Direct consent had lowest ICU-admission, compared to deferred consent (HR: 2.02 95%CI: 1.20 – 3.39, $p < 0.005$) and opt-out (HR: 3.16, 95%CI: 2.11 – 4.72, p<0,005). Consent type also influenced patient demographics, and clinical severity scores.

Conclusion

Participation bias due to consent in acute care research affects rates of survival, ICU admissions, and clinical assessments, which could impact the validity and generalizability of research findings. As a consequence, the design of acute research should balance patient autonomy, and ethical guidelines, but also realize the risk of participation bias due to consent to enhance the quality of research in acute care.



Poster session II

RADIOLOGY & NUCLEAR MEDICINE

Presenters:

- Mohammed Hasan Raheem Alsaedi
- Alessandra De Meis
- Anna Lena De Souza
- Ehsan Hassannejad
- Jingling Huang
- Marta Lo Cirio
- Bas Willemsen

Exploring Telemedicine's Significance in Handling Nutritional Care for Elderly Patients: A Cross-Sectional Study on Feasibility and Physicians Perspectives

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Introduction

Nutritional care is a vital aspect of geriatric healthcare, but it poses a challenge for family physicians who have to deal with a large number of elderly patients. Telemedicine, the use of technology to deliver remote healthcare, offers a promising solution to this problem. This cross-sectional study aims to evaluate the feasibility and effectiveness of telemedicine-based nutrition care interventions for elderly patients and to explore how they can improve healthcare access and reduce the need for frequent appointments.

Method & Materials

A self-administered questionnaire was developed for family physicians, covering demographic characteristics, telemedicine experience, self-assessment of patient outcomes, communication and technical skills, and encountered challenges. Attitude scales regarding telemedicine technology use were included. Descriptive statistics, percentages, and correlation tests were employed for analysis.

Results

Among the 60 targeted doctors, 40 (66%) participated, with an average age of 34 years Ò 1.34. The majority of family physicians (66.7%) reported using telemedicine for nutritional consultations with elderly patients, live video conferencing (37.1%) is preferred over voice calls (34.3%). Although 98% believed telemedicine addressed transportation issues for patients, 66.7% of doctors faced challenges in taking accurate anthropometric measurements, and 24% had difficulties in taking a medical history. At the level of family physicians' view, only 41% expressed positive expectations for telemedicine nutrition care outcomes. Attitudes correlated significantly with both the family physicians' technical abilities ($p < 0.01$), and also with years of experience ($p = 0.01$).

Conclusion

This study indicates the potential of telemedicine as a promising platform for delivering nutrition care to elderly patients. Despite positive attitudes, challenges in accurate assessments and communication exist. Further research is warranted to evaluate the elderly abilities to deal with technology and also to check the efficacy of telemedicine-based interventions in enhancing clinical outcomes for elderly patients. The findings contribute valuable insights into the feasibility and challenges of implementing telemedicine in geriatric nutrition care.

Unraveling the molecular mechanisms of radiation-induced dysfunction on rat vascular cells

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Introduction

Radiotherapy is used to effectively treat thoracic cancer. However, it can also lead to radiation-induced heart diseases (RIHD) and lung injuries (RILI), including valvular disease and pulmonary fibrosis. Radiation can damage healthy Endothelial Cells (ECs) and Smooth Muscle Cells (SMCs) in the blood vessels, causing vascular remodeling. Moreover, exploring the impact of irradiation on ECs and SMCs could improve understanding of primary Pulmonary Arterial Hypertension (PAH), as radiation-induced vascular remodeling was found to resemble the one observed in primary PAH. We aimed to develop an in vitro model to unravel the molecular mechanisms of radiation-induced dysfunction in the cells of the blood vessel. To validate it, we first explored the crosstalk between ECs and SMCs post-irradiation by assessing the effects of irradiated ECs on SMCs? proliferation, migration and fibrogenic phenotype occurrence. Later, we examined three specific signaling pathways to check for potential correlations with PAH.

Method & Materials

A co-culture model of primary rat aortic ECs and SMCs using cell culture inserts was established to assess the effects of 2 Gy-irradiated ECs on non-irradiated SMCs proliferation, migration and fibrogenic phenotype occurrence through Ki-67 staining, scratch assay and _-SMA staining, respectively. The concentration of PAH-related factors, including ET-1, 6-keto-PGF1_, and cGMP, was measured through ELISA assay.

