ISCOMS
science beyond borders

BOOK OF ABSTRACTS

29th International Student Congress Of (bio)Medical Sciences

ISCOMS 2022
SCIENCE BEYOND BORDERS

umcg

university of groningen

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Preface

Tom Lieverse
Prof. Marian Joëls PhD

Tom Lieverse

President ISCOMS 2022

Dear participants,

It is with great pleasure that I welcome you to the digital version of the 29th edition of the International Student Congress of (bio)Medical Sciences.

Due to the COVID-19 pandemic, the Organising Committee of ISCOMS 2022 had an extremely difficult task in organising a congress both physically and digitally of the very high quality that ISCOMS has been over the past 29 years. I am extremely proud of all of them, but we could not have done it without the enthusiasm and support that our participa nts have always shown us.

I hope that ISCOMS 2022 can be a great example that adaptability and ingenuity can be drawn from hard work and passion. I am proud that we are always handling according to our slogan; ''Science Beyond Borders'', and that we can continue to provide students the opportunity to present their research on an international platform, to acquire knowledge by attending the programme, and to expand their network by interacting with other participants, even during difficult times.

Our programme consists of a physical programme and a digital platform on which participants are able to attend three full days of inspiring lectures and student presentations. Furthermore, on Tuesday the 7th of June, we will start with the pre-course, a day in which enthusiastic students can improve their research skills by physically attending informative masterclasses. During the following three congress days, we will welcome Nobel Laureate regental prof. Bruce Beutler MD, prof. Jeffrey Friedman MD PhD, prof. Hanneke Schuitemaker PhD, and prof. Karl Deisseroth MD PhD.
On Friday we will kick-off with a keynote lecture by prof. Beutler, who won the Nobel Prize in Physiology or Medicine in 2011. Prof. Beutler is best known for his discovery concerning the activation of innate immunity. The subject of prof. Beutler's lecture is 'From phenotypes to genes in immunity' . This lecture will outline how TNF is being used for inflammatory diseases.

After the congress, fourteen young and talented foreign (bio)medical students will start with the ISCOMS Research Fellowships where they will join the two-week online research internships at Research Institutes of the UMCG.

This year, we chose a congress theme that fits very well to the current global (bio)medical improvements. Everyone involved in the (bio)medical world is constantly looking for a therapy that best fits a patient and are more and more involving the patient when choosing a therapy. That is why we called the theme of the congress: 'Personalised Medicine'. During the congress, you can discover the theme in a variety of manners, such as the Keynote lectures, speed-Keynote lecture and workshops.

On behalf of the entire Organising Committee, I wish you all a wonderful time and I hope you will enjoy ISCOMS 2022 as much as I did organising it

Prof. Marian Joëls PhD

Dean/Member of the Board of Directors University Medical Center Groningen

Dear participants of ISCOMS 2020,

It is my great pleasure to welcome all guests to the 29th edition of the International Student Congress Of (bio)Medical Sciences in Groningen. An annual event organised by students from Groningen for students from all over the world, something to be very proud of.

ISCOMS has become a tradition and is regarded by many as one of the highlights of the University Medical Center Groningen (UMCG) academic year. We would like to congratulate the Organizing Committee for putting together yet another exciting scientific programme. This year's ISCOMS edition again hosts an impressive number of renowned speakers, including prof. Jeffrey Friedman MD PhD, prof. Roel Nusse PhD, prof. Bruce Beutler MD, prof. Hanneke Schuitemaker PhD and prof. Karl Deisseroth MD PhD. No doubt these and other speakers will be a source of inspiration to the participants.

International contacts and collaborations are essential to push science forwards. The UMCG and the University of Groningen foster such international contacts, not only in their research collaborations but also at all levels of our educational system. We have strategic partnerships with many institutions across the world. ISCOMS is one of the examples through which international ties are strengthened, in this case by bringing together students from a great variety of countries.

ISCOMS offers a wonderful opportunity to all participants to get a taste of what science can offer. Often it is the starting point for new collaborations and friendships for life.
Please enjoy the excellent science, the relaxed atmosphere, the intense discussions and above all the beautiful city of Groningen!

Marian Joëls PhD
Professor of Neuroscience
Dean of the Medical Faculty
Member of the Board of Directors
University Medical Center Groningen

Organisation

Executive Board
Advisory Board
President, Secretary, Treasurer
Scientific Programme
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Executive Board

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, to acquire knowledge by attending the programme, and to expand their network by interacting with other participants.

During the intensive start of the year, despite the COVID-19 difficulties, we accustomed ourselves to the functions and responsibilities. During the meetings we had twice a week, we made sure every task was done and everyone was informed accurately.

Besides our professional collaboration, we also became very close friends. It is impressive that a group that is filled with completely different personalities made sure everyone complemented each other and helped each other in case it was needed. We all learned a lot this challenging year and are very proud of the result.

We want to express our gratitude towards the entire Organising Committee for their amazing effort they have put into this edition. Furthermore, we want to thank the advisory board and everyone else who supported us this year.

We are honoured to welcome you to the 29th edition of the International Student Congress Of (bio) Medical Sciences! We wish you an extraordinary time!

Tom Lieverse
Anne von Hebel
Mark Broekman
Justine Zijlstra
Willemijn Vrijlandt
Willemijn van Dijk
Julian Vrij
Judith Brinkman
Bart Wijntjes

Advisory Board

ISCOMS is a congress organised for and by students. 33 biomedical students are responsible for all scientific, financial, and organisational aspects of the congress. 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 organising ISCOMS for many years now. Their expertise, experience and contacts are of great support for the Organising Committee. The advisory board consists of three seniors from the University Medical Center Groningen (UMCG).

Advisory board:

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

Prof. Paul de Vos PhD

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

Matijs van Meurs MD PhD

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

Robert A. Pol MD PhD

We would like to thank the advisory board for their continuous support and useful advice.

President, Secretary, Treasurer

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

The main task of the president, **Tom Lieverse**, is to lead the Executive Board. He is responsible for the whole organisation towards and during the congress. Additionally, his task is to find suitable day chairs and jury members.

The secretary, **Anne von Hebel**, 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**, Mark Broekman**, 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 2022!

Anne von Hebel, Tom Lieverse, Mark Broekman

Scientific Programme

The Scientific Programme committee consists of seven young and enthusiastic (bio)medical students. It is our responsibility to organise the scientific part of ISCOMS 2022. We are in charge of the keynote lectures, workshops, pre-course, interactive operation, the ISCOMS Research Fellowships (IRF) and the digital scientific programme. It is our aim to make the scientific programme of ISCOMS challenging and diverse. Besides this, we 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), we organise the two-week ISCOMS Research Fellowships. These short internships will take place directly after the congress and brings 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 are convinced ISCOMS is the perfect opportunity for students and young researchers from all around the world to present their recent work, meet fellow researchers and get enthusiastic about research. We enjoy creating a challenging and diverse scientific programme for ISCOMS 2022 a lot and we are looking forward to meeting you all in June 2022!

Justine Zijlstra
Julia Bakker
Anaïs van Haaren
Martijn Bouwman
Eva Hadderingh
Elisa Wiersma
Feyo Putker

Sponsors & Fundraising

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

Due to the fact that we are one of the biggest student congresses for biomedical sciences within Europe and due to the numerous national and international students attending, we have 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 a stand or they can choose for an appearance of their logo on for example our website or our congress bag. A new initiative that has started three years ago, is the networking lunch. Selected motivated students will get acquainted with different companies during a luxurious lunch in a private space. Our sponsor program is available on the website under the heading 'supporters'.

Apart from contacting potential sponsors, we will also subscribe several funds to support ISCOMS. Besides that, one of our committee members is going to assist the treasurer with the finances during the congress. We are also responsible for the journal subscriptions which the presenting participants can win during the congress. And last but not least, we carry the responsibility to provide the participants with a full congress bag which contains a variety of gadgets, magazines and information.

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 go to our site! If you have any questions, please contact us and we are more than willing to give you all the information you need.

Willemijn Vrijlandt
Aniek Schurink
Guusje van helden
Marts van Rietschoten
Lars Zandbergen

International contacts

The International Contacts Committee takes care of the international part of ISCOMS. Our daily responsibilities include the worldwide promotion of our congress, and taking care of participants who encounter problems with their registration, visa application, or other difficulties while organising their trip to Groningen, the Netherlands.

We take care of the promotion by e-mailing, calling, and sending promotional materials across the globe. In this worldwide promotion we are supported by our highly motivated 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. Furthermore, we are responsible for the social media community of ISCOMS, including Facebook, Twitter, Instagram and LinkedIn.

All incoming emails of students who want to submit their abstract or who are seeking additional information about ISCOMS are answered by us. We are also the committee that has contact with the embassies when aiding students in obtaining their visa. Lastly, we 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 2022. If you believe you can help, please send an email to iscoms@umcg.nl.

If you have any other questions regarding promotion, visa application, 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 2022.

Willemijn van Dijk
Arthur van der Vlis
Coen de Vree
Lobke van Dijkhuizen
Danielle Lieverse

Hosting & Logistics

The Hosting and Logistics committee is not only responsible for the social programme, but also for the accommodations, the City Tour, the Post Congress Tour and the plan of action during the congress.
The social programme is the perfect way to extend your social contacts. While enjoying dinners and informal drinks you can meet people from many different countries and cultures.

On Sunday, there will be a City Tour through the center of Groningen and a welcoming party afterwards. At this welcoming party there will be a pub quiz for both the participants and the housing providers. On Monday we will have a completely new social programme this year! Due to last year's success we have decided that the additional third congress day will remain in our programme. Therefore, on Tuesday the recreational evening will be held again. There you will be able to choose one of five activities like visiting a museum, a cheese tasting or a cycling tour.

On Wednesday there will be a formal dinner with 350 participants. This beautiful dinner will be at an historical location in Groningen. We will conclude the last congress day on Thursday with the unforgettable World Wide ISCOMS Night. At this party you can show everyone some great things your country has to offer by bringing your typical national snacks and by putting on your traditional clothing.

To finish off the excellent congress, there will be a Post Congress Tour on Friday. On this day, we will show you a piece of our beautiful country. Together with about 100 foreign participants we will enjoy a day full of fun to blow off some steam after an intense week full of science.

We, as the Hosting and Logistics committee, will provide you with options for accommodation during the congress. One of the options is 'Staying with a Student'. This gives you the perfect opportunity to get a better view of what the student life in the city of Groningen has to offer. Furthermore, you can stay at an international student accommodation or we can give you advice on hostels or hotels.

We ensure you we will do everything to make this congress memorable. We hope you are as excited as we are and we are looking forward to seeing you at ISCOMS 2022!

Julian Vrij
Noor Hakker
Merel Huiskamp
David Warlich

Public Relations

The Public Relations committee is responsible for the appearance of ISCOMS and for the promotion of ISCOMS in Groningen and in The Netherlands.

To reach as many students as possible we are in contact with all other (bio)medical faculties in the Netherlands. They help us to get a lot of attention to ISCOMS, for example, by hanging posters in their faculties and by posting information about the congress on their website. Furthermore we communicate with faculty coordinators to make sure they stimulate their students to visit ISCOMS. Besides this we are setting up a promotional campaign and communicate with the press.

Together, we are also responsible for the graphical design of all material that will be handed out at the congress and of all flyers, posters, booklets and cards that are spread all over the world by our colleagues from the International Contacts committee. Last but not least we compose and design the Book of Abstracts that will be handed out at the congress to all participants. This book contains information about the congress and the people involved and contains all abstracts of participants who present their research at ISCOMS 2022.

Judith Brinkman
Mas Arendsen
Gijs Stuart
Maud Hubbelmeijer
Julia Rikken

Research & Development

The main goal of the Research & Development (R&D) committee of ISCOMS is to innovate and improve every upcoming edition of the congress. We establish this by extensive evaluation that helps us determine what we can and should change. Also, we try to think of how it could be changed. The R&D committee makes sure the improvements are implemented at the upcoming congress. Brainstorming is a great part of our 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 R&D and we will try to keep improving it every year.

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

We maintain partnerships, because these are vitally important to the improvement of medical congresses. Each year we evaluate these partnerships and look for possible new ones. As partners, ISCOMS tries to become an even more inspiring congress.

Each year ISCOMS chooses a charity to support. By organising activities our committee raises money to support this charity. This year we chose the UMCG Alzheimer Foundation. This foundation supports research in the UMCG to find out the cause, develop new treatments, and find ways to lower the risk of dementia. We have collected money for this foundation among others by organising a pub quiz and by participating in a run called the 'Nacht van Groningen'.

Bart Wijntjes
Anne van Gelderen
Guido Feringa
Karien van de Wetering

Ambassadors

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 had the opportunity to attend ISCOMS 2019 as a poster presenter. It is a great experience, if you are looking to increase your knowledge on medicine and to meet people who share as much as enthusiasm as you do on research and medicine, around the globe. ISCOMS has a unique program with the patient lectures, workshops, keynote lectures and more. It is very well-organized by the organizing committee whom you can reach out for help anytime.“ Birce Ataş, a third-year medical student at Izmir University of Economics, Turkey.

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 2020 also excited you and makes you want to share your experience with others, you can apply to become an ambassador for ISCOMS 2021. Help us with our promotional campaign yourself! During the congress you can fill in an application form by contacting the ambassador coordinator or you can apply by sending an e-mail with a short motivation letter to iscoms@umcg.nl in days following the congress.

Akinsola Akinyemi

China

Alex Araya

Chile

Ashwini Priyadarshini Singh

India

Avichal Dani

India

Bahram Askarpour

India

Benson Oguttu

Uganda

Bernard Annan

Ghana

Birce Ataş

Turkey

Boyan Zhang

China

Collins Kofi Frimpong Osei Owusu

Ghana

Faizan Akran

Pakistan

Farid Masoud

Iran

Felipe Calderón Salazar

Mexico

Gita Nur Siwi

Indonesië

Grace Thandekire Sibande

Malawi

Gulfairuz Tukinova

Kazahkstan

Ishani Desai

Georgia

Ishika Mahajan

India

Jordan Popović

Serbia

Khusronasir Mohamedfaruq

Georgia

Kritika Pathak

India

Mahsan Divanbeygi Kermani

Iran

Mashkur Abdulhamid Isa

Ukraine

Montserrat Miranda

Mexico

Nadá Majerníková

Slovakia

Natalya Chepelova

Russia

Nazanin Hazrati

Iran

Nikhil Chauhan

Georgië

Onyeka Kingsley

Nigeria

Prrinisha Kanabathy

Malaysia

Raful Navarro

Mexico

Rizana Riyaz

Ukraine

Ruby Owusua Diabene

United Kingdom

Ruchika Sukhwal

India / Kyrgistan

Schonza Felicitee

Rwanda

Siddharth Agrawal

India

Suranjana Banik

India

Veronika Shinkevich

Belarus

Viral Dave

India

Yaa Owusuaa

Ghana

New ambassadors

Ammas Mohammed

Harar Ethiopia

Anamarija Pavlovska

Skopje Macedonia

Anis Al-Maleki

Sanaá Jemen

Anna Chelchowska

Oxford UK

Arash Khojasteh

Theran Iran

Aryan Mehta

Amritsar India

Bernardinus Pradipta

Malang Indonesia

Beyza Nur Su

Malatya Turkey

Elif San

Malatya Turkey

Fatemeh Hazrati

Mashhad Iran

Hatice Goncu

Malatya Turkey

Iruoma Osonwa

Lagos Nigeria

Johannes Stalter

Germany

Karla Elena Rodriguez Rocandio

Mexico

Kunj Badiani

Dar es Salaam Tanzania

Lean Suiton

Laguna Philippines

Ljupka Pavlova

Macedonia

Marina Vidal Dos Santos

Brazil

Mohammadamin

Iran

Nadiia Mytrokhina

Ukraine

Nataliia Shapovalenko

Ukraine

Parth Gupta

India

Rhea Singh

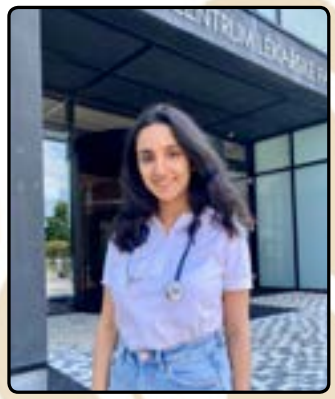
Ukraine

Ruchi Jani

India

Rutvee Patel

India



Saaz Sahani

Hradec Kralove Czech Republic

Sahar Sabaghz

Iran

Sai Ganehs Upputuri

India

Shweta Kharosekar

India

Sisasenkosi Grace Muguwu

Malawi

Urja Parekh

India

Valeriia Vartanova

Yethindra Vityala

India

Yoko Yamashita

Japan

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 March. 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.

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!

Partners

AMSA

The Asian Medical 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 Member Nations and 11 Associate/Observer Nations combine to share knowledge, undertake activities and social services and create international and transcontinental friendships. AMSA was 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 globe AMSA has an active student-exchange program, regularly undertakes national and regional projects, provides humanitarian assistance at times of need, produces quarterly student publications and liaises 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 established in 1979 and the first confreence was held in Mahidol University of Thailand, the Asian Medical Student's 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 INTERNATIONAL

Partners

AMSC

The Antwerp Medical Students' Congress is a project of the European Medical Students Association in Antwerp, Belgium. The AMSC has seen 13 editions. 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. The 14th edition will take place from the 9th to the 12th of September 2020. 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 workshops.

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 next edition of BRAINCOMS will take place in São Paulo, at UNIFESP - Universidade Federalde São Paulo, Brazil, from the 13th till the 15th of August 2020.

For more information, please, check our website: http://braincoms.com/2020/

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 16 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 seventeenth congress in a row will take place in 2021, at the School of Medicine University of Zagreb, Šalata 3.

This year's topic is Neuroscience. (This topic is only regarding lectures.) Topics for poster presentations may differ. For more details about how to register and participate in CROSS 16 visit our website: https://cross.mef.hr/en

CROATIAN STUDENT SUMMIT
SIXTEEN

EMSA

The European Medical Students' Association (EMSA) is a politically neutral, non-governmental, non-profit 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

ESC

Since its foundation in 1989, the ESC has become one of Europe's most established student biomedical conferences. It is our mission to promote the scientific exchange between students, scientists, and researchers worldwide. Every year, more than 500 participants from over 50 countries take the opportunity to attend keynote lectures by renowned experts, participate in exciting workshops, present their research, and explore the vibrant city of Berlin!

For more information, visit our website at https://esc-berlin.charite.de/en/ !

EUROPEAN
STUDENTS'
CONFERENCE
CHARITÉ BERLIN

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

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).

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-NL

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. The 12th Edition of LIMSC will take place 10th to 14th March in 2021.

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) 2020 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 29 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/

15TH WIMC
15TH WARSAW INTERNATIONAL MEDICAL CONGRESS

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 fourteen 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 15th YES Meeting, which will take place between the 17th and 20th of September 2020, whether as a Presenting or a Non-Presenting student. We are waiting for you!

YES MEETING
YOUNG EUROPEAN SCIENTIST MEETING

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

Organisation

Junior Scientific Masterclass
Graduate School of Medical Sciences

Research Institute

Junior Scientific Masterclass

Prof. Robert J. Porte MD PhD, Chair Junior Scientific Masterclass

The route to become a physician-scientist

Are you dreaming of becoming a physician who is trained to combine the care for patients with clinical science? The Junior Scientific Masterclass (JSM) of the University Medical Center Groningen (UMCG) presents you a unique possibility to realise this dream.

Because of the major growth in biomedical knowledge, there is a dire need for physicians who can translate fundamental insights into new clinical applications and, simultaneously, generate scientific questions based on clinical observations (i.e. translational research). In order to enforce clinical research, it is essential to immerse medical students into research during the pre-clinical phase of their curriculum. Therefore, the JSM educational programme encourages motivated students to seek research experience from the start of their medical education.

The JSM educational programme also enables medical students to apply for MD/PhD projects. The MD/PhD programme consists of clinical internships ('co-schappen') combined with a financed period of two extra years within the medical curriculum. This programme gives medical students the opportunity to successfully finish both their medical education (MD) and a PhD project within a period of eight years. The JSM educational programme in the Bachelor phase, the 'Bachelor Honours programme', consists of two phases.

The first phase entails getting familiar with research within (the Graduate School Medical Sciences of) the UMCG (GUIDE, BCN, SHARE and Kolff Institute). The second phase is meant to be a turning point and consists of a one-week course of intensive training in clinical research for a (selected) group of students, called the COMPASS week. In the second phase the students are also stimulated to choose their own line of research and apply for research grants.

The JSM programme has grown considerably since it started in 1999. In the period of 2001 until 2014, more than 850 students have been awarded Pilot Projects and 480 students an MD/PhD project. Until now, more than 200 students successfully mastered the MD/PhD programme. In 2008, the 'Mandema-stipendium' was introduced which enables young physician-scientists (MD PhD) to combine their specialist training with research and establish their own line of research.

The route to become a physician-scientist is challenging, but also highly rewarding. It represents an investment for a lifelong learning in the field of academic medicine.
Additional information: www.jsmgroningen.nl or j.s.masterclass@umcg.nl

Graduate School of Medical Sciences

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

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.

Personalized programmes

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

Research Master's programmes (2 years)

The Graduate School of Medical Sciences administrates two selective master programmes:

1. Clinical and Psychosocial Epidemiology

Clinical and Psychosocial Epidemiology (CPE) is a selective two-year research master. The programme is unique in the sense that students are encouraged to focus on their individual development as a researcher. Therefore, classes are taught in small groups. Students can choose additional courses that suit their personal interests and moreover, research will be conducted side by side with scientists who are leading experts in their field. Mental and physical health and the reciprocal relationship between these two forms the basis of the programme. There is a strong focus on prevention, diagnosis and treatment of physical and mental health conditions. The central idea is that psychological, biological and social aspects all play a role in any physical condition. Students conduct research in several populations, including children, adults and elderly, with or without a physical or mental condition.

Health Systems and Prevention track

The HSP track combines cutting-edge interdisciplinary research with practical policy questions, aiming to solve complex public health problems related to societal issues like an ageing population, increasing levels of chronic diseases, widening health inequalities, migration and urbanization. You learn to tackle issues like these from various academic disciplines, as you are taught and supervised by experts in economics,

2. Clinical and Psychosocial Epidemiology (CPE-SHARE)
The selective two-year master programme Molecular Medicine and Innovative Treatment (formerly known as Medical and Pharmaceutical Drug Innovation) offers research-minded students small-group interactive teaching in an international and multidisciplinary environment. You will learn how to creatively apply knowledge and we will train you to become a critical and analytical scientist. You will be challenged with exciting cutting-edge research and methodologies and will learn how to critically read the literature, design novel research questions, translate hypotheses into testable research plans, and write scientific essays. As a student you can focus on your interests and ambitions by participating in one of the following specializations after the first semester: Oncology, Neuroscience, Infection and Immunity, Nutrition and Metabolism, Systems Medicine and Drug Innovation.

If you are interested in applying for one of these programmes, please consult the How to Apply page on the website of the Graduate School of Medical Sciences.

Abel Tasman Talent Programme
The Abel Tasman Talent Programme (ATTP) supports high-potential international students to excel in the field of (bio)medical or pharmaceutical sciences. Two types of financial support can be distinguished: Financial support for students from one of our so-called 'preferred partner universities' and financial support for exceptionally talented students from other institutions.

More information: https://www.groningenbiomed.com/practical/abel-tasman-talent-programme/

Research Institutes

Our dynamic and innovative research ranges from fundamental to clinical, and translational research. All of our research focuses on Healthy Ageing. Our Research Institutes develop coherent multidisciplinary research programmes. All Institutes collaborate in the Graduate School of Medical Sciences to educate students for future scientific leadership.

Research Institute BCN-BRAIN
Director: prof. Iris E.C. Sommer MD PhD
Central theme: Behavioural and Cognitive Neurosciences

The Research Institute BCN-BRAIN was established in 2005 and is part of the Graduate School of Medical Sciences and of the Research School of Behavioural and Cognitive Neurosciences. BCN-BRAIN promotes research that is aimed at understanding the function of the healthy brain and dysfunction of the nervous system with reference to neurological and psychiatric disorders. Research is focused on translational collaboration between lab-based (molecular- and cell biological) and hospital-based (clinical) researchers integrating different levels of neuroscience research.

Research Institute GUIDE
Director: prof. Jos G.W. Kosterink PhD
Central theme: Chronic Diseases and Drug Exploration

The main asset of the Groningen University Institute for Drug Exploration (GUIDE) is the integration of clinical, biomedical and pharmaceutical research stimulating translational research and researchers with a keen eye on the complete spectrum of biomedical research: from bed to bench to drugs. Ageing is a central theme as most chronic diseases are age-dependent. Research focuses mainly on 1. Lead discovery, development of new drugs, drug delivery and advanced formulation technology and 2. Translational research on molecular and cellular mechanisms underlying disease (etiology and pathophysiology) and on research related to treatment of disease, e.g. in the context of clinical trials and by using relevant animal models.

Cancer Research Center Groningen (CRCG)
Director: prof. Mark van Vugt PhD
Central theme: Cancer Research

The Cancer Research Center Groningen (CRCG) organizes and facilitates high-quality, oncology-related research activities within the UMCG and University of Groningen. All research activities at CRCG share the overall perspective of 'healthier and longer lives of cancer patients through improved care'. Research is performed at the fundamental, translational and clinical levels and organized in a coherent and effective manner in several research programmes to achieve fundamental, clinical and societal relevant research output. Ultimately this leads to personalized cancer therapy, thus reducing the unintended side effects of treatment on normal tissues and improving the quality of life of cancer patients.

Research Institute SHARE (Science in Healthy Ageing and healthcaRE)
Director: prof. Maarten J. Postma PhD
Central theme: Prevention in Health Research

SHARE's mission is to identify determinants and consequences of illness and Healthy Ageing, conducted within inter-/multidisciplinary programmes, in close connection with societal parties and often based on observational data. The institute investigates and evaluates factors and interventions that are population-, patient- and/or healthcare-system-related.
It adds knowledge on prevention of and adaptation to disease, enhancing societal participation of patients with chronic somatic and mental disease and cost-effectiveness and efficacy of pharmaceutical, medical, life-style and psychosocial interventions.
Notably, a life-course perspective is taken, addressing research questions spanning from the preconception period, through infancy, reproductive and working ages to old age.

Research Institute W.J. Kolff
Director: prof. Yijin Ren DDS PhD
Central theme: Biomaterials

The primary objective of the W.J. Kolff Institute for Biomedical Engineering and Materials Science is to bring together pre-clinical and clinical research groups and to establish a center of expertise for the entire stage of biomedical materials science and its application involving basic materials science, medical product development and clinical evaluation that will contribute to the long-lasting well-being of patients in need of biomaterial implants and extra-corporal support systems. Research is conducted within four thematic research programmes each with their own specific theme: 1. Bioadhesion, biocompatibility and infection, 2. Nanobiotechnology and advanced therapeutic materials, 3. Restoring organ function by means of regenerative medicine and 4. Maintaining oral health and oral function.

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 fellows
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 www.eriba.umcg.nl

Congress

- Programme ISCOMS 2022
- Day chairs
- Jury chair + members
- Awards
- Focus: Personalised medicine
- Keynote lectures
- Interactive Operation
- Workshops
- ISCOMS corporate member meeting

Programme ISCOMS 2022

Tuesday 7th of June - Pre-course

08:15-09:00	Registration
09:00-09:30	Day opening
09:30-11:10	Course 1
11:10-11:50	Break
11:50-13:20	Science Elective
13:20-14:30	Lunch
14:30-16:00	Course 2
16:00-17:00	Speed keynote lectures
17:00-17:30	Your Future at the UMCG
17:30-17:45	Day closing
19:00-23:00	Social programme

Wednesday 8th of June - Congress day 1

07:45-08:30	Registration
08:30-09:00	Opening ceremony
09:00-10:00	Keynote lecture: Jeffrey Friedman
10:00-11:05	Poster session I
11:05-11:50	Break
11:50-13:05	Workshop I
13:05-14:20	Lunch
14:20-15:45	Oral session I
15:45-16:15	Break
16:15-17:15	Keynote lecture: Hanneke Schuitemaker
17:15-17:30	Closing ceremony
19:00-22:30	Recreational evening

Programme ISCOMS 2022

Thursday 9th of June - Congress day 2

08:30-09:00	Registration
09:00-09:15	Opening ceremony
09:15-10:15	Keynote lecture: Karl Deisseroth
10:15-11:20	Poster session II
11:20-11:50	Break
11:50 – 13:05	Workshop II
13:05-14:05	Lunch
14:05- 15:05	patient lecture
15:05 – 15:20	Break
15:20-16:20	Keynote Lecture: Roel Nusse
16:20 – 17:20	Plenary session I
17:20-17:35	Closing ceremony
19:30-23:30	Formal Dinner

Friday 10th of June - Congress day 3

08:30 - 09:00	Registration
09:00 - 09:15	Opening ceremony
09:15 - 10:35	Operation
10:35 - 11:35	Plenary session II
11:35 – 12:05	Break
12:05 - 13:20	Workshop III
13:20 – 14:20	Lunch
14:20 – 15:45	Oral II
15:45 – 16:15	Break
16:15 – 17:15	Keynote lecture: Bruce Beutler
17:15 - 18:00	Award & Closing ceremony
19:00 - 22:00	Buffet
22:00 - 02:00	World Wide ISCOMS Night

Saturday 11th of June – Post Congress Tour

08:30-20:30	Post Congress Tour

Day chairs

Wednesday the 8th of June
Prof. Debbie van Baarle MD PhD

Prof. dr. Debbie van Baarle is a pr ofessor in Immunology of Vaccinations at the University Medical Center Groningen since September 2020 and topex pert at the Center for Infectious Disease Control (CIb) at the National Institute for Public Health and the Environment (RIVM) since 2003. She is an immunologist with specific expertise in the immune response to viral infections. Her main research interest is to identify critical features of the T-cell response associated with 'protection' from viral infection or disease progression in order to improve vaccination strategies. More recently, she is focusing on understanding changes in immune health as a consequence of specific exposures (including age and shiftwork) in relation to vaccine responsiveness and finding ways to improve immunity to vaccination in risk groups. For the latter she is leading an H2020 IMI project on vaccination strategies for elderly (VITAL) which includes both induction of proper immunity to vaccinations, identification of biomarkers as well as communication on these strategies. Furthermore, she is a leading immunologist in several large multicenter ZonMW funded clinical COVID19 vaccine studies in patient groups. Prof. Debbie van Baarle is (co-)author of over 175 scientific papers published in peer-reviewed, international journals (H-index: 49), which have been cited around 8000 times. She successfully supervised 21 PhD students and currently has 7 PhD students in training, 2 postdocs and a team of 4 technicians.

Thursday the 9th of June
Prof. Barbara van Leeuwen MD PhD

Prof. Barbara van Leeuwen MD PhD is a professor in surgical oncology with the elderly patient as main interest. She was employed by the Dutch Cancer Foundation 2006-2008 as a clinical and research fellow in "cancer in the elderly". As such she gained valuable working and research experience in Uppsala University Hospital, Sweden, Whiston Hospital in Liverpool and the MD Anderson Cancer Center in Houston, USA. Her clinical work focuses on melanoma, sarcoma and peritoneal disease. She started work in the University Medical Center Groningen in September 2008 and was rewarded a tenure track fellowship by the University. Ever since then she has been the primary investigator in several clinical studies focusing on the elderly cancer patient. Related subjects include: value based healthcare, the decision making process, preoperative risk stratification, the surgery evoked inflammatory response and its detrimental effects, postoperative complications and telemonitoring. Preclinical research focuses on the surgery evoked inflammatory response and its detrimental effects, including neuroinflammation and postoperative cognitive decline. With her international consortium CHANGE, she contributes to knowledge necessary to change the healthcare system from disease centered to patient centered.

Collaborative partners include: LUMC, AMC, MUMC, Prins Claus Conservatorium Groningen, NFK, NFU, Menzis, Zilveren Kruis, Eurecat, Danone, Hanzehogeschool (University of applied sciences) Groningen, Institute for Evolutionary Life Sciences, research institute within the Faculty of Mathematics and Natural Sciences of the University of Groningen (GELIFES) and others.

She is the author of over 120 scientific papers and supervisor of many medical students and PhD candidates.

Friday the 10th of June
Prof. Ody Sibon MD PhD

Dr. Ody Sibon is a professor at the University Medical Center of Groningen (UMCG), Department of Biomedical Sciences of Cells and Systems. She obtained both her MSc degree in Biology (1989) and PhD degree in Molecular Cell Biology (1994) at the University of Utrecht. She worked as a postdoc at the State University of New York, Stony Brook (USA) where she was trained in genetics and development of Drosophila melanogaster (fruit fly). In 1998 she started her independent research group at the UMCG. She is the recipient of several prestigious Dutch fellowships (VIDI and a VICI) and was appointed as full professor in 2012. The main focus of her lab is to understand coenzyme A homeostasis in healthy cells and how this is affected in a class of neurodegenerative diseases. This fundamental knowledge is translated into therapeutic strategies for specific Neurodegenerative Diseases with Brain Iron Accumulation (NBIA). She participated in several European consortia dedicated to rare diseases and currently she is the coordinator of the first Dutch clinical trial investigating a vitamin B5 supplement for the rare disease: Pantothenate kinase Associated Neurodegeneration.

One of the most enjoyable aspects of working in an academic environment like the University of Groningen is the constant exposure to and interaction with interested and curious young people, like MSc and PhD students. The uninhibited curiosity and questioning of MSc students were the inspiration for key experiments that led to the development of the vitamin B5 derivative currently tested in the clinical trial." Therefore, it is a great honour for me to participate in ISCOMS, the world largest meeting for medical students, organized by medical students. ISCOMS always has had great success in featuring world leading scientists as key-note speakers, including many Nobel prize winners, making the ISCOMS experience, from young to old, and from novice to emeritus professor, an unforgettable one. I very much look forward to this upcoming ISCOMS and wish you all an inspiring and motivating meeting!"

Jury members

Prof. Dr. Martin de Borst MD PhD

Consultant nephrologist at the UMCG and professor of medicine at the University of Groningen

Prof. Martin de Borst is consultant nephrologist at the University Medical Center Groningen and adjunct professor of medicine at the University of Groningen.

His clinical duties include the care for patients with chronic kidney disease and kidney transplant recipients. This includes the prevention and treatment of allograft rejection and infections, and cardiovascular risk management. At the UMCG, each year ±180 patients undergo a kidney transplantation, the majority from a living donor.

Prof. de Borst's research focuses on cardio-renal medicine: the interaction between chronic kidney disease and cardiovascular complications. His main scientific aim is to identify targetable factors and innovative treatments to prevent progressive kidney function loss and the development of cardiovascular disease. So far, he has published over 200 peer-reviewed articles in leading scientific journals including the New England Journal of Medicine, Lancet Diabetes and Endocrinology, and Nature Reviews Nephrology. His work is embedded in several national and international research consortia, and is supported by the Dutch Organization for Scientific Research (ZonMW/NWO), Dutch Kidney Foundation, Dutch Heart Foundation, and the European Union. Prof. de Borst is also involved in multiple public-private collaborations, supported by the Dutch Ministry of Economic Affairs (TKI grants). He supervises a team of twelve PhD students, three post-docs, two research analysts and many students. He is the co-founder of NOVO, a national platform that facilitates clinical trials and large cohort studies in the Netherlands. He is (co-)Principal Investigator of several multicenter clinical trials, including the K+ in CKD trial (clinicaltrials.gov NCT03253172) and the EFFECT-KTx study (NCT03769441). In 2020, he received the Stanley Shaldon award for young investigators from the European Renal Association (ERA).

Prof. de Borst is Associate Editor of Nephrology Dialysis Transplantation, the flagship scientific journal of the ERA-EDTA. He is also past chair of the Young Nephrologists' Platform, an ERA-EDTA committee dedicated to promoting the development of young kidney specialists in Europe.

"I vividly remember my participation in ISCOMS as a medical student in 2002. I was very excited when I received both the Public's Award and the First-year-student-Jury Award at the time. Presenting and discussing my work at ISCOMS was one of the fine opportunities that set the stage for my future as a clinical researcher. I hope you will have the same experience, and look forward to meeting you at the congress!"

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 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 in Management of Transfusion Medicine, which is now part of the Master programme of the University of Groningen Graduate School of Medical Sciences.

emProf. Cees Th. Smit Sibinga is still deeply involved in transfusion medicine and related health sciences research focused on developing countries. He serves WHO Eastern Mediterranean Region as a Lead Technical Adviser in their Strategic Framework for Blood Safety and Availability 2016-2025 and its priority interventions.

Prof. Karina Meijer MD PhD

Professor of Thrombosis and Haemostasis at the UMCG

Karina Meijer (1970) is professor of Thrombosis and Haemostasis at the University Medical Center Groningen (UMCG), The Netherlands.
She started her career as a PhD candidate studying liver disease in haemophilia. From that time on, she is fascinated with coagulation. After she finished her training in internal medicine, haematology and thrombosis, she returned to the Haemophilia Treatment Center (HTC) Groningen.

In her clinical work, she focuses on diagnosis and treatment of bleeding disorders and on academic and regional consulting for coagulation issues. Much of this work intermingles with teaching: with the clinical team, she provides coagulation training for internal medicine and other teaching programs.

As director of the HTC Groningen, she led research on arterial disease in haemophilia and on bleeding disorders in women with heavy menstrual bleeding. However, her real research focus is on the optimal use of anticoagulant treatment. She contributes to translational projects, but her own research is strictly clinical, answering questions that arise in daily clinical practice. Recently, one of her PhDs finished a multicenter RCT on the best strategy for dosing antidote to patients who bleed while on vitamin K antagonist anticoagulation. Other ongoing projects include development of prediction tools for substandard anticoagulation, choice of anticoagulant in elderly patients and low molecular heparin dosing in ICU patients.

The Haemostasis and Thrombosis unit participates in numerous investigator initiated national projects, and in phase 1, 2 and 3 trials in haemophilia and thrombosis. The most exciting development in the past years is the application of gene therapy in patients with severe haemophilia B, who were effectively cured from their genetic disorder.

Karina Meijer loves to work in the academic environment of the UMCG, where teaching, research and clinical work form a daily mix and she has the opportunity to work with enthusiastic, smart and dedicated people.

Prof. Marthe Walvoort MD 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 recently received the KNAW Early Career Award and NWO Athena Award. In her research, Walvoort combines her expertise in (organic) chemistry and biochemistry to unravel the impact of sugars in health and disease.

Joost Beusekamp MD PhD

ANIOS Cardiology at University Medical Center Groningen (UMCG) and President of ISCOMS 2015

Joost was the president of the organising committee of ISCOMS in 2015. Seeing all the enthusiastic students from all over the world, convinced him to explore a scientific career for himself as well. After ISCOMS, he successfully applied for the MD/PhD programme of the Junior Scientific Masterclass in Groningen. This programme provides you with a personal grant to fulfil your own research projects and to combine this with your clinical rotations. During the MD/PhD programme his research focussed on the interaction between serum potassium levels and the optimal use of (guideline directed) medication in patients with heart failure. Additionally, he participated in the execution of a clinical trial on the safety and effect of the relatively novel drug empagliflozin (on in the class of the SGTL2-inhibitors) in patients hospitalised for acute heart failure. In February 2022, he successfully defended his thesis at the University of Groningen.

"Dear participants, I am looking forward to welcoming you all in Groningen. Hopefully, the majority of you will be able to attend the congress in person and for the others, the organizing committee will do everything they can to make sure you can experience all ISCOMS has to offer online as well. Let us use this combination of online and in-person sessions to expand our scientific network across all borders ."

Marieke Goodijk

Medical student and President of ISCOMS 2020

Dear participants,

My name is Mar ieke Goodijk 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. Soon I will travel to Deventer to complete the last part of my medical study. ISCOMS also inspired me to do medical research when I became aware of the importance of this during my board year. 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 an unique platform to do so.

As president of ISCOMS 2020, I am honored to be a jury member of the 29th edition of ISCOMS this year! After almost 30 years of experience, ISCOMS has grown to become the leading student congress in biomedical sciences. Despite the many challenges the organising committee faced due to the COVID-19 outbreak, interaction with participants and international exchange of research remained possible through a digital platform. Switching to an online congress and creating something entirely new would never have been possible without the immediate support from all our participants. It was encouraging to see how many of you were enthusiastic to present research online and interact with each other in this way. I am very proud of this year's organising committee, because they managed to create a wonderful programme in these exceptional times.

I would like to wish you all a great time at ISCOMS 2022, 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,-, the second prize of €750,-, and the third prize of €250,-. You can spend this money on visiting biomedical congresses of your choice. All of these winners will also receive a one-year online subscription to world's leading multidisciplinary science journal 'the New England Journal of Medicine' (NEJM). The winners will be selected by a jury of renowned medical scientists and (bio)medical students.

Plenary presentation: Audience award
The winner of this award will be determined by the audience. The plenary presenter most appreciated by the audience will receive a cheque of €150,- to spend on visiting a biomedical congress of his or her choice.

Plenary presentation: First Year Jury Award
This is a special award, as the jury consists of first year (bio)medical students only. Despite not having much research experience, they will judge the plenary sessions open minded and with great care. The winner of this award will receive €150,- and a one-year online subscription to world's leading multidisciplinary science journal 'the New England Journal of Medicine' (NEJM).

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 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 with either an abstract award for the Clinical Sciences, the Basic Sciences or the Community Health. Our official jury will select three winners out of all different oral topics. Winners will receive a cheque of €100,- to spend on visiting a biomedical congress.

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

Please note, all of the prizes which include money, should be claimed within a maximum of three years after this 29th edition of ISCOMS. The awards can only be spent on visiting (bio)medical congresses, and only the travel costs and the costs for the congress itself can be declared.

Focus: Personalised Medicine

Personalised Medicine
Every individual patient is unique. Therefore, the theme of the 29th edition of ISCOMS is Personalised Medicine. Personalised Medicine refers to a medical model that uses individual phenotypic and genotypic characteristics to choose a balanced therapeutic strategy specific to the patient.

Healthcare continues to innovate and new tailor made diagnostic and therapeutic strategies are being developed. As a result, healthcare is becoming increasingly personalised. Personalised Medicine can be found in all areas of healthcare, both diagnostic and therapeutic. In addition, in the University Medical Center Groningen (UMCG) shared decision making is one of the most important aspects of healthcare. The choice of treatment is hereby made by the specialist and the patient together. In this way the patient participates in the decision making of the following treatment. As a result, each patient is treated in the best way possible.

During the three days of the congress, the theme will be visible in various parts of the congress.
For this theme, we will introduce a Personalised Medicine logo. This logo will be coupled with keynote speakers, workshops and presentations who have Personalised Medicine processed in their research. The parts of the congress that represent the theme will be marked with the Personalised Medicine loge on our website.

Keynotes

Prof. Jeffrey Friedman MD PhD

"Leptin and the Regulation of Food intake and Body Weight."

Dr. Jeffrey Friedman is currently a Professor at the Rockefeller University, an Investigator at the Howard Hughes Medical Institute. Professor Friedman is a physician scientist studying the physiologic and genetic mechanisms that regulate food intake and body weight. Dr. Friedman's research on a genetic basis of obesity received national attention in late 1994, when it was announced that he and his colleagues had isolated the mouse ob gene and its human homologue. They subsequently found that injections of the encoded protein, leptin, decreases body weight of mice by reducing food intake and increasing energy expenditure. They showed that leptin is an afferent signal in a negative feedback loop that maintains homeostatic control of body weight. Current research is aimed at understanding the neural and physiological mechanisms by which leptin transmits its weight-reducing signal.

Professor Friedman's lecture will be about 'Leptin and the Regulation of Food Intake and Body Weight'.

Prof. Hanneke Schuitemaker PhD

"The development of the Janssen COVID-19 vaccine: a marathon at sprint speed."

"The development of the Janssen COVID-19 vaccine: a marathon at sprint speed."

Hanneke Schuitemaker PhD is the Head of Viral Vaccine Discovery and Translational Medicine and Disease Area Stronghold Leader for Viral Vaccines at Janssen Vaccines & Prevention B.V. She has been in these roles since 2010 and oversees Janssen's viral vaccine programs including investigational vaccine candidates for HIV, respiratory syncytial virus (RSV), Ebola, Zika, COVID-19 and HPV. In addition, she is a Professor of Virology at the Amsterdam University Medical Center.
Janssen started in January 2020 with the development of a COVID-19 vaccine. Thirteen months later, the vaccine was approved for emergency use. During Professor Schuitemakers' lecture, the most important data of this development trajectory will be discussed as well as the complexity of working on vaccine development during the pandemic. After the baccin was approved, the developmental process was far from finished so an overview of additional activities will also be shared. The name of her lecture will be "The development of the Janssen COVID-19 vaccine: a marathon at sprint speed". Because it truly is a marathon at the speed of sprint with no clear finish line.

Prof. Karl Deisseroth MD PhD

"Inner workings of channelrhodopsins and brains."

Karl Deisseroth is Professor of Bioengineering, and of Psychiatry and Behavioral Sciences, at Stanford, and Investigator of the Howard Hughes Medical Institute . He continues as a practicing psychiatrist (inpatient and outpatient) at Stanford with specialization in affective disorders and autism-spectrum disease, employing medications along with neural stimulation. Deisseroth also serves as Director of Undergraduate Education for Bioengineering at Stanford.

In exploring how properties of the brain arise from activity of its cellular components, Deisseroth has pioneered the basic science discoveries that enabled this goal, including resolving the structural and functional mysteries of natural light-gated ion channels and discovery of the neural cell types and connections that cause adaptive and maladaptive behavior. His laboratory has created and developed technologies for observing and controlling biological systems at high resolution, while maintaining these systems in the intact state; these technologies include optogenetics, hydrogel-tissue chemistry, and a broad range of enabling methods.

Professor Karl Deisseroth's lecture will be about 'Inner workings of channelrhodopsins and brains'. The lecture will outline a new cryo-electron microscopy structure of ChRmine at 2.0 Å resolution. The structure reveals striking architectural features never seen before in channelrhodopsins.

Prof. Roel Nusse PhD

"WNT Signaling Leads To Cell Division. But How?"

Professor Nusse has been a Howard Hughes Medical Institute Investigator since 1990 and has been the chair of the department of Developmental Biology at Stanford from 1999 to 2020. Currently, he is the Virginia and Daniel K. Ludwig Professor of Cancer Research. Roel Nusse has made major discoveries in developmental biology and adult stem cell research. His pioneering research has elucidated the mechanism and role of Wnt signaling, one of the paradigms for the fundamental connections between normal development and cancer. These discoveries relate to fundamental questions on embryogenesis. Roel Nusse co-discovered the gene 'Wnt', which is involved in both embryonic development and cancer. He went on to show that this gene is at the heart of a signaling pathway which directs the growth and development of tissues.
Professor Roel Nusse's lecture will be about 'Wnt Signaling Leads To Cell Division. But How?'.
The lecture will outline how Wnt signaling leads to cell division and how it regulates stem cell differentiation and self-renewal.

Regental Prof. Bruce Beutler MD

"From phenotypes to genes in immunity."

Regental Professor Beutler is an American immunologist and geneticist. He has won the Nobel Prize in Physiology or Medicine in 2011 for his discovery concerning the activation of innate immunity. Regental Professor Beutler surmised that Tumor Necrosis Factor (TNF) mediated much of the acute systemic inflammatory response triggered by administration of LPS to mammals. This pointed the way to the later use of antibodies against TNF in chronic inflammatory diseases.

After this, Beutler developed chimeric proteins in which the TNF receptor was attached to antibody heavy chains. These proteins strongly and specifically inhibited TNF, were non-antigenic, and ultimately helped many patients suffering from TNF-mediated inflammatory diseases. Beutler resolved to find the receptor for lipopolysaccharide (LPS), one of the classical inducers of these cytokines. Beutler and his group also reported that toll-like receptor 4 (TLR4) was the essential membrane-spanning component of the LPS receptor and was highly specific as an LPS sensor.

Regental professor Bruce Beutler's lecture will be about 'From phenotypes to genes in immunity'. The lecture will outline how TLR's detect microorganisms and activate our innate immunity and how TNF is involved in inflammatory diseases.

Interactive Operation

The operating theatre of the future: Fluorescence Guided Surgery

Prof. M.J.H. Witjes MD PhD

During ISCOMS 2022, we will show an example of a potential surgery of the future; Tongue cancer removal guided by fluorescence molecular imaging. Prof. M.J.H. Witjes MD PhD, Oral and Maxillofacial surgeon and principle investigator of the Optical Molecular Imaging Group (OMIG), will guide you through the surgery and show the added value that fluorescence during surgery can have.

The University Medical Centre Groningen is one of the seven academic centers for the treatment of patients with oral cancer in the Netherlands. For these patients, the main pillar of treatment is surgery, and without treatment mortality is up to 100% within six months. The biggest challenge during these procedures is to remove the complete tumor. However, tumor positive tumor margins after surgery remain high which has a mayor impact on patient prognosis. Tumor margin control has not improved in the last decades, mainly because the only intraoperative feedback surgeons have is their visual and tactile information. Fluorescence molecular imaging is a technique that can highlight disease such as cancer and aid surgeons in detecting tumor deposits not visible to the naked eye. The data from our clinical trials show that this technology is able to identify tumor positive margins during surgery. Using this technique, might lead to an improvement in oral cancer surgery and prognosis.

Workshops ISCOMS 2022

1. Suturing
2. Lab on a chip
3. Dental implants
4. Positive Energy
5. The miracle of giving birth
6. Basic life support
7. Transgender workshop
8. Fix a mandibular fracture yourself
9. Guided tour in the central animal facility of the UMCG
10. Macro- and microscopic suturing
11. Inside the psychotic experience
12. Interactive trauma lecture
13. SW: Surgical anatomy of the heart and surgical treatment of end-stage heart failure: LVAD
14. Diagnosis of liver tumors with emphasis on macroscopic features; what is the role of normal habitat of non-neoplastic cells
15. Introduction to medical radiography
16. Lab visit with PhD students
17. Real sounds sent out by your ear
18. Revalidation with exoskeleton
19. Laparoscopy box
20. An introduction in life threatening situations in the ICU
21. 3D lab Groningen
22. Surgical anatomy of the heart and surgical treatment of atrial fibrillation

Workshop: Suturing

Department: Surgery, UMCG
Supervisor: H. Sijbrand Hofker MD
Days: Wednesday June 8th, Thursday June 9th, friday June 10th

Get a head start on learning a fundamental surgical skill. Our suturing workshop provides you with the training and materials to practice a variety of suturing methods (simple interrupted, simple continuous and, subcutaneous) on real porcine skin. The workshop consists of two parts. The first part is a theoretical outline of several aspects of wound closure, illustrated with pictures and short animations. The second part is a practical session that features the guidance of an attending surgeon, allowing personal instruction for every participant. By the end of the workshop, students leave with basic skills necessary to practice basic suturing and achieve mastery.

Note: The practicing will be on real pig's legs.

Workshop: 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
Days: Thursday June 9th, friday June 10th

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 (10-6 to 10-15 µL) 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 becomes possible to think about assembling tissue constructs or actual tissue samples in physiological configurations in specially designed lab chip systems, so-called “body-on-a-chip” or “human-on-a-chip” system. 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 a short glimpse into how a laboratory is actively involved in the realisation of lab chip systems for sensing/analytical chemistry and cell culture and analysis. Participants will see the fabrication of those devices and the basic principles of microfluidics. Besides that, they have an opportunity to discuss about other possible medical uses of the lab-on-a-chip technologies with researchers in the lab.

Workshop: Dental implants

Department: Oral Maxillofacial Surgery, UMCG Prosthetic Dentistry, UMCG
Supervisors: Prof. Henny J.A. Meijer DMD PhD, Prof. Gerry M. Raghoebar DMD PhD, Wim J.W.A. Slot DMD PhD, Charlotte Jensen DMD PhD
Days: Thursday June 9th

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 the 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.

Workshop: Positive Energy

Department: Radiation Oncology, UMCG
Supervisors: Prof. Stefan Both PhD MD PhD
Days: Wednesday June 8th

Radiation oncology is a rapidly evolving field where innovative technology, physics, and medicine merge and enhance one another. Pencil beam scanning (PBS) is a relatively new radiation therapy technique that involves protons instead of traditional X-rays. PBS offers new opportunities for cancer patients, who benefit from significant reduction of radiation exposure to normal tissues. In certain patients this may lead to less side effects and consequent irreversible late complications of treatment.
During this workshop, you will have the opportunity to participate in our 'radiotherapy operating room'. In an interactive manner, you will experience the processes of radiation treatment planning and radiation delivery. You will be part of discussion on patient selection including ethical issues and cost effectiveness, and ongoing scientific investigations to compare PBS to other radiation therapy techniques."

Workshop: The miracle of giving birth

Department: Clinical Training Center, UMCG
Supervisors: Marco A.C. Versluis MD PhD, Dennis Beekhuis MD
Days: Wednesday June 8th

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 categorised 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.

Marco Versluis

Bauke van Minnen

Workshop: 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
Days: Wednesday June 8th, Thursday June 9th, friday June 10th

During this workshop you will be invited to engage with fellow students (3-4 people) to show us a perfect resuscitation (with AED) and continue the resuscitation for some time (5-7 minutes). The students who do not participate in the cardiopulmonary resuscitation-action (CPR) are invited to assess this resuscitation: what is going well and what could go better. If you are working as a doctor, it is necessary to take the leadership on a resuscitation team and to have the ability to coach your CPR-team. A good observation of skills is a requirement of a doctor in order 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 minimise interruption. At the end of this workshop you can exercise your CPR skills with the AED. The workshop will end with a certificate of participation "Workshop: heroes aren't born, they are trained" given by the Wenckebach Training Institute of the UMCG. To prepare for this workshop you 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.

Workshop: Transgender workshop

Department: Genderteam UMCG
Supervisor: A. G. Schuringa
Days: Wednesday June 8th

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 gender queer 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 includes 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, 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 you will be able to ask questions to a member of the UMCG Genderteam and a transgender patient.

Workshop: Fix a mandibular fracture yourself

Department: Oral and Maxillofacial Surgery, UMCG
Supervisors: Prof. Ruud R.M. Bos DMD PhD, Dr. Baucke van Minnen
Days: Thursday June 9th

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 is to give insight in the widely accepted treatment modality of mandibular fractures: internal fixation with mini plates and screws. After a short introduction of the principles of mandibular fracture treatment, the participants will perform an osteosynthesis of mandibular fractures in a polyurethane mandible with mini plates and screws.

Workshop: Guided tour in the central animal facility of the UMCG

Department: Research Support Facility – Central Animal Facility
Supervisors: Catriene Thuring VMD PhD en Annemieke van Oosten PhD
Days: Wednesday June 8th, friday June 10th

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 consists of a guided tour in this facility. During the tour the current status of laboratory animal experimentation within the UMCG will be presented to you.

Please note:

For permission to participate in the tour it is important that you have not had contact with rodents or rabbits in the 24 hours prior to the tour. In this way we want to prevent unwanted transmission of pathogenic micro-organisms to our laboratory animals.

Workshop: Macroscopic suturing

Department: Research Support Facility – Central Animal Facility
Supervisors: Annemieke van Oosten PhD, Catriene Thuring VMD PhD
Days: Thursday June 9th

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 is 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 micro suturing.

Please note:

For permission to participate in the workshop it is important that you have not had contact with rodents or rabbits in the 24 hours prior to the workshop. In this way we want to prevent unwanted transmission of pathogenic micro-organisms to our laboratory animals.

Workshop: Inside the psychotic experience

Department: Psychiatry, UMCG
Supervisor: F. D. van Es MD
Days: Thursday june 9th, friday june 10th

Psychosis is a generic psychiatric term for a mental state often described as 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 cause 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 you will be able to ask questions to a psychiatrist and a patient who has suffered from psychosis.

Workshop: Interactive trauma lecture

Department: Orthopaedics / Trauma
Supervisor: Patrick Nieboer, trauma surgeon
Days: Wednesday June 8th

What would you do when more patients enter the emergency room than you can handle? How would you decide which patient gets a ticket to the Intensive Care Unit (ICU) / Operating Room (OR) when there are only limited resources available? What would you do if patients' conditions are, or become life threatening and help is not directly available?

In this workshop you, as a group, will have to make and motivate decisions about which patients you are going to treat and which patients not. Together we will reflect on the choices you make.

Workshop: Surgical anatomy of the heart and surgical treatment of heartfailure: LVAD

Department: Cardiothoracic Surgery, UMCG
Supervisors: Michiel Erasmus MD PhD, Wobbe Bouma MD PhD, Massimo Mariani MD PhD
Days: Thursday June 9th

Heart failure is an increasing world-wide problem. Until recently, heart transplantation was the only effective option to prolong 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.

Workshop: Diagnosing of liver tumors with emphasis on macroscopic features: What is the role of normal non-neoplastic cells?

Department: Pathology
Supervisor: Marius van den Heuvel, MD PhD
Days: Thursday June 9th, friday June 10th

Despite the introduction of sophisticated techniques in modern pathology, macroscopic interpretation of resection specimens remains the cornerstone in diagnostic surgical pathology. Participants are invited to describe and interpret the macroscopy of liver tumor resection specimens. There will be emphasis on diagnosing tumors on their macroscopic features (in relation to normal, non-tumoral counterparts) and staging of tumors on macroscopy.

Workshop: Introduction to medical radiography

Title: Introduction to medical radiography
Department: Radiology, UMCG
Supervisor: Arjen van Hulzen, Msc

At every radiology department in the world radiography is the trusted workhorse of medical imaging since the discovery of X-rays in 1895. Today most radiographic systems are fully digital and the technique has matured to a steady level. In this workshop basic principles of radiographic imaging are explained and examples from daily practice are demonstrated with the help of life like phantoms. After this workshop participants will have a basic understanding of the use of X-rays in radiography. The relation between dose and image quality and the different factors that influence image quality are explained and demonstrated.

Workshop: Lab visit with PhD students

Days: Thursday June 9th

During this workshop you will get the opportunity to visit research laboratories in the UMCG. You will get a guided tour from a PhD student. Meanwhile you can ask this student anything you want to know about doing research in Groningen. Also, they will show the kind of research that is performed in the labs, and tell their own experiences with doing research here.

Workshop: Real sounds sent out by your ear

Department: Otorhinolaryngology, UMCG
Supervisor: A. (Bert) Maat MSc
Days: Friday June 10th

72% of healthy human ears are emitting acoustic energy just below the hearing threshold. This phenomenon is called Spontaneous Otoacoustic Emission (SOAE). The origin of this acoustic signal lies within the cochlea. Outer hair cells (OHC's) in the cochlea are believed to play a key role in generation of Otoacoustic Emissions (OAE's). OAE's have been found in other mammals, but in non-mammals as well, such as lizards, frogs, and birds, sharing this fundamental biophysical mechanism. What can we learn from this fundamental mechanism, do they interact with incoming sounds, why do they exist, and can we make use of OAE's in diagnostics? But the bigger question is: do you have SOAE's? In this workshop you will find out.

Workshop: Revalidation with exoskeleton

Title workshop: Spinal cord injury; Lets Walk!
Department: UMCG Center for Rehabilitation, Physical and Rehabilitation medicine
Speakers: Dr. G.E. van der Wal, MD PhD and Drs. M. Tepper MD

Spinal Cord Injury (SCI) is an event in which the individual experience reduced or complete loss of mobility below the lesion level. Worldwide SCI has an incidence of 3.6-195.4 cases per million worldwide1. In the Netherlands the incidence of traumatic SCI is about 200 cases per year, the non-traumatic SCI is much higher2. Individuals with motor-complete SCI use, generally, a wheelchair to move toward a destination in their daily activities3. 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 had been a key and challenge within rehabilitation medicine3. In the past decades, 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 the different possibilities to improve walking or make walking able will be discussed. Especially the exoskeleton possibilities and when to use them. Several walking devices will be demonstrated. After this workshop, medical students will know when to indicate certain exoskeletons or other walking devices for individuals with loss of mobility, particularly individuals with spinal cord injury.

Workshop: Laparoscopy box

Days: Wednesday June 8th, Thursday June 9th, friday June 10th

Stupnik Simulator

Video-Assisted Thoracoscopic Surgery (VATS) offers a minimally-invasive approach to lung resection that studies show offers less pain, lower risk of infection, and shorter length of hospital stay compared to traditional thoracotomy. Yet today less than half of lung resections utilize a VATS approach.
One reason is that VATS is a complex procedure that requires a significant amount of training. This training can be expensive and infrequent, and not all surgeons have access.
To address the problem, Johnson & Johnson collaborated with Tomaž Stupnik, M.D., PhD from University Medical Centre Ljubljana in Slovenia, to develop a transportable surgical simulator and structured curriculum to help both trainees and surgeons hone their core VATS skills.
"Training of core VATS skills outside of the operating room can help surgeons gain competency in a safe, efficient manner," said Dr. Stupnik.
To complement the simulator, the Johnson & Johnson Institute professional education team in Europe designed and developed a low-cost, 30-degree thoracoscopic training camera which can be powered via a USB port. This enables the simulator to be run via a standard laptop rather than with expensive hospital equipment.

Simendo Simulator

Using the Simendo simulators you will be able to train and secure the skills needed for Minimal Invasive Surgery that are frequently applied by surgeons, gynaecologists, urologists and orthopaedists. With these training solutions there is no supervisor required to make sure the required skills are obtained.

Workshop: An introduction in life threatening situations in the ICU

Department: Department of Critical Care, UMCG
Supervisors: A. (Annalies) de Bont-Prins and M. (Marije) Smit MD
Days: Friday June 10th

Implementation of interdisciplinary teams in the ICU 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.

Workshop: 3D lab Groningen

Department: 3D-lab / Orthopedic Surgery / Trauma Surgery
Supervisor: Peter Pijpker, Anne Meesters en Nick Assink (Technical Physicians and 3D specialists)
Days: Thursday June 9th, Friday June 10th

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

Workshop: Surgical anatomy of the heart and surgical treatment of atrial fibrillation

Department: Cardiothoracic Surgery, UMCG
Supervisors: Prof. M. Mariani MD PhD, W. Bouma MD PhD
Days: Friday june 10th

Atrial fibrillation is an increasing world-wide 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 surgical treatment modalities. The different surgical 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 surgical treatment.

Pre-Course

Day Chair on Tuesday the 7th of June
Prof. Geert van den Boogaart PhD

Prof. Van den Boogaart his laboratory studies human immune cells in a range of diseases, including infectious diseases, autoimmune diseases and cancer, and is positioned at the interface of chemistry, microscopy and immunology. The goal of his lab is to understand and ultimately tailor membrane trafficking pathways in immune cells to cure and prevent disease. The central focus of our research is the cellular mechanisms that lead to the uptake and degradation of foreign antigen and the trafficking cascades that underlie antigen presentation and cytokine release by phagocytes of the immune system. To resolve the membrane trafficking routes of immune cells, we develop and apply advanced microscopy techniques and novel chemical tools. His lab follows a multidisciplinary approach which combines advanced cell biology on primary blood-isolated immune cells, with a bottom-up approach where complex trafficking pathways are reconstituted in precisely definable in vitro systems.

His research is funded by several prestigious (inter)national grants and received the following prestigious awards such as the Dutch Society Prize for Young Talent from the Royal Dutch Society of Sciences for best Master's research in biochemistry (2004) and the Heineken Young Scientist Award for Biochemistry and Biophysics from the Royal Dutch Academy of Sciences (2012).
He has published over 70 papers, many in top journals such as Nature, Science, eLife, Nature Communications, and Nature Struct. and Mol. Biol. His laboratory consists of 6 PhD students, 2 post-docs and 1 technician. He has over 5000 citations resulting in an H-index of 33 (Google Scholar). He has lectured at over 20 invited talks all over the world and several times acted as a member of evaluation committees for NWO (TOP/ECHO and VENI).

Although this is his first experience with ISCOMS, he had the pleasure to be invited to meetings organised by students from Heidelberg University (Germany), the MRC Laboratory of Molecular Biology (Cambridge, UK), and the Max Planck Institute of Molecular Cell Biology and Genetics (Dresden, Germany). He likes these meetings, as they are excellent opportunities to engage and discuss science with the next generation of scientists. Moreover, the program of ISCOMS is fantastic with a strong lineup of world-renowned speakers. I really look forward to meeting you at the congress!

Speed keynotes

Dr. Laura M.G. Meems MD PhD

"Sex-specific differences in heart failure."