Results

The co-culture model including primary ECs and SMCs was established. By co-culturing SMCs with irradiated ECs, no significant differences in _-SMA expression were observed in SMCs. Similarly, the detected concentration of ET-1, 6-keto-PGF1_, and cGMP were too low to draw any conclusion regarding any potential correlation with radiation-induced PAH. However, a slight increase of the percentage of proliferating and migrating SMCs was observed.

Conclusion

Primary ECs and SMCs were successfully set up for the co-culture model. Moreover, EC irradiation influenced SMCs' proliferation and migration, indicating potential in vitro interaction. This interaction between the two cell types resulting in a slight increase in SMCs proliferation mimics in vivo effects occurring in irradiated lung vasculature, indicating the model's potential for studying primary PAH. Nevertheless, further improvements are required to facilitate its use to better study the mechanisms behind radiation-induced vascular remodeling and its potential correlation with PAH.

Evaluating the Effects of Mitophagy Induction on Senescence in Irradiated Salivary Gland Organoids

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Introduction

Adverse side effects like xerostomia and salivary gland hypofunctioning can be caused by the co-irradiation of the salivary glands during radiotherapy of head and neck cancer (HNC) patients leading to a severe impairment of their quality of life. Importantly, ionizing radiation can induce cellular senescence in salivary glands contributing to hyposalivation. Mitochondrial dynamic processes, such as mitochondrial fusion, fission and mitophagy play a crucial role in tissue regeneration and their downregulation after irradiation can lead to an accumulation of dysfunctional mitochondria and subsequent senescence. This study aims to investigate the impact of the mitophagy inducers Urolithin A (UA) and P62-mediated Mitophagy Inducer (PMI) on radiation-induced senescence and mitophagy dysfunction in murine and HNC patient-derived salivary gland organoids (SGOs).

Method & Materials

Mitophagy and senescence markers were assessed upon irradiation with 7 Gy photons in murine and patient-derived SGOs by rt-qPCR, western blot, flow cytometry, senescence-associated-_-galactosidase and immunofluorescence staining. To modulate mitochondrial fission and mitophagy, Mitochondrial Division Inhibitor-1 (Mdivi-1), UA and PMI were used, and both senescence and organoid formation efficiency (OEF) were evaluated.

Results

Irradiation enhanced senescence but reduced mitochondrial fission and mitophagy in mouse and patient-derived SGOs. Notably, inhibition of fission with Mdivi-1 increased senescence in murine organoids, confirming a link between mitochondrial dynamic dysregulation and senescence. Interestingly, both mitophagy inducers were able to attenuate senescence in irradiated murine SGOs. However, with PMI appearing to be slightly more effective. After irradiation, both UA and PMI treatment increased the OFE of both human and mouse organoid cultures, indicative of enhanced stemness. Nonetheless, PMI was not able to attenuate the senescence-inducing effect of irradiation in patient-derived SGOs.

Conclusion

This study shows the link between mitophagy and senescence after irradiation and it demonstrates that mitophagy induction improves post-irradiation salivary gland stem/progenitor cell function. Moreover, it suggests that mitophagy inducers might offer a new treatment strategy for improving the function of salivary glands after radiotherapy in patients with HNC.

Correlation of ADC values of adult brain tumors with the diagnosis and pathological grade

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Introduction

Brain tumors are common, requiring physicians to have a precise understanding of them for accurate diagnosis and treatment. Diffusion Weighted Imaging (DWI) has been used to evaluate the tumor grade or tumor type differentiation and to diagnose other brain space-occupying lesions. Considering that various histological tumor types present different cellularity, we conducted this research to examine the role of ADC values in the differential diagnosis and pathologic grading of brain tumor types

Method & Materials

In this cross-sectional study we gathered pathology reports of histological samples of adult brain tumors from Birjand medical centers. The tissue sample of brain tumors were examined histologically by a pathologist and the grade and type of tumors were evaluated. The MRI data of these patients, including ADC and DWI sequences, were interpreted by a neuroradiologist. The measured ADC values and ADC ratios were calculated. Standard mean ADC values were expressed as _10_^(-6) _mm_^2/s. The findings were compared according to the histological diagnosis of each tumor.

Results

: Sixty-eight patients were included in the study; 34 (50%) were male and 34 (50%) were female. The average age of the patients was 51.69+16.40 years. In the examination of tumor type, 16 (23.5%) were astrocytoma, 9 (13.2%) were oligodendroglioma, 20 (29.4%) were glioblastoma, 4 (5.9%) were medulloblastoma, and 19 (27.9%) were metastatic tumors. the average value of ADC was statistically significantly different according to the pathological type of tumor. (P<0.001) The two-by-two comparison of average ADC among tumor types revealed significant differences, except for oligodendroglioma and glioblastoma (pvalue=0.87) and glioblastoma and medulloblastoma (pvalue=0.347). The average value of ADC and ADC ratio was statistically significantly different according to the pathological grade of the tumor. (P<0.001) In the two-by-two comparison of average ADC between all pathological grades of the tumor showed significance difference except for Grade I and Grade II (pvalue=0.355). The average value of ADC and ADC ratio was statistically significantly different according to the low and high tumor grade. (P<0.001) The mean value of ADC and ADC ratio for glioblastoma and metastatic tumors showed no significant difference.

Conclusion

The assessment of brain tumor grade through ADC examination will help to estimate prognosis and devising suitable therapeutic strategies.

MRI radiomics for predicting response to neoadjuvant therapy in local advanced head and neck squamous cell carcinoma.

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Introduction

Neoadjuvant therapy plays a significant role in local advanced head and neck squamous cell carcinoma (LA-HNSCC) , while identifying patients who may benefit most from neoadjuvant therapy is a major clinical challenge. This study aims to establish models based on clinical features and MRI radiomics features for predicting neoadjuvant therapy efficacy and screening out neoadjuvant therapy beneficiaries from LA-HNSCC patients.

Method & Materials

This retrospective study included 64 LA-HNSCC patients who underwent neoadjuvant therapy. The radiomics features extracted from the pre-treatment contrast-enhanced T1WI of the primary tumor site and Clinical features were incorporated into study. Patients were categorized into partial response (PR) and non-partial response (non-PR) groups after 2 cycles treatment based on RECIST1.1. Multivariate logistic regression analysis was employed to established Clinical model, radiomics model and combined model. The performance of the models were assessed and compared using ROC analysis, calibration plot and Akaike information criterion (AIC).

Results

The clinical model yielded an area under the curve (AUC) values of 0.867, which included age(HR=18.072,95%CI:3.476-93.947), treatment plan(HR=9.022,95%CI:1.137-71.609), smoking status(HR=5.479,95%CI:1.101-27.269), platelet level(HR=0.170,95%CI:0.034-0.840) and globulin level(HR=6.626,95%CI:1.293-33.955). The model indicated that age and globulin level were positive correlated with better treatment response, while platelet level was opposite. In other words, the elderly patients with higher globulin level and lower platelet were more responsive to neoadjuvant treatment. Importantly, compared with neoadjuvant chemotherapy, immunochemotherapy tended to achieve better therapeutic effect. The radiomics model had an AUC of 0.833, composed of three wavelet-related features: wavelet.HLH_glcm_Correlation(HR=3.575,95%CI:1.419-9.003),wavelet.HHH_glcm_JointEnergy(HR=0.020, 95%CI:0.001-0.484) and wavelet.HHH_glszm_SZHGE(HR =0.367,95%CI:0.160-0.842). The model suggested a significant difference in wavelet-related features between LA-HNSCC patients who could benefit from neoadjuvant therapy and all other patients. The combined model with age(HR=6.403, 95%CI:1.428-28.710), treatment plan (HR=11.751,95%-CI:1.534-90.048), wavelet.HLH_glcm_Correlation(HR=4.392,95%CI:1.507-12.806), wavelet.HHH_glcm_JointEnergy(HR=0.010,95%CI:0.001-0.784) and wavelet.HHH_glszm_SZHGE(HR=0.335, 95%CI:0.130-0.866)demonstrated the most optimal performance with an AUC of 0.905.

Conclusion

Radiomic features, especially the wavelet-related features, may serve as the potential biomarkers for early noninvasive prediction of neoadjuvant treatment response in LA-HNSCC patients. When combined with relevant clinical features, MRI radiomics can perform well in predicting neoadjuvant treatment response.