Heart failure is a major and global disease with an extremely high healthcare burden. In the USA, annual median medical costs for heart failure care are estimated at $24,383 per patient, mostly driven by hospitalizations due to heart failure (median $15,879 per patient). In the case of heart failure, the heart becomes sick and unable to adequately supply organs with blood and nutrients. Patients with heart failure typically suffer from shortness of breath, swollen ankles or legs, orthopnea, nocturia and reduced exercise tolerance. Causes of heart failure are diverse and may result in different subtypes of heart failure. Typically, men are diagnosed with heart failure with a reduced (<40%) ejection fraction (HFrEF), while women suffer from heart failure with a preserved (>50%) ejection fraction (HFpEF). Dr. Meems and her team are interested in why these sex-specific differences in heart failure exist and they designed an experimental study to further investigate heart failure development in males and females. Details and newly obtained, non-published results of this interesting study will be shared in this Speed Keynote Lecture.

Otto van Leeuwen PhD

"Transplantation of high-risk donor livers: exploring the boundaries."

Liver transplantation is the standard treatment for patients with end-stage liver disease. Unfortunately, the success of liver transplantation is strongly inhibited by the shortage of donor organs. With an ageing population and increasing rates of obesity, diabetes mellitus and cardiovascular disease, the quality of the average donor organ has been decreasing for decades. Therefore, more and more donor livers (up to 35% in the Netherlands) are not used for transplantation because they are considered too high risk. In this speed keynote lecture, dr. Otto van Leeuwen presents his work on enabling successful transplantation of these discarded donor livers, using a novel technique called machine perfusion. The use of this technique resulted in 20% extra liver transplants in the University Medical Center Groningen over the last years.

Masterclasses

Medical Statistics
Dr. 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?
- How do we calculate a sample size?

Based on the article of Selles et al. (2021) analyzing the effect of treatment (operative vs nonoperative) on the functional outcome in patients with a displaced intra-articular distal radial fracture, we will go through several steps of the statistical process. Starting with descriptive statistics, and refreshing the theory of hypothesis testing, we will end up with how to interpret the results of the analyses and integrate the findings across similar studies using meta-analytic thinking.
Emphasis will not be on formulas and mathematics, but on understanding the logic behind the statistical tools to avoid biased conclusions. Depending on the interest of the participants, more time can be spent on elementary or advanced statistics.

Preparing oral presentations
Prof. Anton J.W. Scheurink PhD

This masterclass will provide strategies for preparing interesting and engaging presentations. The essence of an effective presentation is 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 provides the audience with cues and information in an orderly structure, allowing them to form expectations on what they will hear and when they will hear it. Tips for doing so, along with tips on what not to do, will be supplied. The presenter will engage participants in a highly interactive format by crafting storylines and structures from material that they provide. The focus of this masterclass will be on oral presentations but at the end we will give some dos and don’ts on poster presentations as well.

How do scientific reviewers review your article?
Prof. Dr. J.A. Lisman MD PhD

After years of meticulous study design, data analysis and perfecting your article, there is only one task left; getting your article published!
How do you choose the right scientific journal for your manuscript, and what happens after the submission of your article to your journal of choice? Which features render your paper attractive to the editor and how do you increase the likelihood that your manuscript will be sent out for review? What will convince the reviewers that your work is good and how do you respond to their comments? How do you react to a rejection by the editor, would you accept it or fight for your article?
Prof. Dr. J.A. Lisman will help you to find the answers to all these questions in this very interactive Masterclass.

Predictive models in healthcare
R.G. Pleijhuis MD PhD

What is the probability that an individual patient will respond to a certain therapy? Or will it develop serious side effects? Clinical prediction models can be used to provide answers to these important questions, therewith providing a solid basis for clinical decision making.
The amount of clinical prediction models published in the literature has increased exponentially over the past few decades. Also, more and more attention is being paid to machine learning algorithms for clinical application. But when is it then that only a few prediction models make it to the clinic? And do machine learning algorithms perform better than conventional prediction models?
In this interactive masterclass, R.G. Pleijhuis MD PhD, internist, and founder of prediction platform Evidencio, will provide an answer to above-mentioned questions. You will learn how to create a fully functional web-based prediction model yourself in just a few simple steps. Finally, possibilities to judge clinical prediction models on their merits will be discussed.

Critical Reading
Girbe Buist PhD

Medical students are supposed to read an enormous amount of information in textbooks, on the internet, and in medical journals. Research is progressing fast, and textbooks often contain dated information. Recent manuscripts provide up-to-date information. However, are we certain that the presented information is valid and should be implemented in patient care? Critical appraisal of a manuscript enables the assessment of the validity of the study results. In this pre-course class, participants will be provided with a general approach to critically appraise clinical research papers and assess research design, identify selection bias, information bias, and confounding factors. Different research designs will be presented, and strengths and weaknesses will be discussed. Participants will assess a paper critically. The results of the assessment will be discussed in the masterclass.

Famelab
Bart van de Laar, MSc

X-factor, Got Talent shows, MasterChef, you name it. Talent scouting is a big thing and results in prize winning television. However, do we embrace science communication talent just as passionately as we embrace young singers and chefs? Or is science communication too important to be in the hands of young talents? On the other hand, they do shape the future of science.

FameLab is the number one international science communication contest, inviting scientists, mathematicians, and engineers across the globe to take part. The FameLab contestants only have three minutes to convey a scientific concept of their choice to a professional jury. It is not allowed to use a PowerPoint or any other tool to facilitate the clarity of the presentation. All contestants are judged on the three C's: content, clarity, and charisma. An unforgettable presentation might make one the winner of a national or international FameLab competition someday. Moreover, you'll learn to master an essential skill for a PhD-student or post-doc: engage future research partners, funders and all sorts of audiences.

This hands-on masterclass challenges participants to prepare and present a three-minute presentation according to the FameLab rules. The masterclass is convened by Bart van de Laar, Dutch FameLab pioneer and regular local/national convenor, together with one of the winners of last year's FameLab heat.

Scientific Electives

Dr. House MD
Dr. Marco Versluis MD PhD

In this Science Elective we will analyse a gynaecological episode of the fascinating House MD series. During this Science Elective, a specialist on the topic of the episode will discuss the facts and myths of a House MD episode.

Doctor Gregory House is not known for his commitment and empathy towards his patients, staff, or interns. These characteristics often place him, his colleagues, and patients in problematic situations. However, to what extent is an episode realistic? Are the disease characteristics of the patients like those in real life? And are the used diagnostic tools suitable? What can we learn from this television programme?

These questions will be answered during this interactive course, where participants will be able to judge and discuss the authenticity of a House MD episode.

WHO: Towards Eliminating Avoidable Harm In Health Care

emProf. Cees Th. Smit Sibinga MD PhD FRCP Edin FRCPath

Every point in the process of health care can contain an inherent risk. Its nature and scale vary greatly based on the context of health care provision and its availability, infrastructure, and resourcing within and across countries. The challenge for all health systems, and all organizations providing health care, is to maintain a heightened awareness to detect and ameliorate safety risks as well as address all sources of potential harm.

Patient safety is a framework of organized activities that creates cultures, processes, procedures, behaviours, technologies, and environments in health care that consistently and sustainably: lower risks, reduce the occurrence of avoidable harm, make error less likely and reduce its impact when it does occur.

Patient safety is also a strategic priority for modern health care and is central to countries' efforts in working towards Universal Health Coverage (UHC). In more recent years, the focus has also been on economic losses and access problems due to unsafe care, that may become a major barrier in achieving UHC. Research studies have shown that an average of 1 in 10 patients is subject to an adverse event while receiving hospital care in high income countries. The estimate for low- and middle-income countries (LMICs) suggests that up to 1 in 4 patients are harmed, with 134 million adverse events occurring annually due to unsafe care in hospitals, contributing to around 2.6 million deaths. Overall, 60% of deaths in LMICs, from conditions amenable to health care are due to unsafe and poor-quality care. Mostly, people link patient safety with hospital-based care, though unsafe care is a system-wide problem. Half of the global disease burden arising from patient harm originates in primary and ambulatory care.

The WHO launched in 2020 a Global Patient Safety Action Plan 2021-2030 towards eliminating avoidable harm in health care, with 6 Strategic Objectives.
This ISCOMS 2022 Science Elective will provide a more detailed insight in the global burden of unsafe health care and how to mitigate at least avoidable harm.

Huntington's disease: fascinating insights in a fascinating disease

Prof. Berry Kremer MD PhD
Chairman Dept. of Neurology at UMCG

Huntington's disease (HD) is an autosomal dominant hereditary neurodegenerative disorder with an estimated prevalence in the western world of about 10/100,000. Characteristic clinical features are a gradual deterioration of cognition and behavior, with manifestations such as apathy, mood disorder, impulse control impairment and violent outbursts, and motor impairment. The best-known motor manifestation is chorea (hence the old name: Huntington's chorea), but other hyperkinetic motor impairments such as dystonia, myoclonus and tremor as well as hypo- and bradykinesia can be observed in many patients.

The signs and symptoms are related to the distribution of the neuropathology: a progressive degeneration of medium sized spiny interneurons in the neostriatum and, to a lesser extent, of cortical neurons. Although motor manifestations are the most obvious disease manifestations, patients and their families suffer particularly from the cognitive and psychiatric deterioration. Due to the gradual progression and the multi-domain impairments, onset age is difficult to pinpoint but onset is generally after age 25. Onset range is remarkably broad, with many patients starting after age 60 but, also, 10% before age 20.

Although HD is yet incurable, modern genome wide association studies have identified modifier genes that retard or, alternatively, speed up onset age and disease progression, thus suggesting potential targets for disease modifying therapies. An exciting development are trials with intrathecal anti-sense oligonucleotides that target intraneuronal translation of the mutated gene product.
In this lecture, prof. Kremer will present videos of patients with HD and will highlight aspects of this fascinating disease.

Social Programme

Monday 6nd of June 2022
Welcoming night: city tour & pub quiz

If you are already in Groningen on Sunday, you can participate in the city tour we organise Sunday evening. We will walk through the historic city centre of Groningen and show you the most beautiful and fun spots in the city. The tour will end at a local pub in the city centre, where the welcoming night will take place. At this pub, we will join a pub quiz together 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.

Tuesday 7th of June 2022
Salsa workshop

Most of you will arrive today. When you have registered for the pre-course, the evening social programme is included. During the day you can participate in the pre-course to improve your research skills. When the educational programme is finished, we will guide you to the location where the dance class will take place. On arrival, a buffet will be served and we will have dinner together. Afterwards, there is a salsa workshop. After the intensive day, you have the opportunity to blow off some steam and show everyone your dancing skills!

Wednesday 8th of June 2022
Recreational evening

We will start the evening by having dinner with the entire group. Afterwards, you will have the opportunity to join the activity you chose. We will prepare different activities which you can choose. Some examples of activities we organised last year are: biking tour of Groningen, a yoga workshop, bowling and many more!

Thursday 9th of June 2022
Formal dinner

After the second congress day, we will have a formal dinner at one of the most prestigious places of Groningen: the historical "Der Aa-Kerk". This church will be transformed into a fancy dining room with a capacity of 350 people! An outstanding three-course dinner will be served, among which you can choose between meat or vegetarian dishes. You will have the opportunity to get to know the other ISCOMS-participants and to meet some of the professors who will be present at the formal dinner. For an amazing appearance it would be great if you bring an elegant dress or your best suit. Bring some cash for the evening for drinks!

Social Programme

Friday 10th of June 2022
World Wide ISCOMS Night

After the last congress day and the closing ceremony, we will go to 'Huize Maas' where the World Wide ISCOMS Night will take place! 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 the traditions of the different countries represented at ISCOMS. Dress up in traditional clothes and bring a traditional snack of your country. We would love to play music specifically from your country, so please bring a USB-stick with your favourite music. The DJ will take care of the rest and make sure you have an unforgettable night!

Saturday 11th of June 2022
Post Congress Tour

Unfortunately, the congress will be over after the World Wide ISCOMS Night. But don't worry because we have one last activity for you: the Post Congress Tour! During this day we are going to make a city trip to Zwolle, the capital of the province of Overijssel! This day we organise some fun activities and you can relax and learn a lot about the Dutch culture, food and lifestyle.

Plenary Session

Presenters:

Tolstoluzhinskaya, A.E. (Anastasiya Evgenievna)
Patkó, E.P. (Evelin)
Weening, EH (Eerde)
Sahani, S (Saaz)
Salem, H.M.A (Hagar)
Ebrahim Soltani, Z.E.S. (Zahra) M.D
Laupp, A.L. (Alexander)
Shumkova, D.

Combination immunotherapy with immune checkpoint inhibitors for Hodgkin's lymphoma: An in-vitro study

Sahani, S (Saaz)[1], *Visser, L (Lydia)*[2]

[1] *Charles University in Prague, General Medicine, Hradec Kralove, Tsjechië*
[2] *UMCG, Cancer Biology, Groningen, Netherlands*

Introduction

Most classical Hodgkin's lymphomas express PD1/PD-L1, indicating a significant role in immune cell evasion. Immunotherapy with checkpoint inhibitors is a promising treatment strategy, showing marked response to cytotoxic T lymphocyte-associate protein-4 (CTLA-4) and programmed cell death-1 receptor (PD-1). The approved checkpoint inhibitors targeting these antigens are Ipilimumab and Nivolumab, respectively. It is important to provide a rationale for targeting multiple immune checkpoints. The study aimed to examine the response of these drugs in PD-L1-expressing and non-expressing cell lines for optimization of the treatment regime.

Materials & Methods

Two human lymphoma cell lines were cultured at the Department of Pathology, at UMCG. SUPHD1 cell line expressed both PD-L1 and PD-L2 while L428 expressed only MHC class II. The cell lines were treated with peripheral blood mononuclear cells (PBMCs) from 3 healthy HLA-matched donors to reproduce an in vitro T-cell response. Each subject was treated with monotherapy of Nivolumab(1ug/ml) Ipilimumab(1ug/ml) and then combined Nivolumab/ Ipilimumab therapy. The IL-2 and IFN-gamma response(biomarkers of T-cell activation) was measured using ELISA after 8 and 11 days. Statistical analysis was carried out using GraphPad Prism.

Results

In the PD-L1 negative cell line (L428), there was no additional T-cell response to Ipilimumab. The response with Nivolumab was low and comparable to the untreated subjects. However, in the PD-L1 positive cell line (SUPHD1), there was a marked response of T-cells activation with Nivolumab; seen in both IL-2 and IFN-g bio-assays ($p=0.031$). In this cell line, the most pronounced response was with combination therapy where there is an 80-90% increase in IL-2 secretion in comparison with untreated subjects ($p=0.031$).

Conclusion

Our results suggest that Ipilimumab monotherapy is more effective than Nivolumab for PD-L1 negative tumours. However, Ipilimumab in combination with Nivolumab has a synergistic response for tumours expressing PD-L1. This also highlights the importance of screening patients for PD-L1 in order to personalize their treatment and increase the likelihood of positive outcomes.

Sex differences and selenium deficiency in heart failure

Weening, EH (Eerde)[1], Bomer, N (Nils) Dr.[2], Al-Mubarak, A (Ali) drs.[2]

[1] *UMCG, Experimental Cardiology, Groningen, Nederland*
[2] *UMCG, Experimental Cardiology, Groningen, Netherlands*

Introduction

Sex differences are observed in the epidemiology, phenotyping and prognosis of heart failure. Though the causative mechanisms of sex differences remain controversial, distinct nutritional demands and metabolism of males and females are thought to play a role. Selenium is an essential micronutrient that is needed for the enzymatic function of 25 selenoproteins, which serve various functions in cardiovasular physiology. In this study, we aim to elucidate effect modification by sex in the association of selenium with multiple clinical parameters in heart failure.

Materials & Methods

In this study, 2328 patients from the BIOSTAT-CHF cohort, a multinational, prospective, observational cohort that enrolled patients with worsening heart failure, were included. Baseline characteristics and effect modification of sex between selenium deficiency and cardiovascular outcomes were investigated. Cox regression analyses were performed for selenium and primary and secondary endpoints, stratified by sex and multiple subgroups.

Results

Of all measured clinical parameters, five were found to show significant interaction effects (p<0.1). Female sex was an effect modifier between selenium deficiency and older age (p=0.080), higher systolic blood pressure (p=0.012), higher ANP levels (p=0.088), and increased risk of hypertension (p<0.001) and atrial fibrillation (p=0.099), whereas these parameters remained relatively unchanged in males regardless of selenium status. Moreover, higher selenium concentrations were associated with lower risk of all-cause mortality or hospitalization in both males (HR 0.94; 95% CI 0.91 – 0.97) and females (HR 0.94; 95% CI 0.88 – 0.99).

Conclusion

Effect modification by sex is seen in the clinical presentation of heart failure, varying with selenium status. Females especially showed a hypertensive phenotype (hypertension, increased SBP and ANP levels) with increased risk for atrial fibrillation (AF) when selenium deficient. An association between higher selenium and a decreased risk of all-cause mortality or hospitalization for HF was present in both sexes and several subgroups. While sexual dimorphism in selenium biology may explain the clinical differences in HF, interventional research is needed to confirm this link.

Elucidation of the effect of mesenchymal stromal cell extracellular vesicles on fibrosis.

Tolstoluzhinskaya, A.E. (Anastasiya Evgenievna)[1,2], Basalova, N.A. (Natalia Andreevna)[3], Karagyaur, M.N. (Maxim Nikolayevich)[3,4], Efimenko, A.Y. (Anastasia Yuryevna)[3,4], Eremichev, R.Y. (Roman Yurievich)[3]

[1] *Lomonosov Moscow State University, Medical research and education centre, Institute for Regenerative Medicine, Moscow, Rusland*
[2] *Lomonosov Moscow State University, Faculty of Biology, Department of Embriology, Moscow, Rusland*
[3] *Lomonosov Moscow State University, Medical research and education centre, Institute for Regenerative Medicine, Moscow, Russian Federation*
[4] *Lomonosov Moscow State University, Faculty of Fundamental Medicine, Moscow, Russian Federation*

Introduction

Fibrosis is a process of an active growth of connective tissue that can lead to a violation of the tissue architecture and even to a complete loss of organ function. The unit of fibrosis named fibroblastic focus is a locus of extracellular matrix (ECM) surrounded with myofibroblasts producing ECM and activated fibroblasts on the edge. It was found that mesenchymal stem/stromal cells (MSCs) are able to secrete extracellular vesicles (EV-MSC) that can suppress fibrogenesis and even lead to fibrosis reversion. MicroRNAs within EV-MSC may play a key role in the process. To understand better the mechanisms mediating the effects of microRNAs transferred by EV-MSC on the processes of fibrogenesis we developed a 3D model of fibroblastic focus.

Materials & Methods

In order to study fibrogenesis in vitro we used a 2D model of TGF-β-induced fibroblasts differentiation into myofibroblasts and also 3D model of a fibroblastic focus based on decellularized matrix spheroid reseeded with myofibroblasts. With the method of ultrafiltration of conditioned MSC medium we obtained EV-MSC which were added to these models. The function of specific fibrosis-related microRNAs was modulated by EV-MSC transfection with synthetic microRNA inhibitors. Immunocytochemical analysis, dot-blot, collagen gel contraction assay were used to test the antifibrotic properties of EV-MSC in cellular models of fibrogenesis.

Results

With the addition of EV-MSC the number of myofibroblasts and fibrotic ECM markers decreased in 2D fibrosis model. Using 3D cellular model which was closer to the real structure of fibroblastic focus in vivo we showed, that the treatment with EV-MSC resulted in a reduction of myofibroblasts features and the destruction of the structure of fibroblastic focus. We conducted an inhibitory analysis and revealed that the effect of EV-MSC was mostly due to microRNAs miR-129 and miR-92a transferred into myofibroblasts within the focus.

Conclusion

Thus, using 2D and 3D cellular models we confirmed the contribution of EV-MSC to the processes of fibrogenesis and their ability to inhibit fibrosis. These data further can be used to consider EV-MSC and specific antifibrotic microRNAs as one of the promising candidates to the treatment of fibrosis. The study was conducted by RFFI (#20-315-90120).

The protective effects of PACAP1-38 on the retinal vasculature and hypoxic molecules in rat glaucoma model

Patkó, E.P. (Evelin)[1], Szabo, E.S. (Edina)[2], Vaczy, A.V. (Alexandra)[2], Molitor, D.M. (Dorottya)[2], Tari, E.T. (Tari)[2], Li, L.L. (Lina)[2], Csutak, A.C. (Adrienne)[3], Toth, G.T. (Gabor)[4], Reglodi, D.R. (Dóra)[2], Atlasz, T.A. (Tamas)[2,5]

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[2] *University of Pecs Medical School, Department of Anatomy, MTA-PTE PACAP Research Team, Pecs, Hungary*
[3] *University of Pecs Medical School, Department of Ophthalmology, Clinical Centre, Pecs, Hungary*
[4] *University of Szeged Faculty of Medicine, Department of Medical Chemistry, Szeged, Hungary*
[5] *Szentagothai Research Center, Department of Sportbiology, Pecs, Hungary*

Introduction

Despite the critical impact of glaucoma on blindness, its cause is not fully understood. Animal models are important for better understanding the mechanism behind this disease. Elevated intraocular pressure (IOP) is a risk factor for glaucoma. In our previous study, we described an inducible, microbeads model in Sprague Dawley (SD) rats in which we were able to prove the neuroprotective effects of PACAP1-38 eye drops treatment. Vascular factors have been suggested to play an important role in the development of glaucoma, based on numerous studies. In our present study, our aim was to examine the possible protective effects of PACAP1-38 eye drops on the retinal vasculature and the molecular patterns of hypoxia in the hypertensive glaucoma model.

Materials & Methods

We induced hypertension through injection of polystyrene microbeads into the anterior chamber of SD rats, PBS receiving rats served as controls. Intraocular pressure was recorded every two weeks. Optical coherence tomography images were made at the end of the study to examine the retinal structure. We assessed retinal degeneration, vascular and molecular changes through immunofluorescence. HIF1α A protein level was also measured by western-blot.

Results

Significantly increased IOP was observed in the glaucomatous vehicle-treated group (Beads+S) however, in the PACAP1-38 treated group (Beads+P) the IOP remained in a normal range. Optical coherence tomography images suggested severe retinal degeneration in the glaucomatous group, although protective effects were measured after topical administration of PACAP1-38. We also found several vascular parameters changed in the Beads+S group. The examination of molecular patterns suggested hypoxic conditions in the Beads+S group, however after PACAP1-38 administration retinoprotective effects were observed in HIF1α protein level.

Conclusion

Our results show that PACAP1-38, given in form of eye drops, is retinoprotective in glaucoma, providing the basis for potential future therapeutic administration.

Prediction of tumor primary site based on brain metastases using deep learning

Shumkova, D.[1], VanderBroeck, L.W.A.J.[1], Hassan, A.[2], Renne, I.W.S.[2], Pereira Bourlios, K.[1], Baggerman, K.[1], Daanen, A.S.[2], Speldenbrink, J.B.[1], Moharam, H.E.[2], Beuque, M.P.L.[3], Keek, S.[3], Woodruff, H.C.A.[3]

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[2] *Maastricht University, FHML, Maastricht, Netherlands*
[3] *Maastricht University, Precision Medicine, Maastricht, Netherlands*

Introduction

Patients with brain metastases have a poor median survival of 3.7 months (Lyu, 2021). Therefore, fast and effective therapy choice is vital. Treatment results are determined by the tumor primary site and its histology. Currently, clinicians conduct a biopsy to define the origin of the brain metastases when primary lesion site is unknown (Yu, 2020). This is an invasive procedure performed on severely diseased cancer patients. This emphasizes the significance of creating a non-invasive technology for determining the main tumor location in order to benefit patients' treatment. This research was aiming to automatically classify brain metastases by their origin using the Xception deep learning model with MRI input data.

Materials & Methods

The dataset from University of California – San Francisco (USCF) medical center included 1390 gadolinium-enhanced T1w MRI's of the patients with brain metastases mainly coming from lung, melanoma and breast. The dataset already included delineations, however all patients were manually checked and corrected when necessary. Dataset was split in train, validation and test sets of 60%, 20% and 20% respectively. Images were pre-processed and different techniques, such as histogram matching, z-score equalization and white-stripe equalization were compared. Xception model was used for binary and multi classification of metastases based on their site of origin. Evaluation techniques included confusion matrix and area under the curve (AUC).

Results

When using the Xception CNN model, testing AUC of 0.805 was achieved for classification of Breast-derived and Melanoma-derived brain metastases. Z score pre-processing increased AUC for Lung-derived versus Breast-derived metastasis classification from 0.705 to 0.755. The lowest AUC score of 0.656 was observed when distinguishing Lung-derived metastases from Melanoma-derived. Multiclass classification resulted in 0.660 AUC.

Conclusion

Binary classification allowed good discrimination between metastases of different origins. The highest AUC of 0.805 was generated by Melanoma-derived and Breast-derived metastases. Multiclass classification outperformed Lung versus Brest-derived melanoma classifier. These results could be further improved by our planned experiments. Ultimately the accurate determination of metastases origin may aid clinical practice in terms of pre-therapeutic assessment.

Molecular Mechanism Of Melatonin Induced Modulation Autophagy Induced By High Glucose In Schwann Cells

Salem, H.M.A (Hagar)[1], Soi Moi, C (Chye) Associate Professor[2]

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[2] *International Medical University, School of Health Sciences, Biomedical Science, Applied biomedical sciences and biotechnology, Kuala Lumpur, Malaysia*

Introduction

Diabetic neuropathy is a condition in which nerve fibres are continually exposed to high glucose-induced free radicals. Melatonin is an indole hormone that has strong anti-oxidant properties and autophagy-modulatory effects. Autophagy is the process in which toxic and unwanted cellular components are degraded. Thus, in this study, we investigated if melatonin counteracts the high glucose induced cytotoxicity in Schwann cells by modulating autophagy and the pathways involved. Schwann cells are known to be involved in the pathogenesis of diabetic neuropathy and RT4 D6P2T cells are one kind of neuronal Schwann cells that were proven to be an appropriate diabetic neuropathy cell model.

Materials & Methods

RT4 D6P2T cells were cultured and used for this study. The cells were treated with a high glucose concentration, with or without various concentrations of melatonin, and the cell viability was measured via 3-(4,5-Dimethylthiazol-2-yl)-2,5-Diphenyltetrazolium Bromide (MTT) assay. Next, autophagy was determined by acridine orange (AO) staining. Finally, western blot analysis was used to assess the involvement of autophagy and endoplasmic reticulum stress pathways.

Results

Following treatment with glucose, the results demonstrated high glucose induced cytotoxicity and autophagy in RT4 D6P2T cells. After treatment of the cells with melatonin, the results showed that melatonin not only prevented glucose-induced cell death and autophagy, but also decreased the levels of cytotoxicity and autophagy in a dose-dependent manner. Furthermore, the results demonstrated that high glucose up-regulated LC3, ATF4, ATF6, CHOP, PERK and eIF2alpha protein expression; however, melatonin attenuated these changes, by down-regulating the expression of LC3 and the ER stress markers ATF4, ATF6, CHOP, PERK and eIF2alpha.

Conclusion

It was concluded that melatonin alleviates high glucose-induced autophagy in RT4 D6P2T cells, through PERK-eIF2α-ATF4-CHOP signaling pathways. These results support the potential use of melatonin for the therapeutic treatment of diabetic neuropathy. Understanding the molecular mechanism by which melatonin inhibits autophagy will assist us in tracing back any unintended consequences of its use, when testing it for treatment of diabetic neuropathy in humans. There is, therefore, a need for further research into the involvement of other cellular molecular pathways in melatonin's inhibition of autophagy.

ENHANCED CATHETER: Electrochemical sensor device for in-vivo real-time blood testing at the bedside

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Introduction

In critical care, measurement of key laboratory parameters (e.g. pH, lactate, glucose, pO2, CO2) is currently only available as separate blood-consuming tests. Real-time monitoring in-vivo would certainly improve patient individual treatment, safety and would be a great step towards personalized medicine. For this purpose, we are developing a smart sensor device, applicable to clinically used catheters.

Materials & Methods

Real-time measurements require unreactive biosensors that integrate all necessary components in a multisensory approach on a catheter. The basic module of the electrochemical sensors is a set of three electrodes. They are coated with a selective, biocompatible hydrogel to protect the surface from deterioration as well as to detect specific molecules. Polyaniline-modified sensors can monitor the pH level in a physiological range via the open circuit potential. Spiked phosphate-buffered saline was employed as representative media. Glucose and lactate can be detected by cyclic voltammetry via the specific reaction of enzymes integrated into the sensor coating.

Results

Our multidisciplinary team successfully fabricated an electrochemical sensor on a central venous catheter using additive cutting-edge nanotechnology manufacturing (thickness < 100 nm). Additionally, we conducted several in-vitro experiments to benchmark its functionality and hemocompatibility.

The pH level was measured in a range between 2 and 8 with an expected increase of potential due to rising acidity. The sensor exhibits a low determination coefficient of 94.16% and indicates the need for further improvement of this measuring technique. The glucose measuring by cyclic voltammetry at -0.5 V in solutions between 0 mM and 20 mM shows an increasing current saturated at 1.65 µA and correlated to the soaring amount of electrons. The hemocompatibility tests of the modified hydrogel biosensors exhibit just a few adhesive leukocytes to their surface compared to the sensors with uncoated electrodes, which show a major platelet and leukocyte adhesion.

Conclusion

Future research involves the sensor’s miniaturization, material synthesis (metals, polymers) and testing (e.g. mechanical properties, toxicology, biostability and sterilization). The in-vitro development of the sensors will be followed up by an in-vivo validation in an experimental pig model.

Mesenchymal stem cells (MSCs)-derived exosome for treatment of rat Proctitis Model.

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Introduction

Proctitis is a significant concern of inflammatory bowel diseases (IBD), especially ulcerative colitis(UC), causing bleeding, rectal pain, and diarrhea. This condition puts patients at risk of anemia, fistula, and ulcer of the rectum. Medications and surgery are the conventional methods for treating patients. On the other hand, exosome is trending these days as a new method for treating so many diseases by its immunosuppressive and tissue repairing potential. Here we tried an MSCs-derived Exosome for treating the proctitis model of rats.

Materials & Methods

Twenty-four rats were randomly assigned into four groups; A. sham, B. control, C. local exosome, and D. systemic exosome group. Exosome was derived from human allogeneic mesenchymal stem cells and prepared for injection. First, rats were anesthetized, and the proctitis model was induced by rectal administration of 3% acetic acid in all groups except the sham group. Next, the exosome was administered through rectal and intraperitoneal injection in groups C and D, respectively. After three days, rats were sacrificed, and their rectum samples were harvested and assessed for histopathological, IHC, and PCR analysis.

Results

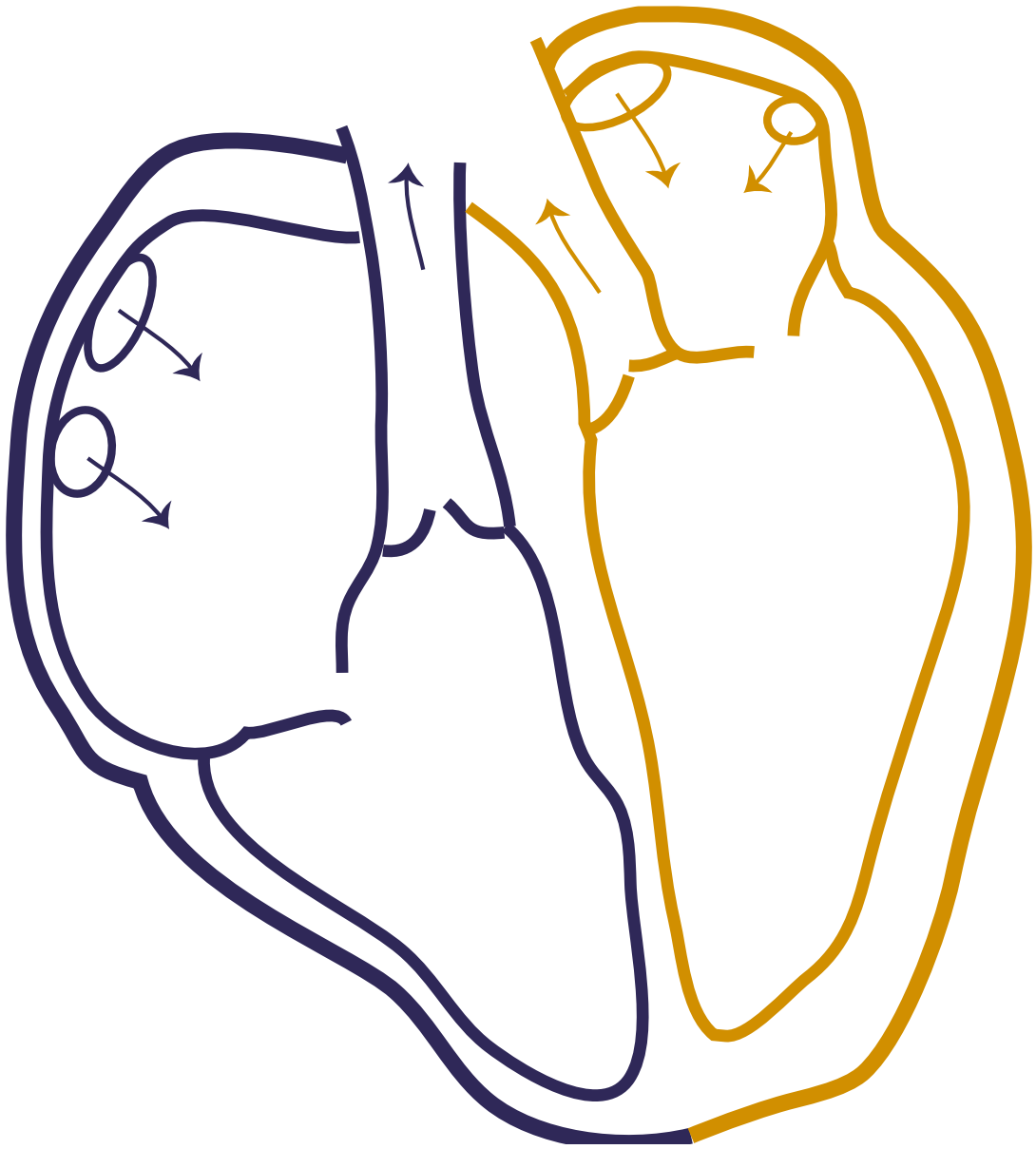
The gene expression of inflammatory-related pathway and cytokines had shown NF-κB (p-value<0.01), TLR4 (p-value<0.05), and TNFα (p-value<0.01) were suppressed significantly in systemic exosome group compared to control rats, while the result was not promising for local exosome. Meanwhile, the anti-inflammatory and anti-oxidative factors, IL-10, TGFβ, and super oxidase dismutase-1 (SOD-1), were higher in the systemic exosome group than other groups (p-value<0.01, <0.01, and <0.001 respectively). Moreover, the expression level of IL-6 in IHC of the rectum was decreased significantly in group D compared to B and C (p-value< 0.01). Also, the pathologic score for neutrophil infiltration and Mucosal ulceration and necrosis were lower in Group D.

Conclusion

Exosomes can suppress the inflammatory response in the proctitis model and improve the healing process of the rectum. Showing anti-inflammatory, anti-oxidative, and healing promotion attributes of the exosome in this study implicates the therapeutic benefits of the exomes in the treatment of proctitis.

Oral Sessions I

Cardiology



Presenters:
Holthaus, MH (Michelle)
Fallahzadeh, A.F (Aida) Dr
Dehghan Tarazjani, A. (Amireza)
Staferov, A.S. mr. (Aleksei)
Kokkorakis, M (Michail)
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PAD4 deficiency affects inflammatory responses and cardiac recovery after myocardial infarction in mice

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Introduction

Myocardial infarction (MI) is one of the most life-threatening diseases worldwide. Characteristic after acute MI is the rapid recruitment of leukocytes to regulate inflammation and the subsequent healing process. Excessive inflammation leads to an adverse cardiac remodeling, resulting in ventricular dilatation and fibrosis. The enzyme peptidylarginine deiminase 4 (PAD4) plays a crucial role in various pathological conditions. First, PAD4 was reported to regulate the formation of extracellular traps (NETs) in neutrophils. Here, we investigated the influence of PAD4 on macrophage polarization in vitro as well as after MI in vivo.

Materials & Methods

For in vitro polarization, bone marrow-derived wild type (WT) and PAD4-/- macrophages were treated with

IFN-ɣ and LPS or IL-4 to induce M1-like and M2a-like macrophages, respectively. MI was induced by permanent ligation of the left coronary artery (LAD) in 9-12 weeks old, male WT and PAD4-/- mice. On days 1, 3 and 7 after MI, plasma IL-6 levels were quantified by ELISA. Additionally, cardiac leukocyte recruitment and reactive oxygen species (ROS) were assessed by FACS analysis and malondialdehyde quantification, respectively. The infarct sizes and fibrotic area were quantified by 2,3,5-triphenyltetrazolium chloride (TTC) or Masson's trichrome staining at days 7 or 28 after MI. Cardiac function was analysed by echocardiography at days 1 and 7 post-surgery.

Results

Significantly reduced expression of pro-inflammatory genes was observed in M1-polarized PAD4-/- macrophages as well as in WT macrophages treated with the PAD inhibitor Cl-amidine in vitro. After MI, reduced ROS levels were detected in cardiac tissue of PAD4-/- mice at days 1 and 7 accompanied by smaller infarct sizes. PAD4-/- mice had significantly fewer leukocytes including monocytes/macrophages than WT mice on day 1 after MI, but the number of these increased significantly over time, so that ultimately more anti-inflammatory M2-like macrophages were detected in the hearts of PAD4-/-mice on day 7 after MI. Accordingly, less fibrosis and improved cardiac function was found in PAD4-/- mice.

Conclusion

PAD4 deficiency is associated with cardioprotection after MI due to diminished inflammation, altered leukocyte recruitment, less tissue damage and fibrosis.

In hospital and one-year outcomes of patients without traditional coronary risk factors presenting with acute coronary syndrome: A single-center landmark analysis

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Introduction

Noticeable proportion of patients admitting with acute coronary syndrome (ACS) have no standard modifiable cardiovascular risk factors (SMuRFs; hypertension [HTN], diabetes mellitus [DM], dyslipidemia [DLP], and cigarette smoking [CS]). Outcome of this population after percutaneous coronary intervention (PCI) and differences between in male and female population are debating topics. Thus, in the present study, we analyzed data from patients with ACS who underwent PCI to evaluate clinical characteristics and outcomes in patients with and without modifiable risk factors and to compare adverse outcomes between women and men in each group.

Materials & Methods

In this registry-based design, we included 7847 patients with ACS who underwent PCI between April 2015 and December 2019. Outcomes were compared in two groups; with and without SMuRF (SMuRF-less). The main outcomes were in-hospital mortality, all-cause mortality and major adverse cardiovascular and cerebrovascular events (MACCE) occurrence. A separate landmark analysis with the landmark (cut-off) set at 30 days after the index procedure was performed.

Results

Almost 11% of patients undergoing non-elective PCI have none of traditional coronary heart disease (CHD) risk factors. During 12.13 months follow-up, in-hospital mortality (OR 1.46, P value= 0.18), all-cause mortality (HR 1.06, P value= 0.76) and MACCE (HR 0.90, P value= 0.37) were statistically similar between patients with and without SMuRFs. Results were the same after performing landmark analysis. In patients who had at least one SMuRF, women had higher one-year mortality compared to men (HR: 1.427, P value=0.038); however, this association was not significant among SMuRF-less patients (HR:1.982, P value=0.197).

Conclusion

SMuRF-less patients had the same in-hospital mortality, one-year all-cause mortality and MACCE compared to patients with at least one risk factor. Women have higher one-year all-cause mortality if they had at least one SMuRF.

The prognostic value of E/Em and DT in heart failure patients with preserved ejection fraction

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Introduction

Heart failure with preserved ejection fraction (HFpEF) is a worldwide growing issue. Several prognostic echocardiographic parameters have been proposed so far but they lack a reliable cut off. The aim of our study was to suggest a cut-off for these parameters including E/Em.

Materials & Methods

The study included 100 HFpEF patients according to Framingham criteria and ejection fraction>45%, pro-B type Natriuretic Peptide>500 pg/ml, and diastolic dysfunction. Neither of the patients suffered from atrial fibrillation, myocardial infarction, valvular disorders, congenital heart disease, ejection fraction (EF) less than 45%, previous lung, liver, and kidney disease wereincluded in our longitudinal study. We performed trans-esophageal tissue Doppler imaging (TDI) for every patient and measured TDI parameters including E/EM, DT. After a six month follow up, the patients were classified into two groups (with or without morbidity). For data analyses we used SPSS 16.0. Regression test, Chi-square, and student t-test were performed. We also designed ROC curve to show the specificity and sensitivity. The best cut-off for parameters, were measured Youden index.

Results

At the end of our follow up, 24 cases developed morbidity. None of the patients died in our study period. Higher mean values of E/Em and E/A correlate with higher incidence of morbidity (all parameters, p<0.001). Also lower mean values of DT showed considerable association with morbidity (<0.001). There was not any notable prognostic application for LVEDD, LAVI, and underlying diseases (all parameters, p>0.05). Regression test presented E/Em and DT as an independent factors in HFpEF prognosis. At the cut-off of 13.5, E/Em was 97.1% sensitive and 55.3% specific.

Conclusion

At the cut off of 13.5, we observed E/Em as a sensitive, specific, and independent prognostic parameter for HFpEF. Also, we found DT an independent prognostic parameter. Early determination of patients which may develop HFpEF, can reduce their mortality rate

Comparison of the results of percutaneous coronary interventions using balloon angioplasty and rotational atherectomy for calcified coronary artery lesions.

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Introduction

Coronary artery disease (CAD) became a 21st-century pandemic that causes deaths of approximately 9,5 million people worldwide annually. Advancements in cardiology allow physicians to treat CAD in a minimally invasive way via percutaneous coronary intervention (PCI) with further implantation of drug-eluting stents (DES), which doesn't require to make traumatically severe incisions and sternotomy. Nonetheless, severe calcifications often cause post-procedural complications after PCI and worsen clinical outcomes. Recently, a new technique called rotational atherectomy (RA) has emerged, allowing to cut hard calcified plaques from the inside of the vessel, therefore theoretically improving the results. Our research is designed to prove that RA improves the clinical outcomes of PCI.

Materials & Methods

We examined the clinical outcomes of 51 patients who underwent treatment from 2016 to 2017. Categorical variables were described as percentages and were compared using Pearson's chi-square test or Fisher's exact test. Continuous variables were expressed as mean ± standard deviation or median unless otherwise specified and were compared using the t-test or Wilcoxon rank-sum test, as appropriate. A two-sided p-value of 0.05 was considered statistically significant.

Results

Two groups were formed depending on the treatment strategy – only balloon-dilated PCI (25 patients) and RA-assisted PCI (26 patients). 84,0% and 84,6% of patients in both groups were men. The mean age was 68,2±9,5 and 69,1±8,2, respectively. SYNTAX score was 42±8 and 46±9. Left ventricle ejection fraction was 46,2±8,1% and 45,4±7,0%. Diabetes mellitus was seen in 24,0% and 19,2% and hypercholesterolemia was seen in 100,0% and 96,2% of patients. The duration of intervention was 100±24 and 65±20 minutes (p=NS). On average 2,5±0,5 and 3,8±1 DES were implanted (p<0,05), technical success was in 84,0% and 100% (p<0,05). Major adverse cardiac events (MACE) rate was 24,0% and 7,7% (p<0,05) in Group 1 and Group 2 respectively.

Conclusion

The use of RA was associated with a higher rate of technical success and lower risk of MACE, shorter duration of intervention despite more complex lesion variants, and, based on the findings, can be considered as the preferred initial strategy in patients with calcified native coronary artery lesions.

Diagnostic performance of Quantitative Flow Ratio (QFR) vs Fractional Flow Reserve (FFR) in nonculprit lesions in patients with ST-Elevation Myocardial Infarction (STEMI)

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Introduction

Fractional Flow Ratio (FFR) is the gold standard method to guide the decision to perform revascularization procedures, among stable coronary artery disease (CAD) patients. Previous studies have demonstrated that the new alternative to FFR, namely Quantitive Flow Ratio (QFR), has a good diagnostic performance when compared to FFR. Next to that, QFR is less invasive because there is no need to administer adenosine and insert a pressure wire in the coronary arteries, faster, and cheaper than the gold standard method. Since no large study has investigated the diagnostic performance of QFR in comparison to FFR among ST-Elevation Myocardial Infarction (STEMI) patients, this has been the main focus of this research project.

Materials & Methods

Angiogram QFR analysis was performed on 100 images to obtain fixed- and contrast-flow QFR values. Diagnostic performance of QFR (sensitivity, specificity, positive and negative predictive value, and overall accuracy) for evaluation of the presence of flow-limiting CAD was determined using FFR as the golden standard. Pearson's correlation coefficient and a Bland-Altman plot was used to demonstrate the correlation and agreement between QFR and FFR.

Results

The mean value of FFR was 0.82 ± 0.12, and the mean values of cQFR and fQFR were respectively 0.81 ± 0.12 and 0.80 ± 0.12. The diagnostic performance of QFR when compared to FFR is: accuracy, sensitivity, specificity, PPV and NPV were 67%, 73%, 63%, 56%, 78% for cQFR and 67%, 65%, 68%, 57%, 75% for fQFR at a cut-off value of >0.80, respectively. No significant difference was found between the AUC for fQFR (AUC 0.725, 95% CI 0.62-0.83)) and cQFR (0.727, 95% CI 0.62-0.83), p = 0.05. Furthermore, its diagnostic accuracy was generated for three different cut-off scores and separately only for the main coronary arteries. The relationship between QFR and FFR was found to be moderate and agreement seemed to be better for higher values (>0.8), further highlighting QFR's strong specificity. Setting the QFR cut-off value to define presence of flow-limiting CAD at ≤0.9 can confidently rule out the presence of flow-limiting CAD.

Conclusion

QFR is a relatively new method that showed reasonable diagnostic performance for evaluation of ischemia presence in STEMI patients with non-culprit lesions. Further analyses on outcome after QFR analysis compared to current clinical care using FFR should be conducted before drawing a solid conclusion on its safety and possible use in the clinic. So far, setting the QFR cut-off at 0.9 yields high sensitivity and NPV and could be useful to apply QFR as a gatekeeper to further FFR in a clinical setting, aiming to safely rule out CAD.

Association between cardiac symptoms and NT-proBNP levels in patients with post-COVID syndrome

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Introduction

Long-term effects of COVID-19 infections have become increasingly relevant since the beginning of the COVID-19 pandemic. Recent studies mention these symptoms as long-COVID syndrome (LCS). Abnormalities behind these long-term effects could not have been objectified so far by currently available methods, which significantly prevents patients from receiving adequate care or professionals carrying out further research on the topic.

Objectification of the symptoms of LCS is yet an unsolved issue, therefore, we aimed to search for objective parameters and differences in patients who has symptomatic LCS without any other primary disease or observable pathological deviation by non-invasive cardiac examination.

Materials & Methods

Through a prospective cohort study, a total of 153 patients' data from the Heart and Vascular Center of Semmelweis University's post-COVID outpatient care has been analysed between 2021.03.23. and 11.16. Patient election criteria consists of previously documented COVID-19 infection and remaining cardiac symptoms (fatigue, chest pain, dyspnea or palpitation) after excluding cardiological and non-cardiological diseases with laboratory tests, echocardiography and ECG. Elevation of NT-proBNP levels have been the most frequent deviation after extensive diagnostic tests, hence, two groups have been created based on normal or elevated level of NT-proBNP, including 126 and 27 patients, respectively.

Results

Significantly higher average age (43,39±11,86vs.58,36±14,05, p=<0,0001) and BMI (25,94±5,23vs.28,68±6,3, p=0,0188), moreover, elevated creatinin (71,09±12,96vs.83,96±23,38, p=0,0001), glucose (5,38±1,03vs.5,97±1,17, p=0,0093), LDH (180,47±52,34vs.227,96±108, p=0,0008), hs-troponin T (5,09±2,81vs.8,89±6,54, p=<0,0001) and D-dimer (0,37±0,18vs.0,61±0,83, p=0,0037) level have been detected throughout the comparison of the two groups with normal or elevated levels of NT-proBNP. In the group with elevated levels of NT-proBNP significantly lower LVEF (60,24±3,17vs.58,93±4,92, p=0,0029) has been observed.

Conclusion

Throughout the comparison of the two groups of patients with normal and elevated level of NT-proBNP, significant difference has been detected in terms of cardiological laboratory parameters. All the test results of the two groups has been in the range of standard parameters, however, they have been closer to the pathological interval. Our results suggest that there is an objective deviation behind the symptoms of LCS, however, it could not have been characterized by this current research. Hence, it is necessary to define further parameters, which indicate ultrastructural dysfunction.

Oncology I

Presenters:
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Bereuter, J.P. (Jean Paul)
Alhadi Alshareef, Mr (Abdul-mueti)
Firigato, I.F. Miss (Isabela) BSc
Gawel, A.M.G. (Agata)
Shokooh Saremi, S. (Sara) Ms.

Aptamer-targeted biomimetic porphyrinic MOF for chemo-photodynamic therapy against metastatic breast cancer

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Introduction

Porphyrin-based metal-organic-frameworks (MOF) have been widely explored as a promising candidate for therapeutic photodynamic therapy (PDT) owning to their desirable physicochemical properties. Although, several limitations such as low selectivity and fast clearance may restrict their biomedical applications. To overcome these barriers, we aimed to develop an efficient therapeutic strategy with augmented specificity, lower side effects and enhanced PDT efficacy.

Materials & Methods

In this study, a porphyrin-based MOF with Cu (II) core was synthesized as the PDT sensitizer. Afterwards, Doxorubicin (DOX) was loaded into the porous structure of MOF. The resulted MOF@DOX was coated with prepared RBC membrane to lower the clearance rate of nanoparticles. To obtain targeted nanoparticles, MUC1 aptamer was conjugated onto RBC-MOF@DOX. The in-vitro production of singlet oxygen was determined under the irradiation at 630 nm using fluorescent probe. In-vivo and in-vitro efficacy and cytotoxicity of Apt-RBC-MOF@DOX were assessed in comparison to free DOX, RBC-MOF, RBC- MOF@DOX, Apt-RBC-MOF. For this aim, MTT assay and PDT experiment were performed against 4T1 and MCF7 breast cancer cells and cellular uptake was evaluated using flow cytometry and fluorescence microscopy. In-vivo experiments and ex-vivo fluorescent imaging were performed in Balb/c mice model, treated with the mentioned samples and irradiation. All values were reported as the means ± mean errors. Statistical analysis was done using Two-way ANOVA, and the p-values < 0.05 were considered significant.

Results

In-vitro singlet oxygen assay proved the PDT capability of Cu-MOF. MTT assay showed the cytotoxicity of Apt-RBC-MOF@DOX, while confirming the non-toxicity of MOF. The higher tumor accumulation of Apt-RBC-MOF@DOX in comparison to RBC-MOF@DOX demonstrated the targeting efficiency of aptamer. In-vivo treatment with Apt-RBC-MOF@DOX-PDT represented significantly higher inhibitory effect comparing to other groups, which proves the higher efficacy of targeted dual therapy. Ex-vivo imaging displayed the favorable biodistribution and enhanced residency in tumor sites.

Conclusion

This work provides strong evidence for the synthesized Apt-RBC-MOF@DOX as a clinically translatable nanoplatform for synergistic chemo and photodynamic cancer therapy.

Investigation of colorectal cancer liver metastases in the context of liver regeneration using patient-derived tumour organoids

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Introduction

Patiently-derived tumour organoids (PDTOs) have become a promising tool for investigating the properties of metastatic colorectal cancer. Liver resections remain the only curative treatment option for patients suffering from colorectal cancer liver metastases (CRCLM). Major surgical liver resections are followed by a substantial release of mitogenic cytokines during liver regeneration. Here, we aim to investigate the impact of specific liver regeneration associated cytokines on CRCLM PDTOs. Moreover, our objective is to find potential targets to inhibit pro-proliferative effects on malignant cells without impairing the process of liver regeneration.

Materials & Methods

KRAS wildtype (WT) and mutated (MT) CRCLM PDTOs (n=9) were treated with different cytokines involved in liver regeneration and measured on their proliferative capacity by using 5-ethynyl-2'-deoxyuridine (EdU). A 36-compound drug screening was performed to reveal potential targets for treating KRAS WT and MT PDTOs. Validation drug assays, including normal liver organoids, were performed to confirm the drug screen and assess normal-liver side effects.

Results

KRAS WT CRCLM PDTOs showed divergent responses to the cytokine treatment depending on their overall mutational landscape, whereas KRAS mutant CRCLM PDTOs showed no change in their growth behaviour. Targeted inhibition of the involved cytokines is ineffective for treating KRAS MUT CRCLM PDTOs and predominantly affects normal liver PDOs. By applying AURKA inhibition at the appropriate dosage, these issues can be prevented.

Conclusion

Our study emphasizes the potential of PDTOs to model tumour dynamics in response to the regenerative microenvironment. We have shown that the cytokines involved in liver regeneration have a profound impact on the outgrowth of CRMLM PDTOs. Perioperative treatment after liver resection has the potential to inhibit the proliferative effects of liver-regeneration associated cytokines on CRCLM growth.

Risk of thyroid dysfunction among advanced and metastatic NSCLC patients treated with Pembrolizumab: Meta-analysis of randomized trails.

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Introduction

Using the immunotherapy such as Pembrolizumab has gained precedence in the treatment of several type of malignancies especially in cure of advanced or metastatic non-small cell lung cancer (NSCLC). However, as Pembrolizumab acts mainly on the immune-system checkpoints , it can also provoke T-cells to attack the healthy cells, leading to several autoimmune-diseases which known as immune-related adverse events (irAEs). On the other hand, thyroid dysfunction have been reported as one of the adverse effects in NSCLC patients treated with Pembrolizumab as referred to immune-related adverse events. Therefore, we have performed a meta-analysis study to investigate the incidence and risk of thyroid dysfunction among advanced and metastatic NSCLC patients treated with Pembrolizumb.

Materials & Methods

A literature search was performed using the electronic databases and engines including; PubMed, Google Scholar, Scopus, Embase, from inception to May 2020. Eligible studies were prospective randomized controlled trials with advanced or metastatic NSCLC. We excluded Phase I studies, single-arm Phase II studies and observational studies. The pooled incidence, risk ratio (RR), and 95% confidence interval (CI) of thyroid dysfunction were calculated using the random-effect model. We used the random-effect model rather than the fixed-effect model using a Comprehensive Meta-Analysis program software 3.3 version.

Results

A total 1678 patients with advanced or metastatic NSCLC from 5 randomized controlled trials were eligible for anal ysis. The incidence of all-grade thyroid dysfunction among these patients ranged from 9% to 27%. However, The pooled incidence of all-grade thyroid dysfunction was 9.5% (95% CI: 7.7-11.6%)from all the trails . In addition, we found that Pembrolizumab was associated with significantly increased risk of thyroid dysfunction of all grades, yielding a risk ratio of 3.94 (95% CI: 2.32-6.68, p= <0.05) among advanced and metastatic NSCLC patients compared with control group.

Conclusion

In patients with advanced or metastatic NSCLC, Pembrolizumab have shown a remarkable incidence of all grade thyroid dysfunction as immune-related adverse events. Furthermore, this treatment was associated with significantly increased risk of thyroid dysfunction comparing to control group. Even with limited number of studies that investigate such immune-related adverse, these findings should being further explored in an ongoing international, randomized, double-blind clinical trials.

Counting is needed: the CNV of GSTM1 related to oral squamous cell carcinoma relapses and death

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Introduction

Oral squamous cell carcinoma (OSCC) mortality rates have kept elevated over the last decades, which is mainly supported by the progression of the disease and the therapy failure. The prediction of these events might lead the decreasing of death numbers and there is an effort to seek prognostic factors as the copy number variation (CNV) of GSTM1 and GSTT1, genes related with carcinogens and chemotherapy drugs detoxification, whose metabolism level becomes altered by the CNV. This study aimed to investigate whether the CNV of GSTM1 and GSTT1 are related with the overall survival and progression-free survival of OSCC patients.

Materials & Methods

A total of 234 OSCC patients were recruited from the Heliopolis Hospital (Brazil) and followed up from 2000 to 2019. The CNV of GSTM1 and GSTT1 was determined by TaqMan qPCR real-time and the software CopyCaller (version 2.1). The overall survival and the progression-free survival were estimated by the Kaplan-Meier method and the hazard ratio (HR) and 95% confidence interval (95%CI) values were calculated by the Cox regression analysis on the SPSS software.

Results

OSCC patients showed a variation from zero to two copies of GSTM1 and for the overall survival analyses, the proportion of death frequently occurred among patients with zero copies of this gene, while those that carried two copies of GSTM1 presented the highest rate of the survivorship. Furthermore, the OSCC death risk decreased in 37% among patients that presented one copy of GSTM1 (HR 0.63; 95%CI 0.44-0.91). About the progression-free survival results, the OSCC relapses occurrence was inversely proportional to the CNV of GSTM1 and patients that carried one copy of this gene presented a diminished OSCC relapses risk (HR 0.50; 95%CI 0.33-0.75). Regarding the CNV of GSTT1, this gene varied from zero to three copies but none of the copies were related with the risk and the occurrence of OSCC progression and death.

Conclusion

The results suggest that the CNV of GSTM1 may be considered a promising OSCC prognostic factor candidate, which can be applied to estimate the risk of relapses and death occurrence and aid the chosen of the appropriate therapy strategy for each patient.

Study on the molecular machinery and regulators of entosis in cancer

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Introduction

Entosis is a still not well-defined "cell-in-cell" phenomenon observed in various cancer tissues. It is considered that formation of entotic structures may enable the escape of cancer cells from the host's immune system or administered therapeutic drugs. It also proposed that entosis allows the outer cell to exploit the engulfed cell, which may lead to enhancement of the cancerous cell, and subsequently, to tumor progression. Importantly, the molecular mechanisms engaged in promoting the internalization of cells are still unclear.

To elucidate the molecular factors promoting formation of "cell-in-cell" structures, we studied the role of two proteins, SRC tyrosine kinase and PDPN (a membrane glycoprotein), in the formation of entotic structures.

Materials & Methods

Two cell lines, MCF-7 and BxPC3, derived from breast and pancreatic cancer, respectively, were used in the study. The expression of the SRC- and PDPN-encoding genes was knocked-down using specific siRNAs. RT-qPCR and Western blot were used to assess the mRNA expression and protein yield, respectively. The frequency of entotic structures was evaluated using haematoxylin/eosin and fluorescent staining, followed by light and confocal microscopy imaging. Data analysis was conducted using CFX Maestro, Prism and ZEN software.

Results

The obtained data showed that silencing the expression of the PDPN or SRC genes affects the number of entotic cells in both tested lines. It was found that depletion of SRC resulted in a reduction of cell-in-cell structures. In contrast, inactivation of the PDPN gene resulted in a significant increase of entotic structures. We further discovered that cells with depleted PDPN were characterized by activation of ezrin, a previously proposed molecular factor regulating entosis.

Conclusion

The results indicate that PDPN acts as an inhibitor, while SRC as an enhancer in the process of formation of "cell-in cell" structures. Additionally, the ezrin-PDPN axis likely acts as a molecular trigger controlling the development of entotic structures.

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developing a high loaded liposomal formulation of lapatinib with enhanced therapeutic effects on breast cancer cells

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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 effects 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.

Materials & Methods

First empty liposomes consisting of HSPC, DPPG, mPEG and cholestrol were formed and the drug was loaded into the inner aquatic phase by means of remote loading method. After purification steps, the final liposomal formulation were evaluated and the 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.

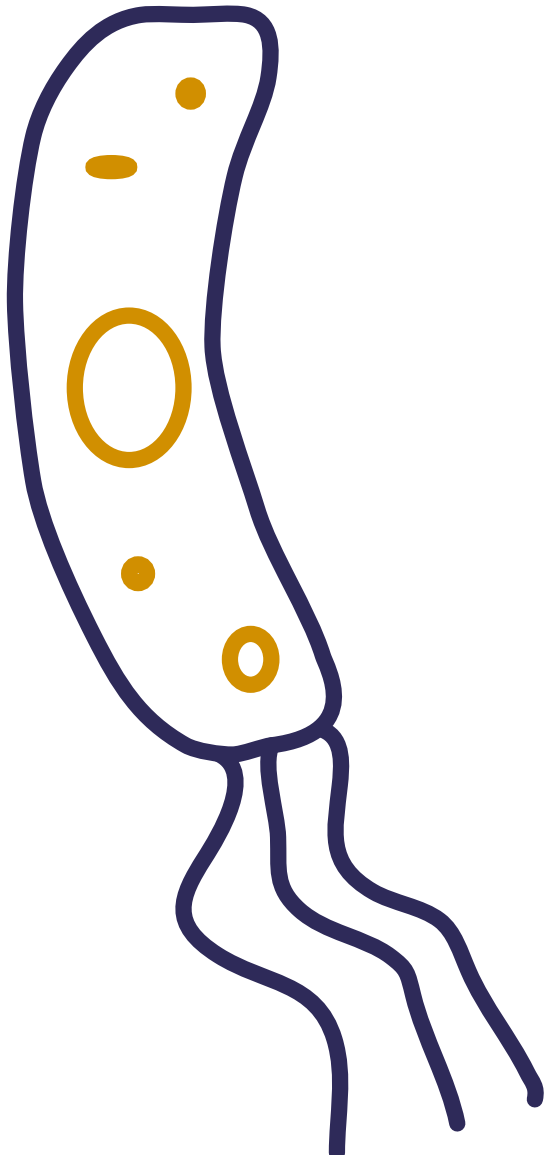
Results

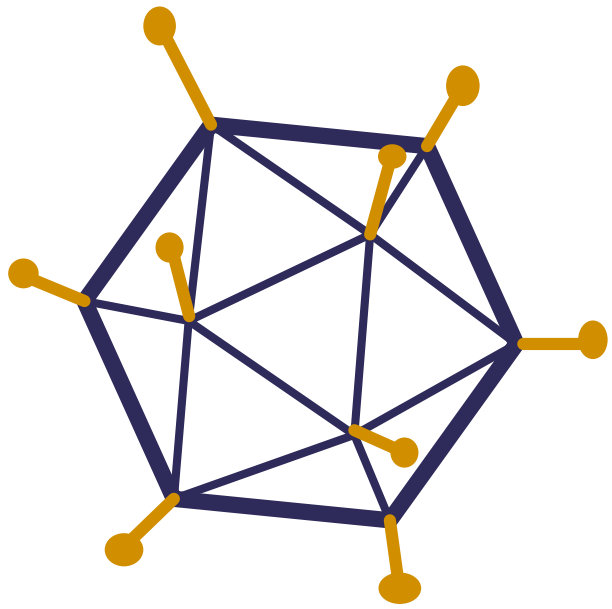
The final liposomal formulation was negatively charged and its particle size was about 128±0.2 nm. The poly dispersity index was 0.142±0.02 ,which confirms the homogeneity and 90±1.3 (1100±11.7 milligrams) percent of the total drug was loaded into liposomes. According to MTT tests results, the formulation was able to inhibit TUBO cells growth, successfully. Tumor growth study indicated that the liposomal formulation was able to hinder the tumor growth, especially in comparison to oral lapatinib (p<0.005).

Conclusion

Incorporating drug molecules in drug delivery systems can play a major role in increasing their clinical benefits. According to our results, by entrapping lapatinib into liposomes, promising effects are shown on inhibiting her2 positive breast cancer tumor cell growth. However, further studies are needed to introduce this effective formulation into the clinics.

Infectious Diseases





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Interleukin 27 as inducer of antiviral response against Chikungunya Virus infection in human macrophages

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Introduction

Chikungunya virus (CHIKV) is the etiological agent of chikungunya fever (CHIKF), a self-limiting disease characterized by myalgia and severe acute or chronic arthralgia. CHIKV is known to have a wide range of tropism in human cell types throughout infection, including keratinocytes, fibroblasts, endothelial cells, monocytes, and macrophages.

Previously, we reported that monocytes-derived macrophages (MDMs) are susceptible to CHIKV infection and induced a robust antiviral response dependent of interferon-stimulated genes (ISGs) expression, in an Interferon (IFN)-independent manner. Therefore, our aim here was to elucidate the molecular mechanism of induction of ISGs in CHIKV-infected MDMs based on transcriptomic analysis by RNA-seq.

Materials & Methods

Healthy human monocytes were enriched from PBMCs (from healthy donors) by adherence to the plastic. Then, monocytes were differentiated to monocytes-derived macrophages (MDMs) for 6 days. Then, MDMs were infected with CHIKV at MOI 5. Cell supernatants and total RNA was obtained at 6, 24 and 48 hpi, and mRNA sequencing was performed by RNA-seq at 24 hpi. Furthermore, quantification of pro-inflammatory and antiviral factors was performed by ELISA and RT-qPCR, respectively.