Investigation of nanoparticle?assisted radiosensitization in GBM cells exposed to photons and protons

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Introduction

Glioblastoma (GBM) is an extremely aggressive and clinically difficult to treat cancer that is in part caused by the presence of glioma stem cells (GSCs) and the formation of a tumor cell network interconnected by microtubes (MTs). Here, we investigated the potential of metal-based nanoparticles (NPs) to enhance radiosensitivity in GBM. Gold (GNP) and super-paramagnetic iron oxide nanoparticles (SPION) either coated with dextran or polyethylene glycol (PEG) were used in combination with photon and proton irradiation in human GBM cells. Additionally, we explored the effects of NPs on mitochondrial content and function in established GBM cell lines.

Method & Materials

First, we established the cellular network in GBM cells and investigated the effects of the NPs when combined to radiation treatment on MT formation. For this, primary GBM cell lines were used, cultured either as neurospheres, known to be enriched in GSCs, or in medium supplemented with 10% FCS that promotes differentiation. Immunofluorescence with GAP43 and Phalloidin was performed for MT characterization. Additionally, we explored the effects of NPs on mitochondrial content and function in established GBM cell lines (U87 and U251). Mitochondrial content was assessed through immunofluorescence of TOM20 and the regulation of fusion and fission with Western Blot analysis of DRP1, OPA1, and MTF2.

Results

Interestingly, serum-induced differentiation was found to promote MT formation. Irradiation alone significantly led to a reduction of MTs in differentiated GSCs, whereas the co-treatment with NPs showed an increase on MT formation. Findings indicated a significant increase in mitochondrial content following irradiation, while the co-treatment with NPs led to a decrease.

Conclusion

This study shows the potential of metal-based nanoparticles to enhance radiosensitivity in GBM cells, highlighting the necessity for additional research to elucidate the underlying mechanisms.

A deep learning approach to identify mammograms with increased risk of lesion masking.

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Introduction

The Dutch National Breast Cancer Screening Programme has made a major contribution to improve breast cancer care by using mammography for the earlier detection of breast cancer. However, mammography has limitations, such as the risk of lesion masking, which can decrease its sensitivity. Lesion masking can occur when lesions are superimposed on fibroglandular tissue, rendering lesions indiscernible and therefore increasing the risk of them being missed. Identifying mammograms with a high lesion masking risk can flag cases that require more attention. A study by Mainprize et al. has shown that it is possible to identify breast tissue with a higher risk of lesion masking with a model observer. This method reached an area under receiver operating curve (AUC) of 0.79 (95%CI 0.69-0.87) on the original North-American cohort. However, it only reached an AUC of 0.62 (95%CI 0.59-0.65) on a Dutch screening cohort. Therefore, this study focuses on finding an alternative deep learning-based method to predict the risk of lesion masking, that is suitable for the Dutch screening cohort.