Results

Differential expression of genes at 24 hpi showed that CHIKV infection abrogated the expression of all types of IFNs in MDMs. However, we observed that CHIKV-infected MDMs activated the JAK-STAT signalling and induced a robust antiviral response associated with control of CHIKV replication. Then, we identified that the IL27 pathway is activated in CHIKV-infected MDMs and that kinetics of IL27p28 mRNA expression and IL27 protein production correlated with the expression of antiviral proteins in CHIKV-infected MDMs. Furthermore, we showed that stimulation of THP-1-derived macrophages with recombinant-human IL27 induced the activation of the JAK-STAT signalling and induced a robust pro-inflammatory and antiviral response, comparable to CHIKV-infected MDMs. Furthermore, pre-treatment of MDMs with recombinant-human IL27 inhibits CHIKV replication in a dose-dependently manner (IC50= 1.83 ng/mL).

Conclusion

Altogether, results show that IL27 is highly expressed in CHIKV-infected MDMs, leading to activation of JAK-STAT signaling and stimulation of pro-inflammatory and antiviral response to control CHIKV replication in an IFN-independent manner.

Lactoferrin reduces the risk of respiratory tract infections: A meta-analysis of randomized controlled trials

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Introduction

Lactoferrin (Lf) is one of the key immunomodulatory substances found naturally in various body fluids, such as saliva, tears, and breast milk, and forms a vital part of the innate defense against invading pathogens. Various studies have demonstrated antibacterial, antifungal, and antiviral properties of Lf and its protective role against respiratory tract infections (RTIs). The present meta-analysis aims to elucidate the association of Lf administration in reducing the risk of RTIs by systematically reviewing the data from randomized controlled trials (RCTs).

Materials & Methods

We systematically searched PubMed, Cochrane Library, Medline & CINAHL, Turning Research into Practice (TRIP), ProQuest Theses & Dissertations Databases, and China National Knowledge Infrastructure (CNKI) from inception till March 15, 2021. The primary outcome measure was a reduction in respiratory illness; decrease in frequency, symptoms, and duration. Random-effects model was used to estimate the odds ratio (OR) and 95% confidence interval (CI). We used Cochrane's RoB-2 to appraise the risk of bias of included RCTs.

Results

A total of nine RCTs were eligible for this review, of which six were included in the meta-analysis. Overall, two studies demonstrated a high risk of bias. The meta-analysis revealed a significantly reduced odds of developing respiratory infections with the use of Lf relative to the control (pooled odds ratio = 0.57; 95% confidence interval 0.44 to 0.74, n = 1,194), with sufficient evidence against the hypothesis of 'no significant difference' at the current sample size.

Conclusion

The administration of Lf shows promising efficacy in reducing the risk of RTIs. Current evidence also favours Lf fortification of infant formula. Lf may also have a beneficial role in managing symptoms and recovery of patients suffering from RTIs and may have potential for use as an adjunct in COVID-19, however this warrants further evidence from a large well-designed RCT.

Age related intestinal barrier dysfunction in SARS-CoV-2 infection

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Introduction

In about 20% of patients with SARS-CoV-2 extrapulmonary hyperinflammatory state develops due to cytokine release syndrome which may damage the intestinal mucosa. Damages of intestinal mucosa have also been observed in hypovolemic, hemorhagic and septic shock, aortic dissection, major surgeries, burns and acute pancreatitis. Bacterial translocation following intestinal damage may complicate these conditions increasing systemic inflammation and multiple organ dysfunctions. Several reports have demonstrated that SARS-CoV-2 infection is more severe in older population. The reasons for this are not fully understood and differences between younger and older population related to intestinal barrier dysfunction have not been previously investigated. In this study, we evaluated an intestinal barrier damage marker, intestinal fatty acid binding protein (i-FABP), and other cytokines in different age groups with SARS-CoV-2 infection.

Materials & Methods

We studied 89 patients (48 patients 61 year age or more and 41 patients with less than 60 year age) from Hospital das Clinicas da Faculdade de Medicina da Universidade de São Paulo - Brazil with SARS-CoV 2 infection. Plasma levels of i-FABP was determined by competitive enzyme-Linked immunosorbent assays and plasma levels of Interferon-gamm (INF-y), Tumor Necrosis Factor (TNF-ɣ) and interleukines 10,1 beta and 4 were determined using MILLIPLEX Human Cytokine. Statistical analyses were performed using Graph Pad Prism. Results were analysed using Mann-Whitney test. A p-value < 0.05 was considered significant.

Results

Plasma interleukines levels obtained in the younger group were similar to the older group. There was no statiscal difference when comparing these two groups regarding interleukines (INFgamma, p= 0.8432; IL-10, p =0.6326; IL-1beta, p=0.0597; IL-4, p=0.1078). However iFABP level was higher in aged population (892,3±191 pg/mL) when compared with younger patients (777,5±126,9 pg/mL) with statically significance (p=0,001).

Conclusion

In the present study we observed for the first time higher plasma levels of i-FABP in older patients with SARS-CoV-2 infection when compared with younger population without increased levels of cytokines. The intestinal damage and increased bacterial translocation may therefore be one possible factor related to the higher morbidity and mortality of SARS-CoV-2 infections in the older populations besides the primary lung and vascular damages.

Influence of host genetic factors on liver steatosis in chronic hepatitis C infection

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Introduction

Chronic hepatitis C virus (HCV) infection affects approximately 58 million people worldwide; liver steatosis is a frequent histological feature. Furthermore, single nucleotide polymorphisms (SNPs) related to lipid metabolism may be involved in the development of steatosis. In the present study, the possible relation between SNPs in the MTTP (microsomal triglyceride transfer protein) gene and their combination with other host and viral factors on the presence of liver steatosis in patients with chronic hepatitis C were investigated.

Materials & Methods

The -493G/T (rs1800591), I128T (rs3816873), Q95H (rs61733139) and Q244E (rs17599091) SNPs in the MTTP gene was genotyped with PCR-RFLP assays using serum of 236 patients with chronic hepatitis C admitted to the Clinical Hospital of the School of Medicine of the University of Sao Paulo (HCFMUSP) in Brazil. These patients were divided into two groups; 125 (53%) with steatosis and 111 (47%) without steatosis. In addition, bivariate and multivariate statistical analysis was performed to assess the effect of SNPs on steatosis in patients with chronic hepatitis C.

Results

Of the patients included in the study, 56.4% were female and the mean age was 55.5 years. Mean body mass index classification was 26.6 kg/m2 ± 4.3. The frequency of mutated alleles of each SNP was >5% and genotype distributions were according with the Hardy-Weinberg equilibrium (p≥0.05). Patients with moderate to high-intensity inflammatory activity of the liver (66.1%), HCV genotype 3 infection (18%) and female gender had an increased risk of liver steatosis (p=0.011, p=0.013 and p<0.001, respectively). This study identified a significant interaction, in the multivariate analysis, between the presence of the mutated allele of the -493G/T and I128T SNPs and the HCV genotype 3 infection increased by 11.51 times (p=0.005) and 8.51 times (p=0.012), respectively, the chance of developing liver steatosis in patients with chronic hepatitis C.

Conclusion

Our data indicate that host factors associated with viral factors may increase the risk of developing liver steatosis in patients with chronic hepatitis C. These results may provide useful information to identify the mechanisms underlying the steatosis and may enable strategies to use markers for early detection of steatosis.

The anti-arbovirus activity of di-halogenated derivatives of L-tyrosine is dependent on structural changes

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Introduction

In the last decade, several regions around the world have reported the emergence, re-emergence and co-circulation of three mosquito-borne viruses: Chikungunya (CHIKV), Zika (ZIKV) and Dengue (DENV). None of these arboviruses have specific licensed antiviral drugs to treat or prevent the infection. These facts increase the necessity of investigation and development of new synthetic compounds with potential antiviral activity and to evaluate small structural changes that could improve the antiviral activity. Then, the aim was to evaluate the potential antiviral in vitro activity of di-halogenated L-tyrosine derived compounds against three arboviruses of public health importance.

Materials & Methods

Phenolic synthetic di-halogenated L-tyrosine compounds (brominated and chlorinated) and its derivatives with methylations in the phenolic hydroxyl (O-ME) or/and in the hydroxyl of the carboxyl group (esterified), were synthetized and tested. Antiviral screening (combined treatment) and individual PRE and POST-treatment strategies were accomplished in VERO cells against CHIKV/Col, ZIKV/Col and DENV-2/S16803. The inhibitory effect was quantified by plaque assay, RT-qPCR and Cell-ELISA. The interactions between the compounds and viral and cellular proteins, were evaluated with Autodock-VINA® software and analyzed with PMV.

Results

In the antiviral screening, CHIKV model viral particles and viral protein were inhibited by phenolic compounds, and esterified compounds also inhibit genome copies. The O-ME modification decreases or eliminates anti-CHIKV activity. ZIKV was inhibited by esterified, O-ME and chlorinated O-ME/esterified compounds inhibiting viral particles and viral protein. DENV-2 was only inhibited by O-ME brominated compound and O-ME/esterified compounds; Then, hydroxyl methylation enhances anti-flavivirus activity.

In the individual treatment strategies, phenolic compounds inhibit CHIKV-viral protein in pre-treatment and CHIKV-viral particles in post-treatment. Esterified compounds inhibited CHIKV and ZIKV viral protein and genome in post-treatment; O-ME brominated compound inhibited ZIKV-viral protein in pre and post-treatment and genome in pre-treatment. Finally, O-ME/esterified compound inhibited ZIKV-viral particles, protein and genome in pre-treatment, and viral protein of both flaviviruses in post-treatment. The free binding energy of the compounds and cellular proteins were better than the obtained with viral proteins.

Conclusion

The antiviral activity of the different compounds can be modulated by small structural differences depending on the viral model as well as its mechanism of action.

Clinical Characteristics and Comorbidities in Patients with Down Syndrome associated with worst outcomes in COVID-19 in Brazil: An Observational Study

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Introduction

Previous studies demonstrated the worst outcomes in COVID-19 patients and with Down syndrome (DS), as longer hospitalization time, worse severity, and enhanced mortality rate. However, these studies presented a low number of patients and the real effect of the COVID-19 in DS patients is not completely elucidated yet.

Materials & Methods

This retrospective study analyzed hospitalized patients due to SARS using demographic and clinical characteristics from a public open-access database. The patients included were further divided into three groups: (Group 1; G1) patients with DS and SARS-CoV-2 RT-PCR-positive (COVID-19); (Group 2; G2) patients with DS who were diagnosed with a non-COVID-19 respiratory infection (other etiological agents related to SARS); and (Group 3; G3) non-DS (without comorbidities) patients with COVID-19. We performed a multivariate analysis using the logistic regression model to (i) differentiate the SARS patients from the G1 and G3; (ii) to differentiate the DS patients from G1 to those from G2; (iii) to differentiate the patients with DS and COVID-19 who died from those who had clinically recovered.

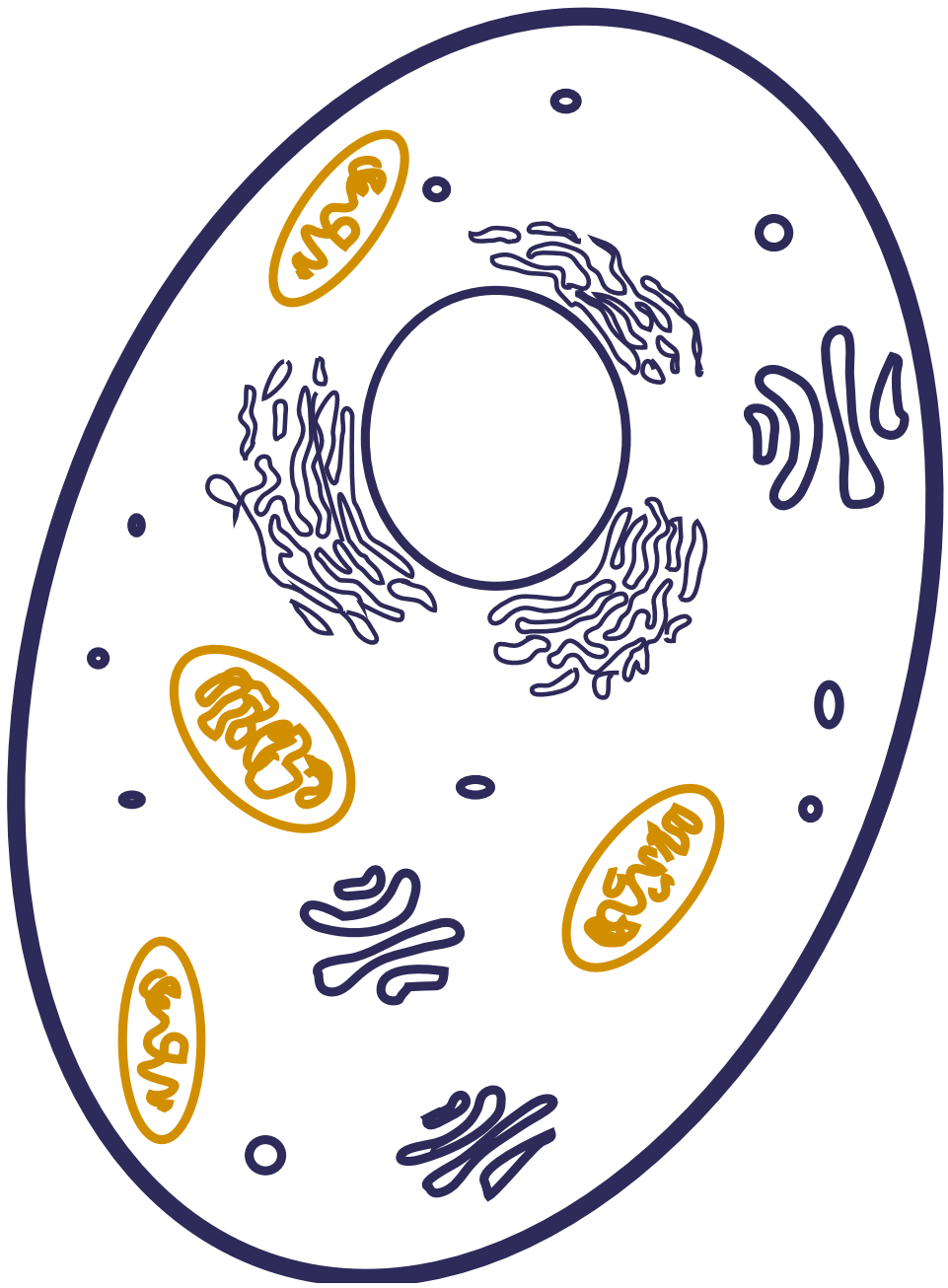
Results

A total of 225,231 patients were included, being G1 [1,619 (0.7%)], G2 [1,431 (0.6%)]; and G3 [222,181 (98.6%)]. The death was more frequent among the patients with DS and COVID-19 (G1: 39.2%), followed by the death among the individuals from G3 (18.1%) and G2 (14.0%). In the multivariate analysis, several characteristics were more common in the G1 when compared to G2, as living in a flu outbreak region [OR=2.054[95%CI:1.406-2.999], loss of smell [OR=4.146[95%CI:1.745-10.174] and inappetence [OR=4.146[95%CI:1.324-12.986]. When G1 was compared to G3, characteristics as age (between 13-24 years old) [OR=3.119[95%CI:2.387-4.075], nosocomial infection [OR=2.741[95%CI:1.711-4.389], oxygen saturation <95% [OR=2.110[95%CI:1.763-2.524], vomit [OR=1.311[95%CI:1.030-1.667], coryza [OR=2.201[95%CI:1.571-3.083], inappetence [OR=1.905[95%CI:1.264-2.872], cyanosis [OR=11.339[95%CI:5.098-25.219] and prostration [OR=3.014[95%CI:1.914-4.745] were more common in the G1. Finally, obesity [OR=1.740[95%CI:1.035-2.924], need of intensive care unit [OR=1.640[95%CI:1.032-2.607] and need for invasive mechanical ventilation [OR=10.742[95%CI:5.197-22.203] were associated with enhanced death in the G1.

Conclusion

Patients with DS are affected by COVID-19 presenting a high lethality rate. Patients with DS infected by the SARS-CoV-2 demonstrated particularities regarding comorbidities, clinical symptoms, and treatment during the hospitalization when compared with other populations.

Cell Biology I



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Influence of melatonin on the content of TBA-active products under the experimental nephropathy

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Introduction

One of the current areas of experimental medicine are the processes that occur in the development of nephropathy. Various etiological factors cause the development of nephropathy, and one of the central mechanisms is the strengthening of free radical oxidation, which leads to changes in the structural and functional properties of membranes, the activity of enzymes of antioxidant defense and activation of proinflammatory processes. The promising antioxidant is melatonin, which has demonstrated its cytoprotective properties in various organs and tissues.

The aim was to investigate the effect of melatonin on the content of TBA-active products in the mitochondria of the kidneys of rats under experimental nephropathy.

Materials & Methods

Simulation of nephropathy was performed by a single intraperitoneal injection of folic acid at a dose of 250 mg / kg. Animals were divided into 5 groups: 1st - control animals; 2nd - experimental animals with simulated nephropathy (3 days); 3rd - animals that were given melatonin daily at the rate of 10 mg / kg intragastric for 3 days on the background of simulation of experimental nephropathy; 4th - animals with simulated nephropathy (7 days); 5th - animals with experimental nephropathy, which were daily administered melatonin at a dose of 10 mg / kg for 7 days. The mitochondrial fraction was isolated by differential centrifugation in isolation buffer. The content of TBA-active products in the cortical layer of the kidneys of rats was determined by reaction with TBA.

Results

The content of TBA-active products in the mitochondrial fraction of the cortical layer of the kidneys of rats with experimental nephropathy has increased by 14.9% - on the 3rd day and 36.0% - on the 7th day of the experiment, compared with the control group indicating an increase in the processes of lipid peroxidation. The introduction of melatonin reduced the content of TBA-active products on the 3rd and 7th day by 13.6% and 26.1% respectively.

Conclusion

In conclusion, the oxidative stress that occurs in experimental nephropathy leads to increased content of TBA-active products. Melatonin improves the action of mitochondria to participate in the generation of ATP due to its direct antioxidant properties.

3D organization of the genome tissue-specifically regulates activity of the development genes Pdgfra, Kit, Kdr in mouse

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Introduction

The three-dimensional (3D) organization of the genome is assumed to contribute to the gene regulation, especially topologically associating domains (TADs) — loops of the chromatin, bordered by the binding sites of the CCCTC factor (CTCF). It is known that TADs regulate gene activity by maintaining enhancer-promoter interactions. Nevertheless, do TADs restrict nonspecific interactions? We studied the regulation of the development genes Pdgfra, Kit, Kdr; each insulated in a corresponding TAD, so the shared borders are Pdgfra/Kit and Kit/Kdr. The genes aberrant activity is associated with several malignant transformations (e.g. glioma, acute myeloid leukemia). Importantly, the genes possess contrasting tissue-specific expression: Pdgfra — fibroblasts; Kit — melanocytes, mast cells; Kdr — endotheliocytes. We aimed to determine the genes activity in an absence of the TADs borders, which we expect to resolve enhancer ectopic interactions.

Materials & Methods

We obtained the cell cultures (embryonic fibroblasts, melanocytes, mast cells) from the five strains of the transgenic mice carrying different deletions of the boundary CTCF sites (CBSs) at the TADs. To study the changes of the 3D organization of the genome, cell cultures were used to perform capture Hi-C, CTCF and H3K27Ac ChIP-seq. For the transcriptome analysis, RNA was obtained from the cell cultures to proceed with RNA-seq.

Results

The deletion of the CBSs at the Pdgfra/Kit TADs borders has little effect on the 3D genome organization and no effect on the transcriptome in the embryonic fibroblasts. The deletion of the CBSs at the Kit/Kdr TADs borders in the mast cells demonstrates a similar effect. We observed an exciting change in the melanocytes: Kit/Kdr TADs fusion leads to Kdr activation. There are at least two factors for such a difference. Firstly, unlike the mast cells, the melanocytes do express Kdr slightly. Secondly, in the mast cells Kit enhancers locate upstream of the Kit, while in the melanocytes — downstream, closer to Kdr. We presume that a locus epigenetic status and an enhancer location might restrict TADs fusion.

Conclusion

The tissue and locus specific TADs fusion in the Pdgfra/Kit/Kdr locus leads to ectopic gene activation. The result implies a new possible parameter to consider in the disease-associated gene activation.

An investigation of the mechanism of action of arsenic exposure in prostate cancer development.

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Introduction

Arsenic is found naturally in the environment at low concentrations. Over 200 million people, largely from South Asian countries, are exposed to toxic levels of arsenic present in ground-water used for drinking. Chronic exposure to arsenic, through such supplies, has been linked to the development of various cancers, as well as many cardiovascular and neurological disorders. Recent epidemiological evidence has associated arsenic exposure to increased incidences of prostate cancer (PrCa) worldwide, most commonly among Asian and American populations.

To date, much of the research has focused on carcinogenicity following chronic exposure of individuals to arsenic; however, there is a lack of research on the effects of low-dose, acute arsenic exposure on early prostate carcinogenesis. Our project aims to analyse the in vitro effects of acute and chronic arsenic exposure on healthy and malignant prostate cells.

Materials & Methods

Healthy (RWPE-1) and malignant prostate cell lines (WPE1-NA22, WPE1-NB26, PC-3 and DU145) were cultured in 2D, were individually treated with incremental arsenic concentrations (0.5nM, 5nM and 50nM) and investigated for their morphology, migratory nature and viability. Cell lysates / supernatants are being collected at different time points for analysis of potential changes to protein expression, particularly those involved in mitochondrial function, carcinogenesis and metastasis.

Results

Preliminary results show that following acute arsenic treatment (24 hours), low concentrations (0.5uM and 5uM) slow down migration significantly in malignant prostate cell lines, with slight changes to cell morphology. However, higher concentrations (50uM) appear to cause cytolethality, with the appearance of rounded cellular phenotypes in all cell types. Interestingly, when supplemented with arsenic-free medium, cells previously exposed to lower concentrations of arsenic restored their normal phenotype, whilst cells treated with higher concentrations remained unchanged.

Conclusion

Results thus far suggest that acute treatments are implicated in altering cell behaviour and may exacerbate the initial development of cancer. Ongoing analysis of protein expression profiles following both acute and chronic treatments will hopefully provide insights into mechanisms underlying cancer development.

Parallel osteogenic and endothelial differentiation of cells in ADSC-derived spheroids.

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Introduction

The problem of proper vascularization is still one of the most challenging questions of regenerative medicine that limits the formation of full-thickness artificial bone tissue. Thence all in vitro bioengineering techniques are aimed at pre-vascularization of osteogenic bioequivalent to provide better regeneration after transplantation. The general approach to generate vascularized tissue involves co-cultivation of the osteogenic and endothelial precursors. Adipose-derived stromal cells (ADSCs) cultured as 3D spheroids provide a favorable spatial context for the induction of angio- and osteogenesis and can model their communication in vitro. An objective of our study was to establish the possibility of simultaneous activating of angiogenic and osteogenic cell differentiation in ADSC-derived spheroids.

Materials & Methods

The study was conducted using human ADSCs isolated from an adipose stromal-vascular fraction. Experimental groups included control spheroids; spheroids with osteogenic induction; spheroids with endothelial induction and spheroids with double-induction.

At a different time of 3D cultivation electron microscopy (SEM), immunocytochemical (ICC) staining, real-time PCR, Western Blot, and angiogenesis assay in fibrin gel were performed.

Results

SEM images confirmed that spheroids had surface epithelial-like cells and central stromal cells surrounded by extracellular matrix during the whole period of cultivation. Complex analysis of expression and synthesis of key factors indicated that ADSC spheroids were capable of spontaneous differentiation in both directions but with a predominance of osteogenic differentiation. ICC showed the synthesis of early osteogenic marker Osteopontin and endothelial marker CD31. Angiogenesis assay demonstrated that spheroids from all groups were able to grow tubule-like structures in fibrin gel and the addition of osteogenic factors led to the formation of more branched, but less structured net of tubules, which were formed by CD34+ cells (endothelial progenitor cell marker).

Conclusion

The current study showed that ADSC spheroids are capable of spontaneous differentiation, while double induction stimulated osteogenesis, also providing angiogenesis. These findings can contribute to a better understanding of the cross-talks of differentiation processes and open new approaches to the generation of vascularized bone tissue bioequivalent.

Impaired trafficking and reduced hemichannels permeability are the main consequences of a rare variant c.516G>C (p.Trp172Cys) in GJB2 gene associated with hearing loss

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Introduction

Mutations in GJB2 gene encoding transmembrane protein connexin 26 (Cx26) are the most common cause of hereditary hearing loss in most populations. Six Cx26-molecules combine to form intercellular channels necessary for the passage of ions and other small molecules, which is a key process for maintaining ion homeostasis in the inner ear tissue. Mutations in GJB2 lead to irreversible hearing loss. This study aims to elucidate the functional consequences of a rare GJB2 variant c.516G>C (p.Trp172Cys) found with high frequency in deaf patients from indigenous populations of Southern Siberia (Russia).

Materials & Methods

HeLa cell line was chosen to generate the panel of transgenic cell lines. CRISPR/Cas9 system was applied to knockout endogenous GJB2 in HeLa cells (KO-HeLa). Transgenic cell lines carrying wild type (wt) and mutant variants c.516G>C (p.Trp172Cys), c.224G>A (p.Arg75Gln) or c.35delG (p.Gly12Valfs*2) of GJB2-coding region were established using Sleeping Beauty transposon system. The presence of Cx26 protein was confirmed by Western blot (WB). Cellular localization of Cx26 was analyzed by immunocytochemistry (ICC). Propidium Iodide (PI) dye uptake assay was used to evaluate Cx26-hemichannels permeability, defined as the proportion of PI-positive cells detected on fluorescent microscope images or by flow cytometry.

Results

We performed a functional analysis of Cx26-p.Trp172Cys protein compared to wild type and other mutant forms of Cx26. The presence of Cx26 was detected by WB in cell lines carrying Cx26-wt, Cx26-p.Trp172Cys and Cx26-p.Arg75Gln. ICC revealed that mutant Cx26-p.Trp172Cys exhibited small puncta diffusely distributed predominantly in cytoplasm of majority of cells however some cells contained discrete protein granules on membrane. Cx26-wt and Cx26-p.Arg75Gln presented distinct protein conglomerates on cell membranes. No specific signal was detected in cell lines KO-HeLa and Cx26-c.35delG. Analysis of fluorescent microscope images revealed significantly reduced hemichannels permeability in cell lines KO-HeLa, Cx26-p.Arg75Gln and Cx26-c.35delG (0.9%, 0.7%, 1.5% of PI-positive cells, respectively) compared to Cx26-wt, whereas 16.9% of Cx26-p.Trp172Cys cells accumulated PI. Similar results were obtained by flow cytometry.

Conclusion

Impaired trafficking of mutant Cx26-p.Trp172Cys protein to plasma membrane and reduced hemichannels permeability support pathogenic effect of GJB2 variant c.516G>C (p.Trp172Cys) and its association with hearing loss. Study was supported by the grant FSUS-2020-0040.

Ecdyteroids exert protective effects on cultured human brain endothelial cells under oxidative stress

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Introduction

Ecdysteroids are members of polyhydroxylated steroids. Althought they were discovered in arthropods as molting hormones they are abundantly present in plants as well. The health benefits of these hormones were discovered in mammals including humans, due to their anabolic, antidiabetic and antioxidant effects, while their acute toxicity is negligible. The 20-hydroxyecdysone (20E) is the most studied plant ecdysteroid. Recently a derivative of the 20E, calonysterone has been synthesized and used for biological testing. Blood-brain barrier (BBB) dysfunction occurs in many neurovascular diseases, therefore it is important to find new agents which are protecting barrier functions in health and disease. Our aim was to test the effects of 20E and calonysterone on human brain capillary endothelial cells in healthy conditions and under oxidative stress.

Materials & Methods

As a simple in vitro BBB model we used the hCMEC/D3 human brain endothelial cell line. Oxidative stress was induced by tert-butyl hydroperoxide (tBHP). Impedance-based cell analysis was performed to test the protective concentrations of the compounds alone and in combination with the tBHP. Transendothelial electrical resistance and permeability of fluorescent marker molecules was measured to examine the barrier integrity after treatments. Fluorescent immunostaining for junctional associated molecules was performed and reactive oxygen species and nitrogen-oxide production was tested.

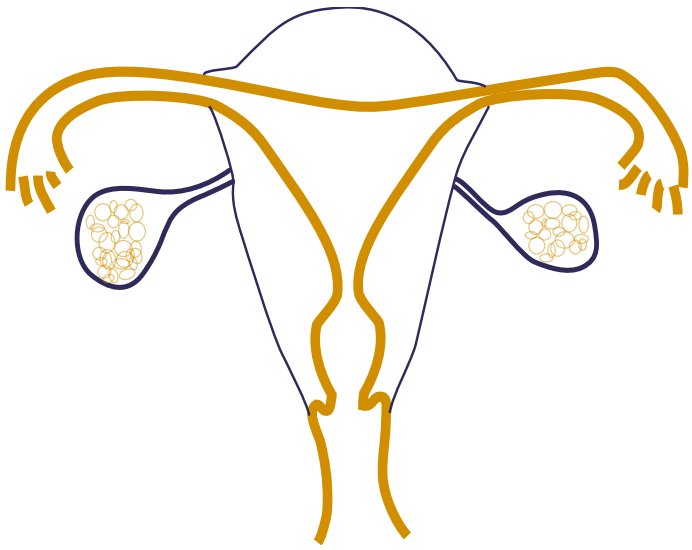
Results

We found, that the impedance of hCMEC/D3 cells increased after treatment with 20E and calonysterone alone. tBHP decreased the impedance of the monolayers, but co-treatment with 20E and calonysterone restored the impedance close to the level of the control. Both agents showed a protective effect on barrier integrity of brain endothelial cells and rescued altered junctional morphology under oxidative stress. These agents could not reverse the tBHP induced elevated reactive oxygen species production, but both agents decreased the basal nitric oxide production.

Conclusion

Our results show that ecdysteroids have a beneficial effect on the barrier properties of cultured human brain endothelial cells. We hypothesize, that these compounds could have therapeutic potential to protect the BBB in neurovascular dysfunctions.

Gynaecology and Paediatrics



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Infant Motor Predictors of Later Neurodevelopmental Delay at School-Going Age: A Longitudinal Study.

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Introduction

There are strong indications that atypical motor development in infancy is correlated with later neurodevelopmental disorder (NDD) in both the high-risk and general infant population. However only 30% of affected children are identified prior to school-going age, thereby delaying early clinical intervention whilst the brain is still highly plastic.

AIM: This study seeks to determine whether atypical motor development in infancy, measured using the Infant Motor Profile (IMP), is associated with atypical development at school-going age, measured using the Ages & Stages Questionnaire (ASQ).

Materials & Methods

Between January 2017 and March 2019, as part of the IMP-SINDA norms study, infants (3-18 months) from the general population were examined using the IMP. Between October 2020 and September 2021, as part of the BIRD study, a cohort of the same children were reassessed using the ASQ (4-5½ years). Crude IMP and ASQ scores were dichotomised into typical and atypical using Dutch norm-group cutoff values. Pearson's χ2 analyses tested the association between atypical IMP and ASQ scores. Multivariate logistic regression analyses were performed whilst correcting for possible confounders.

Results

267 males and 236 females participated. 6.4% were born preterm (<37 weeks). Logistic regression analyses revealed an association between an atypical IMP performance score and atypical ASQ communication and gross motor scores, and between an atypical IMP total score and an atypical ASQ gross motor score. IMP scores were not associated with later atypical ASQ fine motor, problem-solving or personal-social scores.

Conclusion

These findings identify a relationship between infant motor development and later gross motor and communication outcomes.

Neurodevelopmental changes in mice brain following maternal exposure to Bisphenol-S

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Introduction

The growing awareness of Bisphenol-A (BPA) hazard has sparked a massive switch to its analog, Bisphenol-S (BPS), which is deemed to be safer. However, several recent studies have shown that BPS has adverse effects on neurodevelopmental processes. Nevertheless, there is still scarce scientific evidence on the underlying mechanism of the neurodevelopmental effect of BPS. This study aims to investigate the neurodevelopmental toxicity of BPS following maternal exposure at Embryonic day 16.5 (E16.5) and Postnatal day 1 (P1) using a pregnant mice model.

Materials & Methods

BPS was administered orally to pregnant mice at 500 µg/kg BW with corn oil as a control. At E16.5 and P1, the brain of the offspring was isolated, dissected, and subjected to structural and gene expression analysis. For the structural analysis, a histology study was conducted using Hematoxylin & Eosin staining. Meanwhile, the gene expression analysis was conducted by measuring THRα expressions through qRT-PCR.

Results

Histological and morphometric evaluations demonstrated that BPS causes structural impairment in the cerebral cortex of the mice offspring, which could be associated with the inhibition of neuronal migration. This effect was found to be more significant at E16.5 and persisted to the P1 period. Aligned with these structural changes, gene expression analysis found a slight decrease in THRα expression at E16.5 but not at P1, which explains the more significant structural changes in E16.5 compared to P1.

Conclusion

This study suggests that BPS maternal exposure elicits neurodevelopmental toxicity through structural and molecular changes in the brain cortex. This neurotoxicity could lead to adverse neurological effects during the early stage of embryonic brain development which persist until the postnatal period.

Socio-demographic factors affecting Female Sterilization Operation among Couples coming to Tertiary care hospital in Ahmedabad City, India

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Introduction

Unplanned pregnancy may be the reason of many neonatal and maternal adverse effects. Many factors have been reported to be associated with acceptance of female sterilization and the use of contraceptive methods among Indian women is related to several factors such as personal, interpersonal, partner related, service related and/or method related. Various factors like age, education of both the parents, age of the last living child were also reported to be associated with acceptance of female sterilization among Indian women. The objective of this study was to identify various socio-demographic factors affecting the decision of choice of Tubal Ligation (TL) and correlate them with various factors affecting the decision of choice of Tubal Ligation.

Materials & Methods

A record based study carried out at the Family planning unit of Obstetrics and Gynaecology, at one of the tertiary care hospital of Ahmedabad city. Data of the Couples undergoing Tubal ligation (TL) operation at the above hospital during the one year period from April 2018 to March 2019 was collected with permission. The data included the variable like education of couple, their age, and number of children, occupation and age of last child, religion, and time of selection of TL. Odds Ratio (OR) was used for association between socio-demographic variables. P value less than 0.05 was considered significant.

Results

A total of 675 Tubal ligation (TL) operations were conducted. The mean age of females undergoing TL was 28.8 ± 3.9 years and their husbands was 33.25 ± 4.38 years. Out of the total, 484(71.1%) couples were Muslims. 74(10.8%) females were illiterate and 39(5.8%) males were illiterate. 440(65.1%) couples undergoing TL had 3 living children. Majority i.e. 518 (76.7%) had the age of their last living child less than 1 month. Ninety one percent of couples had at least one male child. There was a significant relationship of female education with total number of living children and relationship of total number of living children with religion (p value 0.0001 and OR 2.69).

Conclusion

The study concludes that female education as well as religious and cultural beliefs plays a major role in deciding the female sterilization among Indian women.

Parental satisfaction of phenylketonuria newborn screening in the Netherlands: the role of the general practitioner

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Introduction

Phenylketonuria (PKU) is an inborn error of metabolism caused by a defect in the hepatic enzyme phenylalanine hydroxylase. Newborn Screening (NBS) enables an early start of treatment and helps to prevent severe mental retardation. To date, there is no protocol existing in the Netherlands for the general practitioner (GP) on how to communicate the abnormal NBS result. We hypothesize that parents are not always satisfied with the communication of the NBS result. No studies have yet evaluated the procedure as it takes place in the Netherlands. We therefore aimed to assess parental satisfaction with the communication of an abnormal NBS result for PKU.

Materials & Methods

A web-based questionnaire on parental satisfaction of the communication of an abnormal NBS result was developed and performed in close cooperation with the Dutch PKU Association. An email was sent to all members of the Dutch PKU Association containing the link to the questionnaire. Responses to open questions were grouped and data were analysed with descriptive statistics using SPSS.

Results

Multiple answers per question were possible. 60.2% of all participants (N=113) stated they were unsatisfied with the way the GP communicated the NBS result. Of those, 65.1% indicated the GP was not able to give information or gave wrong information about PKU, and 26.7% was send to the hospital without information. 66.1% of the 113 participants stated they were satisfied because of the house visit performed by the GP, and 25.8% was satisfied due to the involvement of their GP.

Conclusion

Considering this is the first moment young parents get in contact with PKU, there is a lot of space and need for improvement. Further research is necessary, including focus on posttraumatic stress syndrome in parents, to assess the impact of the NBS results. Such research, possibly at an international scale, should also focus at options to improve this communication that may help parents to accept the diagnosis.

Motor development outcomes in children with hydrocephalus up to 2 years of age after treatment with ETV and VPSI at QECH

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Introduction

Ventriculoperitoneal shunt insertion (VPSI) has been the major surgical approach in treating hydrocephalus in children in developing nations. Despite VPSI's success, emerging complications led to the introduction of endoscopic third ventriculostomy (ETV) as an alternative approach. However, the neurodevelopmental outcomes of these procedures have not been largely explored. We aimed to determine motor development outcomes in children with hydrocephalus up to 2 years of age after undergoing ETV and VPSI, to identify which surgical approach yields better motor outcomes and may be most effective for Malawian children.

Materials & Methods

In this cross-sectional study, we recruited two groups of children: post-surgical group which consisted children with hydrocephalus treated with ETV or VPSI, at least 6 months prior to this study; presurgical group were children presenting with hydrocephalus for the first time.The

presurgical were controls for the post-surgical group. Motor development was assessed using Malawi Development Assessment Tool (MDAT).

Results

We recruited 37 participants: 25 post-surgical and 12 presurgical with mean ages of 16.44 months (SD 6.14) and 9.08 months (SD 3.68) respectively. In the post-surgical group, 13 had ETV and 12 VPSI. MDAT revealed significant developmental delays in both groups. Nine of the 12 children in presurgical group had gross motor delays and 8 had fine motor delays. In the post-surgical group, 9 of the 13 with ETVs showed gross motor delays, whilst 6 had fine motor delays; 10 of the 12 who had VPSI showed delays in both gross and fine motor. However, no significant difference was found for all domains (gross p= 0.400; fine p= 0.053, Pearson's chi-squared test).

Conclusion

Our findings reveal that children with hydrocephalus present with motor deficits which do not improve within the first six months of treatment with either ETV or VPSI. These profound developmental deficits may necessitate early and intensive therapy to restore motor function after surgery. Longer follow-up studies with bigger sample sizes and rehabilitation intervention are required to detect the effect of treatment approaches on motor outcomes of treated hudrocephalus.

Knowledge, Attitude and practice of Sudanese women towards cervical cancer and its screening tests in teaching hospital. Khartoum, Sudan

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Introduction

Cervical cancer constitutes the second most common cancer affecting women globally. Most cases occur in developing countries. The human papillomavirus (HPV) constitutes its major cause. The disease precancerous lesions can be detected using Papanicolaou (Pap) smear and visual inspection by acetic acid (VIA). However, the utilization of these tests is limited in developing countries. This study aimed to assess the knowledge, attitude and practice of Sudanese women towards cervical cancer and its screening tests.

Materials & Methods

A cross-sectional study design where a convenient sample of 310 women was collected through total coverage of women who attended the clinics and wards of Saad Abu El Ella teaching hospital in the period between 12 to 30 August 2020. Data was collected using an anonymous questionnaire. Analysis of variance and independent-samples T-test compared the statistical differences of knowledge, attitude and practice scores between groups. Spearman rho correlation assessed the relationship between the scores. Linear regression assessed the impact of predictors on the scores.

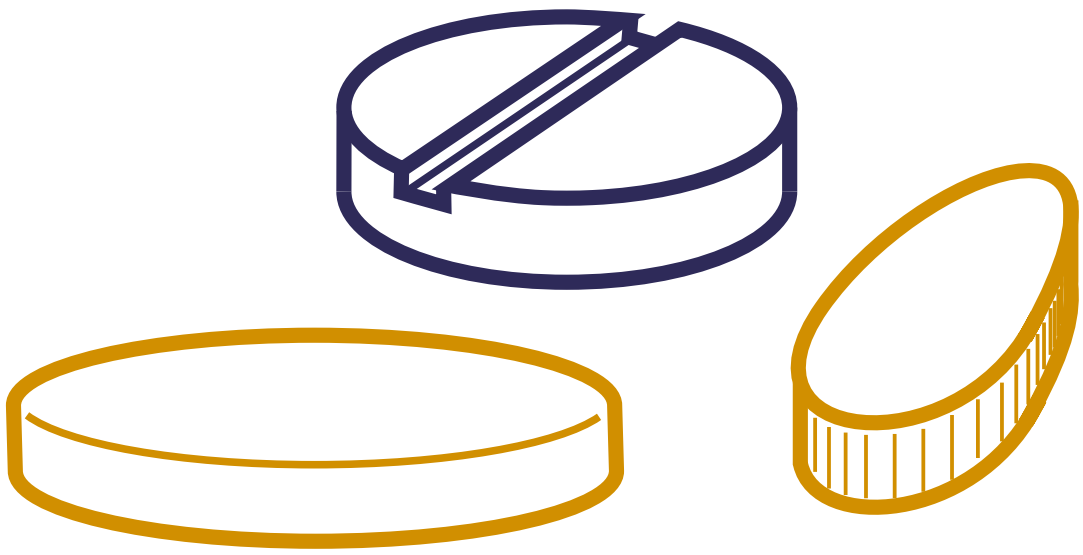
Results

Around50.0% and 27.7% of the respondents heard about cervical cancer and Pap smear/VIA respectively. The highly-rated symptoms and risk factors: abnormal vaginal bleeding between periods, malodorous vaginal discharge, smoking and sexually transmitted infections. 21.3% rated HPV as a causative agentand9.4% heard about its vaccine.65.2% desired to perform Pap smear/ VIA. 2.3% had ever undergone Pap smear/VIA and also 2.3% have ever received the vaccine against the human Papillomavirus. Awareness of cervical cancer was positively associated with attitude score (P-value 0.004) and practice score (P-value 0.016).

Conclusion

Most of the respondents had poor knowledge and practice towards cervical cancer and its screening tests. Health education and screening campaigns regarding cervical cancer should be established. Moreover, the implementation of a vaccination program against HPV is recommended as well.

Pharmacology



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Preparation, characterization and optimization of lipid nanoparticle formulations containing curcuminoids: in vitro and in vivo evaluations

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Introduction

Curcuminoids, the primary active substance of turmeric, are among the most promising phytochemicals with numerous health benefits. However, low aqueous solubility, high metabolism rate, and rapid elimination have limited the application of curcuminoids-based conventional drug delivery systems. Therefore, designing nanoparticulate drug delivery systems such as solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs) provides a solution to this limitation. Accordingly, this study aimed to prepare SLNs and NLCs containing curcuminoids and investigate the effectiveness of the optimized formulations in enhancing the oral bioavailability of curcuminoids.

Materials & Methods

Curcuminoids-loaded SLNs and NLCs were prepared using high shear homogenization and ultrasound technique. Formulations were optimized and characterized regarding particle size, polydispersity index, encapsulation efficiency, morphology, and crystalline structure. In vitro drug release study was conducted using the direct dispersion method. Pharmacokinetic parameters including maximum plasma concentration (Cmax) and area under the concentration-time curve (AUC) following administration of lipid nanoparticles to adult mice were also estimated using PK-solver.

Results

Optimized curcuminoids-loaded SLNs and NLCs showed an average particle size of 160.7±2.69 and 151.4±3.54 nm, respectively. High encapsulation efficiency of 95.3% and 97.4% was achieved for SLNs and NLCs formulations. Transmission electron microscopy revealed the spherical shape of the particles. Differential scanning calorimetry analysis exhibited an amorphous state of the curcuminoids encapsulated into the nanoparticles. The in vitro release profile showed prolonged release of curcuminoids from the nanoparticles, with a higher release rate recorded for NLCs due to the presence of liquid lipid. Furthermore, pharmacokinetic study of SLNs and NLCs demonstrated a 4.48 and 3.41 fold increase in Cmax and a 3.68 and 3.34 fold increase in AUC, respectively, compared to free curcuminoids; indicating a significant improvement of pharmacokinetic parameters following the administration of the nanoparticles.

Conclusion

The finding of this study suggests that SLNs and NLCs could be promising carriers for increasing the oral bioavailability of curcuminoids, with SLNs being superior to NLCs in improving the pharmacokinetic properties of curcuminoids.

A 3D in vitro model of impaired osteocytes activity in CKD-mimicking conditions

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Introduction

Patients suffering from chronic kidney disease (CKD) experience multiple comorbidities, among which mineral bone disease (MBD) contributes to high morbidity and mortality rate due to increased risk of facture. CKD affects the quality of bones which become more fragile and susceptible to fracture incidents. Recently, endogenous metabolites, such as protein-bound uremic toxins (PBUTs), were reported to play an active role in the development of CKD-MBD as they accumulate in blood due toimpaired kidney function. PBUTs have been suspected of their role in exacerbating CKD-MBD, as they have been shown to have catabolic and anti-anabolic effects in bone. However, a thorough analysis of the quality of the bone matrix still needs to be performed. In addition, the development of a fully representative 3D in vitro model of human bone that would contribute to the better understanding of mechanisms underlying both healthy and diseased conditions of bone has not been achieved yet.

Materials & Methods

We assess the effects of indoxyl sulfate (IS), one of the most representative PBUTs, on the osteogenic differentiation of human adipose-derived stem cells (hASCs) in both 2D and 3D environments by mainly focusing on the quantity and quality of the deposited bone matrix. The composition and mineralization of the produced extracellular matrix (ECM) was analyzed through the gene expression of major marker genes, collagen immunostaining, calcium quantification and mCT scanning. We also examined the potential of fibrin hydrogels as tool for developing a 3D in vitro model of human bone, where we checked the ability of the system to permit the succesful osteogenic differentiation of hASCs into osteocytes that producing bone-like ECM.

Results

Overall, our results demonstrate that IS affects the quantity and quality of the extracellular matrix (ECM) produced by differentiated osteoblasts and osteocytes resulting in reduced collagen and calcium deposition and decreased homogeneity of calcium distribution. Our study also indicates that fibrin hydrogels permit the successful generation of osteocytes and their embedding into their own produced collagenous and mineralized matrix.

Conclusion

Further to be validated, our results indicate (a) that IS action on bone ECM could be (one of) the underlying mechanisms of CKD-MBD and thus a possible therapeutic target, and (b) that our 3D system based on fibrin hydrogels and hASCs holds a great potential for the development of a 3D in vitro model of human bone.

Detection of CYP2C19*2 allele among Helicobacter pylori-infected patients in two tertiary hospitals of Khartoum, Sudan, 2019

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Introduction

Helicobacter pylori (H. pylori) is considered the most common bacteria diagnosed in chronically infected stomachs in patients with chronic gastritis. It is infecting more than half of the population worldwide. CYP2C19*2 has been identified as the most common allelic variant of CYP2C19 affecting the response to Proton pump inhibitors (PPI). This study aims to detect CYP2C19*2 allele in H. pylori-infected Sudanese population, owing its probable effect on H. pylori eradication.

Materials & Methods

Antral biopsies were collected conveniently from 30 patients attending endoscopy units for upper GI symptoms in two tertiary hospitals in Khartoum, Sudan. Extraction of DNA was performed through QIAamp® DNA Mini Kit. Samples were screened for Urease C (UreC) gene of H. pylori using conventional PCR (Genebank No. NG_008384.2). Detection of CYP2C19*2 was performed in positive H. pylori samples using Real time-PCR. Informed consent was taken verbally form each patient. Ethical approval was obtained from the ethical committee of Central Laboratories, Ministry of Higher education and Research (Ref. No: CL/85/2019). Analysis was done using Statistical Package for Social Sciences (SPSS) version 23 (SPSS Inc., Chicago, Illinois, USA).

Results

The mean age of patients was 40.7 (±20.2 SE). Positive samples for UreC were 24 (80%) samples. Among them, four samples (16.6%) were found positive for CYP2C19*2 allele presence. Gender was found to be statistically associated with the presence of the allele (p < 0.05). Neither age nor ethnicity were found to be associated with allelic variant presence (p > 0.05).

Conclusion

This study illustrates that CYP2C19*2 is of modest prevalence among H. pylori-infected Sudanese population. Physicians in Sudan should consider this allele as a determinant of suitable drug choice and dosage, which would improve the regimen's effectiveness. The determination of genotypic and allelic frequencies of CYP2C19 gene among different populations will provide data to be used to personalize treatment according to individual genetic profile, and minimize the possible adverse side effects of CYP2C19 substrates.

Antibody production against camptothecin-derived small molecules: a tool for developing pharmacokinetic studies and dose management of chemotherapy

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Introduction

Camptothecin compounds (such as irinotecan or topotecan) are commonly used and the most operative chemotherapeutic drugs for cancer therapy. The active form of all camptothecin derivatives is SN38 released by liver esterase enzyme as the super-cytotoxic form of camptothecin families. Furthermore, in recent years, SN38 is also used as a payload in a new generation of targeted drug delivery systems termed ADCs technology. Pharmacokinetic studies (PK) and side effect management of cancer above medicines have remained a challenge for optimizing patient safety and improving medical practice. To overcome this challenge, developing simple analytical method, non-invasive and amenable to the routine clinical laboratory is the primary goal of our present study.

Materials & Methods

For this purpose, The SN38–20-O-glycine and SN38–20-O-glycine-NHS were synthesized and confirmed by mass, 1 H -NMR, and 13 C -NMR spectroscopic techniques. Then two different immunogens were prepared and characterized, including SN38 conjugated with keyhole limpet hemocyanin (KLH) protein based on linking of SN38 either via its amine-containing SN38–20-O-glycine and SN38–20-O-glycine-NHS derivatives with the tyrosine amino acid residues of KLH by classical glutaraldehyde coupling reaction. The pertinence and efficacy of the coupling reactions of haptens (SN38-KLH and SN38NHS-KLH) were confirmed and characterized by ultraviolet (UV) spectrophotometry and then immunized animals. Antibodies production and isotypes determination were done by enzyme-linked immunosorbent assay (ELISA) and then purified either using handmade SN38 affinity or HiTrapby Protein G prepacked columns.

Results

Immunization of animals with the SN38NHS-KLH generated extraordinarily high anti-SN38 titers that were up to-fold higher than those immunized by SN38-KLH. The animal's antiserum that showed the highest affinity was selected. The collected antiserum (polyclonal and monoclonal antibodies) had a very high affinity to its cognate ligand with high affinity and high specificity, among other irrelevant drug controls.

Conclusion

The produced polyclonal and monoclonal antibodies are valuable for developing highly sensitive and selective immunoassays for camptothecin-containing cancer medicines. The sensitivity and specificity of the ELISA should provide a valuable tool for creating pharmacokinetic studies, dose monitoring, and side effect management of camptothecin-derived small molecules.

Melt-electrowritten tubular scaffolds enhance proximal tubule phenotype in iPSC-derived kidney organoids

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Introduction

Chronic kidney disease (CKD) affects 10% of the global population and severely impacts patients' quality of life, while it also leads to an increased risk of e.g. cardiovascular disease. Researchers have studied kidney diseases by using human primary and immortalized kidney cell lines or animals. However, these approaches often lack physiological characteristics and bring up ethical concerns. Hence, we focussed on the development of a proximal tubule (PT) in vitro model that better mimics the physiology and complexity of this nephron segment. It has been previously shown that melt-electrowritten (MEW) tubular scaffolds with a rhombus geometry can enhance PT function. Here, we aimed to develop MEW tubular scaffolds that can support the differentiation of PT epithelial cells derived from induced pluripotent stem cell (iPSC) derived kidney organoids.

Materials & Methods

Dissociated iPSC-derived kidney organoids with presence of the main four segments (glomerulus, PT, distal tubule and collecting duct) were cultured in highly porous rhombus-shaped (30° angle) tubular MEW scaffolds. Confluent scaffolds were exposed to flow-induced shear stress (FSS) through placement on a 3D rocker for 3 days at 5rpm. Scaffolds were assessed for PT markers through immunofluorescence, RT-qPCR and functional transporter assays.

Results

After staining tubular MEW scaffolds for all nephron segments, cells showed immunolocalization suggestive for PT marker LTL. Basement membrane (BM) formation was shown by staining for collagens, where cells deposited collagen IV, but not collagen I which is in line with the collagen composition of the PT BM. FSS induced directionality of the cells in the scaffolds, as measured by F-actin filaments. Furthermore, FSS exposed cells showed clear polarization and longer cilia (α-tubulin) and enhanced tight junction development (ZO-1). Preliminary data suggests PT-functional organic cation transporter-2 and P-glycoprotein mediated transport in the MEW organoid-derived tubular scaffolds.

Conclusion

Tubular MEW scaffolds with rhombus-shaped pores support PT characteristics of iPSC-derived kidney organoids. This 3D tubular model potentiates the use of organoid-derived cells in drug research and personalized medicine.

Properties of Aspergillus fumigatus alkaline protease – potential target for therapy

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Introduction

Aspergillus fumigatus is an opportunistic pathogen and one of the most common aspergillosis causes. The micromycete synthesizes many extracellular proteolytic enzymes, including pathogenicity factors. Proteases secreted by A. fumigatus could be considered as targets for fungal asthma treatment. However, for the such methods development, the enzymes properties should be studied in detail. Alkaline serine protease Alp1 is one of the known pathogenicity factors of the causative agent of fungal asthma. Thus, the aim of this work was to study the biochemical characteristics of A. fumigatus alkaline protease.

Materials & Methods

A. fumigatus was cultivated under submerged conditions to obtain the target enzymes. Extracellular proteins were precipitated with ammonium sulfate (80% saturation degree) from the culture liquid and then dialyzed prior fractionation by isoelectric focusing in 110 ml column (0-40% sucrose density gradient, pH 2.5-10.0, 800 V, 4 °C, 36 h). A molecular weight of the isolated protein was studied electrophoretically. The ability of the target enzyme to hydrolyze various substrates, such as Hammerstein casein, bovine serum albumin (BSA), horse hemoglobin, was examined spectrophotometrically. The activity was expressed in μmoles of tyrosine formed in 1 min in 1 ml of the sample (U). Thrombolysis in vitro and testing of the protease coagulating effect on human fibrinogen and blood plasma was also performed.

Results

Alkaline serine protease produced by A. fumigatus with a molecular weight of 33 kDa, which corresponds to Alp1, was purified. The protease showed activity against casein (1363.5 U/mg), BSA (201.9 U/mg) and hemoglobin (301.6 U/mg). The obtained enzyme did not have a coagulating ability, but it could hydrolyze blood clots: the thrombus residual weight was 35% after 30 min of incubation, after 90 min – 14%. The blood clot was completely hydrolyzed in 180 min.

Conclusion

The alkaline protease of an A. fumigatus opportunistic pathogenic strain, which apparently may be a pathogenicity factor and serve as a target for the treatment of diseases such as fungal asthma, was isolated. Data were acquired on some biochemical properties of the obtained enzyme, shedding light on the possible protease effect on human blood and being the basis for future detailed study of the enzyme action mechanism.

Surgery and Transplantation

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Metamizole as a potential safe NSAID in donors following living donor nephrectomy: a propensity matched comparison between donors

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Introduction

Nonsteroidal anti-inflammatory drugs (NSAIDs) have long been contraindicated in living kidney donors because of their risk of decreasing kidney function due to constriction of the afferent arteriole in the glomerulus. The NSAID metamizole is regarded to be less detrimental for kidney function with less vasoactive effects and is therefore increasingly used perioperatively in living kidney donors. We aimed to study the association between perioperative metamizole use and post-donation measured GFR (mGFR) in living kidney donors.

Materials & Methods

In this cohort study, 82 kidney donors with perioperative metamizole use were matched to 76 kidney donors without perioperative metamizole use, using propensity matching. We measured mGFR pre- and 3 months post-donation using continuous 125I-iothalamate infusion and tested for differences using an independent t-test. Determinants of a lower post-donation mGFR were assessed using multivariable linear regression analyses.

Results

Baseline characteristics in donors using metamizole (49% male, median age: 56 years) did not differ significantly from donors without perioperative metamizole use (51% male, median age: 56 years). Post-donation, mGFR of donors with perioperative metamizole use was comparable to donors without perioperative metamizole use (70 vs. 69 mL/min/1.73m2, p=0.75). In addition, donors who used higher metamizole doses did not have a lower post-donation mGFR (<2500 mg vs. 2500-7500 mg vs. 7500 mg: 68 vs. 71 vs. 72 mL/min/1.73m2, p=0.60). No association between perioperative metamizole use and post-donation mGFR was found in univariable linear regression analyses (β=0.8 [CI: -3.3;4.8], p=0.70). However, after adjustment for potential confounders, perioperative metamizole use was positively associated with post-donation mGFR (β=3.2 [CI: 0.2;6.1], p=0.04).

Conclusion

Perioperative metamizole use is not associated with a lower post-donation kidney function in living kidney donors. Notably, after adjustments for potential confounders, peri-operative metamizole use was associated with a higher mGFR post-donation. Metamizole may therefore be a valid perioperative pain management strategy in living kidney donors. Further research is needed to assess if metamizole can be used as an analgesic in patients with impaired kidney function.

Atherosclerosis and Intrarenal Resistance Index in Kidney Transplant Recipients

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Introduction

Atherosclerosis of the aorto-iliac vessels can adversely affect kidney perfusion after kidney transplantation (KTx). Post-transplantation kidney perfusion can be determined by the intrarenal resistance index (RI) using Doppler ultrasound (DUS). The severity of atherosclerosis can be determined by means of the Calcium Score (CaScore). This study investigates the association between aorto-iliac CaScore and RI in kidney transplant recipients.

Materials & Methods

Kidney transplant recipients (2004-2019), for which a CaScore and an RI could be determined, were included in this dual-center cohort study (n=389). The CaScore was measured, by means of the Agatston score, in three aorto-iliac segments using non-contrast CT imaging. The RI ((peak systolic rate - end diastolic rate) / peak systolic rate) was determined by DUS. Multivariable linear regression analysis was performed between the CaScore and the RI adjusted for confounding variables which are found with multiple univariate regression analyses.

Results

Median (IQR) RI score (unitless) was 0.70 (0.64 to 0.77) and CaScore (unitless) was 3340 (399 to 7833). In univariate linear regression analyses, with RI as dependent variable, CaScore (β=0.008; 0.004 to 0.013; P<0.001) was associated with RI. In addition, age of the recipient (β=0.091; 95%CI 0.039 to 0.143; P=0.001), history of diabetes (β=0.018; 0.005 to 0.030; P=0.005), history of vascular intervention (β=0.020; 0.007 to 0.033; P=0.002), prior dialysis (β=0.018; 0.006 to 0.029; P=0.003), deceased donation (β=0.026; 0.015 to 0.037; P<0.001), cold ischemia time (β=0.036; 0.020 to 0.052; P<0.001) and preoperative diastolic blood pressure (β=-0.098; -0.174 to -0.021 P=0.013) were associated with RI. In multivariable analysis, CaScore and RI remained significantly (P=0.023) associated, independent of adjustment for potential confounders.

Conclusion

A significant association was found between the CaScore and RI after adjustment for multiple recipient and donor confounding factors. Aorto-iliac atherosclerosis should be taken into account when interpreting the RI and determining the cause of malperfusion and graft failure after kidney transplantation.

Elucidating mechanisms of aspiration-induced lung damage in murine precision-cut lung slices

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Introduction

Lung transplantation is life-saving for patients with end-stage lung disease. Unfortunately, the demand for donor lungs exceeds their availability. Potential donor lungs are often discarded due to pre-existing issues. Gastric aspiration accounts for ~9% of lungs unsuitable for transplantation. To increase the potential donor pool it is of interest whether aspiration-induced lung damage (AILD) can be repaired. In order to develop therapeutic approaches, we need to elucidate the pathophysiology of AILD. We, therefore, investigated the effects of acid on lung tissue, using precision-cut lung slices.

Materials & Methods

Slices were prepared from murine lung tissue using a Krumdieck slicer, producing slices with a diameter of 5 mm and thickness of 200-300 µm. They were then exposed to saline solutions with pH values ranging from 1.5 to 5.5, for 15 min. Slices were subsequently cultured for 48h. We also assessed the effects of dexamethasone (0.5 or 1 µM), as this drug is used in an attempt to treat AILD. In each experiment (n = 3), we analyzed the mitochondrial activity and general morphology as well as inflammation and apoptosis. Data was analysed using a one-way ANOVA followed by Dunn's multiple comparisons test.

Results

Slices subjected to saline with pH of 1.5 and 2.5 – corresponding to the pH of gastric juice – contained no ATP (p < 0.0001), indicating a complete loss of mitochondrial respiration and, therefore, cell viability. These findings were corroborated upon analyzing the general morphology. We also observed a significantly reduced secretion of IL-1β (p < 0.05), IL-6 (p < 0.01) and TNF-ɣ (p < 0.001) for slices exposed to pH 1.5 and 2.5. This suggests severe damage was inflicted, incapacitating virtually all the cells that were present. There were no beneficial effects observed for dexamethasone.

Conclusion

Taken together, these findings suggest brief (15 min) exposure to very acidic saline solutions (pH 1.5 and 2.5) causes immediate cell death. Dexamethasone did not affect this process. Our future studies will investigate how healthy lung tissue responds to neighbouring damaged tissue, and whether the use of dexamethasone affects this process. Then we can assess the implications for the field of transplantation medicine.

histologic and biomechanical evaluation of the thoracolumbar fascia graft for massive rotator cuff tears in a rat model

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Introduction

Fascial autografts, which are easily available grafts, have provided a promising option in patients with massive rotator cuff tears. However, no fascial autografts other than the fascia lata have been reported, and the exact healing process of the fascia-to-bone interface is not well understood. The objective of this study is to histologically and biomechanically evaluate the effect of the thoracolumbar fascia (TLF) on fascia-to-bone healing

Materials & Methods

A total of 88 rats were used in this study. Eight rats were killed at the beginning to form an intact control group, and the other rats were divided randomly into 2 groups (40 rats per group): the TLF augmentation group (TLF group) and the repair group (R group). The right supraspinatus was detached, and a 3 × 5 mm defect of the supraspinatus was created. The TLF was used to augment the torn supraspinatus in the TLF group, whereas in the R group, the torn supraspinatus was repaired in only a transosseous manner. Histology and biomechanics were assessed at 1, 2, 4, 8, and 16 weeks postoperatively.

Results

The modified tendon maturation score of the TLF group was higher than that of the R group at 8 weeks (23.00 ± 0.71 vs. 24.40 ± 0.89, P = .025) and 16 weeks (24.60 ± 0.55 vs. 26.40 ± 0.55, P ≤ .001). The TLF group showed a rapid vascular reaction, and the peak value appeared at 1 week. Later, the capillary density decreased, and almost no angiogenesis was observed at 8 weeks postoperatively. Immunohistochemistry results demonstrated a significantly higher percentage of collagen I in the TLF group at 4, 8, and 16 weeks postoperatively. Biomechanical tests revealed that the ultimate failure force in the TLF group was significantly higher than that in the R group at the final evaluation (29.13 ± 2.49 N vs. 23.10 ± 3.47 N, P = .022).

Conclusion

The TLF autograft can promote a faster biological healing process and a better fixation strength. It could be used as an alternative reinforcement or bridging patch when the fascia lata is not appropriate or available for SCR.

Amniotic membrane patching for repairing the surgical Model of colonic anastomosis in male rats

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Introduction

Colonic anastomosis is a standard procedure following different conditions such as obstruction, tumor, inflammatory bowel diseases, trauma, and polyps. Blockage, stricture, or anastomosis leakage can be some of its complications. The Amniotic membrane (AM) patch is recently used for treating different types of wounds and corneal injuries. Inhibiting protease and inflammatory response and reducing scare formation are beneficial effects of using AM in ophthalmology and dermatology procedures.

Materials & Methods

Twenty-four male Wistar rats were allocated into two groups of study; control and AM patch group. The Am was obtained from the human placenta and prepared for the procedure. First, all rats were anesthetized, then the median laparotomy incision, colon resection, and colocolonic anastomosis were performed on them. Next, a fragment of AM patch was warped and fixed by suture around the anastomosis part of the colon in AM patch group. Samples from the anastomosis site were resected on days 3, 7, and 14, and then morphological, histological, and molecular analyses were performed on them.

Results

Modified scoring system for surgical wound healing had shown significant increase in AM patch group on day 7 and 14 compared to control (p-value< 0.001 and <0.01 respectively). Gene expression of NF-κB (day3; p-value<0.05; day7; p-value <0.01; day 14, p-value<0.01), TNFα (day7; p-value <0.01; day 14, p-value<0.05), TLR4 (day7; p-value <0.05; day 14, p-value<0.05) were significantly decrease while TGFβ (day7; p-value <0.05) and IL-10 (day7; p-value <0.01; day 14, p-value<0.05) were increased in AM patch group. Also expression level of TGFβ (day7; p-value <0.05; day 14, p-value<0.05) and TNFα (day7; p-value <0.01; day 14, p-value<0.001) in IHC had shown similar results.

Conclusion

AM patch is a proper and reasonable choice for colorectal anastomosis repair, which may prevent postoperative complications and accelerate wound healing.

Healing Full-thickness Wounds in Rats using Decellularized Bovine Small Intestinal Submucosa with Enhanced with Cellulose Acetate/ Ag NPs Nanofibers

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Introduction

The formation of chronic wounds accounts for considerable costs in health care systems. Despite the several benefits of Decellularized small intestinal submucosa(SIS) as an appropriate scaffold for different tissue regeneration, it has shortcomings such as lack of antibacterial features and inappropriate mechanical properties for skin tissue regeneration. We aimed to examine the efficacy and safety of decellularized SIS scaffold enhanced with cellulose acetate(CA) and silver(Ag) nanoparticles for healing full-thickness wounds.

Materials & Methods

The scaffolds were prepared by decellularizing bovine SIS and electrospinning CA/Ag nanoparticles and characterized using a transmission electron microscope(TEM), scanning electron microscope(SEM), tensile testing, X-ray diffraction, and Raman spectroscopy. In vivo evaluations were performed using full-thickness excisions covered with sterile gauze as the control group, SIS, SIS/CA, and SIS/CA/Ag scaffolds on the dorsum of twenty male Wistar rats divided into four groups randomly with 14-days follow-up. All in vivo specimens underwent Masson's trichrome(MT), transforming growth factor-β (TGF-β) immunohistochemistry(IHC), and Hematoxylin and Eosin(H&E) stainings. The IHC and MT data were analyzed with the ImageJ by measuring the stained area. IBM® SPSS® Statistics 26 was used for statistical analysis, and the statistical significance was determined as P-value <0.05.

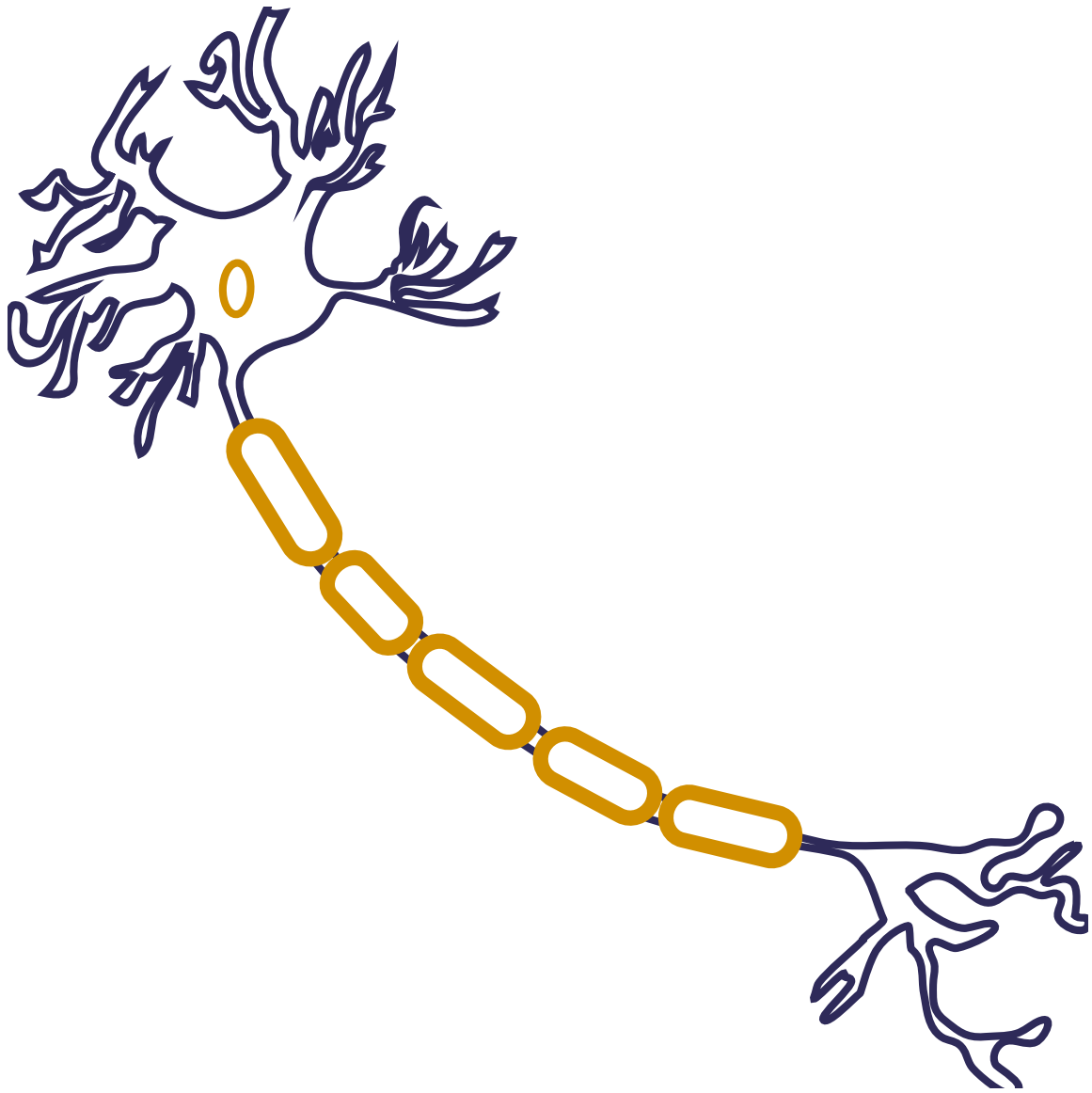
Results

The TEM results revealed that Ag nanoparticles are successfully incorporated into CA nanofibers with an average size of 20±2.67 nm and a diameter of 280±8 nm. Assessment of scaffolds hydrophilicity demonstrated that the contact angle of SIS, SIS/CA, and SIS/CA/Ag scaffolds were 103°±8°, 100°±2°, and 80°±4° respectively. The in vivo results indicated that the SIS/CA/Ag scaffold had the most significant wound closure (89.48%±2.04% on day 14, P=0.039). H&E staining of the in vivo specimens showed the formation of epidermal layers with the skin appendages only in the SIS/CA/Ag group on day 14. The percentage of the stained area of MT and TGF-β IHC stainings was the highest one in the SIS/CA/A group as evidence of greatest expression of collagen and TGF-β(37.17%±6.54% and P=0.002, 27.86%±4.37% and P=0.025 respectively).

Conclusion

The decellularized SIS/CA/Ag scaffolds provided the most significant wound closure compared to other groups and caused the formation of epidermal layers and skin appendages. Additionally, the collagen deposition and expression of TGF-β increased significantly in SIS/CA/Ag group.

Neurology I



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TWO TYPES OF CLOCK-DRAWING TEST PERFORMANCE ASSOCIATE HIGHLY WITH TEMPORAL AND PARIETAL ATROPHY IN ALZHEIMER'S DISEASE

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Introduction

The clock-drawing test (CDT), a screening instrument for cognitive impairment, has high discriminating power between Alzheimer's disease (AD) patients and healthy individuals. Several scoring systems were established for evaluating CDT, that are found to reflect atrophy at different brain regions. Among them, fully-objective Manos&Wu is used widely in research whilst semi-quantitative Shulman method allows faster scoring in clinical settings. In the present study, we aimed to determine the two different scoring systems' neuroanatomical associations to answer the questions whether they can be used interchangeably and are associated with atrophy in similar brain regions.

Materials & Methods

Forty AD patients and 39 healthy controls were participated to the study. CDT was scored according to Manos&Wu and Shulman scoring systems. Grey-matter volumes (GMV) and cortical thickness (CT) measures were obtained from structural magnetic resonance imaging (MRI) scans. The association between GMV and CT with CDT scores were analyzed with Pearson correlation analysis.

Results

Both CDT scores showed moderate to strong correlations with the frontal, temporal and parietal GMV (r>.50). Both CDT scores displayed r-values over.60 with GMV of the left superior temporal gyrus, left and middle temporal gyrus and left fusiform gyrus. Moreover, correlations over .70 was found between left inferior temporal gyrus and both CDT scores. Whereas only Manos&Wu scoring system showed stronger correlations with the left middle temporal gyrus (r>.70). High correlations(r>.60) were found between Manos&Wu scoring systems and the CT measures of the left entorhinal, bilateral middle and superior temporal regions. No correlations over .60 were found between CT measures and Schulman's CDT scores.

Conclusion

Our findings indicate that both scoring systems reflect frontal, temporal and parietal region atrophy. However, CDT scores according to Manos&Wu showed stronger associations with overall CT measures and GMV of the temporal areas. Regardless of the scoring systems, temporal and parietal regions were found to have stronger neuroanatomical associations with CDT scores than frontal regions. These findings suggests that CDT might be a good indicator of visuo-spatial abilities than executive functions. Since AD neurodegeneration begins with parietotemporal lobe atrophy, present findings may explain why CDT has high discriminating power even at early-stages of AD.

Sex-related differences in amyloid plaque burden and microglial activation in Alzheimer's disease

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Introduction

Alzheimer's disease (AD) is a progressive neurodegenerative disease characterised by amyloid plaque deposits, dysregulated microglial activation and chronic neuroinflammation. It is estimated to affect over 50 million people globally, with two-thirds of patients being female. Female AD patients exhibit sex-specific clinical symptoms and generally poorer cognitive ability. This project aims to assess differences in amyloid plaque burden and microglial activation between sexes in order to interrogate one aspect of the sexual dimorphism associated with AD.

Materials & Methods

Sections of parietal cortex and hippocampus of male and female AD patients and age-matched controls were prepared from human post-mortem paraffin-embedded tissue samples, using a microtome. Brain sections were either stained with Congo red to assess amyloid beta plaques or with anti-Iba1 and anti-CD68 to assess microglial activation. Sections were imaged and analysed using ImageJ, and GraphPad Prism.

Results

Congo red analysis revealed that female AD patients had a larger amyloid plaque area in the parietal cortex compared male AD patients. CD68 expression was found to be significantly higher in male AD patients, when compared to male control patients. However, there was no difference seen in CD68 expression between female AD patients and female age-matched controls. Numerous examples of rod-shaped microglia, which are considered to be persistently-activated microglia, were visible in sections from female AD patients whereas amoeboid microglia predominated in sections from male AD patients.

Conclusion

These results suggest that microglia in the brain of female AD patients are not as functionally adept as male microglia, increasing amyloid accumulation in the brain. These findings highlight sex-based dimorphisms in microglial activation and plaque burden and demonstrates the clinical need for further sex-specific research, and sex-specific targeted therapeutics in AD.

BACTERIAL MELANIN PROMOTES AXONAL SPROUTING AFTER PERIPHERIAL NERVE DAMAGE

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Introduction

Injury of nervous system is followed by a local reaction in damaged tissue including inflammation and ischemic necrosis leading to secondary destruction and scaring. Following nerve injury, spontaneous axonal compensatory sprouting takes place aiming to re-innervate synaptic targets. Different therapeutic agents have the potential to suppress expression of inhibitory molecules that hinder the axonal regeneration. Bacterial melanin (BM) was obtained from the mutant strain of Bacillus Thuringiensis at the Institute of Biotechnology in Armenia. The BM was studied in models with central nervous system lesion. Bacterial melanin accelerates motor recovery after CNS lesions and stimulates regenerative processes. We have therefore assessed the mechanism of functional recovery following transection of rat sciatic nerve using injections of melanin solution.

Materials & Methods

Methods

Behavioral and histochemical studies were conducted in 12 rats to study the influence of intramuscularly injected melanin in rats with sciatic nerve damage. The recovery of movements following the nerve damage and injections of melanin were assessed by an initially elaborated instrumental conditioned reflex (balancing on a rotating bar for 250 seconds). The method for Ca2+ - dependent acidic phosphatase activity measurement was used to examine sections of nerve fibers and to trace the sprouting of axons after the injury.

Results

The recovery of elaborated balancing reflex was faster in rats (n=6) treated with melanin after the sciatic nerve injury (in 23 testing days), compared to not treated and operated rats (n=6) (partial recovery in 54 days). Histochemical study revealed expressed proliferation of endoneurium and Schwann cells in nerve sections from animals injected with melanin after the damage. Influence of BM preserves the enzyme activity along almost the whole length of the nerve, with an insignificant prevalence in proximal segments of axons. In the area of transection random alternation in the activity of creatine phosphate is revealed, which is manifested with weak or strong staining zones in nerve fibers. These changes indicate that melanin induces regenerative sprouting in damaged peripheral nerve.

Conclusion

Acceleration of the elaborated conditioned reflex recovery and results of histochemical study showed that bacterial melanin stimulates the axonal sprouting and facilitates recovery of limb movements after peripheral nerve lesion.

Physiological clearance of amyloid-beta by the kidney and its therapeutic potential for Alzheimer's disease

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Introduction

Amyloid-β (Aβ) accumulation in the brain is a pivotal event in the pathogenesis of Alzheimer's disease (AD), and its clearance from the brain is impaired in sporadic AD. Previous studies suggest that approximately half of the Aβ produced in the brain is cleared by transport into the periphery. However, the mechanism and pathophysiological significance of peripheral Aβ clearance remain largely unknown. The kidney is thought to be responsible for Aβ clearance, but direct evidence is lacking.

Materials & Methods

A total of 17 kidney donors and age- and sex-matched controls (1:3) were enrolled. Rabbits were used to investigate the differences in Aβ levels between the renal artery and renal vein. APP/PS1 mice were subjected to ligation of the renal artery, vein, and ureter, and Aβ levels in the blood and interstitial space fluid (ISF) were monitored. APP/PS1 mice were subjected to unilateral nephrectomy to investigate the long-term impacts of Aβ clearance by the kidney. The effects of furosemide on APP/PS1 mice were also examined. To assess the behavioural performance of the mice, the Y-maze test, open-field test, and Morris water maze were performed. Aβ burden, neuroinflammation, neurodegeneration, and tau phosphorylation were measured by immunohistochemistry, double immunofluorescence staining, and ELISA.

Results

In this study, we detected Aβ in the kidneys and urine of both humans and animals and found that the Aβ levels in the blood of the renal artery were higher than those in the blood of the renal vein. Unilateral nephrectomy increased brain Aβ deposition; aggravated AD pathologies, including tau hyperphosphorylation, glial activation, neuroinflammation, and neuronal loss; and aggravated cognitive deficits in APP/PS1 mice. In addition, chronic furosemide treatment reduced blood and brain Aβ levels and attenuated AD pathologies and cognitive deficits in APP/PS1 mice.

Conclusion

Our findings demonstrate that the kidney physiologically clears Aβ from the blood, suggesting that facilitation of Aβ clearance via the kidney represents a novel potential therapeutic approach for AD.

Intravenous Thrombolysis before Mechanical Thrombectomy for Acute Ischemic Stroke due to Large Vessel Occlusion; Should We Cross that Bridge? A Systematic Review and Meta-Analysis of 36,123 Patients

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Introduction

The use of intravenous thrombolysis (IVT) before mechanical thrombectomy (MT) for acute ischemic stroke due to large vessel occlusion (AIS-LVO) is a debatable subject in the field of neuro-interventional surgery. We conducted this systematic review and meta-analysis to synthesize evidence from published studies on the outcomes of IVT+MT compared with MT alone in AIS-LVO patients.

Materials & Methods

We searched PubMed, Scopus, Web of Science, and Cochrane Central Register of Controlled Trials from inception to December 2021 for relevant clinical trials and observational studies. Eligible studies were identified, and all relevant outcomes were pooled in the meta-analysis DerSimonian-Liard random-effects model.

Results

Forty-nine studies, with a total of 36,123 patients, were included in this meta-analysis. IVT+MT was significantly superior to MT alone in terms of successful recanalization (RR 1.06, 95% CI 1.03 to 1.09), mortality (RR 0.75, 95% CI 0.68-0.82), favorable functional outcome (RR 1.21, 95% CI 1.13 to 1.29), and complete recanalization (RR 1.06, 95% CI 1.00 to 1.11). There were no significant differences between the two groups in terms of improvement of the National Institute of Health Stroke Scale (NIHSS) score at 24 hours or at discharge (P>0.05). Complications including symptomatic intracranial hemorrhage, symptomatic intracerebral hemorrhage (sICH), procedure-related complications, and parenchymal hematoma were comparable between the two groups (P>0.05).

Conclusion

For AIS-LVO, IVT+MT is associated with slightly better rates of survival, successful and complete recanalization, and favorable functional outcome as compared with MT alone. Further clinical trials are needed to corroborate such benefits of bridging IVT.

Anticonvulsant effect of minocycline on pentylenetetrazole-induced seizure in mice: involvement of nitric oxide and N-methyl-d-aspartate receptor

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Introduction

Anticonvulsant effects of minocycline have been explored recently. This study was designed to examine the anticonvulsant effect of acute administration of minocycline on pentylenetetrazole-induced seizures in male mice considering the possible role of the nitric oxide/N-methyl-d-aspartate (NMDA) pathway.

Materials & Methods

The following drugs were used: minocycline, pentylenetetrazole (PTZ), NG-L-arginine methyl ester (L-NAME), aminoguanidine, 7-nitroindazole (7-NI), L-arginine (L-arg), ketamine, and MK-801. Except PTZ, all injections were through the intraperitoneal (i.p.) route and with a volume of 5 mL/kg body mass. We induced seizure using intravenous administration of PTZ . The minimal dose of PTZ (milligrams per kilogram of mouse mass) needed to induce a clonic seizure was considered as the index of clonic seizure threshold (CST). To determine the NO level in the hippocampus, we measured the nitrite level as the result of the NO end product via a colorimetric assay. Data were expressed as mean ± SEM of CST. One-way ANOVA followed by Tukey's post hoc comparison was used for analysis and GraphPad Prism software was used to illustrate the results. A P value of less than 0.05 was considered statistically significant.

Results

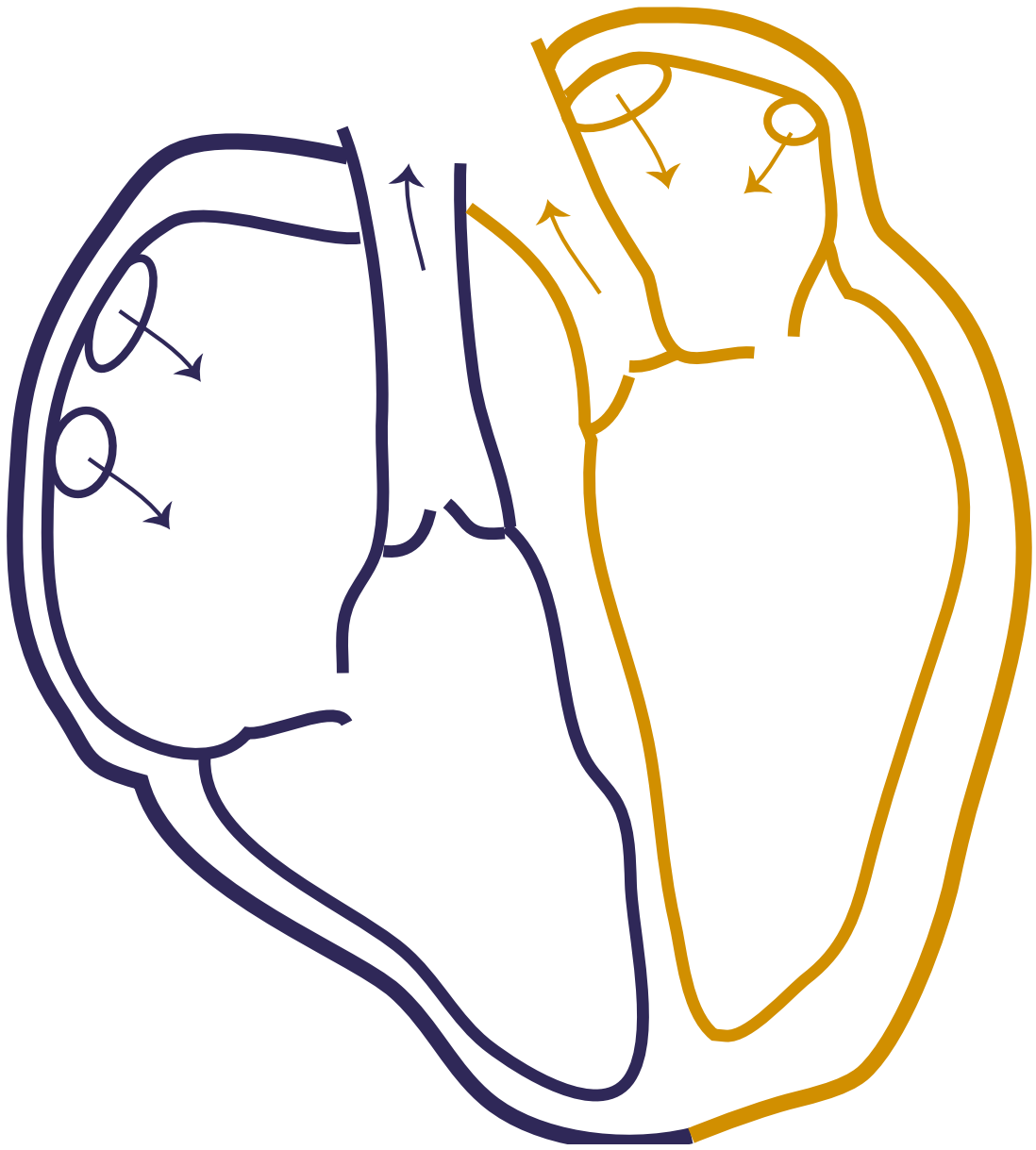
Our results showed that acute administration of minocycline increased the seizure threshold. Furthermore, co-administration of subeffective doses of the nonselective nitric oxide synthase (NOS) inhibitor L-NAME (10 mg/kg) and the neuronal NOS inhibitor 7-NI (40 mg/kg) enhanced the anticonvulsant effect of subeffective doses of minocycline (40 mg/kg). We found that inducible NOS inhibitor aminoguanidine (100 mg/kg) had no effect on the antiseizure effect of minocycline. Moreover, L-arginine (60 mg/kg), as a NOS substrate, reduced the anticonvulsant effect of minocycline. We also demonstrated that pretreatment with the NMDA receptor antagonists ketamine (0.5 mg/kg) and MK-801 (0.05 mg/kg) increased the anticonvulsant effect of subeffective doses of minocycline. Results showed that minocycline significantly decreased the hippocampal nitrite level. Furthermore, co-administration of a neuronal NOS inhibitor and NMDA receptor antagonists augmented the effect of minocycline on the hippocampal nitrite level.

Conclusion

In conclusion, we revealed that anticonvulsant effect of minocycline might be, at least in part, due to a decline in constitutive hippocampal nitric oxide activity as well as inhibition of NMDA receptors.

Oral Sessions II

Cardiology II



Presenters:
van Genderen, O.S. (Olton)
Fogarasi, Cs.E.F. (Csenge)
Steuwer, C.H.
SU, B.N.S. (BEYZA NUR)
Yazdanpanah, M.H. (Mohammad Hosein)
Salazar, C.J. (Cristian)

Elastic Deformation: a reliable, non-invasive, method for the exclusion of endoleak after Endovascular Aortic Aneurysm Repair

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Introduction

Elastic Deformation(ED%) is a non-invasive novel method, based on color duplex ultrasound (CDU), and can be used to evaluate endoleak after endovascular aortic repair (EVAR). If an aneurysm sac, which is completely excluded from the circulation, has a reduced sac pressure; making it more compressible, one can hypothesize that Elastic Deformation(ED%) can serve as a predictor to exclude endoleak(figure 1). We studied whether ED can be used to exclude endoleak post-EVAR procedure.

Materials & Methods

A retrospective cohort study in patients before- and after EVAR-procedure between August, 2020, and September, 2021. Data was collected following our local protocol. Patients were divided into three groups, i.e. patients with an abdominal aortic aneurysm (AAA) (AAA group), patients with an EVAR with endoleak (LEAK group), and patients with an EVAR without endoleak (NO LEAK group).

Results

A total of 109 patients (median (IQR) age: 68 (71-83) years; n=10 [10%] were female) were included. 24 patients in the AAA group, 26 in the LEAK group, and 59 in the NO LEAK group.

The mean ED in the AAA group was 2.0% (SD+/-1.5), 3;3% (SD+/- 2,9) in the LEAK group, and 11,3% (SD+/-5,3) in the NO LEAK group. The diagnostic accuracy in excluding leakage was very reliable (area under the receiver operating characteristic curve = 0.91 (95% confidence interval (CI) = 0.85 to 0.97)) with a sensitivity of 0.64 and a specificity of 1.0. The optimal cutoff was 9.5% ED. A higher ED in the NO LEAK group is associated with absence of endoleak on contrast-enhanced computed tomography (CT-A) (Spearman's p =0,368; p<0,001).

Conclusion

ED reliably excludes endoleak post-EVAR and is well associated with absence of endoleak on contrast-enhanced computed tomography (CT-A).

Myocardial involvement in elite athletes a feared complication after SARS-CoV-2 infection: A cardiac magnetic resonance case-control study

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Introduction

It is well documented that SARS-CoV-2 infection could cause myocarditis but we have a small amount of information about the myocardial involvement in mild, moderate or asymptomatic cases. This data would be necessary with regards to the fact that myocarditis is a relevant cause of sudden cardiac death among young athletes. Therefore, we decided to assess the cardiovascular involvement in post-COVID-19 athletes concerning control groups.

Materials & Methods

All athletes who were referred to our centre for CMR examination between July 2020 and February 2021 were consecutively included after SARS-CoV-2 infection which was diagnosed by PCR or serum immunoglobulin G antibody tests. We recorded the athletes' medical history, symptoms, 12-lead-ECG examination and their high-sensitivity troponin T levels. CMR protocol included functional assessment and specific sequences for oedema and necrosis/fibrosis evaluation. We used T1 and T2 mapping techniques for the objective characterisation of diffuse tissue abnormalities. The CMR parameters of the post-COVID-19 athletes were compared with healthy sex- and age-matched athlete group (n=59) and sedentary controls (n=56) with Kruskal-Wallis test.

Results

Altogether 147 athletes (94 male, median 23, IQR 20-28 years) were included. 12,9% of the athletes were asymptomatic, 83,7% had mild/moderate symptoms and 3,4% had long-COVID symptoms. There were elevated hs Troponin T values in 6 patients (>14ng/l). Only two patients had definitive signs of myocarditis (1,4%) and five had possible myocardial or pericardial involvement. We observed a pronounced sport adaption in the two athlete groups, compared to the sedentary controls. There was no difference between the two athlete groups in any CMR parameter. Comparing athletes with different symptom severities showed that athletes with moderate symptoms had slightly greater T1 values than athletes with asymptomatic and mildly symptomatic infections (p<0.05). However, T1 mapping values remained below the cut-off point for most patients

Conclusion

The results of our study, in a group of young, elite athletes, suggest that SARS-CoV-2 infection with mild/moderate symptoms rarely causes structural myocardial abnormalities.

Our results caution against the routine use of CMR for troponin-negative, asymptomatic, or mildly symptomatic patients with COVID-19.

Short-term incidence of thrombotic complications in male-to-female transgender individuals

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Introduction

Cis-women using estrogen have an increased risk of thrombosis. Estrogens are part of most trans-women's cross-sex hormonal therapy (CSHT). Studies with proper adjudication evaluating this risk in the trans-women population are lacking.

We aimed to determine the incidence of venous and arterial thrombosis in trans-women during the first year of CSHT.

Materials & Methods

Trans-women treated with estrogen-containing CSHT at the gender clinics of the UMCG between 1985 and 2020 were retrospectively followed for one year after the start of CSHT. Data on demographic factors, medical history, and characteristics of CSHT were collected. The outcome was a composite of venous and arterial thrombotic events. If diagnostic data was not available, clinical and treatment characteristics were evaluated (i.e. at least three months of anticoagulation therapy or start of antiplatelet therapy). The incidence rate of thrombotic events was calculated.

Results

242 trans-women contributed 233 person-years follow-up (median 1 year).

Median age was 32 years (interquartile range (IQR 23-44), median BMI was 23,9(IQR 21-25.8) and 75(31%) of the patients were smokers. The estrogen therapy took the form of plasters for 188(78,3%) trans-women, oral supplementation for 48(20,0%), and gel for 3(1,3%). The most common regimen was estrogen plasters 50 mcg/24h, which was administered to 146(40,9%) trans-women. Anti-androgens were also given in 226(93.4%) transwomen and progestagens in 5(2,1%).

Three thrombotic events occurred: one deep vein thrombosis of the leg, one pulmonary embolism, and one ischemic stroke, corresponding to an incidence rate of 1.28/100 person-years during the first year of CSHT. Objective diagnostics were available for these three events. Considering only trans-women treated with the estrogen plasters 50 mcg/24h, the incidence rate was 1.41/100 person-years.

Conclusion

In this population of trans-women predominantly treated with estrogen-containing plasters, the risk of thrombotic events during the first year of CSHT was lower than reported in women on oral contraceptives.

Effects of Fondaparinux against Doxorubicin-Induced Cardiotoxicity in Rats

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Introduction

Chemotherapy-induced cardiotoxicity is the leading cause of morbidity and mortality in patients diagnosed with malignancy. It is believed that reactive oxygen species involve in chemotherapy-induced cardiotoxicity. Therefore, we investigated the possible antioxidant effects of fondaparinux (FDX), an antithrombotic agent, on doxorubicin (DOX)-induced cardiotoxicity.

Materials & Methods

Twenty-eight male Wistar Albino rats were randomized into three groups (n=8 for the control, n=10 for other groups). Control group: Rats were given only saline (vehicle). DOX group: Rats were given DOX (2,5 mg/kg/day, intraperitoneally) for 6 consecutive days. FDX+DOX group: Rats were given DOX for 6 consecutive days and FDX (3 mg/kg, sc.) for 12 days. ECG and hemodynamic parameters (heart rate, systolic, diastolic, and mean blood pressure) were analyzed Also, malondialdehyde (MDA), superoxide dismutase (SOD), catalase (CAT), reduced glutathione (GSH), from the heart and vascular tissue samples; troponin I (TnI), creatinine kinase (CK), cardiac muscle-specific creatinine kinase (CK-MB), myoglobin, blood urea nitrogen (BUN), creatinine (Cr), and lactate dehydrogenase (LDH) from blood samples levels were determined.

Results

A decrease in hemodynamic parameters was observed in the FDX+DOX group when compared to the DOX group (p>0.05). Arrhythmias (AV block, ST depression, T negativity) were observed in the DOX group when compared to the control group. These detrimental changes were significantly reduced in the FDX+DOX group (p<0.05). There was a decrease in the PR interval in the DOX and FDX+DOX group than in the control group (p>0.05). QRS and QT intervals were decreased in DOX, and FDX+DOX groups when compared to the control group (p>0.05). CK, LDH, myoglobin, and TnI values increased in the DOX group when compared to the control group (p<0.05). A significant decrease in these parameters was observed in the FDX+DOX group (p<0.05) however no significant difference was obtained between the groups in terms of BUN and Cr values (p>0.05). CAT and MDA levels were statistically higher in the DOX group (p<0.05) whereas SOD and GSH levels were significantly lower in the DOX group (p<0.05). Histopathologically, interstitial edema in the cardiac tissue samples was significantly reduced in the FDX+DOX group when compared to the DOX group (p<0.05).

Conclusion

FDX might provide clinical benefits on DOX-induced myocardial damage. Further molecular studies are needed to better understand the exact mechanisms of FDX on DOX-induced cardiotoxicity.

The Associations of Electrocardiogram Parameters and Abnormalities with Predicted Risk of Cardiovascular Diseases Among an Iranian Rural Population: The Fasa PERSIAN Cohort Study

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Introduction

Cardiovascular diseases(CVD) are the leading cause of premature mortality globally. Electrocardiogram(ECG) is widely used to diagnose CVD due to its simplicity and high prediction value. This study aimed to assess the associations of various ECG parameters with the Framingham risk score as a 10-year CVD incidence predictor among an Iranian rural population.

Materials & Methods

In this sub-analysis, data was used from the Fasa PERSIAN Cohort study. All the individuals aged 35-70 years with available ECG data and negative history of CVD were entered. Individuals with incomplete ECG data or those with QRS duration >120 and those with a non-sinus rhythm ECG were excluded. The FRS was calculated for each, and subjects were divided into four groups very low(<6%), low(6-10%), intermediate(10-19%), and high risk(≥20%). The 24-bit resolution 12-lead ECGs were obtained by Cardiax® software. The significance level of p-value was considered < 0.05, and all analyses were performed using SPSS v.23.

Results

In this study, 5232 people were studied, 2693(51.4%) were men and 2542 (48.6%) were women with a mean age of 52.32±6.82 years in total. The highest frequency in FRS groups was 4061(77.6%) subjects in the very low-risk while 157(3.0%) subjects were in the high-risk group. All the means of the ECG parameters, including heart rate, P duration and amplitude, PR interval, QRS duration, RV5 amplitude, SV1 amplitude, QTc interval, P, and QRS axis, were significantly different between the FRS groups(P<0.05). After multivariable adjusting, P duration, PR interval, QRS duration, and SV1 amplitude were in significant positive linear relationships with the FRS(P<0.001). Moreover, heart rate, P amplitude, PR interval, RV5 amplitude, and P and QRS axes were in quadratic relationships with the FRS(P<0.001).

Conclusion

In conclusion, all ECG parameters were independently associated with the FRS, either linear or quadratic, except QTc interval. This study also determines the importance of the associations of each ECG parameter in increasing the FRS of subjects. These findings suggested that ECG parameters may be used in early monitoring and prediction of CVD in more extended periods as well as the FRS.

Lipid signature of sleep quality and its relationship with cardiovascular risk in US adults

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Introduction

One of the leading causes of premature death and morbidity worldwide is atherosclerotic cardiovascular disease. Its pathogenesis is multifactorial and strongly associated with unhealthy lifestyles. Evidence suggests sleep quality could have important cardiometabolic effects; however, its impact on the circulating lipid profile –and how it contributes to cardiovascular risk [CVR]– is unknown. We propose to use artificial intelligence to identify the circulating lipidomic profile associated with sleep quality, and its relationship with estimated CVR (ACC/AHA ASCVD).

Materials & Methods

Clinical data, complete lipidomics (1040 serum lipids), and sleep quality assessment (Pittsburgh Index [PSQI]) of 2072 individuals from a large study of middle-aged US adults were used.

A novel PSQI–associated lipid signature [LS] was constructed using Elastic Net regression, prior inverse-rank-normalization. The association between LS and PSQI was evaluated by Pearson's r. The effect of LS on CVR was assessed using multiple linear regression and mediation analysis (considering LS as a mediator of the PSQIɣCVR relationship), adjusting for sociodemographic, metabolic, and behavioral covariates. Finally, lipid pathway enrichment analysis [LIPEA] was implemented to interpret the involvement of the selected lipids in biological systems.

The analyses were performed in R software (v.4.0.1).

Results

A LS highly-correlated to PSQI was identified [r (95% CI) = 0.36 (0.32–0.39); $p=10ɣ^{58}$], comprising 48 different lipid species (mainly glycerolipids, free fatty acids, phosphatidylethanolamines, phosphatidylinositols and sphingomyelins). Correlation and mediation analyses showed that LS was positively associated with CVR [β±SE=0.16±0.02; $p=10ɣ^{19}$], and that it could mediate the relationship between PSQI and CVR [mediated effect = 50%, p<0.001]. According to LIPEA, enriched biological processes include endocrine signaling, energetic metabolism, neuronal synapse, cellular proliferation, circadian entrainment and immune response.

Conclusion

This study allowed us to identify a lipid pattern associated with poor sleep quality in US adults. Interestingly, this lipid profile appeared to partially mediate the relationship between poor sleep quality and higher CVR. These lipids participate in relevant biologic systems, such as neuroendocrine signaling, circadian patterns, energy use and immunoinflammatory status.

These findings contribute to validate the influence of sleep quality on the human lipidome and demonstrate the importance of considering it in cardiovascular disease prevention.

Oncology II

Presenters:
Liu, TD (TingDang) Mr
de Groot, T.M. (Tom) BSc
Onjanson, P. (Phongsathorn)
Rodríguez Solano, K.M. (Karla Monserrat)
Gavrilov, Z.G. (Zoran)
Gotowiec, M.G (Mateusz)

The Expression and potential utilities of CAR-NK antigen CD22 in esophageal squamous cell carcinoma

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Introduction

Background: Chimeric antigen receptor NK (CAR-NK) cell therapy, one the most promising and established engineered immune-cell immunotherapy, specifically combined with membrane antigens on cancer cells and has shown a significant therapeutic effect in the treatment of hematologic and solid malignancies. We aimed to identify an available CAR-NK-associated antigen, CD22, in ESCC and verify the potential utilities of engineered CD22-targeted CAR NK cells against ESCC.

Materials & Methods

Methods: We performed bioinformatic analysis of the RNA-seq data of one normal esophagus and 81 ESCC tissues downloaded from The Cancer Genome Atlas (TCGA) website to examine the significantly different gene expression in ESCC and determined the expression values of the 13 target genes (clinically used CAR-T-associated antigens). The expression of CD22 were determined in ESCC by using qRT-PCR, immunofluorescence (IF) staining, and immunohistochemistry (IHC) staining in ESCC cell lines (KYSE-140 and KYSE-150) and 87 cases of human ESCC samples, respectively. The correlation between experimental results and clinical data was analyzed. Furthermore, the efficacy of engineered CD22-targeted CAR-NK cells against the two ESCC cell lines was verified.

Results

Results: (1) Among the 13 target genes, CD22 were identified specifically expressing in 81 ESCC tissues of TCGA, which was further verified in ESCC cell lines (KYSE-140 and KYSE-150). (2) The IHC results showed that the positive rate of CD22 in ESCC was 80.46% (70/87), and the percentage of cell membrane-expressing CD22 was 27.59% (24/87). (3) The CD22 expression had not shown statistically significant correlation with survival, tumor tissue invasion and lymph node metastasis in ESCC. (4) Engineered CD22-targeted CAR-NK cells exhibited significant growth inhibition capability against the two ESCC cell lines.

Conclusion

Conclusion: CD22 is a novel potential target for CAR-NK therapy in ESCC and Engineered CD22-targeted CAR-NK cells can efficiently inhibited ESCC growth.

Can the SORG Machine Learning Algorithm Predict 90-Day and 1-Year Survival in Patients Suffering from Extremity Metastatic Disease? External Validation in a European Cohort

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Introduction

Accurate survival prediction of patients with long-bone metastases is challenging, but important for optimizing surgical treatment: patients may not benefit from surgery if their life expectancy is less than 90 days, while prosthetic surgery aims to preserve mobility for many years, and intramedullary nailing provides limited durability but faster recovery for patient with life expectancy up to one year.

The Skeletal Oncology Research Group (SORG) machine learning algorithm (MLA) has been previously developed and internally validated to predict 90-day and 1-year survival. External validation showed promise in the United States and Taiwan. To ensure global generalizability, the algorithm remains to be validated in Europe. The purpose of this study was to determine if the SORG ML algorithm accurately predicts 90-day and 1-year survival in a metastatic long-bone disease patient cohort from Groningen, the Netherlands.

Materials & Methods

One-hundred seventy-four patients undergoing surgery for long-bone metastases between 2000-2020 were included at a tertiary referral Orthopaedic Oncology Center in the Netherlands. The median age was 63 years (interquartile range [IQR] 57-70) and 53% (92/174) were female. The most common primary tumors were breast (26%) and lung (21%). Model performance measures included discrimination, calibration, overall performance, and decision curve analysis.

Results

The SORG-MLA retained good discriminative ability, showing an area under the curve of 0.75 for 90-day survival and 0.78 for 1-year survival. However, the calibration analysis demonstrated underestimation of European patients' 90-day survival (calibration intercept -0.54, slope 0.60). For 1-year survival (calibration intercept 0.75, slope 1.22) this was not the case. The Brier score predictions were lower than their respective null model (0.13 versus 0.16 for 90-day; 0.20 versus 0.25 for 1-year), suggesting good overall performance of the SORG-MLA for both timepoints.

Conclusion

The SORG-MLA demonstrated good performance in predicting survival of patients with extremity metastatic disease, thereby providing generalizability to a European population. The SORG model can be accessed freely at https://sorg-apps.shinyapps.io/extremitymetssurvival/

The Added Value of Red Blood Cell Distribution Width for Colorectal Cancer Screening in Primary Care Setting

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Introduction

The incidence of colorectal cancer in Thailand remains high and has increased from 2002-2020. An effective screening on at-risk individuals is indispensable in primary care. Our routine screening determinants include family history, signs and symptoms and fecal occult blood test (FOBT). However, some cases were missed by using these set of determinants. Previous research has shown that red blood cell distribution width (RDW) which indicates the heterogeneity in the size of circulating red blood cells may be used in screening, but results were still controversial. Our study aims to examine an added value of RDW in our colorectal cancer screening.

Materials & Methods

A screening added-values research was conducted in Phrae Hospital, Thailand from January 2018 to December 2020. Data collection was analogous to case-control design. We included 1,059 patients in primary care settings who had been received colonoscopy. Patients were divided into two groups: (i) those diagnosed with colorectal cancer by physicians (n=165), and (ii) those without (n=894). Data on patient's profiles such as age, gender, smoking, family history, bowel habit change, weight loss, FOBT, and RDW were collected from electronic medical records. We performed multivariable logistic regression analysis to compare area under ROC (AuROC) between two models: (i) with routine screening determinants, and (ii) with routine screening determinants plus RDW values. Since missings were >15% in some variables, we additionally performed multiple imputation using MICE (Multivariate Imputation by Chained Equations) to compare the results between imputed and unimputed data.

Results

Age, gender, smoking status, family history of cancer, the presence of bowel habit change, weight loss are significantly different between patients with and without colorectal cancer. In univariable analysis, these screening determinants have sensitivity ranged 55%-60% and specificity ranged 60%-90%. The multivariable model that includes these routine screening determinants has AuROC 0.79 (95%CI: 0.67-0.89), whereas the model that additionally includes RDW has AuROC 0.81 (95%CI: 0.69-0.90). The results from imputed dataset are identical.

Conclusion

RDW may be useful in colorectal cancer screening. Although showing a slight increase in discriminative ability from routine screening, the indicator still provides essential information of blood components from routine laboratory check-up.

Implication of duration of time to diagnosis in survival of children with central nervous system tumors: systematic review and meta-analysis.

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Introduction

Central nervous system (CNS) tumors are the most common pediatric solid tumors and the second leading cause of cancer death in children. A lot of factors has been related with a worse survival one of these is a prolonged time to diagnosis (TtD), defined as the period of time between onset of symptoms and the diagnosis. TtD and survival seem to have no statistically significant relation or may even have an inverse relation: extended TtD associated with better outcome or increased survival, due to this controversy we want to know how TtD affects survival in paediatric patients with CNS tumors.

Materials & Methods

A systematic search was carried out in multiple databases using the keywords: "CNS tumors", "Lag-time", "Survival", "Delayed diagnosis" and its synonyms additionally filters by age (<18 years) and publication date (1998-2021). The localized articles were reviewed by two researchers independently, and by consensus were selected those that would be included in the study, applying the inclusion and exclusion criteria.

Results

A total of 758 articles were located through the search, of which 718 were eliminated after reading the titles and abstracts and duplicates, 40 articles were reviewed in extensive from which 11 were chosen for qualitative analysis and 6 for meta-analysis. In the qualitative analysis in seven of the 11 articles no relationship was found between prolonged TtD and worse survival, in the remaining 4 there was lower survival in short TtD. In the meta-analysis with cut-off point at 1 and 2 months, no difference was found between the duration greater or less than the cut-off point and survival [RR 0.95 (95% CI 0.75-1.2) and RR 1.23 (95% CI 0.77-1.97) respectively].

Conclusion

The duration of TtD in patients younger than 18 years with CNS tumors does not appear to modify 5-year survival. Survival seems to depend more on the site and extent of tumour aggressiveness. High malignant tumours appear to give serious symptoms earlier.

Therefore, we can say that while Lag-time does not appear to be related to the prognosis of survival, it is unquestionable to transmit the prompt start of treatment of these children.

Next-generation sequencing and liquid biopsy in the monitoring of solid tumor patients

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Introduction

Cancer is one of the leading causes of death worldwide and has a significant impact on public health. Therefore, research is focused on improving early detection, clarifying the key biological mechanisms, identifying potential therapeutic targets, precise treatment and monitoring of cancer patients. Research in these areas has been encouraged and intensified by the emergence of massive parallel sequencing which has great application and importance in the design of precise and personalized treatment. Tissue biopsy is the most widely used method for detection, stage and prognosis, but it has a plenty of limitations and disadvantages. Tumor-specific mutations in ctDNA may represent a new type of cancer biomarker and may help for early diagnosis. The aim of the research is to prove the benefits and the potential of NGS together with liquid biopsy in the monitoring of solid tumor patients in order to expose patients to less invasive analysis which at the same time is a powerful and effective tool for monitoring, precise and personalized treatment, determination of resistance to therapy, detection of relapse of the disease etc.

Materials & Methods

Circulated tumor DNA was isolated from the whole blood of 3 patients: patient with colorectal cancer, patient with melanoma and patient with lung cancer using the MagCore® Circulating DNA Large Volume Kit and MagCore® Super extractor. Sequencing was performed on the Miniseq platform using the TruSight® Tumor 15 Kit. This kit provides comprehensive analysis of 15 genes that are most commonly mutated in solid tumors. The analysis of the results was performed using VariantStudio Software and visualization with Integrative Genomics Viewer.

Results

Significant mutations in the patient with colorectal cancer: PIK3CA(c.1624G>A/Glu542Lys), KRAS (c.35C>T/Gly12Asp) and TP53(c.742G>A/Arg248Trp). No significant mutations were detected in the patient with melanoma. Significant mutations in the patient with lung cancer: EGFR(c.2573T>G/Leu858Arg), PIK3CA(c.1624G>A/Glu542Lys) and TP53(c.833G>A/Pro278Leu).

Conclusion

NGS and liquid biopsy based approach is a relatively safe and non-invasive method for monitoring of solid tumor patients. Molecular profiling of tumors with NGS using ctDNA can help to make precise and personalized treatment decisions, monitor treatment response, detect resistance to therapy and relapse of disease.

Comparison of cytotoxic effect of soluble and transmembrane TNF-related apoptosis-inducing ligand (TRAIL) in a rat model of adipose-derived stem cells (rADSC).

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Introduction

Rat TRAIL is a cytokine consisting of 291 amino acids with anticancer potency due to its selective binding ability through p-53 dependent death receptors: TRAIL-R1 and TRAIL-R2 triggering apoptosis. In healthy cells, the pathway is blocked by decoy receptors (DcR1 and DcR2), while many cancer cells lack such receptors, making TRAIL a perfect target of oncologic therapies. However, being primarily transmembrane protein (tTRAIL), its antitumour qualities are limited to juxtacrine signalling. The production of a soluble cytokine (sTRAIL) based on the conserved domain (158-291aa) in rADSC may limit the tumour growth after implanting sTRAIL-expressing rADSC in its vicinity or in a surgical flap.

Materials & Methods

TRAIL cDNA was derived from the kidney of the Sprague-Dawley rat. For constant expression of proteins, two lentiviruses were constructed according to manufacturer guidelines (Takara). Target sequences (tTRAIL containing 876bp and sTRAIL containing 405bp of sole receptor sequence) were inserted in pLvx-IRES-EF1a-PURO plasmid via homologous sequence recombinational cloning (InFusion HD, Takara). HEK293T cells were used for lentivirus assembly. rADSC cells were infected with infection unit = 20. Target gene expression was quantified with qPCR. The protein yield was measured through ELISA and Western Blot techniques. The cytotoxicity assay of supernatants of both sTRAIL and tTRAIL was tested on rat mammary gland adenocarcinoma cell line (RBA).

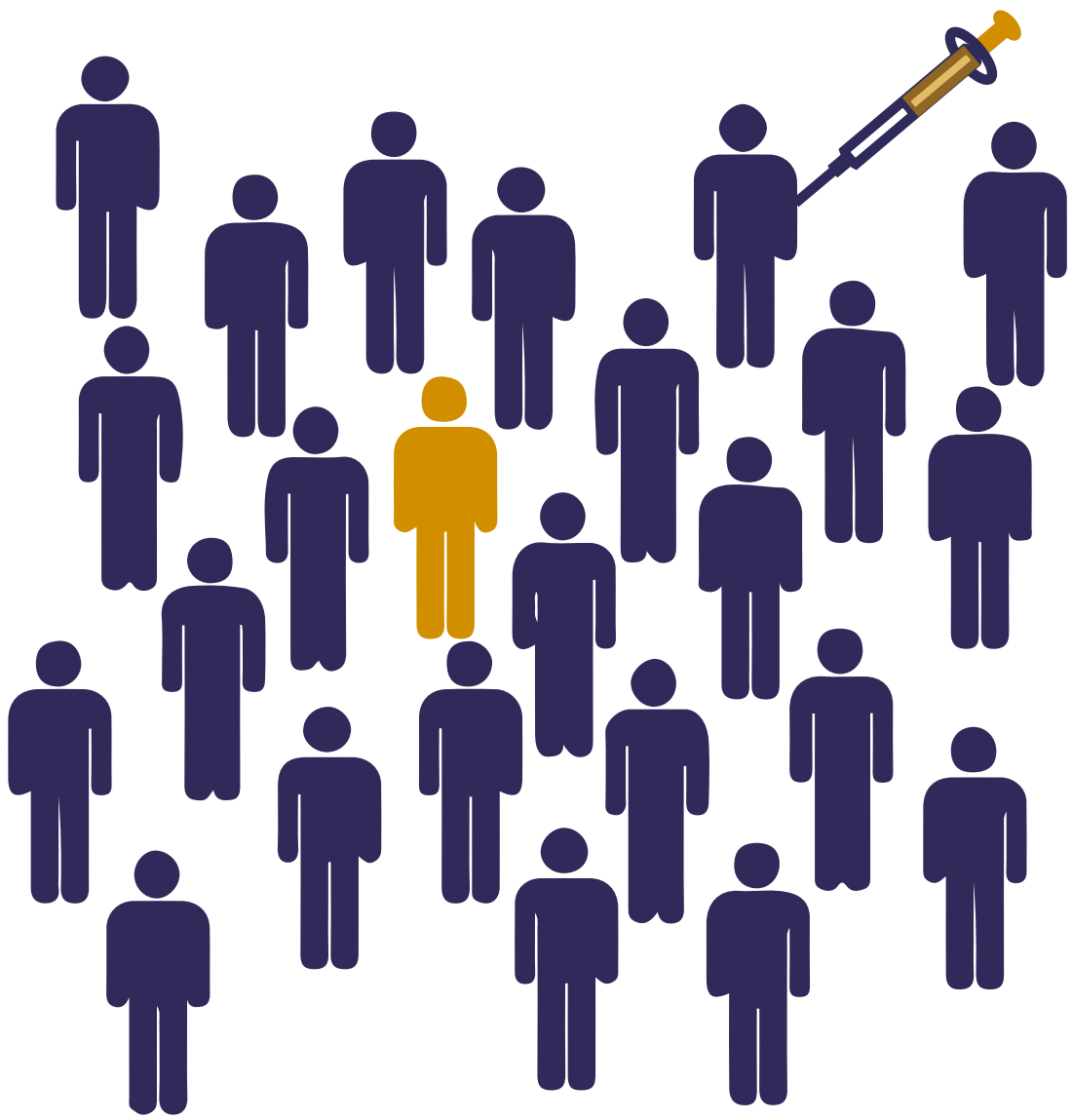
Results

Preliminary results show that a higher concentration of sTRAIL (compared to tTRAIL) is found in rADSC supernatant. Cytotoxicity results show superior efficiency of a supernatant containing sTRAIL in decreasing RBA cells viability.

Conclusion

Although higher sTRAIL concentration was found in cells' supernatant, tTRAIL can still induce a cytotoxic effect in RBA cells. Thus, tTRAIL does not solely act as a transmembrane protein but is also secreted to the surrounding. The cytotoxic activity of tTRAIL/sTRAIL-transduced rADSC towards cancer cells indicates that placing such cells in the vicinity of cancer tissue may limit its growth. Further animal studies are required to establish whether such therapies are viable.

Public Health



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Knowledge Of Chikungunya Disease Among Academic Population In Private Universities, Khartoum State, Sudan - 2019

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Introduction

Chikungunya is a viral disease that could lead to chronic symptoms with no available treatment. Therefore a good understanding and knowledge about all the aspects of the disease are essential to prevent it from spreading. The purpose of this study is to assess the level of knowledge about Chikungunya disease following an outbreak in Kassala Sudan.

Materials & Methods

A cross-sectional study was carried out in three private universities in Khartoum State during April-August 2019. A sample of 376 individuals (346 medical students and 30 teaching staff) was determined. A self-administered questionnaire was distributed to the target population. It included eleven variables about the information regarding Chikungunya disease. Data was imported into SPSS program version 20 and descriptive statistics were presented. Knowledge variables were categorized into scores as adequate, moderate and poor.

Results

Out of 376 study population, 66 (17.6%) had never heard about the Chikungunya disease. Therefore, the knowledge variables were analyzed among 310 individuals who heard about the disease. Out of 310 individuals, 235 (75.8) knew the disease is viral. However, participants who did not know the mode of transmission, diagnostic methods of the disease and management methods accounted for 200 (64.5%), 228 (73.5%) and 174 (56.1%) respectively. More than half did not know the preventive method or if a vaccine is available or not. Moderate to poor knowledge were significantly high among the study population, p value = 0.0002.

Conclusion

Most of the study population heard about the Chikungunya disease but the majority had moderate to poor knowledge about the disease. Medical faculties should open channels with Ministries of Health to facilitate field training of the medical students during outbreaks and control of communicable diseases. Raising conferences and social media about Chikungunya disease is recommended. Clinical manifestations of the Chikungunya virus share similarities with other viral infections, where expensive tests are required for accurate diagnosis. Therefore, spreading awareness is essential in preventing future outbreaks.

Impact of neurocognitive and behavioral disorders on cardiac transcatheter intervention procedures outcome: retrospective cohort study

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Introduction

Strong preoperative evaluation and risk assessment have usually centered on optimizing physical health. However, mental patients' state is given a secondary significance in this process nowadays, while optimization of such kind of aspect may play a significant role in patients postprocedural recovery and improve their short- same as long-term outcomes after cardiac intervention in particular.

Materials & Methods

Patients who underwent TAVI and Mitraclip setting in University Clinical Hospital of Valladolid from 2009 to 2018 were analyzed. They were defined on 2 groups – with or without mental or behavioral disorder. Preoperative and long-term outcomes were compared between both groups. Patients were classified as having mental illness using ICD11. SPSS were used for statistical analysis.

Results

Among 295 patients who met inclusion criteria, 46 (n = 15,6%) individuals had a prior diagnosis of mental disorder. 54,3% had neurocognitive diseases (24% of which were consisting of the diagnosis of Alzheimer's disease). Remaining 45,7% had behavioral and mood disorders with majority of patients with depression (66,7%), while others with anxiety (19%), adaptive disorder (9,5%) and bipolar disorder (4,8%). Patients who did and did not have mental illness were comparable in terms of age and comorbidities. Average age of all patients was 80,3 y.o. and 58,6% were males. Patients with preoperative mental illness had a higher chance of procedural complications (49% main group; 31,9% control, p<0.05). History of depression or other mental/cognitive illness was also associated with higher odds of 1 year (43.5% vs 25.8%, p<0.05) and 2 years readmission (34.8% vs 25%, p<0.05).

Conclusion

4 from 25 cardiac intervention patients had a preexisting mental illness diagnosis, which was associated with worse postoperative outcomes and higher risk of complications. This means that mental illnesses should be paid strong attention during the whole period of cardiac intervention in patients. Furthermore, mental and behavioral disorders may be a significant marker for postprocedural and long-term outcome after the cardiac intervention procedure while improved knowledge and management of such predictors would be expected to increase patient care efficiency and their quality of life.

Comparison of Wrist and Forehead Temperature Measurements as Screening methods during the COVID-19 Pandemic

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Introduction

Temperature screening checkpoints have become prevalent in all public places during the COVID-19 pandemic. Contactless screening methods have been adopted for the early detection and isolation of febrile patients. The tympanic method closely resembles the body core temperature, however, they are not in use due to the disposal charges. The wrist temperature is considered to be stable, as the wrist area is often covered by clothing and the forehead temperature is under the influence of environmental conditions. This study aims to compare the efficacy of wrist and forehead temperature methods with the standard tympanic temperature.

Materials & Methods

This study was conducted in a tertiary care hospital in Perundurai,Tamilnadu. All the visitors who presented to the outpatient department between 6th April-13th May 2020 were included in the study. The exclusion criteria were those with ear discharge or tympanic membrane perforation. All the participants were made to wait for 10 minutes in the waiting hall to ensure temperature-controlled settings. We consecutively collected wrist, forehead, and tympanic temperature readings of all participants using infrared thermometers. Fever was defined as a temperature above 37.5°C. The data was analyzed using the Bland-Altmann plot in MS Excel 2016.

Results

A total of 514 participants were enrolled in the study. The mean temperature for each of the method was calculated (Tympanic temperature: 36.16 ± 0.53; Forehead temperature: 36.19 ± 0.49; Wrist temperature: 36.10 ± 0.62). The mean difference ranged from 2.10 to -2.00 for the forehead measurements and 2.00 to -2.00 for wrist measurements. The agreements for each method with tympanic temperature were calculated (Forehead temperature: 1.23 to -1.17; Wrist temperature: 1.23 to -1.13).

Conclusion

The study concluded that the wrist temperature was more stable than the forehead temperature. However, these methods did not provide any diagnostic cut-off value. Furthermore, the asymptomatic nature of some COVID-19 cases reduced the sensitivity of these tests. Further studies are advised to explore the validity of wrist temperature.

Prevalence and determinants of goiter among children of South Kordofan State, Sudan, 2021: A Need for Action

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Introduction

Iodine deficiency disorders (IDD) threaten 30% of the world's population in 118 countries. Three decades have passed since the adoption of universal salt iodization (USI) in Sudan. South Kordofan has suffered a burdensome war and low socioeconomic status, increasing its susceptibility to nutritional deficiencies. We aimed to determine the total goiter rate (TGR) and its associated factors among children of South Kordofan as an indicator of IDD.

Materials & Methods

We conducted a cross-sectional study among 20 villages of South Kordofan during a medical mission in August 2021. We recruited the 575 school-age children (6 to 12 years) who attended the medical days. Palpation of the thyroid was performed and classified according to the World Health Organization recommendations. We used a semi-structured interviewer-administered questionnaire to assess caregivers' sociodemographic status, knowledge, attitude, and utilization of iodized salt besides children's goitrogens consumption. We used logistic regression to determine the factors associated with goiter.

Results

The TGR among children of South Kordofan was 42.8% (grade 1: 15.7%, grade 2: 27.1%). Only 24.2% of caregivers confirmed using iodized salt. Goiter was significantly associated with mother's work (AOR = 2.984, CI 95% 1.320- 6.747, p= 0.009), iodized salt utilization (AOR = 0.501 , CI 95% = 0.303- 0.830, p=0.007), Darfurian (AOR = 24. 392 , CI 95% 2.794 - 212.979, p=0.004) and African (AOR = 0.483, CI 95% 0.236-0.989, p= 0.046) tribe.

In univariate analysis, we didn't find a significant association between goiter and these factors: child's gender (p=0.11), residence (p =0.3), father's work (p= 0.18), father's education (p=0.18), mother's education (0.065), water source (0.2) and consumption of some goitrogens (p =0.2 and higher).

Conclusion

TGR in South Kordofan state indicates severe iodine deficiency at the population level. Iodized salt consumption is protective. Mother's work rather than father's work was associated with goiter. Parents' educational level and knowledge about iodized salt weren't significantly associated with goiter. Interestingly, local goitrogens consumption didn't increase goiter risk significantly. Mandatory legislation of salt iodization should be enforced by law to make progress.

Determinants of dysmenorrhea among female adolescents; results from a community-based cohort study in Amsterdam.

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Introduction

Dysmenorrhea is menstruation-associated pain, characterized by cramping and lower abdominal pain and/or back pain. This pain results from an elevated concentration of prostaglandins which induces a severe contraction of the uterine muscle. In addition to that, various systematic symptoms appear, which interferes with daily activities of adolescents, leading to problems on social, mental and academic level and a reduced quality of life. Dysmenorrhea is the most prevalent menstrual disorder in adolescents. However, prospective research on possible determinants of dysmenorrhea before and in adolescence is limited. This study investigated the association of potential determinants of dysmenorrhea at age 15/16 using a clustered approach in a population-based prospective birth cohort in Amsterdam.

Materials & Methods

A longitudinal study on 1038 female adolescents at the age of 15/16 from the ABCD-study was conducted. Dysmenorrhea (yes/no) was defined based on the presence of menstrual pain in combination with the intake of medication and/or oral conception. Possible determinants were assessed using self-report at age 11/12 or reported by their mothers and categorized into four clusters: sociodemographic, psychosocial, lifestyle/health-related and obstetrical. Due to the absence of linearity, gynecological age (years since menarche) was divided in quartiles (Q) (Q1: 0.08-2.24, Q2: 2.24-3.10, Q3: 3.10-3.91, Q4: 3.91-8.30). The association between potential determinants and dysmenorrhea was analyzed using multivariable logistic regression. Analyses were performed using IBM SPSS Statistics version 27.

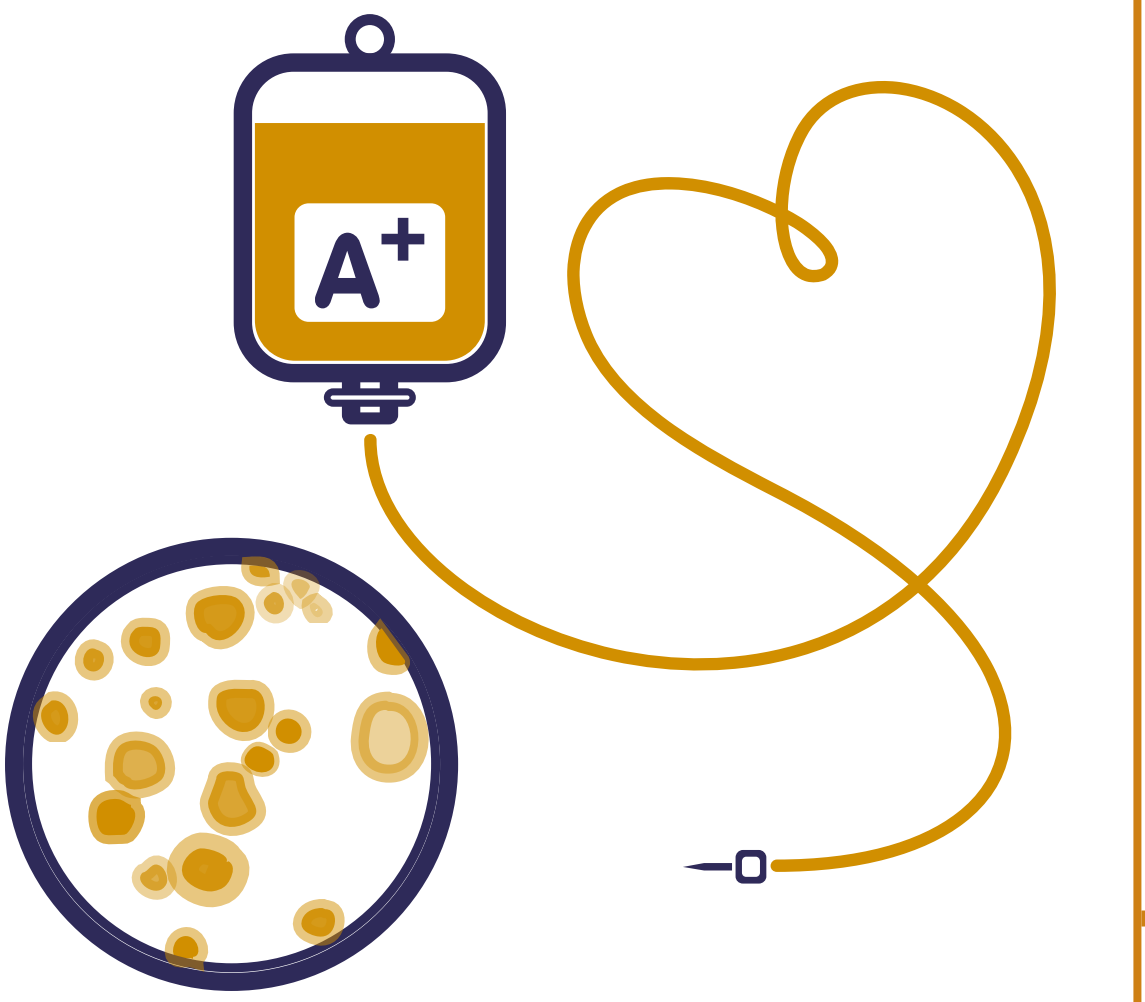
Results

The prevalence of dysmenorrhea was 49.5%. The intake of ≥14 cups of caffeine in a week (Adjusted Odds Ratio (AOR) 1.42, 95%Confidence Interval(CI) 1.01-1.98, p=0.043), the intake of 3-4.5 sugar sweetened beverages a day (AOR 1.45, 95%CI 1.05-2.00, p=0.025) and higher gynecological age (Q2: AOR 2.07, 95%CI 1.44-2.97, Q3: AOR 2.82, 95%CI 1.96-4.08, Q4: AOR 2.94, 95%CI 2.03-4.26, p<0.001) were the only lifestyle factors significantly associated with dysmenorrhea in the final model. None of the sociodemographic, psychosocial and obstetrical factors were significant.