Method & Materials

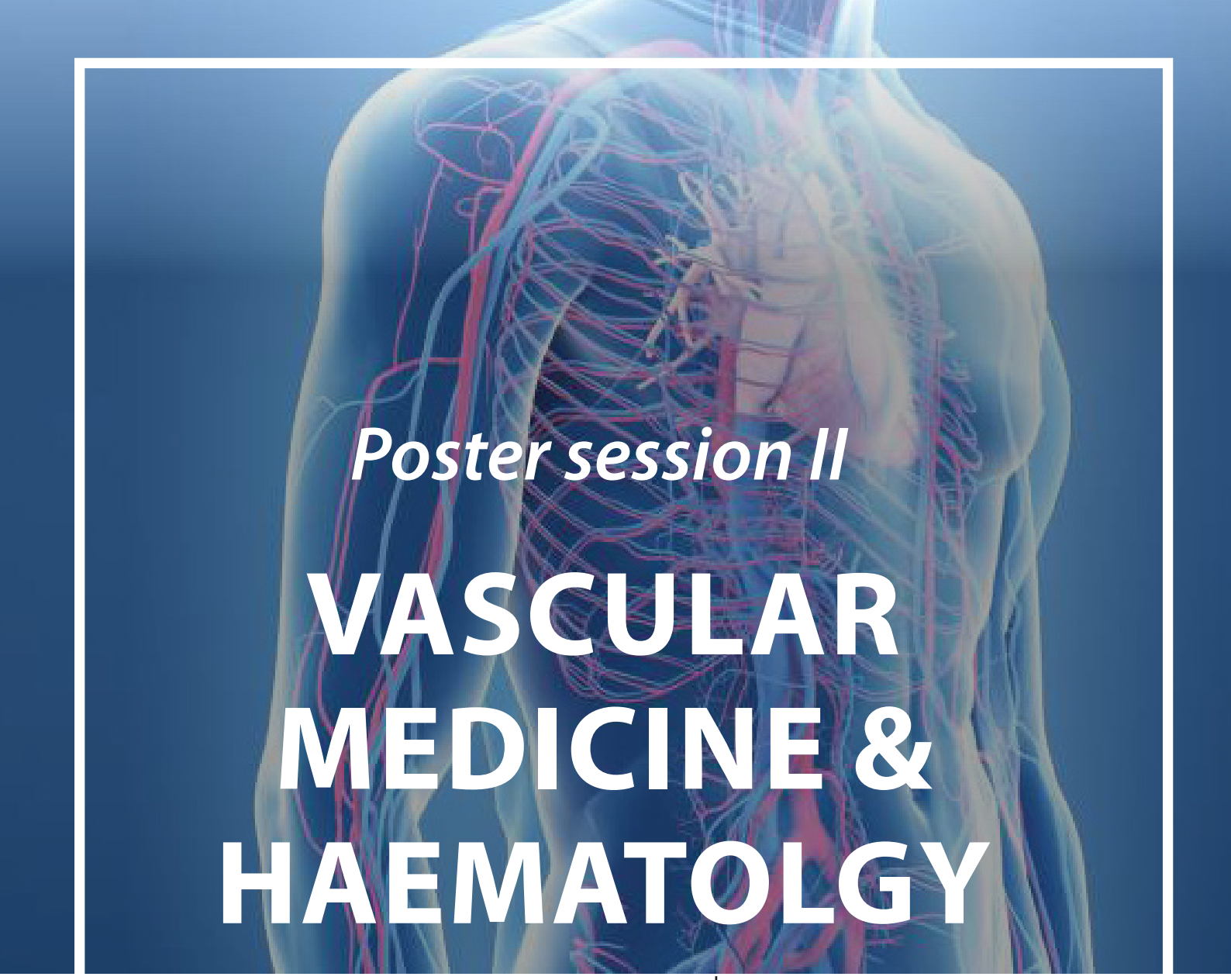
Both a Resnet18 and a SwinV2 model were trained on a dataset containing 2,074 mammograms. 1,534 cases with cancer detected by screening, assumed to have a low masking risk, and 540 with cancer detected in between screening rounds, assumed to have a high masking risk. The models were trained on contralateral images to avoid interference of lesions and allow the model to solely learn from breast tissue structures. In the remainder of this research, both models will be pre-trained with 80.000 negative screening mammograms labelled with volumetric breast density.

Results

The Resnet18 and the SwinV2 both reach an AUC of 0.61Ò0.02 (meanÒstd) without any pre-training, which is similar with the model observer based method from Mainprize et al. when applied to the Dutch dataset.

Conclusion

A deep learning approach trained with a small dataset and no pre-training can identify mammograms with high lesion masking risk with similar performance to the model observer based method developed for a different cohort. It is expected that pre-training with the remaining 80.000 available negative screening exams will improve performance.



Poster session II

VASCULAR MEDICINE & HAEMATOLGY

Presenters:

- Mario Francisco Arreola Rentería
- Aalesh Shah
- Antonia Vásquez
- Yuqing Wang

ISCOMS 2024 SCIENCE BEYOND BORDERS

Experimental analysis of TransfusionMX: Capsule for blood transport, control and conservation

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Introduction

The space initiative will be oriented towards longer trips and less trained users, making it essential to have measures in place for future risks. Blood plays an important role in the state of health, mainly in emergency situations, however there are no projects for its preservation and transport in the space context, so there is not enough information about erythrocyte fragility against mechanical stress. In response to these problems, the present work will seek to evaluate the prototype for the preservation, monitoring and transport of blood products "Transfusi¢nMX" by counting erythrocyte cells from the flight of a drone.