Conclusion

Dysmenorrhea is frequently experienced by adolescents. Determinants of dysmenorrhea are a higher gynecological age, caffeine and the intake of sugar sweetened beverages. More awareness and research on dysmenorrhea is needed to develop guidelines and to provide appropriate care for adolescents with dysmenorrhea.

Medical Microbiology



Presenters:

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Associated Risk of Blastocystis Infection in Colorectal Cancer

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Introduction

Blastocystis species is an anaerobic intestinal protozoan seen in humans and a wide range of animals. Only nine Blastocystis subtypes are seen in humans. The pathogenicity of Blastocystis sp. has long been controversial. Recently, a subtype-dependent association between Blastocystis sp. and colorectal cancer (CRC) is being debated. Thus, this ongoing study aims to assess the possible association between Blastocystis sp. infection, and CRC condition compared to cancer outside the gastrointestinal tract (COGT) and a cancer-free group.

Materials & Methods

Participants are divided into two groups; Cancer patients and Cancer-free participants. The Cancer group is further sub-grouped into CRC and COGT groups. Written consents for fresh stool sample collection are given by all participants. Formalin-Ethyl Acetate concentration technique and a permanent stain (Wheatley Trichrome) are used to identify any present intestinal parasites in stool samples. Furthermore, Molecular and phylogenetic analyses are conducted to identify Blastocystis sp. and its sub-types. Statistical analysis is done using excel and SPSS.

Results

Till January 2022, we collected 127 samples, of which 45 are from cancer patients and 82 from cancer-free participants. Of the 45 cancer patients' samples, 17 are from CRC patients, while the remaining (n=27) are from patients with COGT. A sample is considered positive via microscopy and/or PCR. The prevalence of Blastocystis was significantly higher among cancer patients (n=16, 35.6%, p=0.046) compared to cancer-free participants (n=16, 19.5%). Furthermore, this study revealed that the prevalence of Blastocystis sp. is significant in CRC patients (n=11, 64.7%, p<0.001) to the cancer-free group. Contrarily, Blastocystis sp. prevalence in COGT patients was insignificant compared to the cancer-free group (n=5, 18.5%, p=1.00). Subtype 2 is the most common subtype in the cancer group (n=3), while subtype 3 is the most common in the cancer-free group (n=9).

Conclusion

The highest Blastocystis sp. prevalence was among CRC patients compared to cancer-free and COGT groups.

IDENTIFICATION OF STAPHYLOCOCCI CONTAMINATING CLINICAL WHITE COATS OF 4TH YEAR MEDICAL STUDENTS

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Introduction

Clinical white coats worn by the medical students can be contaminated during their clinical training sessions at the hospital and can be a potential mode for transmission of pathogens including antibiotic-resistant microorganisms. Methicillin-Resistant Staphylococcus aureus (MRSA) and Extended-Spectrum Beta-Lactamase (ESBL) producing coliforms are common two types of antibiotic-resistant bacteria that can be transmitted among themselves (medical students) and between patients by means of contaminated clinical white coats. The spread of these antibiotic-resistant bacteria can bring about serious infections in patients.

Objectives: The purpose of the study is to calculate the prevalence and associated factors of contamination of white coats of medical students with MRSA and ESBL.

Materials & Methods

Cross-sectional study was done with the participation of medical students of the Faculty of Medicine, University of Peradeniya in September 2020. Swabs from sleeves and pockets of the clinical white coats were taken and routine microbiological methods were used to identify the colonization prevalence of Staphylococcus aureus, Enterobacterales. Cefeotoxin is used to test antibiotic susceptibility for MRSA. ESBL screening test used to identify ESBL producing coliforms.

Results

Out of 151 participants, 53 (35.1%) were positive for Staphylococcus aureus, and 12 (7.9%) were positive for Enterobacterales colonization. 15 (9.9%) and 4 (2.6%) were positive for MRSA and ESBL colonization respectively.

Conclusion

There is a considerably high level of prevalence of bacterial contamination of clinical white coats of medical students. As white coats can be a potential source of cross-infection suppose that restriction on the use of white coats from non-clinical areas and to practice a lot of personal hygienic methods and infection control methods in relation to the use of clinical white coats by medical persons.

Genetic improvement of parasporins obtained from PS2Aa1: an approach to colorectal cancer and leukemia treatment

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Introduction

Parasporin 2Aa1(PS2Aa1), is an anticancer protein from Bacillus thuringiensis (Bt), which has shown great selectivity towards different human cancer cell lines, especially colorectal cancer and leukemia. To improve this anticancer activity, we aimed to genetically modify native PS2Aa1 by changing amino acids in the receptor-binding domain, subsequently; we determine key steps in the mechanism of action triggered in treated cancer cells

Materials & Methods

Four critical regions of interaction between PS2Aa1 with h-APN were addressed by molecular docking. Afterward, by site-direct mutagenesis, 4 mutants libraries were generated in which the second nucleotide of each codon triplet encoding these 4 critical amino acids was randomly changed so that mutated strains were generated with random substitutions in each of these amino acids. The mutants were evaluated in vitro by cytotoxicity assays, using its protein extract toward colon cancer cell lines SW480, SW620, and Caco-2 and in leukemia cell lines Jurkat and Molt-4. Subsequently, the activity of caspase 9 and 3, and phosphatidylserine exposure were measured.

Results

By the substitution of 4 critical amino acids in PS2Aa1 to the union with h-APN (GLY254, PRO255, GLY256, and GLY257), 4 mutant libraries were generated through site-direct mutagenesis. Those libraries including PS2Aa1 were sifted, selecting the 2 most cytotoxic variants against cancer cells SW-480, SW-620,caco-2 Jurkat and Molt-4, the mutant 3-35 with an IC50 of 0.966, 1.158, 0.88, 1.94, and 1.07 ug/ml respectively, and the mutant N65 with an IC50 of 0.8488, 1.284, 0.51, 0.73 and 0.6 ug/ml respectively. These two mutants as the PS2Aa1 exert their anticancer activity causing an increase of caspase 9 and 3 activation and the levels of Annexin V positive cells.

Conclusion

Site-direct mutagenesis through a computational approach is a valuable methodology to obtain PS2Aa1 variants with improved anticancer activity. In addition, those enhanced variants of PS2Aa1, 3-35, and N65 seem to generate its cytotoxic activity by the intrinsic way of apoptosis, like the native protein.

Development of a Comprehensive Deep Learning Neural Network Algorithm for Analysis of Gram-Stained Sputum Smears for Adequacy: An Aid for Developing Countries

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Introduction

Sputum is a common laboratory specimen which aids in diagnosing respiratory diseases including Pulmonary Tuberculosis (TB). Gram stain is an easy, cost-effective stain which may be applied to sputum smears to screen out an unsatisfactory sample by applying Bartlett's Criteria (1979), which determines adequacy, or freedom from contamination, of a sputum sample. Lack of trained microbiologists, and a high burden of lower respiratory tract infections, compels a need for developing fast, and accurate methods for screening of slides to be sent for bacteriological cultures.

Therefore, we propose a Faster- Region Based Convolutional Neural Network (F-RCNN) based algorithm to verify our hypothesis, that an Artificial Intelligence (AI) algorithm can automate the process of determining the adequacy of Gram stained sputum smears using Bartlett's criteria, reducing time and human error.

Materials & Methods

The developmental pilot study was carried out by training a F-RCNN based algorithm on 100 Gram Stained Sputum Smear Slides with equal number of adequate and inadequate sputum smears, by using Tensorflow 2 object detection methods on faster_rcnn_resnet50_v1_640x640 pre-trained models. Algorithm was evaluated on Tensorboard. Following evaluation and feedback corrections, the algorithm was then tested on 100 Gram Stained Sputum Smear Slides to determine adequacy as compared to the manual method. Analysis of cell counts, and binary adequacy validation by a cross - classification table was performed.

Results

In 100 Gram Stained Sputum Smear Slides, cell counts matched 76% for Squamous Epithelial Cells, and 91% for Neutrophils. As compared to the manual method, our algorithm reported a Sensitivity of 90.56%, a specificity of 78.72%, and an overall accuracy of 85% in determining whether a slide is adequate or not.

Conclusion

The F-RCNN based algorithm was successful in establishing an approach for detection of Squamous Epithelial Cells and Neutrophils in Gram Stained Sputum Smears, and thus determining their adequacy by Bartlett's Criteria. Therefore, following refinement of the Algorithm, it will be beneficial in the global fight against Tuberculosis, since it finds application in remote and resource limited settings with high burdens of Tuberculosis, like the developing world, where trained microbiologists may not be easily available and, a large volume of screening of slides is mandatory.

Antioxidant Awareness in the Future: The Toxic Effect of Standardized Mangosteen Pericarp Ethanolic Extract on Zebrafish Embryo

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Introduction

The xanthone phytoceuticals/antioxidants in Garcinia mangostana (Mangosteen) are thought to be the most beneficial. It is widely accepted in Indonesia that Garcinia mangostana is the king of the antioxidants, but we already know that every effective drug has a limit on use and a toxicity level. The animal model's mortality and morbidity mechanisms were blamed on another phytoceutical component called mangostin, which was found to have a harmful effect. It has been reported to cause metabolic problems, hemolysis, lymphocytosis and decreased liver and kidney mass if used in excess. Mangosteen pericarp ethanolic extract is being tested on zebrafish eggs to determine its acute toxicity, as measured by mortality, fatal concentration, and teratogenic impact.

Materials & Methods

To conduct the experiment, researchers employed zebrafish embryos housed in 6-well plates. Each plate contained 30 embryos divided into 4 equal groups, with one group receiving physiological embryonic medium and the other three receiving standardized ethanolic extracts of mangosteen pericarp (1250, 1000, 750 g/mL). The experiment was repeated three times. Because the zebrafish (Danio rerio) is 70% human, it is employed for toxicity testing of natural compounds. On 2 hpf, the extract was supplied (hour post-fertilization).

Results

Mangosteen pericarp ethanolic extract at a concentration of 1250 g/mL resulted in a 100% mortality rate at 24 hpf in three separate experiments. First, second, and third repeat death rates are 71%, 70%, and 63%, respectively, at 1000 g/mL concentration. The mortality rates for the first, second, and third repetitions at 750 g/mL concentration are 13%, 33%, and 23%, respectively. The LC50 of mangosteen pericarp ethanolic extract was found to be 716,651 g/mL utilizing the SPSS Ver.22 tool for Probit Analysis. In the 72-hpf observation, defects were discovered with a 750 g/mL concentration of pericardium pigment at the 750-g/mL concentration in the form of a curved-shape body, damaged or expanded pericardium, and undetected heart rate.

Conclusion

We should know that antioxidant agent provided by mangosteen pericarp ethanolic extract should have toxicity effect that should be under consideration of physician or researcher in the future.

The transcriptomic analysis shows that Vitamin D3 induces decreased pro-inflammatory response and enhances IFNβ1-dependent antiviral response in Dengue virus-infected macrophages.

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Introduction

Dengue virus (DENV) is a zoonotic arthropod-borne virus responsible for several outbreaks in tropical and subtropical areas worldwide. Vitamin D3 (VD3) is a fat-soluble vitamin that plays a key role in regulation of calcium/phosphorus metabolism and modulated the immune response.

Previously, we reported that differentiation of monocytes-derived macrophages (MDMs) in presence of VD3 (VD3-MDMs) leads to a reduction of DENV replication and down-regulation of pro-inflammatory response. However, the molecular mechanism involved in control of DENV replication and regulation of pro-inflammatory response in DENV-infected VD3-MDMs are little known.

Materials & Methods

Healthy human monocytes were enriched from PBMCs (from healthy donors) by adherence to the plastic. Then, monocytes were differentiated to macrophages in absence (MDMs) or presence of 0.1 nM VD3 (VD3-MDMs) for 6 days. Then, MDMs and VD3-MDMs were infected with DENV-2 at MOI 5. Cell supernatants and total RNA was obtained at 1.5, 3, 5.5, 10 and 24 hpi, and mRNA sequencing was performed by RNA-seq. Furthermore, quantification of pro-inflammatory factors was performed by ELISA

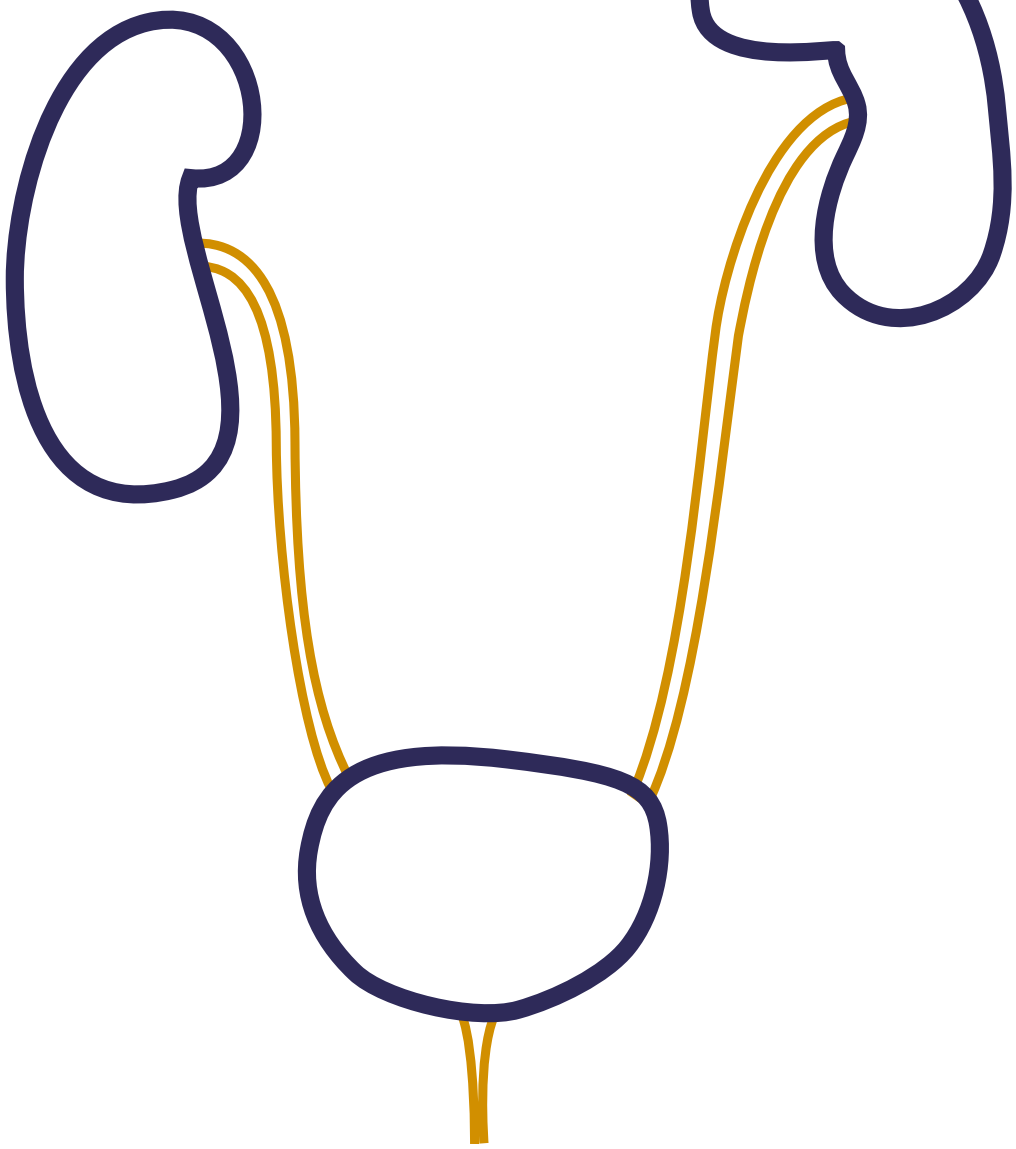
Results

We reported that VD3-MDMs induce a partial control of DENV-2 replication as compared with MDMs. Transcriptomic analysis not showed significant changes in the expression of Toll-like receptors between MDMs and VD3-MDM infected with DENV-2. However, a reduction in the mRNA expression of NF-kB-complex components (NF-kB1 and NF-kB2) and NF-kB-target genes was observed. The decrease of IL6 and COX2 in early times of DENV-2 infection in VD3-MDMs vs MDMs suggests that VD3 treatment contributes to the control of pro-inflammatory response in DENV-infected MDM. Further, we observed that DENV-2 infection induces an early and transient expression of IFNβ1 and antiviral proteins (APOBEC3A, IFIT1, MX1, and Viperin) in VD3-MDMs, but not MDMs, suggesting that VD3-MDMs contributes to control of viral replication by up-regulation of IFNβ1 production

Conclusion

DENV-2-infected VD3-MDMs induce a lower pro-inflammatory response by down-regulation of NF-kB complex and NF-kB-target genes, and induce an increased antiviral response by up-regulation of IFNβ1 and antiviral proteins, as compared with infected MDMs

Endocrinology and Nephrology



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Urinary bladder cancer-derived extracellular vesicles have immunomodulatory effects and signature

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Introduction

Extracellular vesicles (EVs) contribute to tumorigenesis in several cancer types. EVs are secreted by most cell types and the biomolecules they package reveal their originating and target cell. Studies on tumor-derived EVs in urinary bladder cancer (BC) suggest a role for BC-derived EVs in BC progression, recurrence, and dissemination. However, it is not fully understood whether BC-derived EVs play a role in modifying the (tumor) immune landscape. Therefore, this study aims at investigating the immunomodulatory effect of BC-derived EVs.

Materials & Methods

EVs were isolated from the culture medium of human muscle-invasive BC (MIBC) T24 and non-MIBC RT4 cells. Peripheral blood mononuclear cells (PBMCs) were stimulated with EVs followed by flow cytometry phenotyping (Independent Samples t-Test). Additionally, EVs were isolated from bladder urine collected from 33 MIBC and 11 non-MIBC patients. EV protein content was determined by proximity elongation assay (Olink, immuno-oncology panel) (Welch two-sample T-test, Benjamini-Hochberg).

Results

Stimulation of PBMCs with MIBC-T24-derived and non-MIBC-RT4-derived EVs resulted in higher HLA-DR expression on dendritic cells stimulated with non-MIBC-derived EVs compared to MIBC-derived EVs (p<0.001) and PBS-treated controls (p<0.001). To investigate the potential mechanism underlying the immunomodulatory function of these EVs, we characterized the proteomic profile of BC patients-derived EVs. We found higher expression levels of specific cytokines and receptors in/on EVs isolated from MIBC patients compared to non-MIBC patients, such as CCL2 (p<0.001) and PD1 (p=0.001).

Conclusion

The preliminary data on the effect of MIBC-derived and non-MIBC-derived EVs on PBMCs implies an immunostimulatory effect for non-MIBC-RT4-derived EVs but not for MIBC-T24-derived EVs. Upcoming research has to show whether BC-derived EVs have immunomodulatory effects on other immune cells as well as if this is similar for patient-derived EVs. The high expression levels of specific immunomodulatory proteins in/on MIBC-derived EVs are in line with other studies that show a contribution of tumor-derived EV-associated cytokines in modulating the immune landscape in distant organs and thereby facilitating metastasis. Therefore, it is important to investigate the biological activity of these MIBC-EV-associated biomolecules. In summary, this study highlights a role for BC-derived EVs in modulating the (tumor) immune landscape as well as the promising biomarker potential of immunomodulatory proteins in urinary EVs.

Preoperative hematological indices predict higher pathological and histological stages in renal cell carcinoma - A retrospective study from South India

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Introduction

The systemic inflammatory response in cancer can be assessed accurately by hematological indices. These are routine investigations which are inexpensive in developing countries such as India. Hence, they are a potential prognostic tool in predicting pathological and histological grading of various cancers. such as renal cell carcinoma which presents earlier in the Indian population compared to the West. We aimed to assess the ability of preoperative hematological parameters such as neutrophil-lymphocyte ratio(NLR), platelet-lymphocyte ratio(PLR), red cell distribution width(RDW), and RDW to platelet ratio(RPR) in predicting Fuhrman grade (FG) and T-stage in RCC.

Materials & Methods

We analyzed the preoperative NLR, PLR, RDW, RPR, and the FG and T-stages, in 123 patients diagnosed with RCC who underwent nephrectomy at our tertiary-care institution. Patients were divided based on their FGs as high-grade (G3, G4) and low grade (G1, G2) and based on T-stage as high-stage (pT3,pT4) and low-stage (pT1,pT2). Receiver operating characteristic (ROC) analysis was performed to determine the optimal cut-off values for each hematological parameter for FG and T-stage. Values with the highest Youden index were chosen as optimal cut-offs. Pearson chi-square test was used to determine the association between FG, T-staging and hematological parameters. p<0.05 was considered significant, with a 95% confidence interval.

Results

Optimal cut-off values for FG and NLR, PLR, RDW, and RPR were 3.12, 132.46, 15.4%, and 0.005 respectively. The cut-offs for T-stage and NLR, PLR, RDW, and RPR were 2.86, 151.34, 16.3 and 0.007 respectively. High preoperative NLRs and RDWs were statistically significant predictors of T-stage (p=0.0007, p=0.005 respectively). The NLR and FG association was statistically significant (p=0.005). High preoperative PLR and RPR were not associated with higher FG and T-stages.

Conclusion

In an Indian population, preoperative NLR and RDW are useful predictors of high-grade renal cell carcinoma. Thus, they can serve as affordable and early predictors of higher grade disease in renal cell carcinoma.

Prognostic Factors associated with Intradialytic Hypotension in Patients with Acute kidney Injury: an exploratory analysis

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Introduction

Intradialytic hypotension (IDH) is the most common complication in patients undergoing hemodialysis and increased risk of mortality. There was limited evidence on prognostic factors that were associated with IDH especially for acute kidney injury (AKI) patients. Identifying these prognostic factors could help a clinician to closely monitor patients before hemodialysis procedure. Ultimately, a set of these predictors may be used to develop a prediction tool to predict IDH during hemodialysis. The aim of this study was to investigate the effect of pre-dialytic prognostic factors on IDH in patients with AKI who underwent the first hemodialysis.

Materials & Methods

We conducted a retrospective cohort study including 156 patients who were firstly diagnosed with AKI and underwent the first hemodialysis at Phrae hospital, Thailand from January 2019 to August 2021. Candidate prognostic factors were reviewed from previous research. Patients' profiles, clinical signs and symptoms, co-morbidities, and biomarkers such as serum albumin, creatinine, sodium were collected from medical records and hospital database. The outcome was time-to-event data (time-to-IDH, in hours) during 3-hours observation period. We performed the multivariable Cox's proportional hazard regression model as an exploratory analysis to assess the effect of predictors on outcome. The strength of association was reported by hazard ratio (HR) and 95% confidence interval. We set a significance criterion for variable selection using Wald's P-value of < 0.15. This conservative level was chosen to be sure that no potential predictors were missed.

Results

In multivariable Cox regression analysis including 9 prognostic factors, there were two strong prognostic factors that were related to IDH which are: (i) having more than one antihypertensive drug used before hemodialysis (HR=2.74, 95%CI: 1.11-6.76) and (ii) having an initial ultrafiltration rate > 250 ml/hr (HR=2.94, 95%CI: 1.07-8.07). Age ≥ 60 years, having comorbid with diabetes, pre-systolic blood pressure ≥ 140 mmHg, and pre-diastolic blood pressure ≥ 90 mmHg were also associated with increased hazards, but there were not statistically significant.

Conclusion

Concern and special attention should be made on AKI patients receiving antihypertensive drug before the first hemodialysis. Moreover, setting initial ultrafiltration rate for dialysis less than 250 ml/hr would help to prevent IDH.

The Concurrent Therapeutic Potential of Adipose-derived Mesenchymal Stem Cells on Gentamycin-induced Hepatorenal Toxicity in Wistar Rats

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Introduction

Acute kidney injury is a pathological condition in which ischemia or toxic damage contributes to the loss of renal proximal tubule epithelial cells. Also, liver disease is a major health issue which present poor clinical treatment performance. In preclinical studies, it has been reported that MSCs are effective and safe in treating kidney and liver diseases, as they have high potential in aiding tissue and organ repairing. This study aimed to evaluate the therapeutic effect of adipose mesenchymal stem cells (AMSCs) in gentamycin-induced hepatorenal damage in Wistar rats for modelling the kidney and liver functions. Also, assessing its protection potential against oxidative stress and inflammation.

Materials & Methods

18 male Wister rats were assigned into three groups; control, Gentamycin (GM), and GM+AMSCs. GM induced hepatorenal toxicity through daily injection (100 mg/kg, i.p.) for eight days. On the 9th day, AMSC (106 cells/ml/rat) was injected intravenously. The effect of AMSCs was analysed by assessing Kidney and liver functions, oxidative stress and antioxidant markers, inflammatory and anti-inflammatory markers, stem cells homing and histopathological damage.

Results

Adipose mesenchymal stem cells showed significant improvement in the liver and kidney functions through decreasing creatinine, urea, uric acid, AST, ALP, ALT. Also, it provided protection against oxidative stress through significant decrease of MDA level and significant increase in GSH, and CAT levels. Moreover, it reduced the inflammation by significant decrease in the TNF and significant increase in the IL-10. Furthermore, it protected the morphological structure of the kidney and the liver. Finally, stem cells showed homing in the kidney and the liver.

Conclusion

The current study demonstrated the simultaneous therapeutic efficacy of single injection of adipose mesenchymal stem cells. AMSCs induced improvement in the kidney and the liver functions, the inflammation, and the oxidative stress in the treatment of Gentamycin-induced hepatorenal toxicity in animal model. These data showed that AMSCs could be a feasible therapy option for liver and kidney disease.

Lung extracellular superoxide dismutase (EC-SOD) in thyroid states disorders

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Introduction

Thyroid hormones increase the production of free radicals by increasing metabolism. The antioxidant system is activated to fight these free radicals. Superoxide dismutase (SOD) is one of the most abundant antioxidant enzymes in the lungs that protects the lungs against free radicals, inflammation, and fibrosis. Therefore, this antioxidant's amount and activity are expected to be affected by the concentration of thyroid hormones in response to metabolism changes. Considering the relationship between high oxygen uptake in the lungs that results in more production of free radicals, this study was investigated the role of thyroid hormones in the amount of SOD in blood and extracellular lung.

Materials & Methods

Thirty mice were randomly divided into euthyroid, hyper, and hypothyroid groups. Hyperthyroid induction was done by oral treatment of levothyroxine at %0.0012 in the drinking water for 30 days. To hypothyroidism induction, methimazole (1%, in drinking water) was used daily for 14 days. Lung EC-SOD was measured immunohistochemically. SOD enzyme activity was measured in the blood of animals. The results were expressed based on standard Means ± SEM. T-test, paired t-test, Kruskal Wallis, and Mann Whitney test were used to test the differences. p<0/05 was considered as a significant difference

Results

In the present study, the amount of the SOD activity in the blood of hyperthyroid animals (4.64 ± 0.59 mg protein/unit) was significantly less than euthyroid (7. 07 ± 0.44 mg protein/unit) and hypothyroid animals (9.22 ± 0.57 mg protein/unit, p<0/01). Immunohistochemistry study showed a significant decrease of EC-SOD level in the lung of hyperthyroid (26.84 ± 3.34 mg protein/unit compared to hypothyroid (56.71 ± 4.03 mg protein/unit, p<0/01) and euthyroid (39.64±3.02 mg protein/unit, p<0/05) animals.

Conclusion

According to our study, more attention was recommended to the interpretation of oxidative dependent diseases such as lung fibrosis in patients with thyroid state abnormalities.

Investigating the role of leptin signaling in diabetic cardiomyopathy

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Introduction

Previous animal studies demonstrate that the adipocyte-derived hormone leptin mediates cardiac-specific effects by modulating cardiac metabolism and responding to stress conditions with promotion of cardiac remodeling. This role of leptin could be of importance for clinical situations, in which leptin levels are tremendously increased, such as in obesity and diabetes. Although most rodent models demonstrate a cardioprotective role of leptin, this role remains controversially discussed in the clinical situation. In this study, we aim to deeper analyze the mechanisms underlying the proposed cardioprotective role of leptin using an in vitro cardiac diabetic model.

Materials & Methods

Using CRISPR/Cas9, we introduced a patient-specific leptin receptor (LEPR) mutation, known to cause early-onset obesity, in human induced pluripotent stem cells (iPSCs). iPSCs were differentiated into spontaneously beating cardiomyocytes (CMs), which were then cultivated in B27 (11mM glucose, 700nM insulin) or F2 medium (7mM glucose, 50nM insulin, 0.5% Albumax) until 60 days, and stimulated with leptin and insulin. Leptin and insulin signaling was examined by Western blot and cardiomyocyte size was analyzed by immunocytochemistry.

Results

We could show that LEPR-deficient iPSC-CMs express LEPR at a lower level compared to control iPSC-CMs. Leptin and insulin stimulation (5-15 min) significantly induced the activation of the JAK2/STAT3 and the PI3K/AKT pathway, respectively, in control iPSC-CMs independent of culture conditions. However, LEPR-deficient iPSC-CMs showed no activation of both signaling pathways after stimulation. In addition, we found that the size of LEPR-deficient iPSC-CMs is significantly smaller than control iPSC-CMs. Our preliminary results further show trophic effects of 24-hour leptin stimulation on Ctrl-iPSC-CMs cultured in B27 medium. Such a trophic effect was not observed in LEPR-deficient iPSC-CMs cultured in B27, but interestingly in F2 medium.

Conclusion

Our results suggest a crucial role of leptin in trophic signaling in cardiomyocytes cultured under high glucose and insulin, which in part mimics pathophysiological conditions of patients. To explore the long-term effects of leptin under diabetic cardiomyopathy conditions, we are using a medium containing fatty acids, high glucose, and high insulin and leptin to investigate the impact of altered leptin signaling on cardiomyocyte function and morphology.

Immunology

Presenters:

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Milani, A. (Alireza) Dr
Ahmadpour, S. (Sara)

Drug repurposing screen of FDA approved medicines identifies novel anti-inflammatory and NF-κB inhibitory activity of the tyrosine kinase inhibitor sunitinib malate

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Introduction

Macrophage-mediated inflammation is a pathological driver of acute inflammatory disease and chronic conditions such as rheumatoid arthritis and atherosclerosis. Drug repurposing is an attractive strategy for the development of macrophage-targeted anti-inflammatory therapeutics. Currently used anti-inflammatories have their own risk factors, the development of small molecule anti-inflammatory drugs with decreased side effect profiles is thus an ongoing process. The aim of this study was to identify FDA-approved medicines with novel anti-inflammatory effects in macrophages.

Materials & Methods

A murine macrophage NF-κB reporter cell-line was used to screen a library of 159 FDA-approved medicines for NF-κB inhibition upon LPS stimulation. To investigate sunitinib malate in vitro, cytokine production in LPS-stimulated bone marrow derived macrophages treated with sunitinib malate was measured (n=7) and IC50 values were calculated from resulting concentration response curves. To investigate NF-κB inhibitory effects of sunitinib malate in vivo, mice (n=10-11 per group) dosed orally with vehicle or sunitinib malate (30mg kg-1) were exposed to a model of acute endotoxemia (1-hour intraperitoneal injection with LPS, 10mg kg-1). Statistical significance was assessed by one-way ANOVA followed by Tukey's post-hoc test.

Results

Our initial screen identified 18 medicines with NF-κB inhibitory activity. Among these, the type III tyrosine kinase inhibitor sunitinib malate was further investigated and found to reduce pro-inflammatory mediator production in BMDMs (TNFα IC50=0.97μM, IL-6 IC50=1.14μM, CCL2 IC50=1.19μM, Nitrite IC50=0.59μM; n=7) without compromising cell viability. In vivo, sunitinib malate significantly reduces serum TNFα (p<0.05; one-way ANOVA; n=10) and liver tnf mRNA expression (p<0.01; one-way ANOVA; n=10) in a murine model of acute endotoxemia, and reduces nuclear translocation of NF-κB compared to vehicle-treated mice (p<0.01; one-way ANOVA; n=7).

Conclusion

Screening of existing medicines in macrophages allows previously unexplored anti-inflammatory properties to be identified. Here, we have found that the tyrosine kinase inhibitor sunitinib malate has potent anti-inflammatory activity in macrophages in vitro and in vivo, mediated via an NF-κB-dependent mechanism. These results justify further exploration of sunitinib malate in macrophages and its potential as a repurposed anti-inflammatory therapeutic.

Successful Transduction of Cancer-Specific T cells with Self-Renewable Potential

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Introduction

HPV-16 is a leading cause of cervical cancer as well as cancers associated with other genital organs. Therapeutic intervention by means of chemotherapy or radiotherapy have often been used in addition to surgery however, a promising novel therapy may provide hope of better remissive results. Adoptive T Cell Therapy (ACT) is a form of immunotherapy that may provide specific targeting of cancers via editing and "fine tuning" of an individual's immune system.

Materials & Methods

Isolation of donor lymphocytes was undertaken to try to expand a tumour-specific Naïve-T cell population, due to their potential for longevity and specificity. We also aimed to expand a population of T Memory Stem Cells or TSCM, a novel T-cell subset, due to their expected increased specificity and longevity but also their potential for self-renewal. This specificity was generated via lentiviral particles produced from a cell line that had been transfected. This specificity would then allow T cells to recognise the E7 epitope that appears on HPV-16 cancer cells.

Results

Generating a cell line capable of producing the lentiviral vectors was successful as were attempts to induce specificity in T cells via transduction. This was especially true for CD8+ T cells which produced a notably larger successfully transduced population compared to CD4+ T cells. Interestingly however, both populations produced an even greater number of successfully transduced specific cells when the populations were mixed rather than isolated.

Conclusion

In summary, there is great therapeutic potential for the application of such specific cells as those generated by transduction in this study with regard to anti-tumour activity. The next step would likely be introduction of said cells to murine-models possessing HPV-16 induced tumours. Aside from observing any anti-tumour effects, it would be highly interesting to see if there was any significant difference between murine models possessing T cells acquired from Naïve-T or TSCM populations. TSCM's advantageous traits of higher specificity and self-renewability may provide the opportunity to extend the length of time required between treatments compared to other T cell treatments; potentially lowering the overall cost of the course of immunotherapeutic treatments significantly.

Anti-inflammatory effects of sublingual immunotherapy with Lipopolysaccharides-PLGA particles in asthma

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Introduction

Sublingual immunotherapy is a safe disease modifying treatment for asthma. Lipopolysaccharides (LPS), the endotoxin of gram-negative bacteria, is a risk factor for asthma and also can induce systemic inflammation and sepsis if excessive signals occur. However, the effect of LPS is dose, route, and stage dependent. This study was designed to investigate the immunologic and histologic effects of sublingual immunotherapy by LPS-loaded poly (lactic-co-glycolic acid) (LPS-PLGA) nano-particles in asthmatic BALB/c mice.

Materials & Methods

LPS-loaded PLGA (50:50) nanoparticles were prepared using a water-in oil-in water (W1/O/W2) double-emulsion solvent evaporation method. Twenty BALB/c mice were divided into five groups including one group of non-sensitized mice and four groups of asthmatic mice which were treated sublingually with low-dose PLGA-LPS, high-dose PLGA-LPS, and Beclomethasone. The TH1 and TH2 hallmark cytokines (IL-4, IL-10, IFN-γ, and TGF-β) levels were measured in serum and spleen cells supernatant using ELISA. Bronchoalveolar lavage (BAL) fluid inflammatory cells differential counting and lungs histological analysis were also done. The statistical analyses were performed using GraphPad Prism 5 (version 5.01, GraphPad Software, Inc.).

Results

Treatment with low and high dose of LPS-PLGA nanoparticles resulted in significantly lower serum level of IL-4 also BAL fluid level of the IL-5 compared to control group (both are key cytokines responsible for TH2 cell differentiation). IFN-γ Level in serum and splenocyte culture of high-dose LPS-PLGA and beclomethasone groups showed marked elevation (p<0.0001). LPS-PLGA groups showed local weak inflammatory cell infiltration in the lung tissue. This group had a significantly lower inflammation score in comparison to the PBS treated group.

Conclusion

In conclusion, the results of this study suggests that LPS-PLGA nanoparticles can modulate the TH1/TH2 response by stimulating the Th1 cytokines production. Taken together, these findings demonstrate that LPS-PLGA nanoparticles have potential safe immunotherapeutic effects that can assist to reduce the risk of developing allergic asthma.

Potency of HIV-1 proteins in diagnosis and vaccine development

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Introduction

The quality of diagnosis method is fundamental for detecting and monitoring human immunodeficiency virus (HIV) infection. The diagnosis can be achieved through the detection of HIV-specific antibodies produced by the immune system. On the other hand, the combination antiretroviral therapy (cART) could restore CD4+ T cell counts and suppress viral loads, but cART alone cannot eradicate HIV in infected individual. So, development of a therapeutic HIV-1 vaccine is needed to curtail this epidemic. Herein, we evaluated HIV-1 Gp120, Nef and Rev proteins as an antigen candidate in therapeutic vaccine design as well as a possible diagnostic marker between untreated- and treated- HIV-infected individual.

Materials & Methods

At first, the recombinant HIV-Gp120, Nef and Rev proteins were expressed in prokaryotic expression system and purified using affinity chromatography on Ni-NTA agarose column under denaturing condition. Six to eight weeks old female BALB/c mice were immunized with DNA and recombinant proteins using homologous and heterologous prime/boost strategies. To determine the induction of immune responses, mice sera and splenocytes were analyzed for humoral and cellular responses, respectively. Moreover, the anti-HIV IgG antibodies against these antigens were quantified in untreated (Naïve/HIV-infected) compared to treated group using ELISA.

Results

Our results indicated that the Nef and Rev antigens could significantly induce IFN-gamma, IgG2a and IgG2b secretion directed toward Th1 response and granzyme B generation as CTL activity in mice. Whereas Gp120 could increase Th2-directed immune responses in mice. Also, the heterologous DNA prime/ protein boost regimens were more effective than the homologous protein prime/ protein boost regimens. Furthermore, among HIV-1 proteins, the levels of human antibodies against rNef and rRev proteins did not show any statistical differences in Naïve and treated groups. In contrast, the level of antibody against rGp120 in the treated group was lower than the Naïve group.

Conclusion

Our data showed that the Nef and Rev proteins were an antigen candidate for the improvement of the HIV vaccine. Furthermore, Gp120 was known as a potent antigen in diagnosis of treated from untreated HIV-infected individual.

Allergic rhinitis in BALB/c mice is associated with behavioral and hippocampus changes and neuroinflammation via the TLR4/ NF-κB signaling pathway

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Introduction

Allergic rhinitis is a systemic disease with high prevalence, which some of its neuropsychological problems have been reported. The primary pathophysiology and mechanism of the neuropsychological dysfunction of AR patients have not been described yet, so here we subjected an animal model of AR to identify any behavioral or seizure threshold changes and to assess the pathophysiology of the disease.

Materials & Methods

Eighty male BALB/C mice were randomly divided into the allergic rhinitis group and controls. Allergic rhinitis was induced in the first group by administering OVA and aluminum hydroxide intraperitoneally and then nasal injection of OVA for 14 consecutive days. Both groups were subjected to different tests for assessing depressive-like behavior, anxiety, spatial and contextual memory, and learning and seizure threshold. In addition, Hippocampus and plasma samples of mice were subjected for analyzing cytokines and immune modulators and for pathology and immunohistochemistry evaluation.

Results

The depressive and anxiety-like behavior were increased in AR, and the spatial learning and memory were disturbed in the AR group. Also, AR mice had lower seizure thresholds compared to controls. Lab data suggested that TLR4(p=0.008), NF-κB (p=0.02), IL-1β (p=0.011), and TNFα (p<0.001) expressions were increased in the AR hippocampus as well as their plasma proinflammatory cytokines. Likewise, demyelination (p=0.003), cell death (p=0.009), and M1 macrophage aggregation (p<0.001) were increased (the M1/M2 ratio was increased) in the AR hippocampus.

Conclusion

Allergic rhinitis affects mode, behavior, and seizure threshold by inducing inflammation in the hippocampus, and the TLR4/NF-κB signaling pathway probably has an important role in hippocampus neuroinflammation. Therefore, Behavioral and cognitive problems should be taken seriously in patients with AR or other atopic diseases, and more investigating is required to clear the pathophysiology behind it and its treatment.

Evaluation of immunogenicity and efficacy of Human Papillomavirus 16/18 L1 Virus-like Particle (L1VLP) vaccine with glucomannan as an adjuvant in comparison with CERVARIX® in mice

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Introduction

Some specific types of Human Papillomaviruses (HPV) can cause skin lesions and cancers. Although the development of the two prophylactic vaccines Cervarix ® and Gardasil ® into the market has greatly reduced the number of infections, it is still a major problem for the WHO, with 311,000 people dying in 2018. As a result, one of the concerns is to improve the effectiveness of the prophylactic vaccines, and prescribing new adjuvants is one of the suggested methods. Adjuvants are components that are used in vaccines' formulation to enhance efficacy. The adjuvant in Cervarix® is a combination of aluminum hydroxide and monophosphoryl lipid A which is called AS04. In this study, we evaluate the changes in Immunogenicity and efficacy of the HPV vaccine when we add glucomannan as a proven adjuvant.

Materials & Methods

Seventy C57BL/6 mice were divided into five experimental groups and one positive control group (Cervarix®) and one negative control group (PBS). Experimental groups were vaccinated with the mixture of adjuvants, HPV types 16 and 18 L1 virus-like particles (L1VLP) alone, L1VLP in combination with AS04, glucomannan, and also mixture of both adjuvants. Mice were vaccinated subcutaneously twice. The interval of injections was two weeks. The blood samples were taken two weeks after the last injection. And serums were kept for further examination. Dedicated kits with the ELISA technique were used to detect and quantify IgG and different cytokines levels.

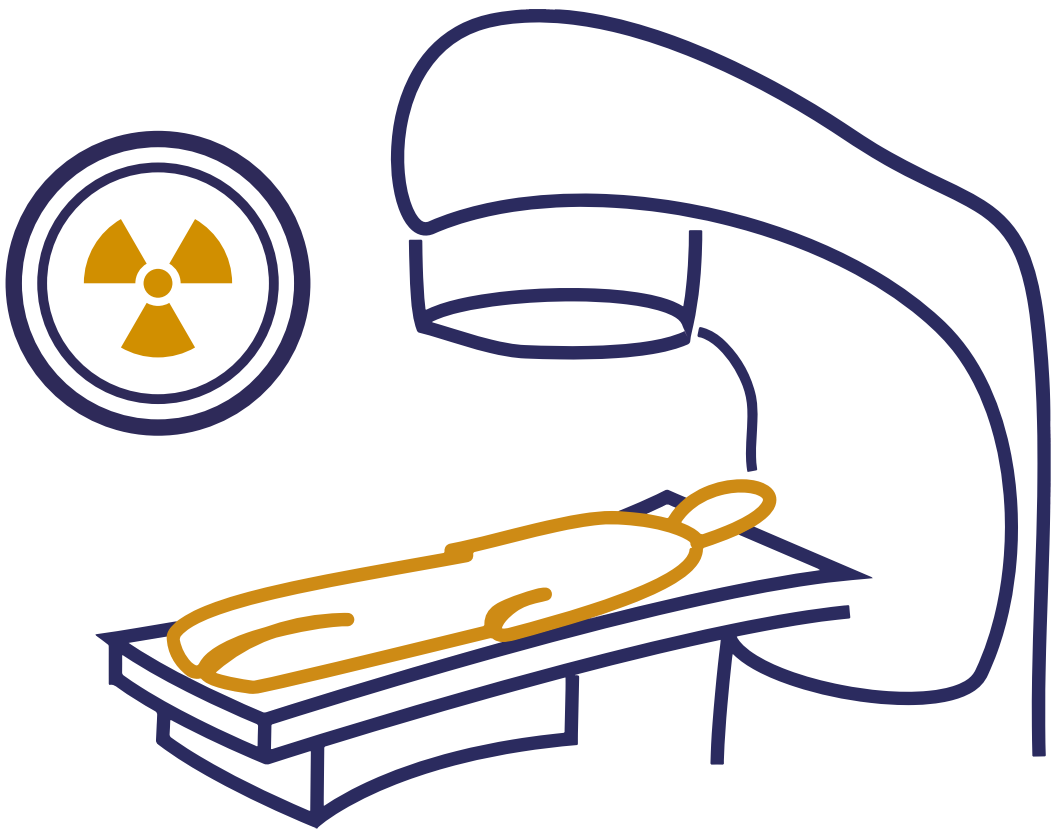
Results

Mice immunized with L1VLP in combination with AS04 and glucomannan showed a higher level of serum anti HPV16/18 L1VLP IgG antibody and also cytokines (IL-12, IL-17, IL-4, IL-10, IFN-γ, TNF-α) in comparison with the other groups.

Conclusion

According to data glucomannan improves both humoral and cellular immune responses to HPV 16/18 L1VLP. As a result, it can be considered as a novel adjuvant for further clinical studies and the development of prophylactic HPV vaccines.

Nuclear and Technical Medicine



Presenters:
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Bedoya, V (Valentina)
Schmude, von, A. (Angelika) MSc.
Frenzel, M. W. W. (Martin Walter Willibald)
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Beneficial effects of repeated UC-MSC derived exosome administration on cutaneous wound healing (in rats)

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Introduction

Wound healing is a multiphase process mainly mediated by paracrine signaling. Exosomes derived from Umbilical Cord Mesenchymal Stem Cells (UC-MSC) have shown promising effects on healing acceleration by modifying intercellular interactions. However, exosomes may not affect all healing phases due to a short half-life and undetectability at the wound site almost two days after administration. This study evaluated the advantages of multi-exosome administration (on days 0, 2, and 7 post-wounding) over its single injection following wound induction.

Materials & Methods

Exosomes were isolated and characterized from human UCMSCs. Male rats were randomly assigned to two groups of single (group A) or multiple exosome administration (group B). Four full-cutaneous wounds were made on the dorsum of each rat. Two right-sided wounds of each animal received exosome subcutaneously either as a single dose immediately after wounding (group A) or three doses on days 0, 2, and 7 post-wounding (group B). Each animal's left side wounds were treated with PBS as a control on the same days. Digital images were used to monitor the wound closure rate on days 0, 4, 7, and 14 (post-wounding). Tissue samples were harvested for further pathologic and PCR analysis.

Results

The wound closure rate was significantly enhanced in group B than group A and controls (p<0.05). In addition, trichrome staining demonstrated enhanced collagen maturity in multi-exosome-treated animals. PCR results suggested lower TNF-α expression in group B compared to the control groups on days 7 and 14 (p<0.001) and group A on day 14 (p<0.05). TGF-β mRNA levels were also higher in group B than PBS-treated wounds on days 7 and 14 (p<0.05 and p<0.0001, respectively) and group A on day 14 (p<0.001).

Conclusion

This study suggests that repeated local administration of UC-MSC-derived exosomes attenuates inflammation and improves wound healing, potentially by maintaining adequate exosome concentration at the wounded site.

Dose-calculation algorithm impact on breast cancer Fast-Forward radiotherapy treatments: what radiobiological parameters have to say.

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Introduction

Hypofractionated radiotherapy schemes, like the Fast-Forward Protocol (FFP) for early breast cancer, allow non-inferior results from the standard fractionation in fewer treatment sessions. FFP was implemented in our clinic due to Covid-19 restrictions, using general dose-volume based criteria to assess plan quality. Nonetheless, radiobiological models may become essential to quantify plan effectiveness on each patient. Normal Tissue Complication Probability (NTCP) and Tumor Control Probability (TCP) are suitable criteria, both in treatment plan approval and in dose calculation-algorithm effect on planning quality.

Materials & Methods

A comparative analysis using AAA and XB algorithms in Eclipse Treatment Planning System (TPS) was performed, for a 315-patient group treated with the FFP, with a schedule of 5 fractions and total prescribed doses of 26 Gy, or 26 Gy with a simultaneous integrated boost of 29 Gy. TCP and NTCP were calculated for each patient using a Python-based code and extracting Dose-Volume Histogram information from the TPS. TCP was determined for the Planning Target Volumes (PTV), whereas NTCP was determined for the ipsilateral lung, heart, and contralateral breast. A paired analysis was performed to determine whether the differences between both algorithms were statistically significant.

Results

The mean TCP was 87.86% and 88.17% for PTV29, using XB and AAA, respectively. For PTV26, the mean TCP was 76.40% and 76.62%. Mean NTCP values were: 1.30% and 1.40% for lung, 1.27% and 1.12% for breast, and 10.53% and 10.57% for heart, using XB and AAA, respectively. Although paired-analysis was statistically significant ($p=0.9$), the difference on both TCP and NTCP between algorithms is at most 0.8%, thus allowing safe use of AAA for FFP dose calculations, even if XB is more recent and physically precise.

Conclusion

NTCP and TCP values between AAA and XB dose calculation algorithms did not differ significantly, even for interface-change structures like lung or heart, where XB shows a greater dose-distribution difference. Radiobiological parameters allow a deeper and more personalized plan assessment than the use of dose-volume constraints or dose distributions alone, and their use should be encouraged in clinical practice.

Spheroid control probability (SCP) assay to compare photon and proton irradiation outcome in head and neck squamous cell carcinoma (HNSCC)

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Introduction

Advanced, curative endpoints in radiotherapy testing are the tumor control probability (TCP) and the tumor control dose 50% (TCD50 = dose required to cure 50% of tumor-bearing animals). The underlying in vivo experiments are economically and ethically problematic. Multicellular tumor spheroids possess radiotherapeutically relevant pathophysiological characteristics of in vivo tumors and facilitate to systematically assess the relative biological effectiveness (RBE) of proton beam irradiation. The aim of this study is to determine a spheroid-based RBE of proton vs. photon irradiation in human HNSCC models by determining TCP/TCD50 equivalent in vitro outcomes via an SCP setup.

Materials & Methods

Two HNSCC spheroid models (FaDu, SAS) with different radiosensitivity are applied. Spheroid integrity and volume (re-)growth are monitored every 48-72 h for up to 60 days after single dose irradiation (0-30 Gy); 30-40 spheroids are included per treatment arm (irradiation dose); 13 treatment arms ≈ 300-400 spheroids ≈ 10,000 images are usually assessed per spheroid type and radiation quality to determine spheroid growth delay, document SCP as function of time for each dose, and calculate spheroid control dose 50% (SCD50) values from SCP dose-response curves.

Results

The first experiment with 500 µm FaDu spheroids irradiated in the center of the proton spread-out Bragg peak (SOBP) resulted in an SCD50 value of 10.2 Gy (95% CI, ±0.5 Gy) as opposed to 11.0 Gy (95% CI, ±0.4 Gy) for photon irradiation. The respective spheroid RBE value was 1.1, which is lower than for most pancreatic cancer spheroid models studied so far by the group but resembles the clinical adaption in proton radiation treatment planning. The project is ongoing and shall also allow to apply the SCP approach to assess the impact of linear energy transfer (LET) variations along the Bragg curve of proton beam irradiation.

Conclusion

Consecutively, the SCP assay can be considered a sophisticated tool to provide gold standard approximation as well as practical and economical advantages.

Effects of high-energy photons on iron oxide nanoparticles

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Introduction

The investigation of the stability and preservation of physical-chemical properties of superparamagnetic iron oxide nanoparticles (SPIONs) when subjected to ionizing radiation is an important issue for their applications in oncology, such as in nanoparticle assisted radiotherapy. In particular, SPIONS may be useful theragnostic agents in the recently developed MRI-guided radiotherapy. In this work, the effects of X-ray and gamma ray radiation on the structure and properties of commercial and lab developed magnetic iron oxide nanoparticles were investigated

Materials & Methods

Commercial grade and synthetized iron oxide nanoparticles (using the coprecipitation method and the polyol route) were used to prepare the targets to be irradiated. The exposures were performed on samples in different forms (thin films on silicon, pellets, and aqueous suspension). The irradiations were performed in a 6-MV Clinac IX linear accelerator from Varian and a cobalt-60 pump. The doses used varied between 10 and 720 Gy at rates around 0,42 and 6 Gy/min. Irradiated samples were analyzed by transmission electron microscopy (TEM), scanning electron microscope (SEM), X-ray diffraction (XRD), magnetic resonance imaging (MRI), vibrating-sample magnetometer (VSM), zeta potential (PZ) and dinamic light scattering (DLS).

Results

Images obtained by TEM do not show significant changes in the morphology of the nanostructures. Analysis by XRD, however, indicates a reduction in crystallinity with increasing dose in the commercial samples. A slight decrease in saturation magnetization was also seen at high doses, exceeding 480 Gy. Measurements of nuclear magnetic relaxation performed on the synthesized nanoparticles coated with dextran demonstrated an increase in transversal relaxation time (T2) with increasing dose, consistent with magnetization data and suggesting the induction of defects in the crystals and changes in the coating permeability to water after the irradiation process.

Conclusion

Irradiation with high energy photons may induce structural modifications in the nanoparticles and changes in the nuclear relaxivity, affecting their behavior as contrast agents in MRI. However, the changes are only clearly detected at doses much higher than those used in the clinical practice for therapy or diagnostics.

BRAF-mutation status beats KRAS-mutation status: a radiogenomic analysis in colorectal cancer

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Introduction

Colorectal cancer (CRC) is one of the leading causes of death worldwide. Genetic variations among the CRC greatly influence survival and therapy. We aimed to identify important radiomic features to predict genetic mutations of CRC, especially BRAF- and KRAS-mutation, based on computed tomography (CT) scans prior to the therapy.

Materials & Methods

A radiogenomic analysis was carried out on 51 subjects who underwent pretherapeutic CT imaging. Using the software LIFEx, radiogenomic feature extraction was performed after manually segmenting the CRC in CT images in the venous phase. The intensity discretization of 64 and 128 grey levels (GL) were also compared. The respective value of 66 radiomic features, the skewness and kurtosis of the belonging histograms were ascertained as predictors for BRAF- and KRAS-mutation. The least absolute shrinkage and selection operator (LASSO) method was used for data dimension reduction and relative feature selection. A balanced random split was applied to separate the data into a training and test set (0.6:0.4 ratio).

Results

Significant values (p=0.034) for the relative importance of significant radiogenomic features were presented in the LASSO method in BRAF-mutation with 64 GL with the following values: accuracy= 0.895, sensitivity= 0.667, specificity= 1.0 and an area under the curve (AUC)= 0.769 (95%CI 0.66-0.99). While with 128 GL the values were slightly worse: accuracy= 0.842, sensitivity= 0.667, specificity= 0.923 and an AUC= 0.667 (95%CI 0.60-0.97). The values for KRAS-mutation status with 64/128 GL cannot be deemed representative: accuracy= 0.445/0.5, sensitivity= 0.375/0.25, specificity= 0.5/0.7 and an AUC= 0.575/0.575 (95%CI 0.22-0.69/0.26-0.74).

Conclusion

The analysis of BRAF-mutation status in CRC shows promise to find significant radiogenomic features, especially with an intensity discretization of 64 GL (AUC= 0.769), identified by LASSO method. Whereas in KRAS-mutation the analysis does not lead to any significant outcome. When results for BRAF-mutation status are confirmed further also using a greater number of subjects, radiogenomic analysis could be considered as a promising tool for determining the BRAF-mutation status of CRC.

Evaluation of Forearm and Hand Joint Positions for Splint Optimization in Carpal Tunnel Syndrome.

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Introduction

CTS is a leading driver of incapacity, with a consequential decline in productivity and income. Splint immobilization is a conservative modality of treatment for Carpal Tunnel Syndrome that mitigates neural compression by reducing carpal tunnel pressure. However, there is a lack of literature investigating optimum splint design and the majority of commercially available splints immobilize only the wrist in a neutral position. This study holistically juxtaposes a range of postures at the proximal radio-ulnar, wrist, and metacarpophalangeal joints to determine the ideal combination yielding the lowest carpal tunnel pressure.

Materials & Methods

In this cross-sectional study, a pressure transducer was introduced between the Flexor Digitorum Superficialis and the Flexor Digitorum Profundus tendons of freshly dissected, unembalmed, cadaveric specimens. The transducer was used to establish the specific degree of immobilization required at each of the aforementioned joints to yield the lowest carpal tunnel pressure. Statistical Package for Social Sciences V.23.0 was used for data analysis. One-way ANOVA analysis was used to analyze differences in carpal tunnel pressure between joints. The Tukey-Kramer post-hoc test was applied to compare the differences among the varying degrees of immobilization at each individual joint. A p-value < 0.05 was considered to be statistically significant.

Results

40 cadaveric specimens were analyzed. The lowest carpal tunnel pressures were procured with 45° of pronation at the proximal radio-ulnar joint, 30° of flexion and 15° of ulnar deviation at the wrist joint, and 30° of flexion at the metacarpophalangeal joints.

Conclusion

This study delves into the pressure analyses of CTS by determining the specific degree of splint immobilization required at the forearm and hand joints for nominalization of carpal tunnel pressure. The data thus acquired paves way for the design of an optimized splint to facilitate recovery and alleviation of symptoms in patients with CTS. Additionally, positions found to critically elevate pressure can be interpreted as risk factors for primary preventive measures. The findings are also paramount with regards to ergonomics, to minimize work-induced hazards by optimizing the design and placement of hand-held tools and furniture. Ultimately, CTS can be managed with a more sustainable approach, socioeconomically, in addition to the patients' best interest.

Psychiatry

Presenters:
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Weijden, D.A.Y van der (Deveny)
Gapchup, TG (Tejal)
Attarbashi, A (Amirhosein) Dr
Dyson, N.G.D. (Nathaniel Gilbert)
Mr.
Liampeng, Stephen (Saharat)

Quality of Life and Mental Health of Hidradenitis Suppurativa Patients in a large prospective, Dutch cohort

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Introduction

Hidradenitis suppurativa (HS) is an auto-inflammatory skin condition, which causes painful lesions in the skin folds, that can contribute to pain, malodorous odour and feelings of shame. HS has a major impact on quality of life (QoL) and affects the emotional and relational life of patients. However, comparisons of mental health between HS patients and the general population are scarce.

Materials & Methods

Data on different aspects of QoL were obtained using the RAND-36 questionnaire through the population-based Lifelines Cohort study, where we identified 1,156 adult HS patients and 5,000 healthy controls. In addition, we determined if participants met the criteria for psychiatric disorder via the Mini International Neuropsychiatric Interview. For analyses, regression modelling was used to assess the association between patient and disease characteristics and mental health outcomes.

Results

Compared to the controls, HS patients scored significantly lower both physical and mental component percentage (respectively, 53.3%[46.5-56.5] and 51.8% [45.5-55.7] versus 54.7%[50.9-56.8] and 53.7%[49.4-58.4] [P<0.001]). For psychiatric comorbidities, HS patients scored significantly higher for major depressive disorder (3.5% versus 1.4% [P<0.001]) and generalized anxiety disorder (7.8% versus 3.3% [P<0.001]). With multivariate regression analysis after adjusting for possible confounders, the mental health component score, physical health component score, major depressive disorder and generalized anxiety disorder remained significantly associated with HS.

Conclusion

In this study, we concluded that the HS patients scored lower in mental health status compared to the general population of the Northern Netherlands and that HS patients had a higher risk of developing psychiatric comorbidities. However, further research on HS disease-specific mental health status analyses is needed to develop multidisciplinary treatment modalities and prevention strategies to improve the QoL of these patients.

Effectiveness of daily self-weighing combined with hypocaloric diet and community personalized-dietary counseling for weight reduction among adults with obesity in a rural community, Thailand: a community-based randomized controlled trial

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Introduction

Significant increase of obesity and average body mass index (BMI) in Thai rural community was found over 6 years. Obesity is one particular risk of noncommunicable diseases. Therefore, effective public health interventions should be implemented to prohibit increased BMI.

Materials & Methods

A randomized controlled trial was conducted in Thakradan rural community, Sanam Chai Khet District, Chachoengsao Province, Thailand. People aged 18-60 years with BMI ≥ 27.5 kg/m2 were invited in the study. A total of 107 individuals were randomly allocated to 70 participants and 30 participants for control group and intervention group, respectively. The health education of hypocaloric diet and how to lose weight were provided to all participants. Additionally, intervention group received digital weight machines and weight-recording calendar to weigh twice daily. The well-trained village health volunteer (VHV) visited the intervention group weekly in order to emphasize on health education for weight loss, personalized-dietary counseling calculated approximately daily intake -500 kilocalories from personal basal metabolic rate, psychological encouragement, and adverse effect records. The interventions were conducted for 20 weeks.

Results

From a total of 107 participants, there were 100 females (93.50%). The average age of participants was 44.0±10.0 years. The average BMI at baseline was 32.45 ± 3.45 kg/m2 and 32.17 ± 4.23 kg/m2, among intervention and control groups, respectively (p =0.744). In intervention group, there were significant differences between average BMI at baseline and average BMI at 8th week (-0.48 kg/m2, p = 0.0496), at 12th week (-0.46 kg/m2, p < 0.01), at 16th (-0.42 kg/m2, p < 0.01) and the end of trial in 20 weeks (-0.51 kg/m2, p < 0.01). While there was an increase in the average BMI compared to their baseline in the control group. Besides, there was a significant decrease in average systolic blood pressure (BP) and diastolic BP from baseline to 4th weeks and 8th weeks in intervention group. The adverse events among all participants were not detected.

Conclusion

In conclusion, this study demonstrated that daily self-weighing combined with hypocaloric diet and community personalized-dietary counseling played an essential role in reducing weight as well as reducing BP levels among individuals with obesity.

Increased mental stress associated with PMS (Premenstrual Syndrome) depression: A pilot study

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Introduction

PMS (Premenstrual Syndrome) is a challenging condition experienced by many women during their reproductive life. The psychological symptoms of this condition, such as depression, may negatively impact their overall well-being. This study explores the impact of pre-existing mental stress on the severity of PMS depression. Awareness about this could pave the way for prioritising mental health and reducing stress in daily life, which could limit the burden of PMS on women and society.

Materials & Methods

One hundred and twenty-three women in the age group of 18-22 years with a regular menstrual cycle were part of this study. Beck Depression Inventory (BDI) questionnaire was used to assess the severity of depression symptoms in the follicular, ovulatory and premenstrual phases of the menstrual cycle. Friedman test with post hoc analysis was used to check if the severity of depression in these three phases was significantly different.

Mental stress levels for the preceding two weeks up to the beginning of the study were assessed using the Perceived Stress Scale (PSS). The calculated stress levels were correlated with the BDI scores in the premenstrual phase, using the Spearman's rho correlation test.

Results

The severity of depression in the premenstrual phase was significantly higher than that in the follicular (z=-6.002, p<0.003) and ovulatory phase (z=-5.766, p<0.003). 44% of participants reported mild-severe depression symptoms in the premenstrual phase, compared to just 16% in the ovulatory phase and 10% in the follicular phase. The spearman's coefficient (0.52911) indicated a positive correlation between pre-existing perceived mental stress and premenstrual depression.