Method & Materials

A flight will be performed with "Transfusion Mx" coupled to the 5-inch FPV quadcopter drone, in which pressure, altitude, time, vibration, acceleration and temperature will be monitorized in real time. Isolation-based protective measures will be applied for the last 3 factors. Six samples of healthy subjects divided into three groups will be used: two no-flight, two exposed to flight without protection and two exposed to flight with the "TransfusionMX" system. After the flight, erythrocytes will be counted using a microscope and a Neubauer chamber, and a direct comparison will be made between the groups to analyze differences in erythrocyte integrity.

Results

The present experimental project will seek to evaluate three blood characteristics from the flight of the drone, using the "TRANSFUSION MX" container: -Degree of hemolysis caused by the low altitude flight of the drone. -Conservation of erythrocytes according to the standard measures of blood protection in the container. -Degree of red cell preservation due to hemoconcentration.

Conclusion

This project will seek to develop transport solutions for blood transfusion and testing, mainly in the aerospace industry but with replicable results on Earth. Conscious of the need to increase the sample size in order to obtain significant advances, the present preliminary results will seek the way to continue the project leading to the progress of mankind in space.

Diagnostic accuracy of Ankle-Brachial Index in patients of Peripheral Arterial Disease: A Meta-analysis

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Introduction

Peripheral Artery Disease(PAD) is a narrowing of the peripheral arteries that carry blood away from the heart to other parts of the body. PAD often goes undiagnosed by health care professionals. Peripheral artery disease diagnosis begins with a medical history and physical examination. If patients? Ankle-Brachial Index(ABI) is abnormal, they may need more tests like: Duplex Ultrasonography(DUS) , Computed Tomographic (CT) Angiography, Magnetic Resonance Angiography (MRA) or Angiography, also called an arteriogram. Ankle-brachial index (ABI) is a painless exam that compares the blood pressure in lower legs to the blood pressure in arms. It takes only a few minutes and can be performed as part of a routine exam. A normal ABI is 1.00 to 1.40. A value less than or equal to 0.90 is considered abnormal, and, in severe disease, it?s less than 0.5. If ABI results are normal or borderline (.91 to .99), an exercise treadmill ABI and/or a toe-brachial index (TBI) test also may be done. The objective of our study was to collect data on diagnostic accuracy of the ankle brachial index (ABI) - also known as the ankle brachial pressure index (ABPI) - for the diagnosis of peripheral arterial disease (PAD) in people who experience leg pain on walking that is alleviated by rest.

Method & Materials

We searched the Medline, Embase, and Cochrane Library databases, and performed a metaanalysis on the diagnostic accuracy of ABPI in patients with PAD. Published clinical trials using ABPI for the diagnosis of PAD have been included in the meta-analysis. After study selection, data and quality assessment, the Sensitivity, Specificity, Positive Predictive Value (PPV), Area Under the Curve of Receiver Operating Characteristic Curve (AUC of ROC) and Youden?s Index (YI) were calculated.

Results

A total of eighteen studies including 2,014 patients with PAD and 2,357 controls (patients without PAD) were available for the meta-analysis. The pooled sensitivity and specificity of ABPI were 64.0% and 78.4%, respectively. The Positive Predictive Value (PPV) was 71.7%. AUC of ROC and the Youden Index (YI) were 0.815 and 0.424 respectively. Some between-study heterogeneity was found in the meta-analyses. However, there was no evidence of a threshold effect.

Conclusion

Our meta-analysis of published studies demonstrates that ABI has a good diagnostic accuracy and plays an important role in the diagnosis of Peripheral Artery Disease.

Hydrogen sulfide reverses gestational diabetes mellitus-altered expression of human equilibrative nucleoside transporters in human umbilical vein endothelium

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Introduction

Human umbilical vein endothelial cells (HUVECs) isolated from women with gestational diabetes mellitus (GDM) show reduced adenosine transport by lower expression and activity of the human equilibrative nucleoside transporters 1 (hENT1) and hENT2. GDM also associates with elevated nitric oxide (NO) synthesis which reduced hENT1 and hENT2 expression. Hydrogen sulfide (H2S) is a gasotransmitter with vascular actions as NO but its role as modulator of hENT1 and hNET2 expression is unknown. Objective. To determine the effect of H2S on hENT1 and hENT2 protein abundance in HUVECs from GDM pregnancies.