Conclusion

The results suggest that women experience more depression symptoms during the premenstrual phase, as compared to other phases. The positive correlation between pre-existing mental stress levels and premenstrual depression may not necessarily imply causation, but it does suggest an association between them. Women experiencing severe depression symptoms during PMS may also be experiencing increased mental stress on a day-to-day basis. With more scientific evidence in this area, we could realise the importance of mental health and its effect on the arduous psychological symptoms of PMS.

Internet-based Cognitive Behavioral Therapy Alleviates Psychiatric Problems Related to Covid-19 Pandemic: A Meta-analysis

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Introduction

The COVID-19 pandemic has resulted in a tremendous impact on mental health, with more than 1 in 3 people worldwide are experiencing psychiatric problems related to the pandemic, ranging from depression, anxiety, and insomnia. An immediate yet effective solution is needed as studies have shown that conventional cognitive behavioral therapy (CBT) had lost its effectiveness due to mobility restrictions and healthcare facility limitations during the pandemic. The utilization of internet-based cognitive behavioral therapy (ICBT) is believed to be the answer to this mental health emergency from getting even worse. This systematic review and meta-analysis aim to quantitatively prove the effectiveness of ICBT for alleviating psychiatric problems related to the COVID-19 pandemic.

Materials & Methods

A systematic literature search was performed in multiple databases including PubMed, Scopus, Cochrane, EBSCOhost, and Google Scholar searching for studies implementing ICBT for psychiatric problems related to COVID-19 up to October 29th, 2021. The quality of studies was evaluated using the Cochrane Risk of Bias 2.0 tool and converted to AHRQ standards. Quantitative analysis of mean differences was performed using Review Manager 5.4 in inverse variance, random-effects model and whenever possible, sensitivity analysis and subgroup analysis were performed.

Results

Our final search resulted in 6 randomized controlled trials with a total of 1,338 participants. ICBT demonstrates promising efficacy, compared to treatment as usual, in reducing adverse psychosocial conditions related to the COVID-19 pandemic situation, including anxiety [pooled mean difference (MD): -8.31 (p<0.00001; 95%CI: -11.81- (-4.80))], depression [(pooled MD: -4.11 (p=0.001, 95%CI: -6.57- (-1.65))], and insomnia [(pooled MD: -1.22 (p=0.004, 95%CI: -2.04- (-0.40))]. In addition, quality of life, work and social functioning, and mindfulness also improved considerably after patients received ICBT.

Conclusion

ICBT presents a promising solution for alleviating psychiatric problems related to the COVID-19 pandemic. Considering the benefits of I-CBT, we believe it would be beneficial for health facilities to consider committing resources for ICBT through online platforms to provide wide coverage of mental health support for patients with psychiatric problems, especially during the COVID-19 pandemic.

Comparative Investigation of Anti-Transglutaminase 6 IgG Antibody Prevalence in Patients with Schizophrenia, First-Degree Relatives and Healthy Control Group

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Introduction

Autoantibody against transglutaminase 6 (anti-tTG6) has been introduced as a marker of neural involvement and has been investigated in some neurologic conditions such as gluten ataxia. As there is a scarcity of studies about tTG6 in schizophrenic patients, in the present study, we assessed and compared serum anti-tTG6 in patients with schizophrenia, their first-degree relatives, and the healthy control (HC) group.

Materials & Methods

In this case-control study, 40 patients with schizophrenia (based on DSM-V criteria) were compared with 40 age- and gender-matched HC and 40 first relatives of patients. Blood samples were collected from all participants at one time, and serum levels of tTG6 IgG were measured by ELISA.

Results

This study included 120 patients (male: 79, 65.8%) with a mean age of 46.2±12.7 years. The positive tTG6 antibody test was observed in 14 (35.0%) schizophrenic patients, 10 (25.0%) subjects in the first-degree relative group, and 2 (5.0%) HC. The frequency of positive tTG6 tests was higher in patients with schizophrenia than in the HC group (P=0.003). Logistic regression analysis shows that the positive anti-tTG6 was associated with an increased risk of illness (OR= 6.7, 95%CI: 1.35-33.3). However, there was no increased risk of illness when schizophrenic patients were compared to their first-degree relatives

(OR= 1.65, 95%CI: 0.61-4.45).

Conclusion

Our findings suggest that the tTG6 antibody could be considered as a marker for autoimmune processes that affect the likelihood of the evaluation of a chronic psychotic disorder. Anti-tTG6 may be a useful marker for the determination of schizophrenic patients, who would profit from a gluten free diet.

Study of Psychological Burden Amongst Family Members of Vitiligo Patients

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Introduction

Vitiligo is characterized by depigmented patches of skin due to the loss of melanocytes. While vitiligo does not pose a significant physical challenge, it does have a significantly detrimental impact on patients' and family members' well-being and QoL (Quality of Life). The assessment of the psychosocial impact of skin disease on a patient can help direct the dermatologists' treatment goals. The study aimed to evaluate the psychological impact on family members of Vitiligo patients using FDLQI and on Vitiligo patients using VIS.

Materials & Methods

A prospective observational study was conducted at Dermatology Outpatient Department at a Tertiary Care Hospital for eight weeks. Impairment in QoL of the total of 80 patients and family members was assessed by using three standardized questionnaires:- Vitiligo impact scale (VIS), Family Dermatology Life Quality Index (FDLQI), and Children's Dermatology Life Quality Index (CDLQI).

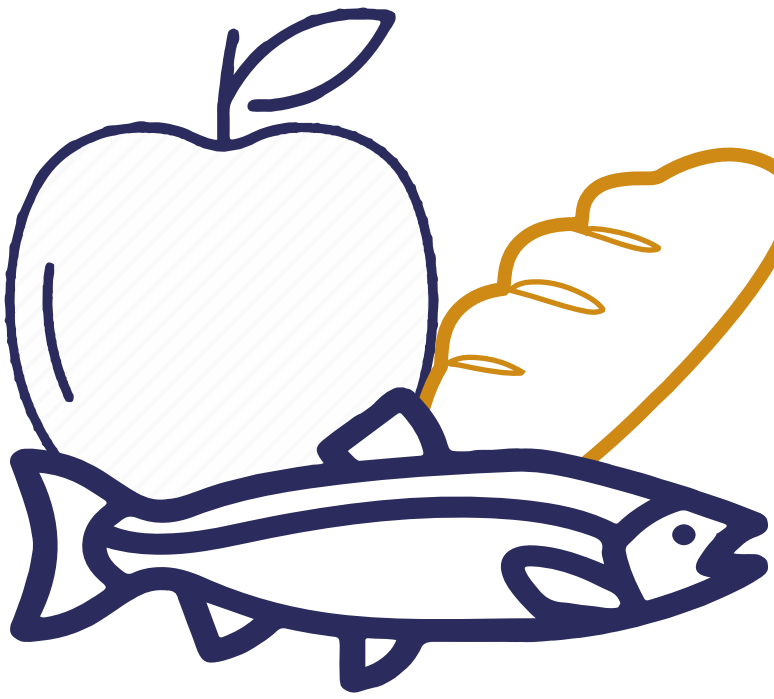
Results

The mean FDLQI score was 6.18 (±5.48), and the mean VIS score was 14.93(±13.10). Higher FDLQI score was associated with female patients (6.87±5.66), unmarried patients (7.59±5.54), those who didn't have children (7.44±5.33), employed (6.78±5.31), patients having lesions on the photo-exposed areas (6.32±5.47) and for Grade 3 BSA involvement (7.00±6.86). FDLQI score was higher for the patients suffering from Vitiligo Vulgaris (6.72±5.71) followed by Focal and Segmental Vitiligo. A similar trend like FDLQI was seen in the VIS score. On comparing the two groups based on marital status and fertility status, we found a significant difference (p=0.0105) & (p=0.0064) respectively in the score of VIS with a mean rank higher in the unmarried group and those who didn't have any child.

Conclusion

Our data indicate that vitiligo has severe impairment in the QoL of patients as well as their family members. Along with the treatment and management of the patient psychiatric consult and counseling should be provided to the patients and their family members to improve their QoL. Future interventional studies in this direction can be planned in the form of psychological counseling of parents, siblings, and patients and also to observe the change in psychological beliefs after the intervention.

GI medicine and Nutrition



Presenters:

Nayun, S.N.Y. (Su) Master degree
Naghibzadeh Gonabadi, N.N.G (Niloofar)
Baidoo, N. (Nicholas)
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Hartman, L M E (Lilian)
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Total collagen content and distribution is increased in human colon during advancing age.

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Introduction

Advanced age is associated with an increased incidence of lower gastrointestinal disorders partly due to structural changes in components that make up this region of the gut. The influence of ageing on the collagen content of the human colon has not been adequately studied. The aim of this study was to determine if ageing altered total collagen content and distribution in the human colon.

Materials & Methods

Macroscopically normal ascending colon was obtained at surgery from cancer patients (n = 31) without diagnosis of diverticular or inflammatory bowel disease. Systematic serial transverse sections of formalin-fixed paraffin-embedded full-thickness were generated; Masson's trichrome and Picrosirus red stains were employed to identify the total collagen content distribution within the sublayers of the colonic wall for adult (22 – 60 years; 6 male, 6 female) and elderly (70 – 91years; 6 male, 4 female) patients. New procedures were used to ensure unbiased image-capturing and analysis with brightfield microscopy was derived using ImageJ. Hydroxyproline assay evaluated the total collagen concentration for adults (30- 64years; 9 male, 6 female) and the elderly (66 – 91 years; 8 male, 8 female). Age-related changes in total collagen content and concentration between the adult and the elderly were compared by a two-tailed independent student's t-test using the Statistical Package for Social science.

Results

Histological studies showed that the percentage mean intensity of total collagen staining in the mucosa, submucosa and muscularis externa was, respectively, 14(1.9) %, 74(3.2) % and 12(1.5) % in the adult ascending colon. Compared with the adults, the total collagen fibres content was increased in the submucosa (mean intensity; 163.1 ± 11.1 vs. 124.5 ± 7.8; P < 0.05) and muscularis externa (42.5 ± 8.0 vs. 20.6 ± 2.8; P < 0.01) of the elderly patients. There was no change in total collagen content of the mucosa. The total collagen concentration was increased in the elderly by 16%. Sex-related differences were not found, and the data were combined.

Conclusion

Greater total collagen content was found in the submucosa and muscularis externa of the elderly human male and female colon. These changes may contribute to a possible loss of function with ageing.

The effect of an angiotensin receptor blocker in lung metastasis of colorectal cancer

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Introduction

Colorectal cancer (CRC) is a common cancer with a high incidence rate. Components of the renin-angiotensin system (RAS) have been reported to be dysregulated in several malignancies including CRC. Here, we have explored the potential anti-metastatic effects of a RAS inhibitor, losartan, in an experimental model of lung metastasis in CRC.

Materials & Methods

A murine model of lung metastasis of CRC was used, which involved the intravenous injection of CT26 cells via a tail vein. Four experimental groups comprised: an untreated group; a group that received 5-FU which was administered intraperitoneally; a losartan group that received a combination group that received 5-FU plus losartan . We evaluated the anti-inflammatory effects of losartan by histopathological method, and the measurement of oxidative or antioxidant markers including malondialdehyde (MDA) and total-thiols (T-SH) tissue levels, superoxide-dismutase (SOD) and catalase activity.

Results

We found that losartan inhibited lung metastasis of CRC and there was a reduction of the IL-6 expression level in the tissue sample. It was also associated with reduced levels of the anti-angiogenic factor Vascular endothelial growth factor (VEGF). Furthermore, we found that losartan induced oxidative stress as assessed by an elevation of MDA level, reduction of T-SH, SOD and catalase activities in lung tissue.

Conclusion

Our findings demonstrated that losartan ameliorates angiogenesis, inflammation and the induction of oxidative stress via Angiotensin II type I receptor (AT1R). This may shine some lights on targeting the RAS pathway as a potential therapeutic approach in the treatment of metastatic CRC patients.

Higher Meat Intake Is Associated with Higher Inflammatory Markers, Mostly Due to Adiposity: Results from UK Biobank

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Introduction

High meat consumption may play a role in promoting low-grade systemic inflammation, but evidence is limited. We therefore aimed to examine cross-sectional associations of habitual meat consumption with serum C-reactive protein (CRP) and total white blood cell count (WBCC) in British adults.

Materials & Methods

We included 403,886 men and women (aged 38–73y) participating in the UK Biobank who provided information on meat intake (via touchscreen questionnaire) and a nonfasting blood sample at recruitment (2006–2010). For a subset of participants (ɣ5%), an additional blood sample was collected (median 4.4 y later). We used multivariable linear regression models to estimate associations of meat intake (total meat, unprocessed red meat, processed meat, and poultry) with logCRP and logWBCC.

Results

The difference in the serum CRP (mg/L) for each 50-g/d higher intake for total meat was 11.6% (95% CI: 11.1, 12.0%), for processed meat was 38.3% (95% CI: 36.0, 40.7%), for unprocessed red meat was 14.4% (95% CI: 13.6, 15.1%), and for poultry was 12.8% (95% CI: 12.0, 13.5%). The difference in the WBCC (×10–9L) for each 50 g/d higher intake of total meat was 1.5% (95% CI: 1.4, 1.6%), for processed meat was 6.5% (95% CI: 6.1, 6.9%), for unprocessed red meat was 1.6% (95% CI: 1.4, 1.7%), and for poultry was 1.6% (95% CI: 1.4, 1.7%). All associations were attenuated after adjustment for adiposity; by 67% with BMI (in kg/m2) and by 58% with waist circumference for total meat and CRP, and by 53% and 47%, respectively, for WBCC, although associations remained statistically significant. Findings of sensitivity analyses in 15,420 participants were similar prospectively, except there were no associations between unprocessed red meat and WBCC.

Conclusion

Higher meat consumption, particularly of processed meat, was positively associated with inflammatory markers in these British adults; however, the magnitudes of associations are small and predominantly due to higher adiposity.

Dietary treatment in Dutch children with phenylketonuria: an inventory of associated social restrictions and eating problems.

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Introduction

Phenylketonuria (PKU) is caused by a defect in the liver enzyme phenylalanine hydroxylase which leads to high blood phenylalanine and consequently, if untreated, severe developmental delay. Therefore, a lifelong phenylalanine-restricted diet is necessary. Eating problems due to the diet are known to exist, but knowledge on both prevalence and magnitude, especially on social restrictions, is scarce. The aim of this study is to evaluate the social restrictions and eating problems PKU children and their caregivers experience due to the dietary treatment.

Materials & Methods

A web-based questionnaire, based on the Behavioural Paediatric Feeding Assessment Scale with additional PKU specific questions, was developed in close collaboration with and distributed via the Dutch PKU Association. All members of the Dutch PKU Association received an email containing the link to the questionnaire. The questionnaire was completed by caregivers of PKU children and caregivers of age matched children without PKU. Data were analysed with the Kruskall Wallis and Mann Whitney U test using SPSS.

Results

In comparison with the control group (aged 1-16; N=50), caregivers of PKU children reported more difficulty in offering food variety, experienced more stress when eating an evening meal outside the home and during vacation, and to be stricter about (accidental) spilling of food during dinner by the child with PKU (p<0.05). They also reported to be angrier, more frustrated and/or anxious when feeding their child, and they more often felt their child's eating pattern had a negative influence on his/her general health (p<0.05).

Conclusion

This study provides further evidence that restriction of social activities and eating problems associated with dietary restrictions are more common in children with PKU, and warrants more awareness on this topic by professionals working with children with PKU.

H.pylori activates LUBAC-NF-κB inflammatory pathway by CagA-SHARPIN interaction

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Introduction

Helicobacter pylori (H. pylori), with the infection rate of nearly half of the world's population, is the main risk factor for gastric adenocarcinoma. Cytotoxin-associated gene A (cagA) has been considered as a significant oncogenic gene responsible for H.pylori-induced gastric tumorigenesis. However, it still remains obscure that how CagA protein is regulated in the process of inflammation-cancer transformation. Playing an important role in the occurrence and progression of cancer, the NF-κB pathway has long been considered a classic pro-inflammatory signaling pathway. LUBAC regulates the activation of NF-κB pathway by promoting the linear ubiquitination of NEMO and increasing phosphorylation of p65 and IκBα. Previous research has shown CagA activates the NF-κB signaling by targeting TAK1, but more molecules need to be discovered to investigate the specific mechanism of this activation.

Materials & Methods

Experiment methods like Dual-luciferase reporter gene study, RT-PCR and western blotting were applied to discern and examine the relationship between CagA and the NF-κB inflammatory pathway. Clinical correlation of CagA and its targets was examined in H.pylori-infected mice models and human samples. Mass spectrometry, co-immunoprecipitation and laser confocal were performed to explore the underlying mechanism of CagA in activating NF-κB signaling.

Results

Compared with the CagA knockout stain, the activation of NF-κB signaling pathway by CagA contributed to elevated mRNA expression of TNF-α, IL-6, IL-8 and protein phosphorylation levels of p65 and IκBα. Through binding with SHARPIN in vitro and in vivo, CagA promoted the Met1 linear ubiquitination of NEMO and the NF-κB activation. CagA-SHARPIN interaction increased SHARPIN binding to NEMO and upregulated the phosphorylation level of SHARPIN. While silencing SHARPIN partially represses the levels of proteins involved in NF-κB signaling of gastric cancer cells.

Conclusion

These findings demonstrated that Met1-ubiquitination of NEMO by CagA-SHARPIN interaction regulates the activation of NF-κB signaling, revealing a novel mechanism for H.pylori-induced activation of NF-κB inflammatory signaling in gastric cancer cells. Thus, targeting CagA-SHARPIN interaction may provide a new strategy to restrain NF-κB signaling and an important perspective for the treatment of gastric cancer.

Introduction of ketogenic diet in epilepsy treatment: the impact on blood glucose levels

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Introduction

The ketogenic diet (KD) is a diet low in carbohydrates and rich in fats which has long been used to treat refractory epilepsy. The metabolic changes related to the diet can decrease the seizure frequency but at the same time may increase the risk of hypoglycemia (glycemia < 3,5mmol/l), especially during the first days. The study focused on the impact of KD initiation on glycemia in non-diabetic patients with refractory epilepsy.

Materials & Methods

The subjects were 10 paediatric patients (6 boys, mean age 6,1±2,4 years, mean BMI 15,4±1,8 kg/m2) treated for intractable epilepsy. Continuous glucose monitoring system (CGM) Dexcom G6 (generating glycemic value every 5 minutes) was used. The system was blinded, the patients and their relatives could not see the results in the real time. Patients started on a regular diet in the first 36 hours of monitoring, followed by an increase in lipids intake and a gradual reduction of carbohydrates (relations 1:1,2:1,3:1, 3,5:1). We analysed changes in glycemia during fat-to-carbohydrates ratio changes when switching to KD using a generalized linear model approach.

Results

The mean monitored time per person was 6 days, 10 hours and 44 minutes. The mean±SD glycemia for regular diet was 4,84±0,20 mmol/l, for the carbohydrates/fat ratio of 1:1 it was 4,03±0,16, for the ratio of 1:2 it was 3,57±0,10, for the ratio 1:3 it was 3,39±0,13 and for the final ratio of 1:3,5 it was 2,79±0,06 mmol/l (p< 0,001). The portions of time spent in glycemia ≤3,5 mmol/l (≤2,5 mmol/l respectively) were: on normal diet 0,88% (0,31%) of the monitored period, during 1:1 diet ratio 1,92% (0,95%), during 1:2 ratio 3,18% (1,02%), and during 1:3 and 1:3,5 ratios 13,64% (2,36%) of the monitored time (P<0,05). Patients did not report any symptoms of hypoglycemia.

Conclusion

Our results show a consistent trend of decreasing glycemic values with increasing ratios in KD. Conjointly, the risk of hypoglycemia (<3,5 mmol/l) as well as severe hypoglycemia (<2,5 mmol/l) increased markedly, thus signifying that blood glucose levels should be monitored carefully in epilepsy patients during the first days of KD.

Poster Sessions I

Oncology I

Presenters:
Farrokhi, P. (Pegah)
Ellaithy, A.S.E (Asmaa)
Rengganaten, V (Vimalan) Mr
WETHERELL MATEU, G.W.M (GUILLEM)
Ravendran, K. (Kapilraj)
Bartha, A. (Aron) dr.
Yaghoubi, A. (Atieh) Dr

Anticancer activity of Pseudomonas aeruginosa derived peptide with iRGD in treatment of colon cancer

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Introduction

As the conventional therapeutic approaches were not completely successful in the treatment of colon cancer, there is still a need for finding the most efficient therapeutic agents to achieve better outcomes with the least side effects. Currently, using bacteria as the therapeutic agent for cancer has aroused attention in medical and pharmaceutical studies. Here we investigated the anticancer activity of Azurin-p28 that was derived from Pseudomonas aeruginosa alone or in combination with tumor-homing peptide iRGD and 5-Fluorouracil (5FU) on colon cancer cell lines (CT26 and HT29) and xenograft models of colon cancer.

Materials & Methods

Inhibitory effect of bacterial peptide (p28) with or without iRGD/5FU was assessed in two colon cancer cell lines (CT26 and HT29) and the normal fibroblast cell line (L929), as well as the xenograft animal model of colon cancer. The effect of p28 alone or along with iRGD/5FU on cell migration, apoptotic activity, and cell cycle of cell lines were assessed. The expression levels of the pro-and anti-apoptotic gene (BAX and BCL2), tumor suppressor gene [(p53 and collagen type I α 1 (COL1A1), collagen type I α 2 (COL1A2)], monocyte chemoattractant protein 1 (MCP-1), and interleukin-1 (IL1) β were investigated by qRT-PCR.

Results

Our results demonstrated that co-therapy of the bacterial peptide (p28) with iRGD and 5FU increased the intracellular level of p53 that upregulates the pro-apoptotic gene BAX and downregulates the anti-apoptotic gene BCL2. Moreover, this bacterial peptide blocks the cell cycle progression in G2/M. Co-administration of p28 with iRGD and 5FU significantly reduced the size and weight of the tumors which also significantly increased necrosis and decreased fibrotic area in the tumor tissues. Furthermore, this bacterial peptide disrupts the oxidant/antioxidant balance.

Conclusion

It seems that p28 can be used as a novel therapeutic approach in the treatment of colon cancer that is able to enhance anti-tumor effects of 5FU as a conventional chemotherapeutic agent.

A proteome based AI algorithm for the differentiation of normal and malignant kidney tissues

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Introduction

Proper diagnosis has the utmost importance in the treatment of clear cell Renal Cell Carcinoma (ccRCC). Novel methods can assist during the diagnostical process to differentiate normal and tumor tissues. We aimed to develop an AI-based model capable to differentiate between normal kidney and ccRCC tissue using a specific protein panel.

Materials & Methods

Using in silico discovery datasets of patients with paired normal tissue samples from gene array and RNA-Seq data repositories, we uncovered the top genes over-expressed in ccRCC. We collected surgically resected ccRCC specimens and employed RNA sequencing of the pathologically validated ccRCC patients' tissue sample pairs to validate the strongest genes. The differential expression was then evaluated at the protein level using targeted mass spectrometry (MS). Finally, a support vector machine-based classification algorithm using the protein-level data was set up.

Results

We assembled a database of 558 renal tissue samples from NCBI GEO and TCGA and used these to uncover the top 30 genes with higher expression in ccRCC which were then further validated in the Semmelweis cohort of 162 renal tumor and normal tissue samples. Mass spectrometry further validated the differential protein abundance of these proteins from the same patient cohort. Using the MS based protein abundance values of the best performing proteins, the support vector machine-based model was capable to discriminate ccRCC with 0.95 sensitivity and 1 specificity.

Conclusion

By employing our model one can perform a differentiation between normal and malignant kidney tissues, which could provide valuable information in the everyday clinical setting.

Differences in epidemiology, biology and survival of patients with invasive ductal and invasive lobular breast cancer in Bulgaria

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Introduction

Invasive lobular breast cancer (ILC) originates from the breast lobules and shows different growth patterns and clinical behaviour compared to the most common invasive ductal breast cancer, non-special type (IDC). The aim of our study was to compare the epidemiology, biology and 5-year overall survival (OS) of patients with ILC and IDC. We also analysed the impact of chemotherapy on OS of hormonal positive (HR+) and HER2- patients.

Materials & Methods

This is a retrospective population wide observational study of 4056 cases registered with breast cancer in the Bulgarian National Cancer Registry (BNCR) in 2013. 155 cases were excluded from the study (122 registered after death and 33 patients with bilateral cancer). From 3901 patients, 458 (11.7%) had ILC, 2763 (70.8%) - IDC and 680 (17.5%) - other pathological subtypes. Patients were divided into 4 groups according to their receptor status: HR+HER2-, HR+HER2+, HR-HER2+ and HR-HER2-. The receptor status was unknown in 1562 (39.9%) patients. We used the Kaplan-Meier curve with log rank, ANOVA and chi-squared tests to estimate the statistical significance.

Results

Patients diagnosed with ILC were significantly older compared to patients with IDC (mean 62.4 vs 60.3, p-value=0.004). 44% of patients from both histological types were diagnosed in stage II. Overall, the 5 years observed OS was better for patients with IDC than ILC (68.3% vs 63.1%, p-value=0.029) The most prevalence receptor status subtype among both types was HR+HER2-, which represented 71.2% of patients with ILC and 65.8% of patients with IDC respectively. We investigated the additional benefit of adding chemotherapy to stage II patients (1-3 positive lymph nodes or tumor>5cm, but N0) and HR+HER2- tumors, where currently treatment decision should be made based on genetic testing. Chemotherapy was applied in 64.8% of ILC cases vs 56.7% of IDC patients. In patients with both histological types, adding chemotherapy to the treatment did not significantly affect the 5-year OS.

Conclusion

In our study ILC had a worse 5-year OS compared to IDC. Overall chemotherapy is still applied to more than half of patients with HR+HER2- tumors, but chemotherapy does not add survival benefit for both patients with IDC and ILC.

Impact of adjuvant chemoradiotherapy on survival outcome compared to other treatment modalities for node positive cervical cancer

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Introduction

cervical cancer is the fourth most common cancer among females. About 99% of cervical cancer is a complication of human papilloma viruses (HPV), a common sexually transmitted infection. Surgery, Chemotherapy and radiotherapy are different treatment options. Although many studies evaluated the efficacy of combined regimens, adjuvant chemoradiotherapy compared to other treatment regimens for node positive cervical cancer, remains controversial. This study aim is to evaluate the survival outcome of adjuvant chemoradiotherapy compared to other regimens in node positive cervical cancer patients.

Materials & Methods

we used Surveillance, Epidemiology, and End Results (SEER) database to extract the data of 3146 patients with node positive cervical cancer diagnosed from 2000 to 2018 . The sample included who were treated with different approaches: adjuvant chemoradiotherapy, adjuvant radiotherapy, surgery without adjuvant treatment , adjuvant chemotherapy and chemoradiotherapy alone .

Results

The 5-year disease free survival DFS is better in patients treated with adjuvant chemoradiotherapy compared to adjuvant radiotherapy, surgery, chemoradiotherapy alone and adjuvant chemotherapy(65%,57.5%,56%,47%,42.5% respectively; p-value <0.00) and the overall 5-year survival outcome was higher for adjuvant chemoradiotherapy compared to adjuvant radiotherapy, surgery, chemoradiotherapy alone and adjuvant chemotherapy (64.8%,57%,55%,46.3%,42.2%; P-value <0.00) . The number of positive lymph nodes, type and age significantly affect the overall survival (P-value <0.00)

Conclusion

Adjuvant chemoradiotherapy has better 5-year Disease Free Survival (DFS) and better overall 5-year survival outcome compared to other treatment modalities . These results highlighted adjuvant chemoradiotherapy as the treatment of choice for node positive cervical cancer . Further evaluation is necessary to determine the best regimen for each patient.

Systematic review and meta-analysis on the adverse events of bortezomib in treatment of relapsed/refractory mantle cell lymphoma

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Introduction

Mantle cell lymphoma is a rare subtype of non-Hodgkin lymphoma that presents with aggressive clinical presentation and poor prognosis which has not established treatment in a relapsed/refractory setting. Studies on several drug categories have shown that the proteasome inhibitor bortezomib is effective in the treatment of MCL patients with relapsed or refractory MCL and improves survival and response to treatment. The efficacy of bortezomib has been investigated in different ways, including both as a single agent or in combination with other drugs, with results showing 95% response to treatment in combination therapy and 46% response in single-agent therapy, though the toxicity profile needs to be evaluated and weighed against its efficacy. The purpose of this study is to provide a comprehensive systematic review and meta-analysis on the safety of bortezomib as a single agent or in combination with other drugs as a treatment for relapsed/refractory mantle cell lymphoma.

Materials & Methods

A systematic search was conducted in the following electronic databases: PubMed, Cochrane CENTRAL, Embase, Web of Knowledge, and Scopus, using the search terms Bortezomib, protease inhibitor, MCL, and Bortezomib. Following that, a team of independent reviewers selected relevant studies and extracted the data. The data were analyzed using STATA software to perform a meta-analysis to evaluate the safety profile of bortezomib.

Results

Five studies were included out of the total of 2571 studies. According to the findings of the analysis, using bortezomib was associated with increasing grade 3 or higher of thrombocytopenia (RR=0.234, 95%CI= 0.188-0.288), fatigue(RR=0.143, 95%CI= 0.101-0.200), peripheral neuropathy (RR=0.125, 95%CI= 0.095-0.163), and neutropenia (RR=0306, 95%CI= 0.252-0.366).

Conclusion

While several studies have shown bortezomib is efficacious as a single agent or in combination with other drugs to treat relapsed/refractory mantle cell lymphoma, the safety profile should be scrutinized carefully along with the toxicity in comparison with the effectiveness in the treatment plan.

Chip microfluidic bubble cell sorter for CTC isolation and characterization

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Introduction

Circulating tumor cells (CTCs) are the ones causing metastases and relapse in cancer patients. In melanoma, CTC research remains a challenge due to their heterogeneity and rarity (0.05%) present in blood samples.

A genetically engineered mouse model (GEMM) expressing tdTomato melanoma cells has been developed, allowing us to trace the melanoma lineage to the bloodstream (CTCs). Together with Fluorescent Activated Cell Sorting (FACS), it could be a great tool to isolate CTCs based on a fluorescent reporter. Traditional FACS technologies perform poorly in CTC isolation. Moreover, they cause sorter induced cell stress (SICS), hampering further downstream analysis.

IMEC has proposed a FACS technology which could overcome the major limitations. It works as a microfluidic sorter, using micro vapor bubbles to sort cells more gently compared to traditional FACS. In this study we investigated its performance for the isolation of CTCs and optimized it to minimize SICS and improve RNA quality.

Materials & Methods

Spike-in experiments of established melanoma cell lines with stable fluorescence reporter expression (NRAS dsRED+) against mice PBMCs was done as a first model, mimicking CTC isolation in a blood sample. Next, using the developed GEMM, tdTomato+ cells (CTCs) need to be isolated.
SICS and RNA quality was studied by comparing sorted samples to unsorted controls.

Results

PBMC samples with a spike-in of 15% NRAS dsRED+ cells, were sorted with an efficiency of 98.09%, recovery of 97.89% and yield of 87.66%. Cell Viability assays showed a 60% viability in the sorted sample, compared to 90% in the unsorted. RNA quality assays showed similar RNA quality to the controls, with an average RIN of 9/10.
Finally, isolation of reporter positive (tdTomato+) cells from the GEMM model was successfully accomplished.

Conclusion

First steps, testing the microfluidic sorter for reporter positive CTCs isolation, decreased SICS and improved RNA quality has been done. Further spike experiments at lower percentages need to be tested. Following steps will be to test the same parameters using the developed GEMM, as a closer model to CTCs in humans.

Through the isolation of CTCs together with sqRNAseq, common biomarkers could be identified, coming closer to melanoma CTC characterization for clinical applications.

A molecular circuitry network of circular RNA-microRNA-mRNA regulating colorectal cancer stemness properties

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Introduction

The existence of colorectal cancer (CRC) stem cell (CrCSC) population has warranted further investigation into the underlying mechanisms that result in cancer recurrence. Re-differentiation therapy of CrCSC population has been a focus as potential eradication therapy by targeting the molecular signatures that govern the stem-cell like features. The discovery of a novel epigenetic regulators knowns as circular RNAs have been shown to be involved in various hallmarks of cancers. The exact involvement of circular RNAs in mediating stemness in colorectal cancer population remains to be investigated.

Materials & Methods

Genome-wide circular RNA sequencing to establish the differential expression profile in colorectal cancer stem cell population was performed. Through deductive bioinformatic analysis, candidate circular RNAs were narrowed using tools such as CircInteractome and Cytoscape. To validate the bioinformatics prediction, qRT-PCR was performed. RNA FISH assays were used to visualize the candiate circular RNA. Autocatalytic self-splicing introns were used in generating cell-free self-circularizing RNA. RNA-targeting CRISPR Cas13D system was used to induce circular RNA knockdown.

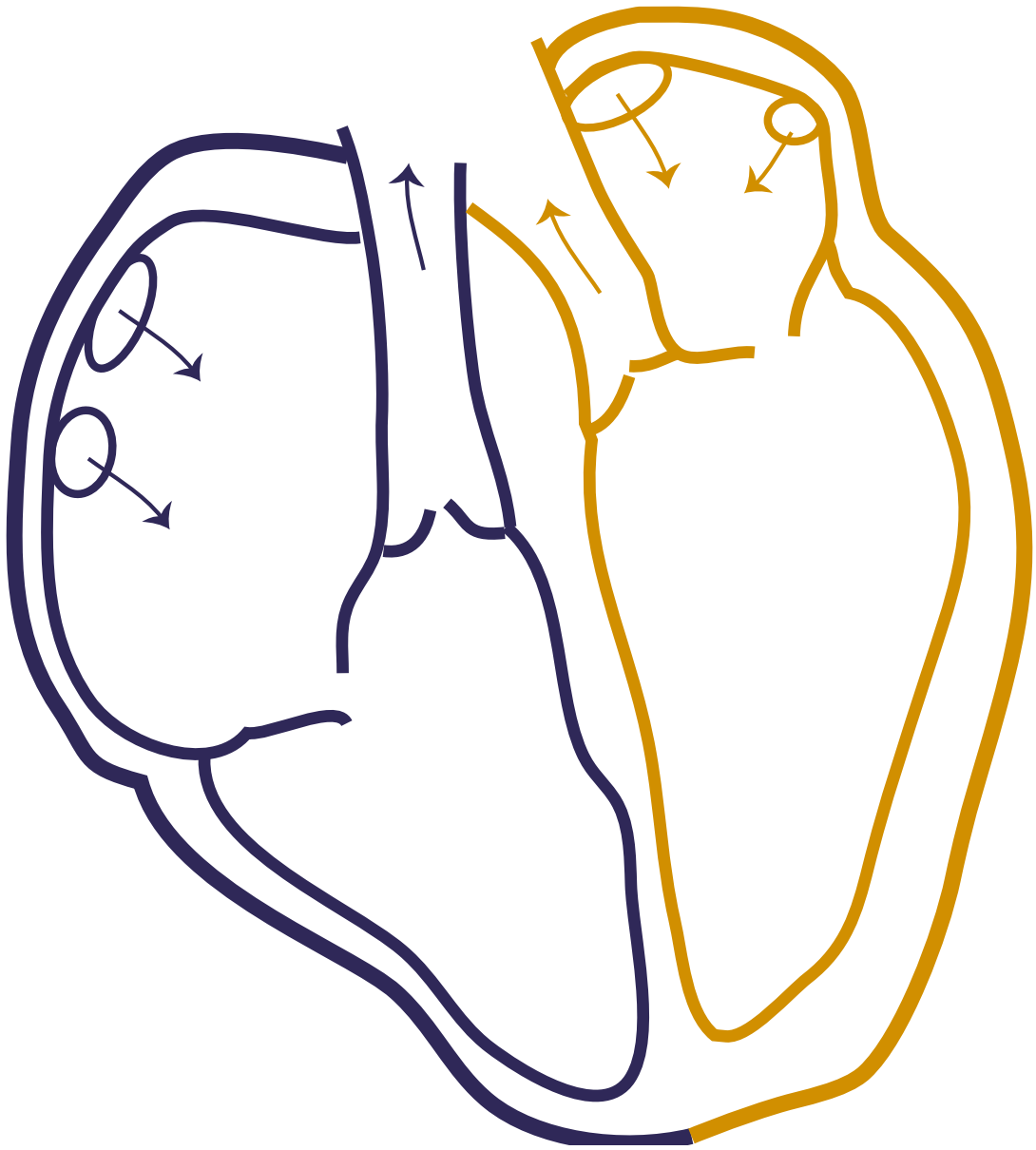
Results

Circular RNA sequencing revealed a differential expression profile of circular RNA in the CrCSC population. Of which, an epigenetic-mediated regulatory network of circRNAs-microRNAs-mRNAs that regulates pluripotency pathways in CrCSC population was identified. Hsa_circ_0082096 and hsa_circ_0066631 were predicted as candidate circular RNAs that are essential in the stemness regulation of CrCSC population. Further investigation revealed hsa_circ_0082096 is consistently upregulated in passage-dependent manner of CrCSC enrichment. Higher expression levels of hsa_circ_0082096 were detected in the cancerous region of CRC patient tissues. Accounting for the high specificity and efficiency, CRISPR Cas13D system was used to establish hsa_circ_0082096 knockdown cells by targeting the unique backsplice-junction. The loss-of-function assay revealed a reduced proliferation and colony-forming ability of CRC cells. Furthermore, flowcytometry analysis showed a reduced expression levels of CSC markers, CD44 and CD133. At the molecular level, hsa_circ_0082096 knockdown reduced the expression levels of the predicted pluripotency genes, ACVR1C and FZD3 by sponging microRNAs; miR-140-3p, miR-382 and miR-579, and other core pluripotency regulators, OCT4, SOX2 and NANOG.

Conclusion

Taken together, the data indicates that hsa_circ_0082096 could be a potent regulator of stemness in CRC population, suggesting a potential target for therapeutic to eliminate CrCSC population.

Cardiology I



Presenters:
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Handheld echocardiographic screening for rheumatic heart disease in rural South Kordofan, Sudan by junior medicals: Supporting task shifting for control of a serious disease

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Introduction

Rheumatic Heart Disease (RHD) is a serious condition precipitated by the heart valves damage associated with acute rheumatic fever (ARF) that is a sequelae of group A streptococcal infection. Early identification of the subclinical valvular insult and the use of benzathine penicillin prophylaxis constitute a mainstay for disease control. Fortunately, The emergence of echocardiography (echo) and the availability of portable and handheld echo (HHE) machines that had proven high sensitivity, resulted in a significant increase in the RHD detection rates with a potential for treatment of the early stage of the disease.

Materials & Methods

A cross-sectional study was conducted in South Kordofan State, Sudan (as part of a medical convoy organized by Khartoum Medical Students Association). A team of shortly trained medical students and newly graduated doctors conducted a handheld echocardiographic screening using a simplified protocol. All suspected cases were recorded and reviewed later by a senior pediatric cardiologist. Demographic and clinical features of screened subjects were studied. Data analysis was performed using the Statistical Package for Services and Solutions (SPSS 25). Descriptive statistics were presented as "number (%)" or "mean ± SD". RHD prevalence was expressed as cases per 1000, and Chi-Square test/Fisher's Exact test was used to compare RHD findings between different groups.

Results

Echocardiographic screening quality was acceptable in 93% of studies. The disease frequency was found to be 50 per 1000. Out of 452 screened subjects (age 10-25 years), 23 were found to have RHD, with a male to female ratio of 1:1.5. The disease was mild in 70% and moderate or involving 2 valves in 30% of patients. Patients were contacted, advised to start penicillin prophylaxis and referred to cardiologists. Risk factors for the disease included father's occupation and village of residence.

Conclusion

Shortly trained junior medicals can assist in RHD echocardiographic surveillance in remote areas. South Kordofan state is highly endemic for RHD and a control program needs to be implemented. Handheld echocardiography is of value for early detection and management.

Proteomic analysis of epicardial effusion collected by a novel device ASD in myocardial infarction

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Introduction

The epicardium is a layer of mesothelial tissue surrounding the vertebrate heart that plays a critical role in cardiac development and repair. However, it is not clear how the epicardium initiates the repair process after myocardial ischemic injury. Therefore, we performed the first proteomic analysis of rat epicardial exudate.

Materials & Methods

Male SD rats were divided into sham operation group and acute myocardial infarction group, and the left anterior descending branch of the coronary artery was ligated to establish a rat permanent acute myocardial infarction model. An active hydraulic ventricular apposition support delivery system (ASD) was implanted and confirmed to be adsorbed to the epicardium. Epicardial exudate was collected within 6 h of early acute infarction, and samples were pretreated for TMT labeled quantitative proteomics analysis.

Results

A total of 1292 proteins were identified. Among them, 77 proteins were upregulated and 49 proteins were decreased in expression. Bioinformatics analysis showed that these differentially expressed proteins were mainly involved in precursor metabolite and energy production, regulation of intracellular protein transport, response to peptides, protein folding, post-translational protein phosphorylation, regulation of neuronal projection development, NF-kB signaling pathway, Hippo signaling pathway, HIF-1 signaling pathway, estrogen signaling pathway, TGF-beta signaling pathway, etc. We also found that the levels of acute inflammatory response and complement response were reduced in the early 6 h of acute infarction. Although inhibition of complement response helped to reduce infarct size, this was contrary to previous studies and may be related to the negative regulation of inflammation. We also found that Trim72, Sirt5 and Prdx6 of the upregulated differential proteins have potential targets for myocardial repair.

Conclusion

In conclusion, we used ASD to explore the proteomic changes of epicardial exudate in the early stage of acute myocardial infarction for the first time, which could help to further clarify the regulatory network of epicardial repair and is expected to lead to cardiac repair by regulating the regenerative potential of the epicardium

A cross sectional study of effects of organophosphorus pesticides on cardio respiratory parameters among farm labourers of North Maharashtra.

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Introduction

The increasing use of organophosphorus pesticides in farming has increased the yield of farm produce all over the world but improper handling of pesticides can cause serious health problems. In this research, we aimed to assess the cardio respiratory parameters of subjects exposed to pesticides as compared to those who were not. The study also aims to promote the use of Personal Protective Equipment.

Materials & Methods

A total of 99 subjects in each group, case and control, were taken according to sample size calculation. The case group had subjects exposed to organophosphorus pesticides for at least 6 hours a day since at least 6 months. The control group had subjects without OP exposure. Individuals with genetic disorder, Chronic Obstructive Pulmonary Disease, substance abuse, diabetes mellitus, thyroid disorder etc. were excluded. The investigations performed were Peak Expiratory Flow Rate (PEFR), Vital Capacity (VC), Timed Vital Capacity (TVC), Heart Rate (HR), Blood Pressure (BP) and the mean values of both groups were compared using unpaired t- test.

Results

Significant difference (p<0.05) in Forced Expiratory Volume 1 (FEV1), FEV1/FVC, PEFR, MVV, was observed between the cases and the controls. The Mean Forced Vital Capacity (FVC), in the cases (3.0723) is slightly lower than that of the controls (3.2615). The Mean FEV1 in the cases (2.6713) is lower than that of the controls (3.1002). The FEV1/FVC ratio in cases (82.3731) is lower than that of the controls (94.7041). The Mean PEFR in cases (5.9639) is lower than that of the controls (7.6078). The Mean MVV in cases (93.9495) is lower than that of controls (123.5455). Systolic blood pressure and pulse rate shows significant difference in cases and controls.

Conclusion

The FEV1, FEV1/FVC ratio, PEFR, MVV are significantly reduced (p<0.05) in cases as compared to controls. Systolic blood pressure and pulse rate shows significant difference in cases as compared to controls. Thus the study helps to identify significant differences in cardio respiratory parameters in farmers exposed to pesticides as compared to the unexposed control group.

Limb remote ischemic preconditioning in rats: discrepancy between meta-analysis and a three-centre in vivo study

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Introduction

Despite promising preclinical results on cardioprotection by remote ischemic preconditioning (RIPC), multicentre clinical trials show no reduction in infarct size. This translational gap might be due to unknown confounding factors and a lack of sufficiently reported, robust in vivo preclinical proof-of-concept studies. Therefore, here we performed randomized, blinded in vivo studies in three study centres using the most often reported methodological settings, as well as a systematic review and meta-analysis of RIPC studies.

Materials & Methods

Male Wistar rats were subjected to 20 to 45 min cardiac ischemia followed by 120 min reperfusion with or without preceding RIPC by 3 or 4×5-5 min occlusion/reperfusion of one or two femoral vessels by clamping, tourniquet, or pressure cuff. Systematic review and meta-analysis focusing on in vivo rat models of myocardial ischemia/reperfusion injury with limb RIPC were performed.

Results

RIPC did not reduce infarct size, microvascular obstruction, or arrhythmias at any study centres. Our systematic review and meta-analysis showed that RIPC reduces infarct size by 21% on average; however, a tendency for publication bias towards positive results was found. In addition, the systematic review showed methodological heterogeneity and insufficient reporting quality in a high proportion of studies.

Conclusion

We report for the first time the lack of cardioprotection by RIPC in rats, assessed in individually randomized, blinded in vivo studies, involving three study centres. Systematic review and meta-analysis revealed that the under-publication of neutral studies is plausible. Methodological

confounding factors leading to the discrepancy between meta-analysis and the present studies cannot be identified; insufficient reporting quality, heterogeneity of the applied settings, and selection bias against studies with neutral outcomes may contribute to this discrepancy. More preclinical studies with adequate quality control, together with the publication of neutral studies, are required to support the development of clinically translatable cardioprotective interventions.

New, non-invasive computational fluid dynamic methods in the prediction of coronary artery disease progression

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Introduction

To date, fractional flow reserve (FFR) is the gold standard procedure for assessing the condition of coronary arteries. Although the pathomechanism of coronary stenosis and plaque progression is a well-known and intensively researched area, the significance of patient-specific characteristics and complex blood flow parameters are less well known. Aim: We aimed to compare the pressure, velocity, and flow values measured by simulation with the invasively measured FFR and coronary flow reserve (CFR) values in patients.

Materials & Methods

Models were retrospectively analyzed from angiograms of 16 patients who underwent elective coronarography. Four groups were formed for inflow and outflow profiles with transient flow simulation 1: pressure-pressure profile; 2: velocity-pressure profile with vascular phase shift; 3: modified coronary velocity-pressure profile; 4: corrected flow-pressure profile. A constant pressure, velocity model was used as a pilot study.

Results

In the stationary simulation, a deviation of 5.9 ± 0.07 FFR and 11.5 ± 0.101% CFR compared to the measured / real values was observed (this showed the best approximation, then the boundary profiles of our transient measurements were examined. In the first group a significant oscillation >100% deviations was seen, in group 2: 10.91% ± 0.091% FFR, 73.41 ± 0.549%, significant CFR deviation, in group 3: 6.93% ± 4.74% FFR, 98.08% ± 49.85% CFR, in group 4: 13.25% ± 5.02% FFR 15.29% ± 8.13% CFR was observed compared to the measured values (the latter shows significantly close reliability, the vasodilated vessels can be attributed to the pressure increase observed during the simulation, which is characteristic of the model, as exactly the appropriate elasticity cannot be fully set in the simulation).

Conclusion

The adjustment system is suitable for non-invasive CFR measurement in coronary arteries. Additional flow influencing parameters can be investigated using CFD simulation. Parameters specific to stenotic vascular sections can be used in long-term prognostic and risk estimation systems.

Demographic Features of First Acute Myocardial Infarction in Iran from 2012–2020: A Retrospective Cross-Sectional Study

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Introduction

Cardiovascular disease has been the leading cause of mortality worldwide for over 25 years. The most frequent manifestation of cardiovascular disease is coronary heart disease, commonly manifested as acute myocardial infarction (AMI). Several studies have documented the role of different risk factors in the distribution of AMI. However, information on trends regarding age and sex distribution in first AMI patients is limited. So, this research was designed to study the demographic features of first AMI patients in Iran.

Materials & Methods

This was a retrospective cross-sectional study conducted in a tertiary hospital in north of Iran. All patients with first AMI from 2012 to 2020 were included in this research. Demographic features and past medical history were collected from Medical Record System of the hospital. SPSS Version 24 was used to analyze the data and p<0.05 was considered statistically significant.

Results

In this study, 1621 patients (male = 75%) were included and the mean age was 58.47± 10.14 years. Interestingly, the percent of patients with first AMI increased slightly from 8% (2012) to 13.85% (2020). However, the mean age of patients increased from 57.6 ±6.5 to 59.2± 9.2 years from 2012 to 2020, respectively (p<0.05). Also, the first AMI was more likely to occur in 60 to 70 years old patients (p<0.05). In addition, it was revealed that the first AMI is considerably lower in women than in men (p<0.05). There was no statistically significant difference in AMI risk factors including smoking, diabetes, hypertension, and obesity frequency during study period.

Conclusion

This study showed an increased incidence of first AMI in 60 to 70 years old patients in north of Iran. Management of cardiovascular risk factors in high-risk patients is necessary to reduce the mortality and morbidity. The elderly patients are at higher risk for recurrent MI and should be managed closely beyond the first year.

Estimation of change and predictive factors of improvement in diastolic function after CABG surgery: a single-center experience in North Macedonia

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Introduction

Although diastolic dysfunction is a common finding in patients with coronary artery disease, its severity is often ignored among clinicians. This study aims to evaluate the change in diastolic function and to determine the role of echocardiographic parameters as predictors of improvement in diastolic function after coronary artery bypass graft (CABG) surgery.

Materials & Methods

91 patients indicated for CABG surgery were enrolled in this prospective cross-sectional study. Echocardiographic evaluation was performed by measurement of the early (E) and late (A) diastolic filling velocity, E/A ratio and DT, the length of isovolumetric relaxation time (IVRT), as well as pulmonary venous flow assessment (systolic and diastolic velocity - S, D, S/D, reversal wave-Ar and Ar/A ratio). Also, the early and late velocities of the mitral annulus (e' and a') were measured by tissue Doppler (TDI) and E/e' ratio was accessed as a parameter.

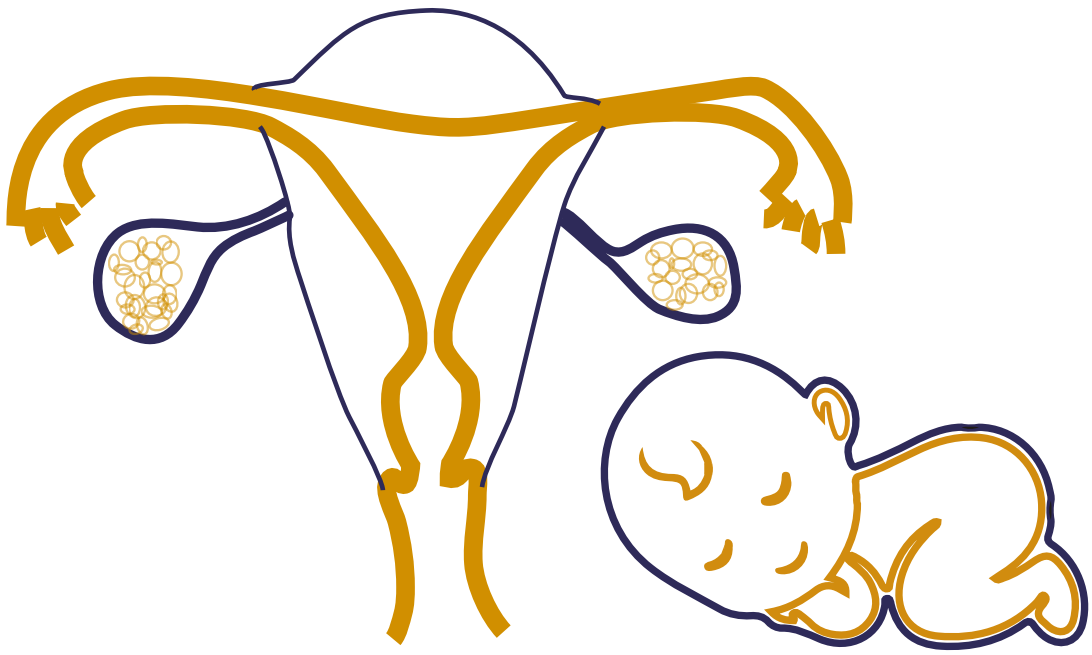
Results

On preoperative evaluation, our patients, as a group, presented with moderate diastolic dysfunction. Both E and DT parameters reduced but not significantly (73.3±21.8 cm/s and 207.8±60.7 ms preoperatively, 79.1±25.4 cm/s and 193.6±64.2 ms postoperatively, respectively), E/A and IVRT slightly increased postoperatively (p values of 0.150 and 0.893, respectively) and in terms of pulmonary venous flow, S/D changed from 1.3±0.5 before to 1.1±0.4 after CABG (p=0.006). Despite the statistically significant increase in e' values (p=0.0001) and decrease in E/e' ratio (p=0.002) after CABG, diastolic function remained moderately impaired. In terms of echocardiographic variables who can predict the diastolic function after surgery, in linear regression analysis, for each unit decrease in interventricular septum (IVS) thickness, the E/e' ratio after CABG decreases by 0.3% (95%Cl 0.004-0.728, p=0.048). For each unit increase in PALS, the E/e' ratio decreases by 0,1% (95%CI -,244-(-0,044), p=0,004) and for each unit of reduction of number of segments with LS<13%, the E/e' ratio after CABG decreases by 0.2% (95% CI 0.026–0.381, p = 0.025).

Conclusion

In our study, postoperatively, there was an improvement in many individual parameters that directly/indirectly indicate diastolic dysfunction, but only TDI measurements were statistically significant. Longer follow-up studies of a larger group of patients referred for CABG surgery are required.

Obstetrics and Paediatrics



Presenters:
Rohm, M.L. (Marie-Luise)
Sokolnyk, I. (Iryna) student
Kairgaliyev, I.
Dourado, D.S.D (Danilo)
Interior, J.S.I (Jasmine)
Khaity, A.M.M.K. (Abdulrhman)
Guerra-Silva, C.R. (Catalina)

Effects of martial arts training on executive function performance and on attention deficit/hyperactivity disorder symptoms in children aged nine to 12 years.

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Introduction

Attention-Deficit / Hyperactivity Disorder (ADHD) is a highly prevalent neurodevelopmental disorder among children and adolescents. Studies suggest that skills acquired in martial arts can favor the development of executive functions (EFs), identified as one of the main factors related to the difficulties of ADHD patients and determinants in its symptoms reduction when stimulated in interventions. This study aimed to investigate the effects of martial arts on EFs, ADHD symptoms, and quality of life.

Materials & Methods

In this context, 12 children (nine boys; three girls) diagnosed with ADHD, whose ages ranged from nine to 12 years, attended a martial arts program (32 sessions of 50 minutes each, twice a week for 16 weeks). Six instruments called Victoria Stroop Test, Digit Span Test, Corsi Block Tapping Test, Wisconsin Card Sorting Test, SNAP-IV, and PedsQL were administered three times (before, after, and 12 months after intervention) to assess inhibitory control, working memory, cognitive flexibility, ADHD symptoms, and quality of life.

Results

Statistically significant improvements were shown in inhibitory control (VST: card 1 - time p = 0.01 errors=0.83/ card 2-time p = 0.005 errors p=0.039 / card 3- time p = 0.002 errors p=0.009), cognitive flexibility (WCST: errors p = 0.009 / perseverative errors p=0.29/ failure to maintain set p=0.96/ categories completed p = 0.029) , visuospatial working memory (CBTT: forward p = 0.04/ backward p=0.31/ total p= 0.02), verbal working memory (DST: forward p=0.509/ backward p=0.964/ total p=0.784), quality of life (PedQL: Parents p= 0.001 / Children p = 0.03) and in ADHD symptoms (SNAP-IV: Parents-inattention p <0.001; hyperactivity / impulsivity p = 0.006; total p <0.001).

Conclusion

The results obtained are promising and show that martial arts can be considered an adjuvant treatment of the disorder. However, future studies addressing the theme are urgently needed.

Saffron Supplementation for Reduced Labor Duration in Term Pregnant Patients: A Systematic Review and Meta-Analysis of Randomized Clinical Trials

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Introduction

Prolonged labor or failure to progress is a common obstetric problem that brings about various maternal and fetal complications. Herbal preparations like saffron (pistil of Crocus sativus L.) have been historically utilized by midwives effectively in labor augmentation. But to date, strong evidence regarding its efficacy is still lacking. In this study, the efficacy of saffron supplementation in reducing the duration of labor among term pregnant patients, was assessed.

Materials & Methods

Randomized clinical trials published from 2000 onwards on the efficacy of saffron supplementation in decreasing labor duration among term pregnant patients of the reproductive age group with cephalic presentation, gestational age of ≥37 weeks, and low-risk pregnancy were reviewed. Primary outcomes measured were durations of the first and second stages of labor, Bishop score, and pain severity index. Secondary outcomes assessed were compliance rate and presence of adverse events. Subgroup analyses on type of intervention (saffron alone or with adjunct), parity of participants, and presence of uterine contractions were also performed.

Results

Five randomized controlled trials, all conducted in Iran, were selected from the initial 608 studies identified through electronic searches and other resources. Analyses revealed significant reduction in the duration of the first [MD -66.82, 95% CI (-95.32, -38.33), P<0.0001] and second [MD -18.53, 95% CI, (-18.63, -18.42) P <0.00001] stages of labor among pregnant women with saffron supplementation compared to placebo. Bishop score analysis showed that there was a significantly higher Bishop score after saffron supplementation [MD -1.16, 95% CI (-0.73, -1.59), P <0.00001]. Review of studies for pain severity index showed a lower pain intensity during labor with saffron supplementation compared to placebo. Compliance rate analysis showed no significant difference between the saffron supplementation group and placebo group [OR = 1.75, 95% CI (0.74, 4.11), P = 0.20]. Only one study reported the occurrence of adverse events (lethargy, palpitations, and nausea).

Conclusion

This study suggests the possible utility of saffron supplementation in reducing the first and second stages of labor, increasing the Bishop score, and lowering the pain intensity during the labor of term pregnant patients. However, evidence for its safety profile remains inadequate.

Retrospective analysis of postoperative complications after circumcision from 2010 to 2020 in Multidisciplinary Children City Hospital №2 (Nur-Sultan, Kazakhstan).

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Introduction

For many decades, circumcision has been one of the most common surgical procedures worldwide. To obtain satisfactory results after circumcision, this procedure requires many factors, one of the most important: technical skills and knowledge from a surgeon, proper equipment, lack of congenital malformation of the penis. In Kazakhstan, due to religious reasons, this procedure is often performed by non-medical workers, which could lead sometimes to unsatisfactory results. The study aimed to evaluate the incidence rate of postoperative complications after circumcision.

Materials & Methods

A retrospective analysis was conducted with patients, who primarily applied to our Multidisciplinary City Children Hospital №2 (MCCH) (Nur-Sultan, Kazakhstan) after poor post-circumcision results in the period from 2010 to 2020. Patients were sorted into groups by age, type of complication, the period when the procedure was done, sterile/nonsterile conditions where were performed.

Results

In total, in the period from 2010 to 2020 there were 443 postoperative cases registered. From this group, 48% had cicatricial phymosis (n=213), infection site occurred in 26% cases (n=26), penile adhesions had 10% (n=44), bleeding in 6% (n=27), buried penis had 4% (n=18), meatostenosis was in 3% (n=13), paraphymosis had 2% (n=9), redundant skin in 1% (n=4) of patients. In age group from 0 to 3 there were 21% of complications (n=93), half of the complications had age group from 4 to 6 years old- 51% of patients (n=226), age group “7-10” had 18% (n=78) of all complications. 33% (n=146) rate of complications occurred after they were performed in nonsterile conditions (at home, mosques, e t.c.).

Conclusion

In a 10-year period the most common complications after circumcision procedure were cicatricial phymosis, infection, penile adhesions. The most vulnerable was the age group from 4 to 6. The variability of the types of complications requires a detailed study of their causes, to develop algorithms for their prevention, as well as crucial to have discussions with religious representatives.

A novel mouse model for congenital adrenal hyperplasia offers new opportunities to test future treatment options

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Introduction

Congenital adrenal hyperplasia (CAH) is an autosomal recessive disease. In 95% of the cases, the cause are mutations in the human CYP21A2 gene resulting in 21-hydroxylase deficiency. They lead to a blocked steroidal pathway and dysregulation of the hypothalamic-pituitary-adrenal axis with an accumulation of adrenal steroid precursors like 17-hydroxyprogesterone, increased production of adrenal androgens, and on the other hand, a decreased mineralocorticoid and glucocorticoid synthesis. In this study, we generated and are currently characterizing a novel mouse model with an integrated point mutation p.Ile169Asn in the homologous Cyp21a1 mouse gen. The goal is to develop a novel 21-hydroxylase-knock-in mouse model for CAH with a milder phenotype to study novel therapeutics.

Materials & Methods

For the generation of the Cyp21a1Ile169Asn mouse strain, we utilized mouse embryonic stem cells and the CRISPR/Cas9 technique. Genotypes were determined by PCR and verified by sequencing. We will examine seven male and seven female homozygote mice compared to Cyp21a1 sex and age-matched WT. After birth, we monitor the health and behavior of the litters. We measure blood pressure, weight, steroid profile in blood and urine samples at different time points. At 20-22 weeks, we take final blood samples and sacrifice the mice for organ collection for histological analyses and RNA studies.

Results

We successfully established the Cyp21a1Ile169Asn mouse strain and got homozygous viable animals. At the current time point, the genotyping and health check of the litters is continuing. We have already collected blood samples and blood pressure data of eight homozygote mice and plan to continue the characterization. In June, we will be able to present partial results.

Conclusion

It is essential to establish preclinical models to investigate new medical treatment options like ACTH- or CRH-receptor antagonists. Complete characterization of this new murine 21-hydroxylase deficiency model will contribute to a better understanding of the human disorder CAH and facilitate the development of novel therapeutics.

The effect of music on pain and anxiety during cesarean delivery: A meta-analysis of 1513 patients.

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Introduction

Music therapy has become a trendy possible solution in many clinical conditions and surgical procedures. However, most previous studies have been shown conflicting findings regarding the efficacy of music in reducing pain, anxiety in women with cesarean delivery. Therefore, in this meta-analysis, we aimed to synthesize evidence class 1 about the beneficial effect of music on preoperative, intraoperative, and postoperative anxiety, pain, and vital signs in women undergoing cesarean section.

Materials & Methods

We searched PubMed, Cochrane Central, and Web of Science for relevant randomized controlled trials (RCTs). Data were extracted from eligible studies and pooled as standardized mean difference (SMD) or mean difference (MD) values in a meta-analysis model, using RevMan software.

Results

Thirteen RCTs were included in this meta-analysis with a total of 1513 patients. Our meta showed that music was superior to control in terms of overall anxiety score (SMD = - 0.26, 95% CI [- 0.39, - 0.14], p < 0.0001), postoperative pain (SMD = - 0.50, 95% CI [- 0.74, - 0.26], p < 0.0001), and the overall effect of diastolic blood pressure (DBP) (MD = -1.58, 95% CI [- 3.11, - 0.04], p = 0.04). The overall effect did not favor either of the two groups in terms of systolic blood pressure (SBP) and heart rate ((MD = - 1.87, 95% CI [-4.04, 0.30], p = 0.09), (MD = - 2.10, 95% CI [- 4.78, 0.58], p = 0.12); respectively).

Conclusion

Our analysis revealed that music has a beneficial effect on anxiety, pain, DBP, and intraoperative heart rate over control in patients with CS. However, the music did not differ significantly from placebo in preoperative anxiety, postoperative heart rate, as well as SBP. Therefore, the current evidence supports using music to alleviate the anxiety and pain of women during and post-cesarean sections. Future randomized controlled trials are recommended to confirm the efficacy of music in the preoperative period and vital signs among women undergoing cesarean section.

Pre-pregnancy maternal obesity reduces human umbilical vein endothelial cell proliferation requiring hydrogen sulfide and activator protein 1

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Introduction

Obesity in pregnancy associates with impaired foetoplacental vascular endothelial function and adverse neonatal outcomes. Several regulatory factors are involved; however, the obesity effect on intracellular pH (pHi) and proliferation of foetoplacental endothelium is unknown. We evaluated the role of hydrogen sulfide (H2S) and activator protein 1 (AP-1) in the pHi and cell proliferation in human umbilical vein endothelial cells (HUVECs).

Materials & Methods

HUVECs were isolated from full-term pregnancies (n = 3) of mothers with pre-pregnancy normal weight (NW) or obesity (OB), from UC-CHRISTUS Clinical Hospital, Chile. HUVECs were cultured in medium 199 plus sera up to passage 2 and incubated (12 h) with 100 µmol/L sodium hydrosulfide (NaHS, H2S donor), 1 µmol/L SR11302 (AP-1 inhibitor) or both. Cell confluence (CCf) and wound healing were assessed. The pHi was measured in cells loaded with a fluorescent pH-sensitive probe (BCECF-AM) and exposed to NH4Cl (20 mmol/L, 2 min). Basal and pHi recovery rate (dpHi/dt) were also quantified.

Results

CCf 80% was achieved on the 5th day in NW but 7th day in OB. Cells from OB showed lower proliferation than NW (final/initial wounded area ratio (f/i) 0.098 vs 0.49 for NW vs OB, respectively). NW cells proliferation was reduced by NaHS (f/i 0.21), SR11302 (f/i 0.25) or both (f/i 0.42). However, in OB cells it was increased by NaHS (f/i 0.09), or both molecules (f/i 0.19), but unaltered by SR11302. Basal pHi was lower in OB (7.19) compared with NW (7.23). NaHS, SR11302, and NaHS+SR11302 increased the basal pHi in both cell types. The dpHi/dt was lower in OB compared with NW (0.002 vs 0.003 pHi units/30s, respectively). NaHS, SR11302, and NaHS+SR11302 reduced the dpHi/dt in cells from NW. However, OB-reduced dpHi/dt was reversed by SR11392 and NaHS+SR11302 but unaltered by NaHS.

Conclusion

Pre-pregnancy maternal obesity-reduced HUVECs proliferation may result from lower H2S generation, via a H+ efflux modulation independent phenomenon, requiring AP-1 activity. In cells from pre-pregnancy maternal NW, H2S and AP-1 are needed to reduce cell proliferation which might involve lower H+ efflux. Differential action of H2S on proliferation is likely in HUVECs from mothers with pre-pregnancy NW or OB. (Support: FONDECYT 1190316, U Talca and UMCG PhD fellowships, VRI and DIDEMUC PUC fellowships).

The content of alpha-defensins in blood of children with ulcer disease

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Introduction

Biologically active endogenous peptides, despite the fact that they belong to category of short-living molecules (rapidly undergo enzymatic cleavage by proteases), are able to work in a coordinated cascade of cellular/intercellular and molecular/intermolecular communications, as their synthesis in human body is constant and does not lead to the formation of microbial resistance, characterized by both selectivity of action and atoxicity.

The aim was to determine the content of alpha-defensins in blood of patients with ulcer disease.

Materials & Methods

Comprehensive clinical-paraclinical and instrumental examination (fibrogastroduodenoscopy with biopsy of the gastric and duodenal mucosa, Ph-metry, ultrasound, tests for Helicobacter pylori (H.pylori)) was conducted in 46 children aged 10-18 years, with ulcer disease (UD), which were divided into two groups: I (n = 36) - children with H.pylori-associated UD and II (n = 10) - H.pylori-non-associated UD. The control group consisted of 35 healthy volunteers, representative by gender and age. Enzyme-linked immunosorbent assay was used to examine the content of antimicrobial peptides of alpha-defensins 1-3 (HNP) in the serum of children. Statistical processing of the obtained results was performed using "Statistica 6.0".

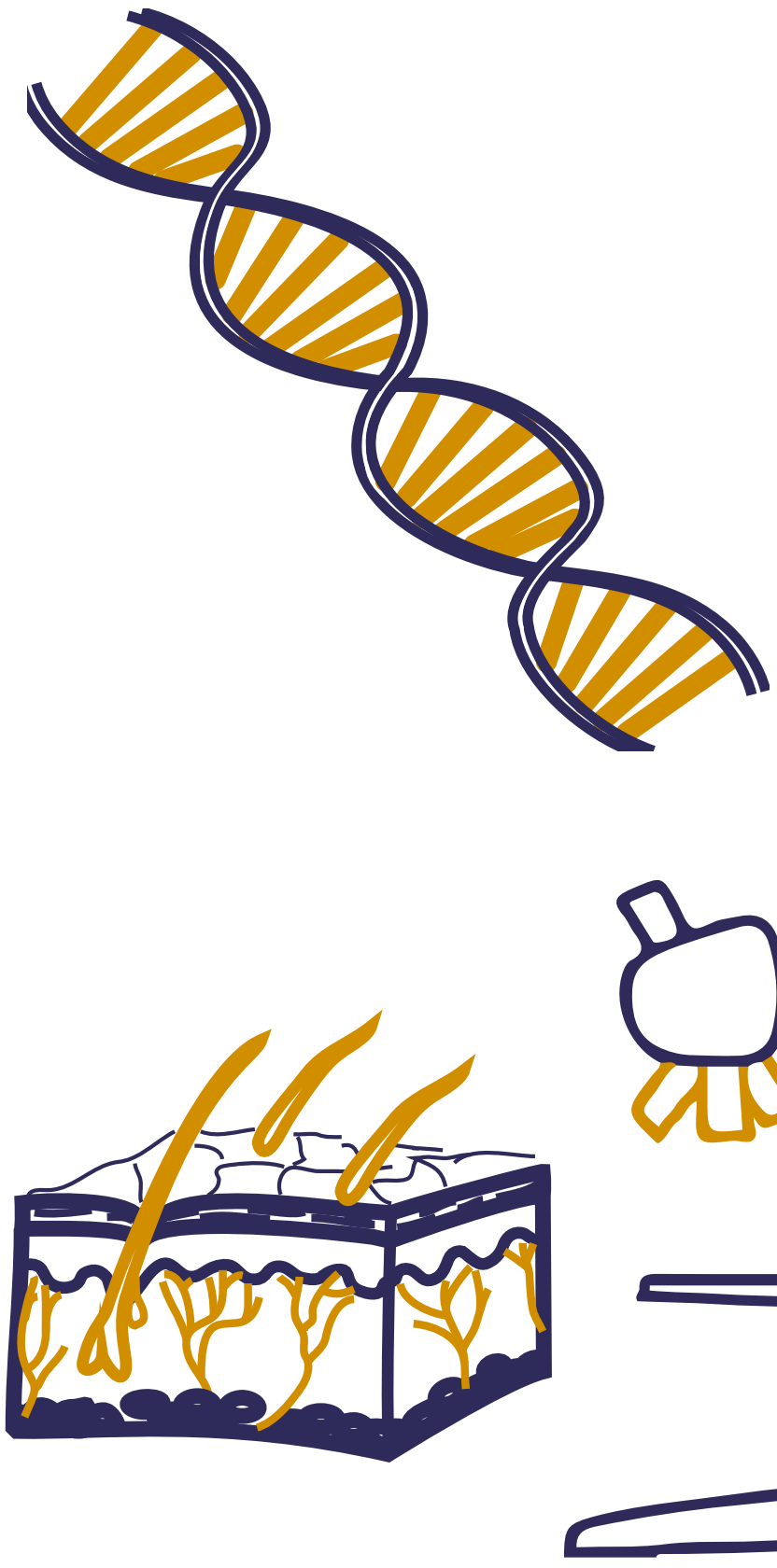
Results

In general, the average HNP content in children with UD was 1421.5±81.3 pg/ml (Me - 1419.4; Min-Max - 1398.8-1435.7; interquartile range 25;75-1384;1449.1), which is significantly higher than in practically healthy children - 498.9±21.7 pg/ml; p<0.05, (Me - 496.0; Min-Max - 379-518; interquartile range 25;75-462;548). In patients with H.pylori-non-associated UD, the mean value of the HNP concentration in serum was 2.0 times higher than the relevant norm values (992.3±19.04 pg/ml, p<0.05; Me - 981.4; Min-Max - 952-1092; interquartile range 25;75-1016;1086); in patients with H.pylori-associated UD - 3.6 times (1801.5±51.7 pg/ml, p<0.05; Me - 1797.1; Min-Max - 1589.3-1987.2; interquartile scope 25;75-1719.6;1891.5).

Conclusion

Under conditions of pathological process, in particular, in UD, the so-called HNP 1-3 in their excessive synthesis/release of neutrophils from the lesion, quickly enter the bloodstream and as "signal" molecules provide recruitment of proinflammatory cells, which are also capable of their synthesis and increase the expression and secretion of other signaling compounds aimed at strengthening the adaptive response. H.pylori infection exacerbates these processes.

Genetics and Dermatology



Presenters:

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Hypericin, Resveratrol, and Naringenin Anti-tumor Activity on Y79 Retinoblastoma Cells; Down-regulating MMP-9 and N-Cadherin

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Introduction

One of the detrimental features of retinoblastoma is highly invasiveness of this type of cancer; the ability to metastasize into distal organs even in the early stages. This phenomenon highlights the importance of experiments targeting this characteristic to diminish the disquieting outcomes. In this study our main aim was to assess the impact of hypericin, naringenin and resveratrol (three main herbal extracts with known anti-cancer properties) treatment on the important metastasis and cancer progression pathways in Y79 retinoblastoma cell line.

Materials & Methods

MTT assay performed for 24 and 48 hours. To further investigate the kind of cell death, AnnexinV/PI flowcytometry performed. Finally the expression of BAX, Bcl-2, E-cadherin, N-Cadherin, and Galectin-3 investigated in different samples by the aid of real-time PCR. Western blotting performed on MMP-9 protein.

Results

The 24h and 48h IC50 for resveratrol, hypericin and naringenin (just48h) was about 100 and 50, 2.5 and 1.25, and 100 µg/ml respectively. All three compounds induced apoptosis in Y79 cells and down-regulated theN-Cadherin mRNA and MMP-9 protein expression level. Treatment with resveratrol or hypericin increased the expression level of the E-Cadherin and diminished Galectin-3 expression.

Conclusion

Hypericin and at the next place resveratrol seems to be more toxic for Y79 cells compared with the naringenin. The three compounds exert apoptotic and anti-metastatic effect on these cells by up-regulating Bax and down-regulating N-Cadherin and MMP-9. Hypericin and resveratrol enhanced the expression of the E-Cadherin, along with the decreasing the Galectin-3 exerts even more anti-tumor activity, and can be proposed as a beneficial reagents in cancer immunotherapy.

Sarecycline in treatment of Moderate-to-Severe Acne Vulgaris: A Meta Analysis

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Introduction

Sarecycline, a novel tetracycline class of antibiotic which was FDA approved in 2018 is specifically used to treat acne vulgaris. By offering a narrow spectrum of activity mainly against cutinebacterium acne and having advantages over older tetracycline by decreasing gastrointestinal side effects. Due to scare data over its efficacy and safety in various treatment regimens and with different dosages, we decided to do a meta analysis on it

Materials & Methods

A total of 6 RCTs following PRISMA guidelines and matching inclusion and exclusion criteria were collected of sarecycline versus placebo in treatment of acne. Studies with treatment response as Reduction in inflammatory lesions at 12 weeks with sarecycline used in different doses of 0.75, 1.5 and 3.0 mg/dl was chosen as clinical outcome measure. Safety in terms of any Investigator-reported adverse events, development of gastrointestinal adverse event like nausea, vertigo, tinnitus, urticaria, pseudotumor cerebri, dizziness or photo-sensitivity was considered. RevMan 5.3 software was used for the calculation of Relative Risk(RR). P value less than 0.05 was considered significant.

Results

Data of 2583 patients were included. Use of Sarecycline was associated with a significant reduction in inflammatory lesions at 12 weeks compared to placebo. Random effect RR was 1.912 and 95% CI 1.760-2.077. P value in random effect was <0.001 and in fixed effect was <0.001. Maximum effect was seen at 1.5 mg/dl daily dose. Sarecycline was well tolerated across all treatment groups. Most common adverse event being Nausea, while other events of vertigo, dizziness and photo-sensitivity was seen but was not significant in sarecycline treated patients compared to placebo (RR=1.19, P=0.004). Other adverse events did not show a significant difference.

Conclusion

Sarecycline in dose of 1.5 mg/dl was the most efficacious in terms of showing a significant reduction in inflammatory lesions from baseline at the end of 12 weeks and was not associated with significant risk of treatment related adverse events.

Designing and fabrication a protective dressing including silver and zinc nanoparticles and evaluation of wound healing effects in bedsore

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Introduction

A pressure ulcer is a localized injury to the skin and underlying tissue that is caused by physical factors. Low adherent dressing such as hydrogels including antibacterial agents are the basic types of wound dressings commonly in use, to restrict microbial penetration and allow air and water vapor through them. So, this research aims to design and fabricate a hydrogel based on poloxamer including silver and zinc oxide nanoparticles and study its wound-healing effects.

Materials & Methods

Initially, silver and zinc oxide nanoparticles were prepared via chemical reduction and green synthesis respectively. Then, characterization of Ag and ZnO NPs was done using UV-Vis spectrometry, DLS, XRD, SEM, and FTIR. Next, the synthesized nanoparticles at a suitable concentration were inserted into the hydrogel of poloxamer 4.5%. The prepared formulation was assessed in terms of physical stability, rheological behavior, water absorption power, and the amount of effective substance. Then, the effects of wound healing on patients with grade 1 and 2 bedsore in the hospital were evaluated

Results

SEM and XRD show that nanoparticles formed are crystalline, pure, and do not aggregate and functional groups were proved by FTIR spectroscopy. It showed pseudoplastic non-Newtonian behavior in terms of rheological properties. The percentage of silver and zinc oxide nanoparticles in the formulation was 91% and 94%, respectively. Then, the efficacy of this formulation on the wound healing process of patients was assessed on days 7 and 14. The mean ± SD surface area of ulcer in the hydrogel receiver group was significantly decreased compared with the control group on the seventh day (2.7± 2.3 vs. 5.5 ±4.3 cm2, p<0.05) and fourteenth day (0.4 ±0.8 vs. 6.2 ± 4.7 cm2, p<0.05) of treatment.

Conclusion

Results of this clinical trial showed that topical application of poloxamer gel 4/5% containing Ag and ZnONPs for 14 days along with standard wound care significantly accelerate the wound healing process in patients with grade 1 and 2 bedsore.

Emergence of G3P[8] rotavirus strains with a potential vaccine-escape P[8] genotype in Blantyre, Malawi

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Introduction

Outer capsid proteins (VP4 and VP7) have been mapped as the main drivers of protection after rotavirus vaccination in under-five children. The VP4 is cleaved into the VP5*(membrane fusion protein) and VP8* (receptor binding protein). The VP8* is prone to mutations hence reads to introduction of vaccine escape strains. Malawi uses a Rotarix rotavirus vaccine to combat rotavirus disease. Rotarix is formulated using a live attenuated G1P[8] strain and is highly effective against homotypic as well as partial homotypic strains. Previously, we saw the emergence of G3 rotaviruses in 2017 in Malawi almost two decades after previous detection. G3P[4] strains emerged first, followed by G3P[6] and G3P[8] strains. Since G3P[8] are partial homotypic, we undertook protein analysis study to assess if Rotarix induced antibodies will be effective against G3P[8] strains.

Materials & Methods

Reference sequences of Rotarix VP4 segment was obtained virus resource in GenBank. Representative VP4 segment sequences of G3P[8] strains were selected and exposed to multiple sequence alignments using MUSCLE. Antigenic sites were extracted from the alignments using modules in Biopython. Protein structures were modelled using Modeller v9.25 while quality assessment of the structures was done using ProCheck and SWISS-MODEL. Protein models were visualized and annotated using PyMol.

Results

Protein analysis revealed the VP5*(membrane fusion protein) structure to be conserved across the VP4 of G3P[8] strains. Amino acid substitutions were observed with the antigenic region 1 (E150D) and 3 (S125N, S131R, and N135D) within the VP8*(receptor binding protein) of the VP4 of G3P[8] strains. Protein modelling revealed structural changes within antigenic region 1 due to the E150D substitution as well as antigenic region 3 due to the S131R substitution.

Conclusion

P[8] of the emerging G3 strains seems to have acquired mutations within antigenic regions associated with neutralization. Mutations within the antigenic regions of the VP8* structure of VP4 had an impact on the structural orientation of antigenic regions. These changes might

reduce the binding ability of vaccine induced antibodies to bind to the newly emerging strains. Further work is warranted to assess the neutralizing potential of vaccine induced antibodies against the G3P[8] strains.

Increased expression of LINE-1 in neurons derived from iPSC of patients with Autism Spectrum Disorder

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Introduction

Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder and is part of a set of complex diseases whose causes and mechanisms of inheritance have not yet been fully unraveled. The phenotypic heterogeneity of the disorder reflects a complex genetic architecture, with more than 800 genes associated with ASD according to the literature. Recent studies demonstrate the correlation between psychiatric disorders and alterations in the expression of transposable element genes. Among the transposable elements, the LINE-1 retrotransposon has been shown to play a role in the pathophysiology of ASD. Thus, the current project aims to investigate the expression of LINE-1 in ASD patients.

Materials & Methods

RNA was extracted from neurons derived from iPSC obtained from PBMC from ASD patients. LINE-1 expression was analyzed by RT-qPCR using primers previously designed for the ORF2 and 5'UTR regions. The transcriptional level of LINE-1 was evaluated and considered differentially expressed when p<0.05 and Log2 Fold Change (LogFC) values greater than 1.25. The data obtained were analyzed using the Software R x64 3.5.3 by the Wilcoxon statistical test.

Results

The data show that LINE-1 expression is differentially expressed in differentiated neurons in the ASD group when compared to the control group (p<0.05) for both primers: for the ORF2 primer LogFC was 2.29 and for the 5'UTR primer LogFC was 1.71.

Conclusion

Thus, LINE-1 expression was higher in iPSC-derived neurons of the ASD group than in the control group. This result is corroborated by data in the literature that indicates a greater expression of this retrotransposon in the somatic cells of autistic individuals. The difference in the expression levels between the two sets of primers may be due to the fact that ORF2 is also present in different forms of LINE-1 that are not retrotransposable, that is, in inactive forms of LINE, since these forms represent the most abundant forms of LINE-1 expressed.

Parental perspectives on Phelan-McDermid syndrome; the results of a worldwide survey

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Introduction

Phelan-McDermid syndrome (PMS) is a rare neurodevelopmental disorder caused by 22q13 deletions or mutations in the SHANK3 gene. Currently, evidence-based recommendations for the care of PMS patients are lacking. For this purpose, a European consortium is developing a guideline. An indispensable part of such a guideline is knowledge of the needs of parents.

Materials & Methods

We developed an online, multi-lingual survey for parents of individuals with PMS, which included questions on experienced problems, knowledge on the genetic cause, level of care, and communication among care providers. We analyzed the answers per age group, genetic background (22q13 deletions and SHANK3 mutations), and country of origin with chi-square tests, including posthoc analysis.

Results

We received 588 answers from 35 countries representing every continent. Sixty-four percent of individuals had a 22q13 deletion, 18% a SHANK3 mutation, and 18% an unknown genetic background. Parents most frequently experienced problems with speech and communication (96%), learning difficulties/intellectual disability (94%), problems with fine motor skills (82%), altered pain perception (77%), and hypotonia (76%). Adult individuals had significantly higher rates of behavioral problems, sleeping problems, constipation, and epilepsy than all other age groups (p<.001, for all four variables). Individuals with 22q13 deletions had significantly higher rates of hypotonia (p=.002), problems with gross motor skills (p=.002), feet (p=.001), and heart (p=.018), while individuals with SHANK3 mutations had significantly higher rates of sleeping problems (p=.017) and constipation (p=.013).

Parents from countries with a very high Human Development Index (HDI) were more likely to know the cause of PMS in their children, experience organized communication among care providers, and receive higher-level care (center of expertise for PMS or academic hospital) than parents from countries with high and medium HDI (p<.001, for all three variables). The level of care did not influence genetic knowledge or experienced communication by parents.

Conclusion

Most of the problems parents reported are present in all age groups and genetic backgrounds. Since some problems develop progressively, patients may have additional care needs in adulthood. The differences among countries are crucial to consider in an international guideline.

Physiochemical properties of oil from Malawian Jatropha Curcas for dermatological applications

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Introduction

Jatropha curcas (Euphorbiaceae family) is a multipurpose shrub native to Central America and has been naturalized in many tropical regions including Africa. In Malawi, the plant is mainly grown along the lakeshore areas and its seeds are traditionally used for treating dysentery and diarrhoea. A variety of pharmacological activities including anthelmintic, antifungal, laxative and antibacterial have been reported for J. curcas crude oil. Until now, the physicochemical properties associated with dermatological applications have not been reported for the oil derived from the Malawian plant species. Therefore, we conducted the study to investigate selected properties of J. curcas oil relevant for dermatological applications.

Materials & Methods

An experimental study was conducted, where J. curcas oil was extracted from seeds and subsequently analysed for the following physicochemical properties; solubility, refractive index, saponification value and acid value. All the analyses were conducted in triplicates and mean ± SD for each parameter was reported. Data distribution analysis was determined by the Shapiro–Wilk test. To compare with USP 28, JP 2001 and PhEur 2005 specifications, a one-way ANOVA was performed, followed by multiple comparisons using Tukey's test.

Results

The results showed that the refractive index, acid value and saponification values of the oil were 1.34 ± 0.08, 1.67±0.57, 76.45±21.10, respectively. According to the pharmacopeia specifications for pharmaceutical excipients, acid values for oils are ≤ 1.5 according to JP 2001 and ≤ 2.0 according to PhEur 2005. Therefore, the J. curcas oil acid value obtained from this study was within the acceptable standard range for vegetable oils. At 25°C, the oil was miscible in all proportions with organic solvents acetone and chloroform while immiscible with polar solvents cold ethanol, ethanol and hot water. Evidently, the results suggested that J. carcus oil is highly lipophilic that it can easily penetrate through the stratum cornea of the skin.

Conclusion

Except for saponification value, the selected physicochemical parameters were statistically comparable to the three international pharmacopeia specifications. This study, therefore, provided scientific information for the potential use of the oil for dermatological application.

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 associated with distressing pruritus (itch). Nitric oxide (NO) is a neurotransmitter, assumed to be involved in pruritus. Based on over-production of NO in cholestatic liver diseases, this project aimed to investigate involvement of NO in cholestasis-related itch in mice.

Materials & Methods

Cholestasis was induced by bile duct ligation (BDL). In order to confirm our BDL as a model of

cholestasis in rodents, we evaluated bilirubin concentration also the plasma alanine aminotransferase and aspartate aminotransferase activities in samples, using commercially available kits. The itch related behaviors of mice were recorded for 60 min, by a camera in an unmanned situation and by using the playback, number of bouts were accounted by an expert, blind to the procedure. Also, to evaluate motor activity, the ambulatory behavior of mice was assessed in an open field test to confirm that variations in the scratching behavior are not subsequent to changes in general motor activity. Serum and intradermal concentration of nitrite were measured using a colorimetric assay.

Results

Our results showed that BDL mice elicited significant itch on fifth and seventh day after the procedure. This scratching behavior was inhibited by treatment of mice with non-selective NOS inhibitor N-nitro-l-arginine methyl ester (l-NAME; 3 mg/kg) and inducible NOS (iNOS) inhibitor aminoguanidine (AG; 100 mg/kg). The inhibitory effects of l-NAME and AG were reversed by pretreatment with l-arginine (100 mg/kg). Administration of l-NAME, AG and l-arginine per se, in BDL and SHAM mice did not produce scratching behaviors. In addition, intradermal injection of l-arginine at dose of 300 nmol/site significantly increased itch in BDL mice. Furthermore, nitrite levels in skin and serum of BDL animals significantly increased after post-operation day 7 and administration of NOS inhibitors decreased this enhancement. l-arginine injection reversed the effects of NOS inhibitors on reduction of nitrite levels in the skin and serum of BDL mice. Finally, cutaneous iNOS expression increased in BDL mice 7 days after surgery.

Conclusion

Taken together, our study showed for the first time that BDL, as a model of acute cholestasis in rodents, induces NO over-production by activating NOS enzymes, especially iNOS, which contribute to pruritus.

Identification of chromatin interactome changes and regulators of H2AK119ub upon cellular stress ubiquitination using the miniTurboID system

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Introduction

The Polycomb repressive complexes (PRC) 1 and 2 play a vital role in cell lineage specification and stem cell self-renewal by epigenetic regulation. PRC1 ubiquitinates H2AK119 and PRC2 methylates H3K27, leading to gene silencing. It is of utmost importance to maintain this repressed state to avoid inappropriate expression of lineage markers, even under cellular stress, since misexpression of genes can lead to cancer development. Strikingly, it was recently found that heat shock (HS), a basic form of cell stress, leads to loss of PRC1/2 chromatin binding, temporary relocalization of these proteins to the nucleolus, and a concomitant reduction of PRC1/2-induced epigenetic marks (Azkanaz et al. eLife, 2019). The fast kinetics of H2AK119ub reduction suggest that this process may be enzymatically driven. Within this project we aim to investigate how the chromatin interactome is changed after HS and identify potential HS-specific regulators of H2AK119ub levels.

Materials & Methods

To this purpose, we employ the miniTurboID system, allowing proximity-dependent biotinylation of nearby proteins. We expressed a histone H2A-miniTurboID fusion protein in K562 cells and screened for changes in the chromatin interactome after HS using streptavidin-mediated purification of biotinylated proteins and subsequent LC-MS/MS analysis.

Results

Initial experiments show that the H2A-miniTurboID fusion protein is stably incorporated and can be ubiquitinated at H2AK119 suggesting the fusion proteins is fully functional. HS experiments show that miniTurboID remains functional during HS, and streptavidin pull outs show that chromatin-associated proteins (EZH2, CBX8) are efficiently biotinylated. Fluorescent microscopy analysis shows that biotinylated proteins are localized to the nucleus as expected.

Conclusion

Taken together, our preliminary data show that our H2A-miniTurboID approach works to identify chromatin associated proteins under normothermic and hyperthermic conditions. Next, we will identify changes in the chromatin interactome during cellular stress (heat shock, low oxygen conditions, and proteasome inhibition) by large-scale isolation of biotinylated proteins followed by LC-MS/MS analysis.

Public Health I

Presenters:
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Tariq, S T (Sana)
Murali, M (Mathangi)
Sharieff, N.J (Noora Jabeen)
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A Cross-sectional study on the Cardiovascular risk associated with the COVID-19 Lockdown

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Introduction

In December 2019, an outbreak of Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV 2), emerged in Wuhan, China causing a global pandemic. Stringent measures were implemented in several parts of the world and a nation-wide lockdown was declared in India to alleviate disease transmission. This confinement severely impacted people's lives and forced them to switch to a sedentary lifestyle.The present study aimed to analyse the cardiovascular risk associated with lifestyle modifications due to the lockdown.

Materials & Methods

This cross-sectional study used a structured online questionnaire with data collection using a convenience This cross-sectional study was conducted using an anonymous online questionnaire consisting of more than 20 questions about living habits during the COVID-19 confinement and the previous time. Convenience sampling was used for data collection and the statistical analysis (Chi-squared test and one-way ANOVA) was performed using PASW Statistics 18.0.

Results

A total of 432 respondents, aged between 20 and 60 years (mean age-33.39 ±10.8 years) were included in the study. The perception of weight gain was observed in 46.06% of the population;19.90% reported an increased carbohydrate intake; a decrease in physical activity was observed in 27.08%; 62.73% reported an increase in screen time; more females complained of having sleep disturbances and stress perception was more in the population group aged between 30-50 years.

Conclusion

Quarantine results in an increased cardiovascular risk due to the associated unhealthy lifestyle and stress. Following quarantine, a global action supporting healthy diet and physical activity should be made mandatory to encourage people to return to a good lifestyle routine. This study would help in execution of public health interventions during the pandemic as well as in future times.

Internet addiction and its associated factors among African high school and university students: systematic review and meta-analysis

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Introduction

Internet addiction is characterized by excessive and uncontrolled use of the internet affecting everyday life. Adolescents are the primary risk group for internet addiction. Thus, this study aimed to determine the pooled prevalence of internet addiction among high school and university students in Africa.

Materials & Methods

A comprehensive literature search was conducted using electronic databases. Heterogeneity between studies was checked using Cochrane Q test statistics and I2 test statistics and small-study effects were checked using Egger's statistical test at a 5% significance level. A sensitivity analysis was performed. A random-effects model was employed to estimate the pooled prevalence and associated factors of internet addiction among students. The primary outcome of measure of this review was the prevalence of internet addiction and the secondary outcome of measures are the factors associated with internet addiction.

Results

A total of 5562 studies were identified among the five databases. Of these, 27 studies from 10 countries with 14,946 high school and university students were included in this review. The overall pooled prevalence of internet addiction among the students was 34.53% (95% Confidence Interval (CI): 26.83, 42.23, I2 = 99.20%). Male sex (Pooled Odds Ratio (POR) = 1.92, 95% CI:1.43, 2.57 I2 =0.00), urban residence (POR = 2.32, 95% CI:1.19, 4.53, I2 = 59.39%), and duration of daily internet use for more than four hours (POR= 2.25, 95% CI:1.20, 4.21, I2 = 0.00%, were significantly associated with internet addiction among adolescents.

Conclusion

Almost one-third of university and high school students in Africa are addicted to the internet. Male students, those from urban areas, and those who use the internet for more than 4 hours per day have higher odds of internet addiction. Thus, we recommend that health planners and policymakers pay attention to the use of the internet and internet addiction in Africa

Overactive Bladder Symptoms associated with BMI in young females: Physiological traits as a treatment option

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Introduction

An overactive bladder is characterized by a persistent urge to urinate, which can lead to spontaneous urination. Treatment of overactive bladder with mild to moderate exercises and lifestyle changes as treatment has caught the attention in the past decade, This study aims to understand the association of Besal Metabolic Index with overactive bladder symptoms and the effect of exercise on Overactive bladder (OAB) in young females

Materials & Methods

This is a prospective cohort study, OABSS was used to determine OAB symptoms, positive results for overactive bladder symptoms were educated for lifestyle changes such as water intake timings, and pelvic floor muscle exercise. After 3 months of 4 times, a week exercises and lifestyle modifications, the OABSS questionnaire was asked to be answered again. Analysis of data included demographic details and OABSS score before and after the intervention were entered and edited in the statistical package of social sciences (SPSS) version 21. Paired sample T-Test and chi-square test were used to analyze the significance of data.

Results

A total of 380 participants were included in the study, mean age of participants was reported as 23.7 ± 3.9 years, further divided into 2 categories of 20-25 years and 25-30 years. The most commonly reported urinary symptom was increased frequency with 172 participants 8-14 times a day and 45 participants indicated > 15 times a day frequency of urination. After 3 months OABSS presented significant improvement in symptoms. 288 (60%) participants were cured, 92 (24%) indicated improved results.

Conclusion

our study indicated approximately 32% frequency of overactive blagger moderate to severe symptoms in females aged between 20 to 30 years, indicating BMI as an independent risk factor and exercise as the first best treatment option for young patients.

EFFECT OF THE SELF-MANAGEMENT PROGRAM ON MEDICATION ADHERENCE AND BLOOD PRESSURE LEVEL AMOMG PERSONS WITH HYPERTENSION IN COMMUNITY

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Introduction

Adherence to prescribed medication is an imperative issue which can be directly linked with the management of hypertension. The problem was a failure to adhere can affect the effectiveness of medication and blood pressure.

Materials & Methods

This study aimed to examine the effects of the self-management program on medication adherence and blood pressure level among persons with hypertension in community.

Method: This study was quasi-experimental research with two groups, pretest-posttest design. There were 48 participants with hypertension, aged 35 to 59 years old, and divided into a control group (24 person) and an experimental group (24 person). The experimental group had been received the self-management program for 8 weeks from July to August 2021. The program was developed by the researcher based on the self-management theoretical framework (Kanfer & Gaelick-Buys, 1991) consisted of 3 steps 1) self-monitoring 2) self-evaluation and 3) self-reinforcement by telephone and home health care visit. The control group received normal care. Data were collected using demographic questionnaire and medication adherence scale in Thais questionnaire (CVI=0.96 with a coefficient of stability= 0.98). Data were analyzed using descriptive statistics, paired t-test and the Mann-Whitney U Test.

Results

The results revealed that after participating the self-management program, the experimental group had an average medication adherence score (x = 37.75, SD 2.33) significantly higher than before receiving program (x = 30.92, SD 3.50) and higher than the control groups (X= 34.68, SD 6.80) (p<0.05). The average blood pressure level of SBP/DBP (X = 129.83/81.17, SD 8.49/10.00) significantly lower than before receiving program (X = 139.54/83.04, SD 12.30/13.24) (p<0.05).

Conclusion

The self-management program can be used to increase medication adherence behaviors and reduces blood pressure level. Nurse practitioners should use telephone and home health care visit continuingly for monitoring medication adherence behaviors and decrease blood pressure level among persons with hypertension.

Variation in lipid profile and glycemic status among diabetic and prediabetic patients and its correlation with their sleep quality and stress levels

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Introduction

Diabetes (DM) is a metabolic syndrome and one of the top 10 causes of death globally. Studies have suggested that sleep disturbances and severe stress are associated with insulin resistance and poor lipid profile. Prediabetic screening has enabled early intervention and prolonged the onset of complications in DM. However, only few studies have commented on the effect of sleep quality and stress on lipid and glucose levels in these patients. Hence, our study is aimed to identify patterns in the above parameters in pre diabetic group (PDG) and diabetic group (DG) of patients.

Materials & Methods

A cross-sectional study was conducted with a total of 90 patients, 45 PDG and 45 DG, from a tertiary hospital in Southern India. Parameters like HbA1c, lipid profile, fasting and post prandial glucose levels were recorded and correlated with their sleep and stress levels which were assessed using Pittsburgh sleep quality index (PSQI) score and Perceived stress scale (PSS) questionnaires respectively.

Results

In PDG, a significant positive correlation was found between HDL and HbA1c (p<0.05), probably due to reverse causation. Their mean triglyceride (TG) and LDL were elevated, and HDL was low.

In DG, significantly higher TC (total cholesterol) was strongly associated with increased stress (p<0.05). TC, LDL and TC:HDL ratio was higher in those with bad sleep quality (p<0.05). 99.6% of DG who had poor glycemic control, had increased stress levels. TG levels were comparatively higher in DG than in PDG (p<0.05).

Conclusion

Our study reveals that hypertriglyceridemia is a major component of metabolic syndrome in DM. It established that poor sleep quality strongly correlates to an elevated lipid profile in these patients. We also reported that dyslipidemia began early in the prediabetics. Poor sleep, deranged lipid profile, and stress may contribute as risk factors to pre-diabetes and poor glycemic control in diabetic patients. Similarly, uncontrolled DM may cause poor sleep and increased stress, and vice versa, leading to a vicious cycle unless kept in check.

Participation in colorectal cancer screening programme in Czech Republic: analysis of the affecting factors.

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Introduction

Screening for colorectal cancer (CRC) in the risk groups decreases both its incidence and mortality. Faecal occult blood test (FOBT) once a year or colonoscopy once in ten years are the two options approved for CRC screening for asymptomatic individuals aged ≥ 50 years in Czech Republic. We aimed to analyse the participation in the screening programme in order to design the strategies for improving the general participation.

Materials & Methods

The data was collected from 4044 participants (1866 men, 2178 women) aged ≥ 50 years by questionnaires as a part of European Health Interview Survey 2014. Individuals who underwent colonoscopy within the last 10 years or FOBT within the last 2 years were classified as participants in the screening programme. The separate binary logistic regression was used to estimate the odds ratio for set of variables.

Results

Among 4044 participants, 1050 individuals (26%) participated in FOBT, 464 (11.5%) in colonoscopy and 558 (13.8%) in both. After adjusting for age, sex and education, the following results were statistically significant (p < 0.05). A higher participation in preventive screening programme was observed in the groups of non-smokers (OR = 1.25; 95% CI 1.051–1.479) and ex-smokers (OR = 1.51; 95% CI 1.257–1.825) compared to smokers; respondents consuming smoked meat products less than once a week (OR = 1.26; 95% CI 1.089-1.453) and those practicing physical activity at least once a week (OR = 1.25; 95% CI 1.033–1.514). A higher participation was observed among individuals hospitalized in the past 12 months (OR = 1.73; 95% CI 1.466–2.048) and those consulting the GP in the past 12 months (OR = 2.26; 95% CI 1.872–2.735). The participation of individuals possessing a risk factor for CRC (obesity, smoking, diabetes, low physical activity, drinking of alcohol) was not higher compared to those without the risk factors.

Conclusion

Respondents having a tendance to a healthy lifestyle and those being in a recent contact with the healthcare system by various means, mainly visiting their GP, have a higher participation in the screening for CRC. However, among the groups with an increased risk for CRC, a higher participation was not shown.

The one-year prevalence of influenza vaccination in Slovak population over 45 years and selected health characteristics with the focus to diabetes population

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Introduction

Patients with diabetes are more likely to have influenza infection as an underlying or contributing cause of death. Therefore, seasonal influenza vaccination is recommended for risky populations including individuals with diabetes mellitus.

The mean IVP in European Union (total population/diabetes/non-diabetes population) was 24,7/41/22,5%. This study shows a year influenza vaccination prevalence (IVP) among diabetic patients in Slovakia and its relation to the selected health characteristics.

Materials & Methods

Slovakian branch of 2014 European Health Interview Survey (EHIS) was the source of analyzed data in this study. The study population consists of 413 (14%) patients with diabetes, and the rest of 2574 (86%) non-diabetic participants forming the control group. Information regarding sociodemographic characteristics, lifestyle characteristics and anamnestic data were collected through health questionnaires from EHIS.The analysis was achieved by a one-way analysis variance (ANOVA) and an X2-test.

Results

Our study showed that the IVP in the whole study population was 10%, among diabetic patients, it was 16,7% and among non-diabetics 8,9% (p<0,001) without signifcant difference between male and female.

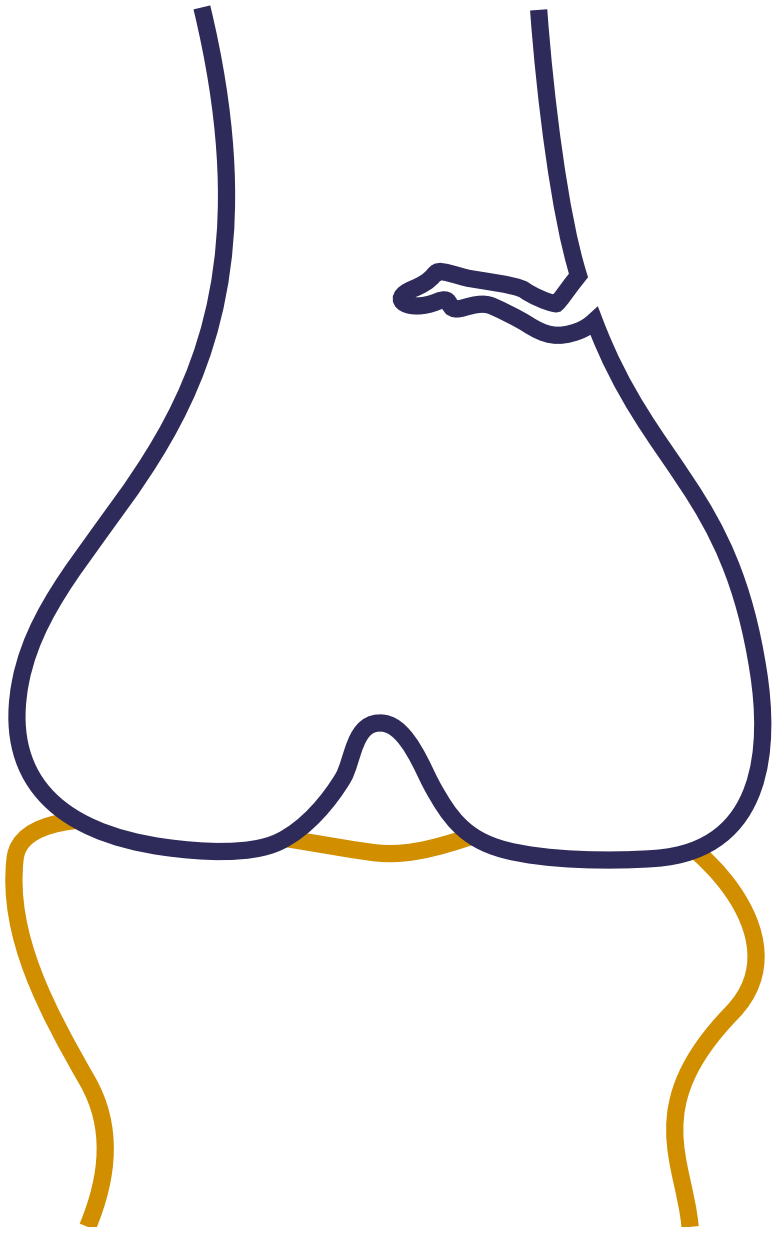
According to age analysis, in diabetic and control group, the IVPs were as follows: 6.3% and 3.5% (p=0.419) in the age group of 45-54 years old; 10.3% and 8.1% (p=0.423) in the age group 55-64; 18.2% and 12.9% (p=0.095) in the age group 65-74; and for the participants older than 75 years, it was 24.1% vs. 17.1% (p=0.091). The frequency of vaccination increases with increasing age within the diabetes population (p=0.012). Comparison within diabetes population revealed that more likely to get vaccination are those with university education compared to other types of education (p=0,045). Within the diabetes population non-smokers are more frequently vaccinated than smokers (p=0.017).

There was no significant difference within the diabetes group regarding: presence of cardiovascular disease or asthma or chronic bronchitis, household income, obesity, frequency of alcohol consumption, and urban settlement.

Conclusion

The one-year IVP in the diabetes group in Slovakia was significantly higher compared to the non-diabetes group. Regarding age, the most notable difference was found among the age group 75 + years. The IVP numbers are lower than EU average. More attention should be paid to population influenza vaccination education.

Orthopeadics and Surgery



Presenters:

Miljkovic, M.M. (Martin) Student
Tadele, FTA (Fitalew) Mr
Mămăligă, M.C. (Cătălina)
GANDHI, K.V.G (KHUSHI)
Schelhaas, R. (Reslin) Drs.
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Radio-frequency ablation versus hepatic surgery for the treatment of hepatocellular carcinoma: a systematic review and meta-analysis

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Introduction

Hepatocellular carcinoma (HCC) is the most common malignant tumor composed of cells resembling hepatocytes. It is the fourth most common cause of cancer-related death on earth.

Treatment involves radio frequency ablation (RFA)or hepatic ressection (HR) . This is a review & evaluation of evidence comparing either methods by using meta-analysis technique.

Materials & Methods

We conducted a database search of the PUBMED,SCIHUB, GOOGLE SCHOLAR etc in which total of 36 observational studies and 3 RCTs following PRISMA guidelines till sep 2020 and matching inclusion and exclusion criteria were collected. These studies include total 16,700patients out of which 8565 were treated with RFA & 8135 with surgery .The following search strings were used: " RFA vs HR", "hepatocellular carcinoma treatment ". The primary end point was overall survival rate in 3&5 years respectively,including hospital stay duration & local recurrence. RevMan 5.3 was used for appropriate statistical tests. Fixed and Random Effect Model Tests was used and p<0.05 was considered statistically significant.

Results

Meta-analysis showed that RFA was associated with significant decrease in the length of hospital stay for RCTs (SMD = -2.171 , CI = -2.381 to - 1.962 , p=<0.001) and non-RCTs (SMD = -1.048 , CI = 1.492 to -0.937, p=<0.001) respectively.

However, it was also associated with significant increase incidence of recurrence (RR = 1.749, 95% CI = 1.444 to 2.119, p=<0.001) and significantly poorer 3-year (RR = 0.850, 95% CI = 0.772 to 0.935 , p=0.001); (RR = 0.941, 95%CI = 0.927 to 0.956, p=<0.001) for RCTs and non-RCTs respectively.

Conclusion

Although RFA was associated with decreased duration of hospital stay, it was associated with increased chances of recurrence compared to hepatic resection. 3-year survival rate was also poorer.

Assessment of complications following gastrectomy for gastric cancer: an observational retrospective study

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Introduction

As surgery remains the main treatment option for gastric cancer, the incidence of postoperative complications following radical gastric resections should become an index which assesses the surgical outcome. The aim of this study was to analyze postgastrectomy complications for stomach tumors by retrospectively collecting data and classifying them according to severity and to investigate the risk factors associated with them.

Materials & Methods

The data of 128 consecutive patients who underwent radical gastric resections have been collected retrospectively. The postoperative complications were graded according to Clavien-Dindo classification. Statistical analysis was performed using the Chi-square test and ANOVA test. A p value of <0,05 was considered significant.

Results

The incidence of postoperative complications was 82,8%. The numbers of grade I, II, III, IV and V according to Clavien-Dindo was 25 (18%), 33 (25, 77%), 58 (45,31%), 8 (6,85%) and 6 (4,75%), respectively. Patient-related variables, like age (p=0,468577), ASA score (p=0,27), sex (p=0,52), TNM staging (p=0,81), previous abdominal resections (p=0,05046), Charlson Comorbidity Index (p=0,65) and operation – related variables, like lymph node dissection (p=0,131) and the extent of resection (p=0,23), weren't found as risk factors, whereas multiorgan resections had an important impact over the postoperative outcome (p=0,0027).

Conclusion

Our results show that the postoperative outcome following open gastrectomies is mainly influenced by the multiorgan resection.

Effects of fecal stream deprivation on human intestinal barrier after loop ileostomy

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Introduction

Intestinal homeostasis is closely related to normal intestinal luminal physiological environment. Temporary loop ileostomy changes the intestinal structure and diverts the fecal stream, thereby drastically disturbing the intestinal environment, but enterogenic infections are rare in loop ileostomy patients, which suggests that a greater ecological tolerance may exist than previously recognized. This study aimed to clarify the changing situation of the human intestinal mucosa barrier in the absence of a fecal stream after loop ileostomy.

Materials & Methods

We obtained paired samples from the fed (fecal stream maintained) and unfed (no fecal stream) portions of the loop ileostomy and subjected these samples to RNA sequencing. We also determined transepithelial electrical resistance. The mucus layer thickness and content of MUC2, tight junction proteins, and common antimicrobial peptides in ileum mucosa were studied.

Results

Transcriptome data revealed that genes related to enhancing the intestinal barrier function of the unfed ileum were significantly decreased and genes associated with immune defense response were significantly increased. The transepithelial electrical resistance was lower and the mucus layer thickness was thinner in the unfed ileal mucosa than in the fed ileum. The MUC2, Occludin, and ZO-1 content was lower in the unfed ileum than in the fed ileum. α-Defensin 5, α-defensin 6, and lysozyme content was higher in the unfed ileum than in the enterally fed ileum.

Conclusion

Intestinal barrier function is weakened after long-term fecal diversion, but antimicrobiota defense function is strengthened. Thus, the intestinal mucosa barrier adopts an alternative stable state during fecal diversion, which may explain the clinical paucity of cases of enterogenic infection caused by loop ileostomy.

Large particles of bone filing material promote superior angiogenesis and bone regeneration - an in vivo experimental study

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Introduction

Considering the angiogenesis precedes spatially and temporally osteogenesis, it is required for new bone formation and bone defect regeneration. Besides the bone defect structure and morphology, both revascularization and bone healing depend on the choice of the bone substitute. For successful graft healing and integration two preconditions are required and they are: blood vessel in-growth in bone defect from the surrounding bone and close contact between surface of bone substitute and vascularized tissue. The main objective of the research was to estimate whether the size of bone substitute have an effect on angiogenesis and consequently on new bone formation.

Materials & Methods

The control experimental study included ten New Zealand rabbits. On both sides of cranial vault two 8mm-diameter defects were formed and filled with bone substitute particles. The tested materials are commercially available in two dimensions and contained the following: deproteinized bovine bone minerals in the form of small and large particles (250-1000µm and 1000-2000µm, respectively), deantigenated equine-derived bone in the form of small and large particles (500-1000µm and 2000-3000µm, respectively). After 4 and 8 weeks the animals were sacrificed and tissue samples were prepared for pathohistological analysis. The angiogenesis characteristics were analyzed using histological, histochemical and immuno-histochemical methods. Besides, micro-CT analyze was used to reckon morphological features as well as differences among all examined bone substitutes.

Results

Research results showed larger number of blood vessels in defects filled with large particles after 4 and 8 weeks of healing regardless the type of xenograft origin. After 8 weeks the mean value of micro-vessel density was significantly higher in defects filled with large equine derived particles than in large bovine-derived ones (55.6 ± 1.67 and 58.6± 0.89, respectively p<0.05). Conversely, regarding to small particles significant difference was noticed in favor of those small bovine derived. In the multivariate regression analysis, size of the bone substitute was found to be significantly associated with number of blood vessels, describing 92% variabilities. (B=27.77; 95% CI =17,75 - 37,78; R2=0.92,1; p<0.001)

Conclusion

Large xenogenic bone substitute particles were found to provide more space for vascular ingrowth and more new bone formation making independent predictor of neo-angiogenesis.

The prediction of the size of the femoral component used in knee replacement surgery in relation to patient's height, weight, body mass index (BMI), gender, and age.

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Introduction

Degenerative knee osteoarthritis is a common medical condition worldwide. Recent research projects proved that Total knee Replacement (TKR) is a successful surgery for treating osteoarthritis after failure of non-surgical interventions to restore the function of the joint and improve patient's quality of life.

The selection of the size of the femoral component is significant to get equal flexion-extension gaps which is also important to get a pain-free range of motion and stability.

The availability of stock is of paramount importance for the surgeon before starting the surgery to allow accurate sizing for the patient intra-operatively. We tried to predict the femoral size pre-operatively by analyzing the association between BMI, gender, age, and the actual size used in the operation.

Materials & Methods

A retrospective review was performed on a group of 385 patients who underwent TKR surgery between 2019 and 2020. Patient demographics included weight, height, BMI, gender, age, and the actual femoral size used in the operation were obtained from the medical records of Jordan University Hospital (JUH). SPSS (Statistical Package for the Social Sciences) version 28.0 (Chicago, USA) was used for data analysis. Pearson Chi-square test was utilized to investigate the association between type of femoral component and gender of patients. Spearman's rank correlation was used to analyze the femoral component size and continuous measures (e.g., weight).

Results

The mean age of the study sample being 68 years (ranging from 26 and 92 years). 88.6% of the sample were females, and 11.4% were males with a mean BMI of 31.

We found a significant positive correlation between gender, height, weight, and the used femoral component size (P-value < 0.001, <0.001, <0.025, respectively); however, BMI and age were not statistically correlated to the femoral component size (P-value = 0.625, 0.138, respectively).

Conclusion

According to the results, we concluded that the chosen size of the femoral component used in the surgery is highly associated with the height, weight, and gender of patients. But not with their BMI and age. These predictive variables can help improve pre-operative planning for the availability of implant sizes and implant supply chain efficiency.

Evaluation of the pre and post-surgery oxidative disturbance among Brain Tumor Patients Attending referral Hospitals of Addis Ababa, Ethiopia 2021: A Comparative cross-Sectional Study

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Introduction

The exact cause of brain tumors is still unknown but disruptions of redox balance are thought to play a significant role in all stages of brain tumor development. However, there has been no recent scientific evidence about the exact impact of redox imbalance in brain tumor tumorigenesis. Moreover, the roles of free radical imbalance at different grades of brain tumor and degree of oxidative stress before and after surgery haven't been addressed in the prior studies.

Materials & Methods

An institution-based comparative cross-sectional study was conducted on a total of 100 participants (50 brain tumor patients and 50 controls). Venous blood samples were collected to measure the activity of serum parameters. Descriptive statistics were used to describe the socio-demographic information of participants. T-test and ANOVA were used to compare serum parameters of cases and control groups and statistical significance was declared at $p \leq 0.05$.

Results

The serum oxidized glutathione and total oxidative stress were significantly higher in the serum of brain tumor patients (0.72 ± 0.03 µM/µg, 9.66 ± 1.76 µmol H2O2 Eq/l resp.) compared to the control group (0.21 ± 0.07 µM/µg, 6.59 ± 0.81 µmol H2O2 Eq/l resp.) ($P \leq 0.05$). The serum TOS gradually increases as the tumor grade increases, with higher in grade four (11.96±0.72) and lower in grade one (8.43±1.56), and the mean differences were statistically significant ($P \leq 0$ 05). A statistically significantly higher total antioxidant capacity (116.78± 5.03Trolox Eq/l) was obtained in the post-surgery than the pre-surgery level (116.78 ± 5.03Trolox Eq/l) ($P \leq 0$ 05).

Conclusion

Higher oxidant and lower antioxidant levels were found in the serum of brain tumor patients than in the control groups. The post-surgery oxidative stress level was lower than the pre-surgery state, therefore a combination of antioxidants with the current treatment strategy may help.

Changes in the flexion-extension axis of the elbow following total elbow arthroplasty – a pilot cadaver study

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Introduction

Total elbow arthroplasty (TEA) is a surgical procedure in which a surgeon replaces the elbow with a prosthesis. Complication rates after TEA are high, and survival rates of elbow prostheses are low. One of the most important changes that could occur following TEA is a change in the location and orientation of the flexion-extension axis of the elbow. Failure to accurately reconstruct the flexion-extension axis affects the elbow load and increases the chance of complications. The primary goal of the current paper is, therefore, to investigate the changes in the location and orientation of the flexion-extension axis of the elbow following TEA.

Materials & Methods

Two series of measurements were performed on the left upper-limb of an anatomical specimen, before and after a Latitude linked TEA (Tornier, Stafford, TX, USA) was performed. Passive flexion-extension movements were performed with the forearm in the neutral position, in pronation, and in supination. Reflective markers were attached to the humerus, radius, and ulna, and movements were recorded with OptiTrack Flex 3 (NaturalPoint, Inc., Corvallis, OR, USA). Based on marker position data, the location and orientation of the flexion-extension axis of the elbow were determined in both the frontal and transversal planes. A Wilcoxon signed-rank test was performed to test whether there was a change in the orientation of the flexion-extension axis after TEA.

Results

The results show that, over all movement trials, there was a significant change in the orientation of the flexion-extension axis post TEA compared with pre TEA in both the frontal plane (median pre-TEA = 11°; median post-TEA = -5°; $p=0.031$) and the transversal plane (median pre-TEA = 12°; median post-TEA = 19° $p=0.031$). Examination of the prosthesis post-operatively revealed that a part of the 7 degrees varus-valgus laxity was already used in the neutral position because of an alignment error of the ulnar component.

Conclusion

In this pilot cadaver study, a significant change is seen in the orientation of the flexion-extension axis post-TEA compared with pre-TEA in both the frontal and transversal planes. The results stress the importance of properly aligning both the humeral and ulnar components during TEA.

Pathology and Medical Biochemistry

Presenters:

Rahmati, M. (Mina)
Monakova, A. (Anna)
Mehta, A (Aryan)
Lytvynets, M. L. (Mykhailo) BSc
Jamali, M (Mounes) DDS,MS
Rachelkar, AV (Anjali)
Sparks, J. (Jason) assistant professor
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Evaluation of CD44 and TGF-B Expression in Oral Carcinogenesis

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Introduction

Oral squamous cell carcinoma (OSCC) is the most common malignancy of the oral cavity. Evaluation of OSCC by using biomarkers provides preventive treatment approach to suppress the disease in early stages. CD44 as a cancer stem cell (CSC) marker may be cleaved by MT1-MMP and plays an important role in migration of cancer cells. TGF-B promotes formation of invasive cancer cells phenotype through epithelial mesenchymal transition (EMT) and induces MT1-MMP formation. Purpose: The aim of this study is to evaluate the expression of TGF-B and CD44 in leukoplakia (premalignant lesion), squamous cell carcinoma (SCC) and normal oral mucosa to determine the role of these markers in the carcinogenesis process of the oral mucosa.

Materials & Methods

The expression of TGF-B and CD44 were evaluated in 55 paraffin-embedded specimens (10normal mucosa, 15 non-dysplastic leukoplakia, 15 dysplastic leukoplakia and 15 OSCC) by immunohistochemistry. Statistical analysis were performed using Kruskal-wallis, Mann-whitney and Spearman's rank correlation tests.

Results

Evaluation of CD44 and TGF-B expression in the four studied groups showed statistical significant difference for each marker (p< 0.001). Pairwise comparison of CD44 and TGF-B expression in all groups except normal mucosa and non-dysplastic leukoplakia demonstrated statistical significant difference. Also there was positive significant correlation between two markers (r= 0.914, p< 0.001) Diagnostic test's accuracy for identification of OSCC and dysplastic leukoplakia from non-dysplastic leukoplakia and normal tissues and also recognition of OSCC from dysplastic leukoplakia showed optimum sensitivity and specificity.

Conclusion

Increased expression of CD44 as a cancer stem cell marker and TGF-B as an EMT marker from normal mucosa to non-dysplastic leukoplakia, dysplastic leukoplakia and OSCC and also significant statistical correlation between two markers demonstrate the role of these markers in the carcinogenesis process of oral mucosa.

The elevation of S100B and downregulation of circulating miR-602 in the sera of ischemic stroke (IS) patients: the emergence of novel diagnostic and prognostic markers

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Introduction

Ischemic stroke (IS) is a major cause of mortality and disability. However, no reliable prognostic or diagnostic biomarker has been utilized to date. Here, we have evaluated the serum S100B concentration and miR-602 expression as potential biomarkers for IS.

Materials & Methods

Fifty-two IS patients and 52 age- and sex-matched healthy volunteers were enrolled. Blood samples were collected from all patients at the time of admission, 24 and 48 h later, at the time of discharge, and 3 months later. Real-time (RT) PCR was used to measure the serum level of miR602. We also measured the serum concentration of S100B using ELISA.

Results

As compared with healthy subjects, IS patients had a higher level of serum S100B and lower serum miR-602. ROC curve analyses revealed that miR-602 (AUC = 0.8168; P < 0.0001) and S100B (AUC = 0.8699; P < 0.0001) had acceptable ability to differentiate between IS patients from healthy subjects. Furthermore, serum S100B was a reliable predictor of the survival outcome at 3 months (P = 0.021). The expression of miR-602 was significantly higher in patients with bigger NIHSS scores.

Conclusion

The lower levels of miR-602 and higher concentration of S100B in the sera of IS patients could be associated with clinically significant diagnostic utilities. S100B could be also introduced as a reliable prognostic marker for stroke and implemented in future research.

Role of PACAP in age-related systemic amyloidosis

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Introduction

Introduction: PACAP (Pituitary Adenylate-Cyclase Activating Polypeptide) is a multifunctional neuropeptide, which can be found in many tissues and organs of the body. Its general cytoprotective, anti-inflammatory, and anti-apoptotic effects have been proven; however, there are just a few data available of its role in aging. The aim of our experiment was to compare the tissues of wild-type (WT) and PACAP (KO) deficient mice of different age groups to explore the role of endogenous PACAP in aging.

Materials & Methods

Materials and Methods: Samples were taken from more than 20 organs of two age groups of WT and PACAP KO mice (n=30). We divided the following age groups: 3-12-months, 13-24-months-old animals. 3-µm-thick sections of the samples were stained with hematoxylin-eosin, Congo-red staining and anti-ß-amyloid immunohistochemistry, after we have found signs of amyloid deposits. A semi-quantitative scoring to grade Congo-positive deposits from 0-3 was performed according to pathological criteria. Complete blood count, serum analysis from the animals' blood and cytokine array examinations from kidney samples were performed.

Results

Results: Histopathological analysis showed that in the PACAP KO mice the lesion in all organs seemed more severe and was present at a younger age. Among the WT and PACAP KO mice, significant difference occurred in the esophagus, kidney, liver, spleen, thyroid, and skin. Complete blood count, serum analysis and cytokine array examinations (BLC, IL-1ra, RANTES) have shown differences, due to the lack of PACAP.

Conclusion

Conclusion: Using young and aging PACAP KO mice, here we demonstrated that in mice lacking endogenous PACAP senile amyloidosis appeared accelerated, more generalized, more severe and affected more individuals. In summary, here we describe accelerated systemic senile amyloidosis in PACAP KO mice, which might indicate an early aging phenomenon in this mouse strain. Thus, PACAP KO mice could serve also as a model of accelerated aging, with human relevance.

Diagnostic and prognostic implication of expression of INSM1 in glial neoplasms.

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Introduction

To evaluate the expression of transcription factor insulinoma-associated protein 1 (INSM1) in different glial neoplasms and reactive glial tissue and its possible diagnostic utility in routine histopathology.

Materials & Methods

Cases of reactive glial tissue (n=37) and cases of low-grade (n=40) and high-grade (n=77) gliomas diagnosed at University Hospital in Hradec Kralove between 2012 and 2020 were used for the construction of 7 tissue microarrays (TMAs). Each case was represented with three 1 mm thick cores. Only cases with known IDH1 status and 1p/19q codeletion were included in the group of low-grade astrocytomas and oligodendrogliomas respectively. Antibodies against INSMI and IDH1 R132H mutated protein were used. Staining was performed with Agilent/Dako Autostainer 48, equipping Envision Flex detection kit. The slides were scanned with Leica Aperio AT2 slide scanner (Leica Biosystems, IL, USA) and the percentage of INSM1 positive cells was evaluated in a double-blinded fashion. Cases with discordant results were reviewed by both authors together. Only cases with at least 1 intact core were included.

Results

The cohort included 32 (27.5%) IDH1mt and 84 (72.5%) IDH1wt tumors. 17 (14.5%) tumors harbored 1p/19q codeletion. 40 (34%) tumors were low-grade (grade 1 and 2), while the remaining 77 (66%) were high grade (grade 3 and 4). In total, 61.5% (72/117) of gliomas expressed INSM1. Of IDH1wt cases, 64.2% (54/84) were positive, in contrast to only 2.7% (1/37) samples of reactive glial tissue (p<0.001, $\chi 2$). INSM1 expression was 64.2% sensitive and 96.7% specific for the diagnosis of glioma. In gliomas, the mean percentage of INSM1+ cell percentage was 7.5 (S.D.±13.819), the median percentage was 2 (IQR 0-8.8). Expression of INSM1 did not differ between IDH1mt and IDH1wt groups (p=0.5; Mann-Whitney test), nor between oligodendroglial tumors with 1p/19q codeletion and non-codeleted tumors (p=0.22; Mann-Whitney test). High-grade gliomas show significantly higher expression of INSM1 compared to the low-grade group (p<0.001; Mann-Whitney test).

Conclusion

INSM1 expression was significantly increased in glial neoplasms vs reactive glial tissue. The results also suggest that INSM1 positivity was seen in IDHwt tumors which would help us to diagnose if a certain tumor is a glial neoplasm or not.

Searching for the pivotal components of mesenchymal stromal cell secretome responsible for the restoration of damaged spermatogonial stem cell niche

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Introduction

Mesenchymal stromal cells (MSCs) take part in sustaining of stem cells and their tissue-specific niches. We have previously shown that MSCs promote the restoration of spermatogonial stem cell (SSCs) niche mostly due to secretome. We assumed that the paracrine regenerative effects of MSC secretome on SSC niche are mainly mediated by growth factors such as vascular endothelial growth factor (VEGF) and glial cell-derived neurotrophic factor (GDNF). GDNF is a crucial factor for the maintaining the viability of SSCs. VEGF is one of major growth factors, which enhances the secretion of testosterone by SSC supporting cells – Leydig cells. Extracellular vesicles (EVs) also could mediate MSC-dependent regenerative effects.

Materials & Methods

To check a contribution of these components into the recovery of spermatogenesis after damage, the murine model of complex spermatogenesis damage by doxorubicin was established. Then we neutralized VEGF or GDNF in MSC secretome with specific antibodies or deleted EV fraction from MSC secretome. MSC secretome or the mentioned substances were administrated locally in mice with doxorubicin-induced disruption of spermatogenesis. A spermatogenesis recovery was estimated by the histological analysis of testicles stained with hematoxylin-eosin and spermatozoa count in the epididymis.

Results

Total (6,251*10^6) and motile spermatozoa (0,123*10^6) fractions increased in the treated with MSC secretome mice more than in doxorubicin animals (0,412*10^6 and 0,0007*10^6 respectively). In animals treated with MSC secretome containing VEGF neutralizing antibodies amount of total and motile spermatozoa was lower (0,25*10^6 and 0 respectively) than in MSC treated group. Percent of animals with normal and recovered tubules increased in a group treated with MSC secretome compared with untreated group. However, VEGF neutralizing MSC secretome injection did not recover damaged tubules. GDNF neutralizing or EVs deletion did not change MSC secretome effects.

Conclusion

Thus, VEGF contributes into the MSC-mediated spermatogenesis recovery after damage whereas GDNF and EVs were not so important for the observed therapeutic effects. Our data are preliminary, but have pharmaceutical value for the standardization of MSC secretome using VEGF measurement.