Method & Materials

Preliminary studies were performed in human umbilical vein endothelial cells (HUVECs) isolated from women with normal pregnancies and pre-pregnancy normal weight (Nnw) or obesity (Nob) (n = 3-7) and GDMnw or GDMob (n = 3-4) (Clinical Hospital UC CHRISTUS, with patients consent; Ethics #012793). HUVECs were isolated by collagenase digestion and cultured until passage 3 when were incubated (13 h) without or with sodium hydrosulfide (NaSH, H2S donor, 100 mmol/L) or DL-propargyl glycine (PAG, H2S irreversible inhibitor, 100 mmol/L). hENT1 and hENT2 protein abundance was measured by Western blot. Data was analyzed by two-way ANOVA and shown as mean Ò S.E.M. with $P<0.05$ as significant.

Results

hENT1 protein abundance was higher ($P<0.05$) in GDMob and Nob compared with GDMnw and Nnw. However, hENT2 protein abundance was higher only in cells from GMDob compared with all other groups. NaSH reversed the GDMob- and Nob-increased hENT1, and the GDMob-increased hENT2 protein abundance. However, PAG did not alter hENT1 and hENT2 protein abundance in all groups.

Conclusion

Exogenously donated H2S modulate the protein abundance of hENT1 and hENT2 in HUVECs from women with pre-pregnancy obesity with a normal and GDM pregnancy. Exogenously donated but not endogenously generated H2S may be protective to GDM-altered hENT1 and hENT2 protein abundance in HUVECs.

Corticosteroids impair hematopoietic microenvironment via inducing senescence of the mesenchymal stromal niche

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Introduction

Mesenchymal stem cells play a crucial role in maintaining the immune homeostasis of the post-transplant bone marrow microenvironment, which is essential for the successful engraftment of allogeneic hematopoietic stem cells. Graft-versus-host disease (GVHD) induced by allogeneic hematopoietic stem cell transplantation is a key factor contributing to transplant failure. Corticosteroids with or without calcineurin inhibitors comprise the first-line treatment option for graft-versus-host disease (GVHD). But there is still up 65% of patients experience steroid-resistant or steroid-refractory GVHD. The pathogenesis of steroid-resistant or steroid-refractory GVHD is complicated, and the impacts of steroid on bone marrow microenvironment are lacking.

Method & Materials

To simulate the changes of bone marrow microenvironment during steroid treatment, mesenchymal stromal cells (MSCs), the pivotal component of bone microenvironment, were isolated from healthy donor and subjected to dexamethasone (Dex) treatment. Bulk RNA sequencing (RNA-seq) was employed to identify the significant molecular changes, followed by in vitro cell-based validation.

Results

Bulk RNA-seq analysis revealed downregulation of genes associated with cell cycle and mitosis following Dex treatment. The percentage of SA-_- gal positive cells increased under Dex treatment. Additionally, Dex-treated BM-MSCs upregulated P16, indicating the potential induction of senescence in bone marrow derived MSCs (BM-MSCs). Besides, in BM-MSCs with glucocorticoid receptor (GR) knockdown, the percentage of Dex-induced senescent cells significantly decreased. Thus, Dex-induced senescence in BM-MSCs appears to be GR-dependent. Moreover, Dex-treatment attenuated the osteogenic ability of BM-MSCs, while concurrently enhancing their adipogenic potential.

Conclusion

Steroid treatment triggers senescence of BM-MSCs, resulting in an elevated secretion of inflammatory factors. This may underlie the diminished capacity of MSCs to support hematopoiesis observed in patients with steroid-resistant or steroid-refractory GVHD patients. And the compromised osteogenic ability of BM-MSCs following steroid treatment may lead to osteoporosis. Elucidating the pathogenesis of steroid on bone marrow environment may provide promising target for refractory/relapsed GVHD treatment.

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Thank you for reading the Book of Abstracts and for participating in ISCOMS 2024.
We hope you enjoyed the congress as much as we did.
We hope to see you next year.

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Ik heb jullie heel hoog zitten. Ik ga jullie missen en hou van jullie.

Kind Regards,

Iza de Wilde