Russian Science Foundation (project 19-75-30007, in vivo experiments) and the State Assignment of Lomonosov; the equipment to be used was purchased as a part of Lomonosov MSU Program of Development.

Content and localization of angiotensin-converting enzyme-2 (ace2) in acute experimental bronchopneumonia

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Introduction

Coronavirus (SARS-Cov-2) affects on almost all systems and organs, but the lungs are most affecting. The main cause of death is the development of acute respiratory distress syndrome and pulmonary fibrosis. SARS-CoV-2 enters the cell by binding to a transmembrane glycoprotein, angiotensin-converting enzyme-2 (ACE2), which is expressed on the surface of the bronchial and alveolar epithelium. Unfortunately, development of animas model with actual SARS-COV-2 infection is limited. That's why we require the model which reproduces the main stages in the pathogenesis of the disease and also discover the influence of acute pulmonary inflammation on the ACE-2 epression.

The aim of this study was to determine changes in the content and characteristics of tissue localization of ACE2 in the model of acute bronchopulmonary inflammation.

Materials & Methods

Acute inflammation was modeled in Wistar rats (n=50) by endotracheal injection of a foreign body (capron thread) and a solution of lipopolysaccharide (LPS; 50 µl at a dose of 12.5 mg/kg) against the background of systemic administration of LPS for two days before surgery (250 mg/kg). Cellular ACE2 localization and quantity were evaluated by immunohistochemical and western blot assays with the use of specific monoclonal antibody (anti-ACE2; clone 4G5.1; Sigma-Aldrich MABN59; EMD Millipore Corporation; Temecula, CA US).

Results

The experiment reproduced acute exudative-hemorrhagic bronchopneumonia with the development of diffuse progressive pulmonary fibrosis with a lethality of 36% of animals. Acute exudative inflammation was accompanied by complete inhibition of ACE2 expression in bronchial epitheliocytes (by 2.0 times compared to the control; P=0.003) and its significant decrease in alveolocytes II type and vascular endothelium. With the development of the proliferative stage of bronchopneumonia, the level of ACE2 was restored, subsequently remaining without significant changes.

Conclusion

The obtained experimental data suggest the existence of a relationship between the features of quantitative changes in the ACE2 level in the bronchopulmonary epithelium and the undulating course of the inflammatory process during SARS-CoV-2 infection.

Correlation between glycated hemoglobin (HbA1c) and oxidative stress status in patients with type 2 diabetes mellitus

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Introduction

Type 2 diabetes mellitus has a heavy disease burden and is also one of the leading causes of death worldwide. It is considered to be evolving from a complex and multifactorial metabolic disorder to an inflammatory condition. The strong link between hyperglycemia and oxidative stress has long been established. Oxidative stress results in generation of inflammatory mediators and reactive oxygen species which results in an inflammatory state, which plays a key role in pathogenesis and progression of diabetes and its complications. We aimed to correlate the levels of HbA1c with oxidative stress of the patients

Materials & Methods

The current cross sectional study included 100 patients with type 2 diabetes mellitus being treated at an outpatient clinic of a tertiary care hospital. The oxidative stress of the patient was estimated by lipid peroxidation assay (activity of malondialdehyde) and superoxide dismutase levels in the patient. Estimation of glycated hemoglobin (HbA1c) was done using ion exchange chromatography. The data was analyzed using t test.

Results

It was observed that the levels of superoxide dismutase increased with increasing duration of diabetes. Similar trend was observed with levels of malondialdehyde (MDA). The change in the levels of both superoxide dismutase (SOD) and malondialdehyde (MDA) was statistically significant (p<0.001) when compared amongst each other. This increase in the levels of SOD and MDA indicate increased oxidative stress and lipid peroxidation in relation to duration of diabetes in these individuals. No significant correlation was found between markers of oxidative stress -superoxide dismutase (SOD) (p=0.995) and malondialdehyde (MDA) (p= 0.877) with glycated hemoglobin (HbA1c).

Conclusion

The results of the study show that as the duration of diabetes mellitus increased, the levels of oxidative stress (SOD and MDA) increased as well. Also no significant correlation was found between markers of oxidative stress -superoxide dismutase (SOD) and malondialdehyde (MDA) with glycated hemoglobin (HbA1c).

Immunohistochemical concentration of vimentin in the vessel endothelium of the myometrium in the projection of the uterine-placental area in iron-deficiency anemia during pregnancy

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Introduction

During pregnancy, the uterus undergoes structural changes - the uterine-placental area (UPA) is formed. Our previous studies revealed that during gestation on the background of Iron deficiency anemia (IDA) placental bed of the uterus morphologically has signs of gestational immaturity, the severity of which correlates with the degree of anemia. In that case increases the production of a number of proteins, which are poorly detected in the UPA during physiological pregnancy, one of them is vimentin.

Materials & Methods

54 biopsies of UPA and myometrium obtained in the Caesareo section were studied (including 30 observations of placental dysfunction and 24 biopsies of UPA of physiological pregnancy). Term of gestation was 37-40 weeks. The material according to the standard technique was objected to immunohistochemical procedure with primary antibodies against vimentin (DAKO, USA). On digital copies of images the optical color density was evaluated (in the range from "0" to "1") based on logarithmic transformations brightness (in gradations from "0" to "255"), that was a measure of immunohistochemical concentration of vimentin.

Results

During physiological pregnancy, the optical density of staining for vimentin in the endothelium was: in the arteries - 0,284 ± 0,0022, in the veins - 0,287 ± 0,0023, vessels of the microcirculatory tract - 0,326 ± 0.0015. At IDA without clinical signs of placental dysfunction optical density of color on vimentin in endothelium was: in arteries - 0,336 ± 0,0021, in veins - 0,295 ± 0,0021, microcirculatory vessels - 0,321 ± 0,0016. In cases of gestation on the background of IDA with the presence of placental dysfunction, the optical density of staining for vimentin in the endothelium was: in the arteries - 0,408 ± 0,0022, in the veins - 0,241 ± 0,0022, in the microcirculatory tract - 0,215 ± 0,0012.

Conclusion

Observations of pregnancy on the background of IDA revealed the features of increasing immunohistochemical concentration of vimentin in the walls of myometrial segments of utero-placental arteries, which should be regarded as a manifestation of endothelial dysfunction, endothelial damage of incomplete gestational transformed spiral arteries. At gestation against anemia with placental insufficiency decrease in immunoexpression of vimentin in the endothelium of the microcirculatory tract is evidence of impaired angiogenesis in the myometrium in the projection of the placental bed of the uterus.

Immunology and Haematology

Presenters:

Alabdallat, Y.J.A (Yasmeen)
Bult, J.A.A. (Johanna)
Montaño Mendoza, V.M. (Vicky) Medical student
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Maleki, R (Reza) Mister
Vazhappilly Jose, A.V.J (Arun)

Construction and evaluation of wild and mutant Ofatumumab scFvs against the human CD20 antigen

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Introduction

Several monoclonal antibodies targeting the CD20 antigen have been produced, and some of these are now being tested in clinical studies. Ofatumumab is a completely human anti-CD20 antibody that was approved in 2009 for the treatment of CLL. Although antibodies are able to target cancer cells effectively, their applications are restricted in some ways. For example, their large size or Fc region could result in slow blood clearance rates and immunogenicity. In bacterial systems, single-chain fragment variable (scFv) generation has become a functional approach for creating a fully functional antigen-binding fragment.

Materials & Methods

The DNA coding sequence of VL and VH of wild and mutant forms of ofatumumab were joined with flexible linker (GGGGS)3 by SOE PCR. Using the E.coli BL21 (DE3) expression system, the VL-linker-VH genes were cloned into the pET-28a, and the associated proteins were produced. SDS-PAGE analysis was used to validate the purity of the scFvs and subsequently, the expression of 6×His tagged proteins was detected using the Western blotting method. Affinity measurement was performed according to Beaty formula. Moreover, Cell ELISA and MTT assay were also used to supplement the evaluation.

Results

The scFv antibodies were successfully cloned, produced, and purified. Both scFvs represented a yield of around 0.7 mg/ml with a molecular weight of about 27 kDa. According to affinity measurement, anti-CD20 scFv-V-3 showed a higher affinity constant compared to anti-CD20 scFv-C.

Cell-ELISA revealed that the recombinant scFvs selectively bind to Raji cells (CD20 positive) but not to Jurkat cells and also anti-CD20 scFv-V-3 binds to Raji cells more efficiently. An MTT test was used to examine the potential influence of scFvs, which demonstrated that anti-CD20 scFvs could affect cell viability in Raji cells but had no impact on Jurkat cells. Moreover, Raji cell viability was affected more significantly by anti-CD20 scFv-V-3.

Conclusion

The resulting antibody fragments demonstrated that they are able to bind to CD20 antigen effectively and also can prevent the proliferation of Raji cancer cells considerably. Moreover, the scFv-V_3 antibody fragment showed a greater tendency to bind to CD20 antigen compared to the scFv-C antibody fragment.

comparative study of diagnostic accuracy between rotational thromboelastometry and conventional coagulation tests

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Introduction

ROTEM(Rotational thromboelastometry) is a point of care viscoelastic hemostasis analyzer test which aids in understanding coagulation pathways and bedside identification haemostasis disorders. When compared to Conventional coagulation tests(CCT) like Prothrombin time(PT), partial thromboplastin time(aPTT), platelet count & fibrinogen, viscoelastic methods like ROTEM resemble in vivo haemostasis, require one device to evaluate multiple coagulation factors, do not require centrifuge, measures cloth strength and dynamics. ROTEM has a faster turnaround time but requires more expensive reagents.

Materials & Methods

It was a cross-sectional- diagnostic evaluation test conducted in a tertiary care hospital in South India, among 109 patients above 18 years requiring coagulation assessment. In all the cases, both conventional tests and ROTEM were performed simultaneously. Comparison between standard conventional coagulation tests and ROTEM test(EXTEM, INTEM, FIBTEM) was done using SPSS AUC-ROC curve, standard error assessment and difference of p<0.05 was taken as statistically significant.

Results

The mean age of the study population was 42.7 years with 52.3% males and 47.7% females. The mean turnaround time (TAT) for ROTEM 11.2 min was around three times lesser than that of CCT 33.5 min. Fibrinogen had an excellent correlation (r > 0.8) with A5(Amplitude at 5th minute), A10(Amplitude at 10 min) and MCF(Maximum clot firmness) of FIBTEM, compared to strong correlation with EXTEM (r > 0.6) and INTEM (r > 0.5). Also, AUC ROC for all these parameters was above 0.9 with > 80% sensitivity and specificity. EXTEM parameters A5, A10, MCF & ALPHA had > 70% sensitivity and specificity in diagnosing coagulopathy. A5 parameters have a strong correlation with MCF parameters and hence help in the early detection of clot firmness and coagulopathy. Platelet count had a significant correlation with A5, A10 & MCF of EXTEM.

Conclusion

We could conclude that FIBTEM, EXTEM, and INTEM parameters can be used as surrogates to fibrinogen levels with great sensitivity and specificity. Significant reduction in TAT by ROTEM leads to early bedside identification & resuscitation of coagulopathy. ROTEM provides a global portrait of the clot formation within whole blood and allows for interaction between whole blood elements including platelet, fibrinogen & coagulation factors.

The Safety and Efficacy of CPX-351 versus 7+3 in Patients with Newly Diagnosed, High-Risk/Secondary AML (sAML): A Systematic Review and Meta-analysis.

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Introduction

The aim of this study was to assess the safety and efficacy of CPX-351 versus 7+3 cytarabine and daunorubicin chemotherapy among patients with newly diagnosed, high-risk/secondary AML (sAML).

Materials & Methods

We performed a comprehensive search for the following databases: PubMed, Cochrane (Medline), Web of Science (WOS), and Scopus. All studies published in English till 2021 were included. These included randomized and non-randomized controlled trials comparing the Complete Response (CR), Incomplete Neutrophil Recovery (CRi), Overall Survival (OS), Event Free Survival (EFS) as well as Treatment Emergent Adverse Events (TEAEs). The risk of bias was assessed according to the Cochrane risk-of-bias tool for randomized trials (RoB2) and the ROBINS-I risk of bias tool to assess non-randomized studies of interventions.

Results

We included 19 trials involving 5,257 participants. The best transformation of the data was converting the HR (Hazard Ratio) of the median OS into RR (Risk Ratio) logarithm. The results of the OS are reported in 10 studies examining 2529 sAML patients. The overall effect favored the CPX-351 group (RR 0.79 with 95% CI, (0.69 to 0.28; I2 = 54%), P < 0.001). Further, the CR's results reported in Five studies examining 1219 sAML patients showed that the overall effect favored the CPX-351 group (RR 1.47 with 95% CI, (1.12 to 1.92; I2 = 59%), P = 0.005). The results of the CR+CRi are reported in Eight studies examining 2083 sAML patients. Results showed that the overall effect favored the CPX-351 group (RR 1.65 with 95% CI, (1.34 to 2.03; I2 = 59%), P < 0.001). The results of the EFS are reported in Four studies examining 1221 sAML patients. Results showed that the overall effect favored the CPX-351 group (RR 72 with 95% CI, (0.63 to 0.82; I2 = 0%), P < 0.001).

Conclusion

Overall survival, Complete remission, both complete remission and incomplete neutrophil recovery as well as event free survival showed a favorable outcome among CPX-351 group in comparison to 7+3 group.

Comparison of humoral immune response following boosting with BNT162b2 COVID-19 vaccine as a heterologous or homologous third dose in healthy individuals from Republic of North Macedonia

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Introduction

The 'mix-and-match' approach in vaccination, has been previously used during the development of vaccines against several microorganisms, including the novel SARS-CoV-2 in 2020. The aim of our research was to compare the titers of antibodies against the receptor-binding domain of SARS-CoV-2, elicited after application of heterologous booster regimen versus application of the same type of primary and booster vaccine doses.

Materials & Methods

Our prospective cohort consisted of 52 healthcare workers who received a booster dose in the period between October and December 2021. We divided the participants in two subgroups, the first group were vacccinees that received BNT162b2 vaccine as a primary immunization, and the second group received Sputnik V. We collected serum samples 4 weeks after receiving the booster. Serological testing was performed using the commercially available CLIA SARS-CoV-2 RBD kit, whose target is the S1 subunit of the viral spike protein. The cut-off value of the test is 1AU/ml.

Results

The mean concentration of RBD IgG antibodies after two doses of Sputnik V was 14.0837±10.651 AU/ml, while two doses of BNT162b2 vaccine resulted in significantly higher mean concentration of 69.5664±58.58 AU/ml (p=0.0001 with 95% CI). The BNT162b2 booster dose elicited strong humoral response in both groups, 606.7126±125.572 AU/ml in the homologous vaccine group and 373.9039±150.527 AU/ml in the heterologous vaccine group. However, when comparing the increase itself, we noted substantially higher increase in the mean antibody concentration in the heterologous group, 26.5 fold vs 8.7 fold increase in the homologous vaccination group.

Conclusion

Our results bring forward the applicability of the 'mix-and-match' principle in the process of COVID-19 immunization and its potential advantages based solely on analyzing the humoral response to vaccines. This principle might have a wider-scale impact, helping countries in shortage of vaccine supplies to combine available vaccines and speed up the vaccine coverage. Another potential benefit from this study is the recommendation to improve humoral response with booster BNT162b2 vaccine in individuals who have unsatisfactory humoral response after the primary immunization. However, the need for confirmation of these findings in a real-world setting remains.

Low mutational burden of extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue in patients with primary Sjogren's syndrome.

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Introduction

Primary Sjogren's syndrome (pSS) is an autoimmune disease characterized by chronic inflammation of the exocrine glands. Patients with pSS are at increased risk of developing extranodal marginal zone lymphoma of the mucosa-associated lymphoid tissue (MALT) type. Unlike recurrent genomic aberrations observed in MALT lymphoma not associated with pSS (non-pSS), it is unknown which somatic aberrations underlie the development of pSS-associated MALT lymphomas. The aim of the current study was to define the genomic landscape of pSS-associated salivary gland MALT lymphomas.

Materials & Methods

Whole exome sequencing was performed on 14 fresh frozen and 3 paraffin embedded MALT tissue samples of pSS patients. Matched peripheral white blood cell samples were available for 12 patients and were used as germline controls. Fluorescence in situ hybridization was performed for the detection of MALT1 translocations.

Results

Presence of a clonal B-cell population, indicative of a MALT lymphoma, was confirmed by IgH PCR (BIOMED-2) for all patients. Whole exome sequencing resulted in a median target coverage of 130x, ranging from 84-163. More than 90% of the target regions had a coverage of >50x. Translocations involving the MALT1 gene were not detected in any of the samples. In total, 222 nonsynonymous somatic variants were detected in 182 genes. The median number of variants was 7 (range 2–78), including 3 cases with a relatively high mutational load (≥24/case). Out of 16 recurrently mutated genes ID3, TBL1XR1, PAX5, IGLL5 and APC are known to be associated with lymphomagenesis. In addition, five recurrently mutated genes are involved in epithelial surface and/or extracellular matrix (MAMDC4, COL14A1, CAMSAP3, TMEM2 and MUC4). A total of 18 copy number alterations were detected in 8 cases. With respect to outcome, only 2 cases with high mutational load relapsed outside of the salivary glands, suggesting a more advanced stage of lymphoma.

Conclusion

The low mutational load and lack of a clear lymphoma-related gene profile suggests that localized pSS-associated MALT lymphomas are genomically more stable than non-pSS MALT lymphoma

and most likely depend on a stimulatory micro-environment.

Immune cells of the endometrium which make pregnancy happen

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Introduction

From a woman's perspective, an embryo is a foreign genetic material. The immune system is specifically designed to protect from foreign genetic material. If we want a normal pregnancy to happen, the immune system must change. Otherwise, we have what is called immunological infertility. If we know how the endometrial immune cells function in a normal setting, which is the subject of our work, we will understand why women have multiple implantation failures. We have used the human endometrium, which makes our work unique.

Materials & Methods

The endometrium was collected from 22 healthy women on day of ovulation (OV) and 23 healthy women on day of implantation window (IW). The features of NK and T-cells were evaluated in the collected endometrium. We have used three-colour flow cytometer FACScan (BD-Biosciences) for measuring CD158 — receptors that prevent NK and T-cells from activating and killing, HLA-DR — a sign of inflammation, CD8α and InStat for Windows for statistical analysis.

Results

The samples collected in IW compared to OV have shown a significant increase of the number of NK-cells (95%CI 42.48-53.13; p-value<0.00001; tStat=-5.26) and increase of CD8 (95%CI 27.33-37.82; p-value=0.002; tStat=-3.26) and CD158a on NK-cells (95%CI 34.18-49.22; p-value<0.00001; tStat=-5.08), as well as decreased HLA-DR expression on NK-cells (95%CI 9.69-15.04; p-value=0.00004; tStat=4.53) in endometrium.

The number of T-cells was lower during IW (95%CI 31.87-42.52; p-value<0.00001; tStat=5.26) without any differences of HLA-DR production on their surface (95%CI 39.21-46.98; p-value=0.628931; tStat=0.48). CD158 expression on T-cells was higher during IW (95%CI 9.41-25.89; p-value=0.01; tStat=-2.69).

Conclusion

There is an immunological reason why IW is the best time for implantation. We investigated the characteristics of endometrial NK and T-cells. The growth and activity of these cells determine if the embryo can successfully implant. Indeed, during IW, the number of NK-cells increases, however, they become more mature by higher CD158 and CD8 expression and less active by lower HLA-DR expression. The number of T-cells decreases without any changes in HLA-DR expression, but T-cells become more mature by higher CD158. All these changes suggest that a woman's immune system changes every month to allow the embryo, a genetically foreign material, to successfully implant and develop.

Immune gene expression by sex and age shapes the antiviral response to SARS-CoV-2 infection

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Introduction

Viral infectious diseases affect humans worldwide and typically behave differently in each sex, influenced by the disease-causing virus itself and the host immune response. For the SARS-CoV-2 infection, clinical manifestations are broad and highly heterogeneous for both sexes; however, older men are more vulnerable to severe and life-threatening presentations than women. Disparities in the immune phenotypes among infected subjects may trigger the distinct disease courses by altering the antiviral response cascade. Here, we aimed to determine how biological sex and age effects in immune gene expression rebound on the immunological profile and influence the humoral neutralizing antibody (NAb) response of patients with COVID-19.

Materials & Methods

We conducted an in silico-in vitro study. Sex differences in immune gene expression were assessed using the whole-genome expression profile of blood proteins from the Genotype-Tissue Expression (GTEx) Portal. Moreover, a plaque reduction neutralization test (PRNT) was performed in 141 individuals with COVID-19 to measure the neutralizing activity of anti-SARS-CoV-2 antibodies. Significant designations were determined by means of a cut-off p-value <0.05. All the analyses were performed using GraphPad Prism version 9.0.1.

Results

Most of the differentially expressed genes (DEG) were identified to participate in antimicrobial and proinflammatory responses. Also, there were more male-biased than female-biased genes and the peak of DEG was higher in the youngest cohort studied, to further decrease with aging. Compared to the higher innate immunity functions represented in female-biased genes, male-biased genes were more associated to cytotoxicity in the adaptive immunity.

Among patients with COVID-19, males had statistically significant higher median PNRT50 titers (320, IQR 80-1280) than females (20, IQR 0-320). Despite that, the difference was non-significant among patients with more severe disease (p= 0.1986). Furthermore, we observed a weak positive correlation between age and NAb titers (rs=0.3262, p= 0.008).

Conclusion

Collectively, our findings suggest that stronger innate responses in women resulting from variations in immune gene expression may be responsible for the distinct outcomes observed between male and female COVID-19 patients. SARS-CoV-2 also induces changes in gene regulation that affect the kinetics of both cellular and humoral responses by sex and age and should be considered in additional studies.

Medical Physiology

Presenters:
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Chronic exposure of unflavoured electronic cigarettes liquid in different nicotine concentrations impairs liver function

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Introduction

Nicotine and flavour in electronic cigarette (e-cig) liquid have been demonstrated cytotoxic effects in acute exposure. The chronic effects of unflavoured and with or without nicotine in e-cig liquid on liver function has not been evaluated. This study purposed to evaluate the chronic effect on liver function in rats after exposure to unflavoured e-cig liquid in different nicotine concentrations.

Materials & Methods

A total of 28 male Wistar rats were randomly distributed into four groups of seven each. Control, as a control group. Nic 0, Nic 6, and Nic 12 groups were exposed to unflavoured e-cig liquid for eight weeks with different nicotine concentrations of 0, 6, and 12 mg/mL, respectively. E-cig exposure in rats carried out an exposure instrument adjusted to real-life exposure to humans. Liver function markers including alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels as well as antioxidant enzyme catalase (Cat) activity in plasma were assessed. One-way ANOVA with Tukey's post hoc was performed for statistical analysis.

Results

Unflavoured e-cig liquids were impaired liver function by significantly increasing (P < 0.001) ALT and AST levels in all exposed groups compared to control, except in AST levels of Nic 0 group (P > 0.05). A significant decrease (P < 0.001) of Cat in all exposed groups also occurred. These results demonstrated that the higher nicotine concentration further impairs liver function.

Conclusion

Chronic exposure to unflavoured e-cig liquids impairs liver function in nicotine concentration-dependent. Thus, these findings highlight the potentially harmful effect of e-cig use even without nicotine and flavour, particularly liver function.

The characteristic and function of the hypothalamus to sublaterodorsal orexin pathway

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Introduction

Stable vigilance states depend on the regulation of diverse neurochemical signals. Among them, hypothalamic neuropeptide orexin/hypocretin is indispensably involved. The deficiency of orexin causes narcolepsy in human and animals. Besides the prominent deficits in maintaining wakefulness state, narcoleptic patients also suffer from the impaired quality of rapid eye movement (REM) sleep. Intriguingly, a brainstem region that is necessary and sufficient in REM sleep generation, sublaterodorsal tegmental nucleus (SLD), receives direct innervation from orexin neurons. Nevertheless, roles of SLD orexin signaling in REM sleep regulation and the related neural mechanisms remain unknown.

Materials & Methods

Multidisciplinary approches including immunostaining, neurotracing, electrophysiology, fiber photometry, optogenetics, chemogenetics and behavioral tests were employed in the present study.

Results

Using in vitro and in vivo electrophysiological investigations, we first found that orexin globally excited the electrically coupled SLD network to promote synchronized firings. We next observed the activity of the orexin pathway from hypothalamus to SLD and found an increased activity during REM sleep. Optogenetic and chemogenetic manipulations reveal that this SLD orexin signaling was employed to stabilize REM sleep episodes. Intriguingly, besides the reduced REM sleep episodes, an abnormal behavior phenotype characterized by severe disruption of muscle atonia of REM sleep was also observed after chemogenetically silencing the orexin pathway. Furthermore, permanent deletion of SLD orexin signalling obviously disrupted REM sleep homeostasis through the abnormal muscle activities.

Conclusion

Collectively, the present study demonstrates a direct stabilization mechanism of excitatory orexin signaling in REM sleep regulation. These findings provide additional insights to understand that both REM sleep symptoms and wakefulness-maintaining deficits exist after loss of central orexin signaling.

The role of intraamygdaloid oxytocin receptors in social interaction in valproate induced autism animal model

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Introduction

The incidence of autism spectrum disorder (ASD) among children is about 1%. Symptoms are variable but in most cases damage to social interaction is present. Proper treatment has not been solved yet since the exact pathomechanism of ASD is still poorly understood. The aim of our research was to study the effect of oxytocin (OT) injected into the central nucleus of amygdala (CeA) on social interaction in healthy rats and in valproate induced autism animal model. We also studied the receptor specificity with OT receptor antagonist (ANT).

Materials & Methods

To induce autism the dams received intraperitoneal valproate injection on the 12.5th day of the gestation therefore most of the descendant animals showed autistic signs. We operated healthy and autistic signs showing male Wistar rats by stereotaxic surgery. Stainless steel guide cannulas were implanted bilaterally above the CeA and were used for microinjections further on. We divided the healthy animals into four categories: 1. vehicle (n=8), 2. 10 ng OT (n=8), 3. 20 ng ANT+10 ng OT (n=7), 4. 20 ng ANT (n=7). Groups among animals with autistic signs were the same: 5. vehicle (n=7), 6. 10 ng OT (n=7), 7. 20 ng ANT+10 ng OT (n=6), 8. 20 ng ANT (n=6). We examined the behaviour of the animals in social interaction test. We used Noldus EthoVision program to measure the time spent with social interaction.

Results

Due to the 10 ng OT treatment the time spent with studying the unfamiliar rat among healthy animals has significantly increased compared to the control group. In autistic signs showing animals impairment in social interaction was detectable. Due to the OT microinjection it has significantly increased and reached the level of healthy animals. The ANT treatment has fended the effect of OT off but given alone has not affected the time spent with social interaction significantly.

Conclusion

According to our results the microinjection of 10 ng OT into the CeA has significantly improved the impaired social interaction in valproate induced autism model and this effect was receptor specific.

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Localisation of sensory nerve endings in the dorsal part of the scapholunate ligament

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Introduction

The dorsal part of the scapholunate (SL) ligament is a key stabilizer of the human wrist. It the is most frequently injured ligament of the human carpus. It is important to surgically reconstruct the SL ligament after injury to prevent alterations in the biomechanics of the wrist joint and carpal collapse. The SL ligament contributes to proprioception due to a rich innervation with sensory nerve endings. We aimed to analyse the three-dimensional intrastructural distribution of sensory nerve endings in the dorsal part of the SL ligament.

Materials & Methods

Two dorsal parts of SL ligaments were excised from two cadaver specimens. Consecutive 70 µm thick cryosections were stained with the immunofluorescence markers for protein S100, neurotropin receptor p75, protein gene product 9.5 and 4ɣ,6-diamidino-2-phenylindole (DAPI). Three-dimensional images of the sensory nerve endings were obtained using a confocal laser scanning microscope Leica SP8. Images were deconvolved using Huygens Professional software. Sensory nerve endings were localised in each section plane and classified according to Freeman and Wyke. Visualisation of the 3D-images was accomplished with Imaris 9.6. Distribution of sensory nerve endings was analysed by dividing the ligament into twelve anatomical subregions.

Results

Significantly more Ruffini-endings were found at the scaphoid (p<0.0005) and lunate insertion (p=0.022) in comparison to the central ligament region. Furthermore, free nerve endings were significantly more frequently located centrally (p=0.003) than lunarly or scaphoidally. No significant difference in the distribution along the scaphoid-central-lunate axis was found for Pacini corpuscles or Golgi-endings. Furthermore, no significant differences in the distribution along the dorsal-palmar and the proximal-distal axis were observed for all mechanoreceptors.

Conclusion

The three-dimensional analysis allows precise localisation of sensory nerve endings in a ligament. The polarised distribution of Ruffini endings at the ligamentous insertion of the scaphoid indicates that this region is essential for the neuromuscular stability of the wrist. In contrast, nociception takes place in the central parts of the ligament.

Vascular adaptation to cancer: Mechanisms involved

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Introduction

Cancer needs to induce vascular adaptation through angiogenesis, changes in vascular reactivity (VR) and in the architecture of the arterial wall. Generating knowledge about vascular adaptation mechanisms contributes to a better understanding of cancer and to develop new strategies for its treatment.

Materials & Methods

Mesenteric arteries from patients colectomized due to colon cancer (vessels that irrigate the tumor -TU- or the surrounding non-tumoral tissue -ET-), or non-cancer (NT) patients were processed. VR (maximum effect, Emax; sensitivity, pD2) to KCl, U46619 (TXA2 analog), phenylephrine, endothelin-1, carbachol, bradykinin, vascular endothelial growth factor (VEGF) and isoproterenol was measured in an organ bath. The contractile response was normalized to a response to 40 mM KCl (%KCl). These arteries will be incubated with nanovesicles (NV) obtained by ultracentrifugation of HeLa and SiHa cancer cell culture medium. In cell culture, changes in the capacity for tube formation in microvascular endothelium HMEC will be measured, and in organ bath changes in VR of new TU, ET and NT human arteries will be measured, to determine adaptation mechanisms affected by NV.

Results

Contraction: Cancer increases sensitivity to KCl (pD2: NT 1.6±0.04; ET 1.8±0.02; TU 1.8±0.03, p=0.02), to phenylephrine (pD2: NT 5.7±0.008; ET 6.2 ±0.09; TU 6.1±0.13, p=0.004; Emax: NT 91±12 %KCl; ET 137±6.5% and TU 117±18%; p=0.04) in ET and TU, and to U46619 (pD2: NT 7.08±0.1, ET 7.3±0.09, TU 7.2±0.1, p=0.06) in ET and TU. There are no differences in VR to endothelin-1(p>0.05).

Vasodilation: Cancer increases sensitivity to carbachol (Emax: NT 1.3±8%; ET 49.6±14% and TU 41.5±13 %relaxation; p=0.009) in ET and TU, and to isoproterenol (pD2: NT 6.5±0.17; ET 8.3±0.3; TU 7.7±0.18, p=0.001) and Emax (NT 8.4±2%; ET 28.2±5% and TU 29.5±9.2 %relaxation; p =0.005) in ET and TU. Cancer decreases sensitivity to bradykinin (pD2: NT 6.2±0.16; ET 6.01±0.2; TU 6.05±0.12, p=0.02) and Emax (NT 91±20%; ET 53.4±5.6% and TU 44.08±1 %relaxation, p=0.03) in ET and TU. No differences were found in VR to VEGF (P>0.05).

Conclusion

Cancer induces a contractile environment in the arteries, which could facilitate a hypoxic environment in the tumor. NV could play a role in vascular adaptation.

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Characterization of vascular models to support strategies against cancer

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Introduction

Generating knowledge about vascular adaptation to cancer contributes to developing strategies for its treatment. Our studies in human colon cancer compare cancerous with non-cancerous arteries to assess the mechanisms altered by the disease, but we do not have healthy human arteries to extend our studies to lung cancer. We present evidence that the pig is an excellent vascular model in colon, and preliminary findings characterizing the pig pulmonary artery branches.

Materials & Methods

In organ bath, we measured vascular reactivity (-VR- maximum effect "Emax"; sensitivity, "pD2") of human and porcine colon, and porcine pulmonary arteries, to contractile agonists and vasodilators. The contractile response was normalized to a response to 40 mM KCl (%KCl). In addition, α1, β2 and thromboxane-prostanoid (TP) receptors were quantified by fluorescence microscopy in each vascular tunic.

Results

Pig arteries differ from humans only in Emax to isoproterenol (Human-Emax: 13.6±3.6%relaxation; pD2: 7.36±0.12; Pig-Emax: 27.4±9.9%relaxation; pD2: 6.36±0.17, p=0.005). The response to the rest of the agonists is the same: to KCl (Human-Emax: 127.9±10%KCl, pD2: 1.6±0.07; Pig-Emax: 136±7.2%KCl, pD2: 1.58 ±0.03), U46619 (Human-Emax: 128.6±8.5%KCl, pD2: 7.05±0.01; Pig-Emax: 113.6±16%KCl, pD2: 6.6±0.07), phenylephrine (Human-Emax: 95.9±14%KCl, pD2:5.68±0.1; Pig-Emax:132.8±16.7%KCl, pD2: 5.82±0.09), carbachol (Human-Emax: 1.3±8%relaxation; pD2: 6.48±0.14; Pig-Emax: 8±8.4% relaxation; pD2:5.93±0.17) and BK (Human-Emax: 96.4±17%relaxation; pD2: 6.6±0.25; Pig-Emax: 86±7.5%relaxation; pD2: 7.3±0.33).

In receptor expression, pig arteries differ from humans only in the tunica media for α1 (Human-intima: 1±0.08, media: 1±0.18; adventitia: 1±0.17; Pig-intima: 1.27±0.15, mean: 1.5±0.3; adventitia: 1.36±0.2; p=0.001) and β2 (Human-intima: 1±0.07, mean: 1±0.11 adventitia: 1±0.16, Pig-intima: 0.65±0.11, mean: 1.3±0.14, adventitia: 0.9±0.16, p=0.009), but not for TP (Human- intima: 1±0.09, mean: 1±0.11, adventitia: 1±0.14, Pig-intima: 1.2±0.13, mean: 1.13±0.14, adventitia: 1,07±0.11).

Preliminary RV in pig lung: to KCl (Emax: 131.4±35%KCl; pD2: 1.52±0.08), epinephrine (Emax: 96.7±11%KCl and PD2: 5.78±0.09), ET-1 (Emax: 74.12±16%KCl and pD2: 5.74±0.06), Bradykinin (Emax 116.1±11% and pD2: 7.18±0.09) and sodium nitroprusside (Emax: 71.09±5% and pD2: 5.64±0.1).

Conclusion

Full characterization and comparisons with human cancer arteries will be presented. This characterization helps identifying the mechanisms affected by cancer, and serves as a model to evaluate drugs.

Adenosine uptake mediated by hENT1 but not -hENT2 is reduced by intracellular alkalization in human umbilical vein endothelial cells from gestational diabetes mellitus

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Introduction

Human umbilical vein endothelial cells (HUVECs) from gestational diabetes mellitus (GDM) pregnancies show reduced adenosine transport by human equilibrative nucleoside transporters 1 and 2 (hENT1/2). Increased NO generation associates with alkaline intracellular medium, and high NO reduced the hENT1/2 expression and activity in HUVECs. GDM associates with intracellular alkalization due to a higher activity of the Na+/H+ exchanger-1 (NHE1). The aim of this study was to evaluate whether GDM alters hENT1/2 transport activity due to intracellular alkalization.

Materials & Methods

HUVECs were isolated (collagenase digestion) from full term normal (n = 11) or GDM (n = 8) pregnancies collected at the Clinical Hospital CHRISTUS-UC (Chile) and approved by the Ethics Committee. The study conformed to the Declaration of Helsinki. HUVECs were cultured in medium 199 plus sera (20%) up to passage 3. The pHi was measured in cells loaded with the fluorescent pH-sensitive probe BCECF-AM (12 µmol/L, 10 min) and exposed to NH4Cl (20 mmol/L). Basal and pHi recovery rate (dpHi/dt) were estimated in cells exposed to 5 µmol/L 5-N,N-hexamethylene-amiloride (HMA, NHEs general inhibitor), 0.1 µmol/L zoniporide (Zn, NHE1 inhibitor. Uptake of 2,3-[3H]adenosine (0-500 µmol/L, after NH4Cl removal) was measured in absence or presence of 1 or 10 µmol/L S-(4-nitrobenzyl)-6-thio-inosine (NBTI), inhibitory concentrations for hENT1 or hENT1+hENT2 transport, respectively.

Results

HUVECs from GDM showed higher basal pHi compared with normal pregnancies (pHi = 7.7±0.2 vs 7.1±0.1, respectively) (values are mean±SEM, compared by unpaired ANOVA, P<0.04, as statistical analysis). The dpHi/dt in GDM was higher (4.2±0.2 fold) than in normal pregnancies. Zn and HMA reversed the GDM-increased dpHi/dt to normal values. The reduced hENT1-mediated adenosine uptake in GDM at basal pHi was reversed by Zn. hENT2-mediated uptake was increased

(2.9±0.3) in an acidic intracellular medium compared with basal pHi, but unaltered by Zn.

Conclusion

NHE1-mediated alkaline pHi inhibits hENT1 and hENT2-adenosine transport in HUVECs from GDM pregnancies. (Support: FONDECYT 1190316 & International Sabbatical (LS) (UMCG/UG, The Netherlands) from the Vicerectorate of Academic Affairs, Academic Development Office of the Pontificia Universidad Católica de Chile. GF, PV, and MC hold PhD fellowships from UT(Chile). GF and MC hold Abel Tasman Talent Program PhD fellowships from UMCG/UG (The Netherlands)).

AP1 activity is required for arsenic trioxide-increased MDCK cells proliferation

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Introduction

The regulation of intracellular pH is essential for all physiological processes; the extrusion of protons is carried out through the Sodium/proton isoform 1 (NHE1) exchanger, which contributes to the regulation of this parameter. An increase in the expression and activity of NHE1 was associated with more significant morbidity and mortality in various neoplasm tissues. However, the presence of heavy metals such as Arsenic Trioxide (ATO) induces an increase in the expression and activity of NHE1, which results in intracellular alkalinization and more significant cell proliferation in MDCK cells. On the other hand, the transcription factor (AP-1) is activated under alkaline conditions, which parallels the increase in the activity of NHE1.Objective: ATO-induced MDCK cell proliferation involves AP-1-dependent NHE1 activation

Materials & Methods

Cells were exposed (48 h) to ATO (0.05 µmol/L), SR11302 (1 µmol/L, AP-1 inhibitor), HOE-694 (100 nmol/L, NHE1 inhibitor) and EIPA (50 µmol/L, NHE1/NHE3 inhibitor) in the presence of S3226 (10 µmol/L, NHE3 inhibitor), concanamycin A (0.1 µmol/L, V-ATPases inhibitor), and Schering (10 µmol/L, H+/K+- ATPase inhibitor). [3H]Thymidine incorporation, cell counting, wound healing assay, and AP-1 activity were determined. The pHi was measured in cells pre-loaded (10 min) with 2,7-bicarboxyethyl-5,6-carboxyfluorescein acetoxymethyl ester (12 mmol/L) and exposed to NH4Cl (20 mmol/L). Basal pHi and recovery rate (dpHi/dt), intracellular buffer capacity (βi) and H+ flux (JH+) were determined. NHE1 protein abundance was measured by Western blotting and immunofluorescence.

Results

ATO increased the cell growth (1.21±4,6-fold, n=6-23) (one-way ANOVA), basal pHi (0.4±0.02 pHi units, n=17-19), dpHi/dt (1.8±0.2-fold, n=6-29), JH+ (1.4±0.14, n=17-29-fold), AP-1 activity and NHE1 protein abundance (1.3±0,04 fold; n=3). ATO also increased (1.45±0.1fold, n=3-5) the nuclear/perinuclear NHE1 immunosignal. SR11302 and HOE-694 blocked ATO effects. All values are mean±SEM, p<0,05

Conclusion

The increase in cell proliferation induced by ATO is dependent on the activation of NHE1-dependent on AP-1 in MDCK cells.

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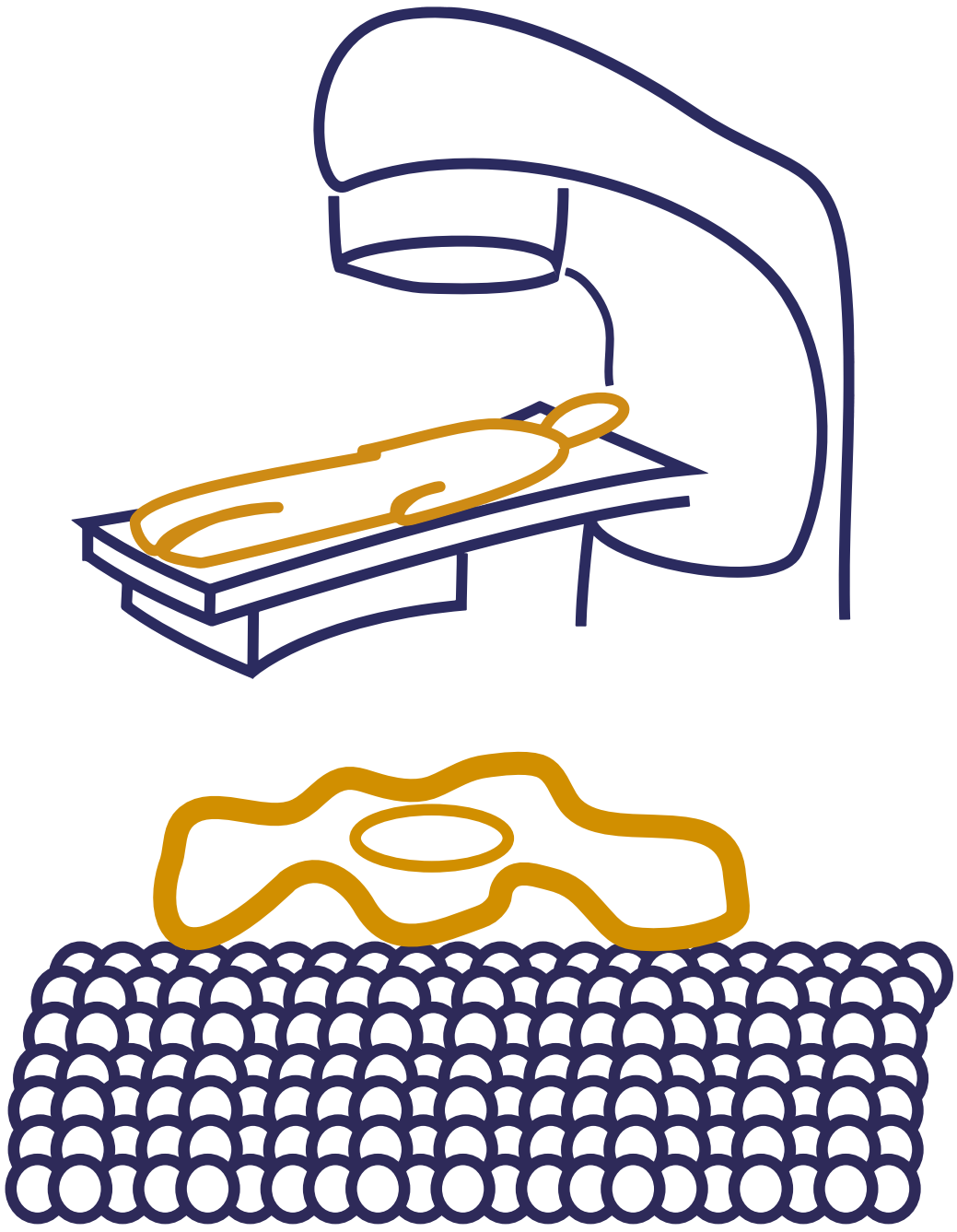

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Association between CTLA4 +49A/G (rs231775) and single nucleotide polymorphism and the risk of acute allograft renal transplantation rejection: a multilevel modelling of meta-analysis

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Introduction

Acute renal transplant rejection believed to be immunological phenomenon which is one of major complications for transplant as the last resort treatment of end-stage renal disease. In the last decades, studies have been widely carried out to assess the association between single nucleotide polymorphisms (SNPs) of cytotoxic T-lymphocyte antigen 4 +49A/G and the risk of rejection, however the results are still debatable along with inconsistency across the studies was reported. Therefore, our current study aimed to perform a meta-analysis concerning the association between the risk of transplant rejection and CTLA4 +49A/G polymorphism.

Materials & Methods

Whether retrospective and prospective analytical Randomized Control Trials (RCTs) published papers from PubMed, Embase, Cohcrane, and Web of science were included for the study in line with PRISMA Guideline, and they were analyzed using fixed or random effect model regarding its heterogeneity. We exclude study that has deviation from hardy-weinberg equilibrium (X2 > 3.84 indicated deviation from HWE)

Results

Fifteen studies were included in the meta-analysis and continued multi-level modeling. We found the association between CTLA4 G allele/GG genotype and acute rejection risk in renal transplantation was found in this meta-analysis with Odds ratio overall analysis G vs A 1.22 and 1.47 (p<0.05). However, the AA genotype was not associated with acute rejection risk in renal transplantation.

Conclusion

Therefore, CTLA4 G allele/GG genotype is associated with the acute rejection risk in renal transplantation, and it should be the hope for personalised medicine.

A mortality rate comparison between liver transplant receptors of donors with positive versus negative hemoculture results

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Introduction

Donor selection is an important factor in the result of solid organ transplants. With the shortage of organs the use of extended criteria for donor selection has been growing, however this leads to the inclusion of donors that may present higher risks for the receptors. Hence, the importance that these expanded criteria be carefully evaluated to determine if its benefits outweigh the risks. The objective of this study is to analyze the impact of using livers from donors with a positive hemoculture on the mortality of the receptors.

Materials & Methods

Transplants done by the Liver transplant program of Hospital Israelita Albert Einstein from 2013 and 2017 were analyzed and included when donors had a hemoculture collected by the program at the moment of the procurement surgery.

For the statistical results the Mann-Whitney Qui-Square and Fisher exact were applied and the R Core Team program software was used. A 5% significance level was considered.

Results

The study analyzed a total of 384 liver transplants, of those 319 had donors with a negative hemoculture and 65 donors with positive hemoculture. The groups were considered homogeneous. The receptors mortality rate of donors with positive hemoculture were compared with the negative hemoculture group and the following results were found respectively: Mortality after 1month 8,8% vs 10,8%(p0,786), after 3months 11,9% vs 13,8% (p0,821), after 6months 14,7% vs 16,9% (p0,795) 1year 17,9% vs 20% (p0,818). All receptors were provided with appropriate prophylactic antibiotic therapy and adjusted according to the culture results when they became available.

Conclusion

Results have shown that there was no statistical difference in survival rate of patients that received a liver from a donor with positive hemoculture and a donor with negative hemoculture. This can be seen as an indication that using donors with positive hemoculture could be considered safe when selecting livers for transplant given that appropriate antibiotic coverage is given prophylactic and modified according to the culture once its available.

Clinical outcomes among patients with Autosomal Dominant Polycystic Kidney Disease (ADPKD) submitted to kidney transplant from deceased donors: results from a Brazilian single-center cohort study.

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Introduction

Beyond the kidney function impairment, the autosomal dominant polycystic kidney disease (ADPKD) patients present abnormal kidney volume, impacting the abdominal venous capacity and the sympathetic / parasympathetic control, which would hypothetically increase the risk of ischemia following the kidney transplantation (KT). Thus, this study aimed to evaluate whether ADPKD is associated with delayed graft function (DGF), a clinical manifestation of ischemia injury after the KT.

Materials & Methods

This single-center cohort study enrolled 245 patients with ADPKD transplanted from a deceased donor between 2013-17. The control group comprised non-diabetic patients transplanted in the same period (n= 2,596), also from a deceased donor. The primary outcome was DGF, defined as a requirement for dialysis within one week after the KT. Logistic regression was performed to evaluate the variables associated with DGF, using SPSS v.25.0.

Results

In the ADPKD-group, recipients were older (57 vs. 49 years, P<0.001), more frequently female (51% vs. 37%, P<0.001), and candidate for a first KT (98.4% vs. 92.1%, P<0.001). There were no differences in other demographic data, donor characteristics, and baseline immunosuppression regimen stratified by groups. The frequency of DGF was significantly lower among ADPKD-group, 52.2% vs. 60.5% (P=0.012), for whom the time in DGF was shorter, 2 vs. 6.5 days, but this difference was not significant (P=0.41). In the multivariable model, the variables associated with the probability of DGF were: male recipients (OR=1.25; P=0.01) and male donors (OR=1.39; P<0.001); hemodialysis as renal replacement therapy, previous to the KT (OR= 1.58; P<0.001) and time waiting for the KT (OR=1.06; P<0.001); KDPI (reference [1-35%], OR[35-51%]=1.47, P=0.01; OR[51-80%]=1.82, P<0.001; and OR[>85%]=1.83, P<0.001); and cold ischemia time (OR=1.02; P<0.001). The ADPKD tended to reduce the probability of DGF: OR=0.76, P=0.05. There were no differences in the 1-yr rate of death, 2.9% vs. 3.3% (P=0.71), and graft loss, 4.1% vs. 4.8% (P=0.62) for ADPKD and control groups, respectively. However, the graft loss due to thrombosis was more frequent in the ADPKD-group: 50% vs. 33%, P=0.02.

Conclusion

Patients with ADPKD did not present a higher risk of DGF; however, they presented a significantly higher frequency of graft loss due to vascular thrombosis.

Creating an immersive 3D digital framework for human neuroanatomy

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Introduction

Although helped by traditional pedagogical methods of cadaveric dissection and two-dimensional (2D) illustration, neuroanatomy remains a notoriously difficult subject for medical students. However, teaching has benefited tremendously in recent years from the increased inclusion of computer-assisted learning into the curriculum. I investigated the development of an innovative three dimensional (3D) digital teaching framework for neuroanatomy.

Materials & Methods

I applied methods for dissection and preparation of a whole brain specimen, which allowed us to take a systematic collection of photographs, representing a 2D image set for the object. I then applied computational methods to create a high-resolution 3D digital reconstruction of the donor specimen, using a process called photogrammetry. I then used the game engine Unity 3D to develop a real-time augmented reality environment for the specimen.

Results

I created a 3D digital brain specimen, that is an accurate representation of the external surface geometry of the donor specimen photographed. Its representation was also physically reproduced through 3D printing. Important, delicate human brain anatomy structures were visibly reproduced. This reconstruction is the closest 3D representation of an individual donor's brain that students would be able to view and manipulate, other than the physical specimen itself. I finally used the game engine Unity 3D to develop a real-time augmented reality environment for the specimen which allows user interaction and manipulation (such as on dissection room touch screens).

Conclusion

This project is the first known investigation into the use of photogrammetry for interactive neuroanatomy education. I showed the feasibility of creating accurate digital 3D neuroanatomical specimens from real-life specimens, for use as a teaching resource to aid the learning and understanding of neuroanatomy. I finally extended this work by creating an optimised protocol for the facilitation of further additions of specimens or functionality. Future work could utilise this protocol to produce personalised 3D recreations of unique patient-specific pathologies for clinicians, and further unique dissection room specimens for medical students.

Liver and/or kidney transplantation after SARS-CoV-2 infection: Prevalence, short-term outcome and kinetics of serum IgG antibodies.

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Introduction

There is a paucity of data on the prevalence, adequate timing and outcome of solid organ transplantation after SARS-CoV-2 infection. Furthermore, the post-transplant kinetics of SARS-CoV-2 IgG antibodies in patients with pre-transplant SARS-CoV-2 infection are unknown. The aim of the present study is to determine the prevalence of SARS-CoV-2 infection in patients undergoing liver and/or kidney transplantation. Additionally, we provide data on the short-term post-transplant outcomes and longitudinally assess their SARS-CoV-2 IgG antibody seroprevalence.

Materials & Methods

All patients receiving a liver and/or kidney transplantation at University Hospitals Leuven between May 1st 2020 and March 18th 2021 were included. Nasopharyngeal SARS-CoV-2 PCR analysis along with assessment of SARS-CoV-2 anti-nucleocapsid (N) and anti-spike (S) IgG were performed 24 hours before transplantation. Prior SARS-CoV-2 infection was defined as a prior positive nasopharyngeal PCR and/or the presence of SARS-CoV-2 anti-N IgG antibodies. In patients with a prior SARS-CoV-2 infection, data on clinical outcome was collected and SARS-CoV-2 anti-N and anti-S IgG were serially assessed.

Results

A total of 168 patients underwent liver and/or kidney transplantation at the University Hospitals of Leuven, of which 11 (6.54%) patients with previous SARS-CoV-2 infection were identified. Median interval between SARS-CoV-2 infection (based on day of PCR positivity) and transplantation was 4.5 months (range 0.9-11). After a median post-transplant follow-up of 4.9 (0.3-8.9) months, 10 out of 11 patients were alive without clinical signs of viral shedding or recurrent / active infection. One patient without COVID-19 symptom resolution at time of transplantation died after combined liver-kidney transplantation. In 9 out of 11 patients with previously PCR confirmed SARS-CoV-2 infection, SARS-CoV-2 anti-nucleocapsid (anti-N) and anti-spike (anti-S) IgG were detectable at day of transplantation. Absolute levels of anti-N and anti-S IgG were positively correlated, and both declined over time in all patients. All patients remained anti-S IgG positive until last post-transplant follow-up, while in three patients anti-N disappeared.

Conclusion

These results support the current recommendation that liver and/or kidney transplantation can be safely performed in patients with complete symptom resolution and a negative PCR at time

of transplantation.

Augmented Lagrangian based full-waveform inversion (FWI) for breast cancer imaging

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Introduction

Medical imaging always seeks for more advanced methods in order to reach better resolution and accessibility. Although conventional methods for cancer imaging relies on MRI and CT scan using electromagnetic waves, utilizing ultrasonic provides a safer, cheaper, more feasible and applicable diagnostic tool. It is worth mentioning that ultrasonic imaging includes various methods like full-waveform inversion (FWI). Development of this method significantly enhanced structural resolution, but it requires a good initial model and the low-frequency data. Iteratively refined wavefield reconstruction inversion (IR-WRI) improves FWI and reduce the sensitivity of the problem to the initial model and the frequency content. In this study, we represent an application of IR-WRI for breast cancer imaging.

Materials & Methods

IR-WRI reconstructs the speed of sound (SOS) and attenuation by breaking the problem into various sub-problems associated with each variable as well as the wavefields. Then this subproblems are solved in an alternating way based on the alternating direction method of multipliers (ADMM). A proper regularization is applied to mitigate ill-posedness of the problem and reconstruct more meaningful biological tissues based according to the prior information that we know about them. In this study, we use total-variation (TV) regularization, which drives inversion towards a blocky reconstruction.

Results

The phantom used in this paper is a type B (scattered areas of fibro-glandular density) left breast containing water, fat, skin, glandular, ligament and malignant lesion. We first create the synthetic data by propagating the ultrasonic waves at different frequencies using finite difference and we implement TV regularized IR-WRI to estimate SOS and attenuation. The estimated SOS and attenuation models are close to the true models and target anomaly (malignant tissue).

Conclusion

In this study, we proposed to use IR-WRI for ultrasound medical imaging. The proposed algorithm can improve anatomical resolution starting from a rough initial guess for SOS and attenuation model. Our analysis in this framework is distinguishable with others in updating SOS and Q factor model. The results illustrated proper reconstruction of the models and detection of anomalies. This can be considered a useful step toward reaching more appropriate settings for breast cancer imaging.

AIM2 inflammasome is implied in inflammation and graft survival in in silico kidney acute rejection analysis

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Introduction

Kidney acute rejection (AR) is currently the main cause of early graft loss, maintaining a prevalence of nearly 10%. Despite the last decades immunosuppression improvement, several available drugs still act on similar pathways, especially of lymphocyte activation and cytokines synthesis. In this sense, we aimed to identify potential novel targets of AR analyzing transcriptome datasets of T-cell mediated rejection (TCMR), antibody-mediated rejection (ABMR) and borderline changes (BL).

Materials & Methods

Human microarrays of Gene Expression Omnibus were searched using the keyword "kidney transplant". Studies were included when comparing AR to stable grafts, and excluded if related to meta-analysis or concurrent chronic rejection. Different expressed genes (DEG) were established considering logFC > 1 or logFC < -1 for FDR < 0.05. Their related processes were accessed with Gene Ontology (GO) and the gene-sets associated with AIM2 were evaluated by GSEA. Correlations and Kaplan-Meier analysis were visualized using GraphPad Prism-6, while meta-analysis was performed by the R package “meta”. Differences were considered significant when p < 0.05.

Results

Eighteen datasets were found filtering the query criteria. Of them, three were selected for initial DEG evaluation, including the ones with higher sample numbers for TCMR, ABMR or BL. Totally, 52 genes were commonly upregulated, being associated with GO lymphocyte and CARD signaling. Since CARD composes inflammasome responses, we accessed NLRP3, NLRC4 and AIM2 levels in AR, identifying a reproductive enhancement of AIM2, which was positively correlated to T-cell surface markers and negatively associated to oxidative phosphorylation (OXPHOS) gene-sets. Clinically, grafts presenting higher AIM2 expression reached more graft failure in a pool of TCMR and ABMR samples (HR = 2.943, 95% CI = 1.649-5.254, p < 0.0005). Meta-analysis comparing AIM2 increasement according to rejection type revealed that the combined effect is significant and remarkable for TCMR.

Conclusion

AIM2 is enhanced in kidney AR, related to a higher T-cell response and lower OXPHOS. The inflammasome increasement is remarkable for TCMR, and is implied in shorter graft survival in a set of either TCMR and ABMR. Since currently used immunosuppressive schemes do not include inflammasome targeting, our study hypothesizes that AIM2 pathway may aid to attenuate graft loss and inflammation.

Prediction of peritumoral infiltration and location of recurrent tumor in glioblastoma by probabilistic tractography based on pre-operatively acquired MR examination

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Introduction

Glioblastoma (GBM) is the most common primary malignant tumor of the central nervous system. Its prognosis is unfavourable, average overall survival is 18-24 months. The GBM originates from white matter, but its tumor cells aggressively infiltrates the surrounding brain via white matter tracts, too. It has typical radio-morfological features (e.g., ringlike contrast enhancement, central necrotic area, perifocal edema), however, it is known that the malignant cells can migrate even a few centimetres away from the tumor mass - beyond the scope of conventional MR imaging. After resection, these are the cells where GBM re-grown from. Diffusor tensor imaging (DTI) based tractography could reveal these otherwise un-diagnosable infiltrated pathways which aids patient-tailored surgical intervention and radiotherapy. Our aim was to investigate whether these infiltrated white matter tracts are identifiable with the use of DTI based peritumoral probabilistic tractography.

Materials & Methods

We retrospectively investigated 12 patients, recruited from SZTE SZAOK, all diagnosed with GBM. We performed a probabilistic peritumoral tractography originated from tumors identified on preoperative MR images based on the „ball and sticks" modell. In order to exclude possible false positives, the results were optimised by 11 thresholds. The brain was divided into 216 standardized regions and we compared the images of recurrent tumors with the 11 tractographic results to determine the overlapping regions. Statistical analysis was made to determine the sensitivity and specificity of every threshold, in order words, the accuracy of our recurrent tumor location prediction.

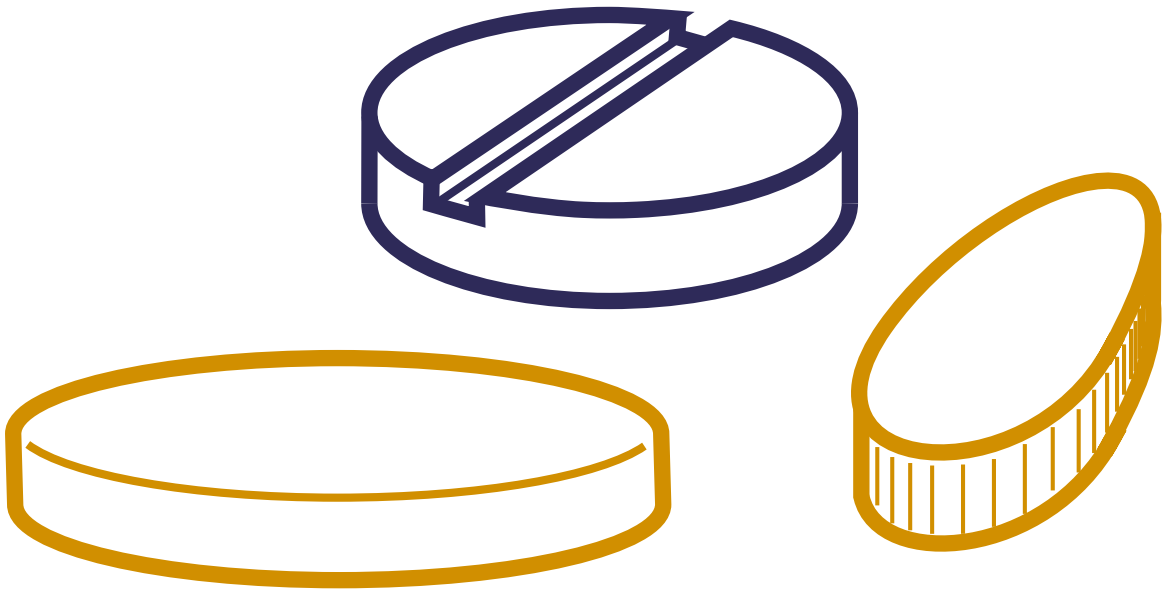
Results

The average age of patients was 49 ± 14.5 years; their average survival time was 21 ± 4.2 months. As the threshold increased, so did the specificity, the sensitivity decreased. The best results was found at the 5% threshold, with the average sensitivity at 81.7% and the specificity at 80.1%.

Conclusion

The possible future location of the GBM recurrence can be determined with good certainity by preoperative peritumoral tractography. It could help surgical and radiotherapy planning, eventually improving the efficiency of treatment modalities and providing a better survival rate for patients.

Pharmacology I



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Comparative efficacy of praziquantel and artemether-lumefantrine in the treatment of urinary schistosomiasis among children in endemic community of Nigeria

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Introduction

Praziquantel (PZQ) remains the drug of choice for the treatment of schistosomiasis, but the problem of reported reduced efficacy makes the need for alternative drug imperative. Some Antimalarial Combination Therapy (ACTs) are believed to be effective against schistosomiasis. This study therefore compared the efficacy of PZQ and Artemether-Lumefantrine (AL) for the treatment of urinary schistosomiasis in Nigerian children.

Materials & Methods

Urine were collected from 625 children, examined using the filtration technique method and Schistosoma haematobium positive children were randomized into PZQ and AL treatment groups. Urine was screened for S. haematobium egg at 4 and 8 weeks post-treatment. Efficacy was determined based on the Egg Reduction Rate (ERR) and Cure Rate (CR).

Results

Prevalence of urinary schistosomiasis was 41.8% (261/625). The 261 S. haematobium infected children were randomized to receive PZQ (129) and AL (132). The ERR at 4 and 8 weeks post-treatment was 94.8% and 95.4% respectively for PZQ and 91.8% and 92.9% respectively for AL. The CR at 4 and 8 week post treatment was 75.2% and 97.3% respectively for PZQ and 61.7% and 93.0% respectively for AL.

Conclusion

Both PZQ and AL were found to be effective and the use of AL could be advantageous in malaria schistosomiasis co-infection cases.

Comparative hypolipidemic evaluation of aframomum melegueta seeds and moringa oleifera leaves

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Introduction

The study was carried out to compare the lipid lowering effects of both crude drugs as well as deducing the extracts with the best lipid lowering property; and the fractions. The research was conducted with an experimental design which involved the use of ninety-six (96) male albino wistar rats to compare the hypolipidemic effects of both crude drugs and respective fractions.

Materials & Methods

Ethanol extracts of both plants were prepared using soxhlet apparatus. Each extract was subjected to VLC fractionation using four solvents : n- hexane, chloroform, ethyl acetate and methanol. The fractions were bulked together after conducting TLC procedures and each extracts bulked into four fractions. The acute toxicity studies (LD50) of both extracts were determined using lorke's method. The crude extracts were screened for the presence and quantity of phytoconstituents using standard methods. The antilipidemic study was carried out using sixty-eight (68) rats randomized into seventeen groups of four(4) animals each. Lipid profile was determined using spectrophotometer. Liver function tests was also carried out using standard procedures.

Results

Administration of various treatments (both crude extracts and fractions) evoked a significant (p<0.05) reduction of TC, TG and LDL-C as well as significant (p<0.05) elevation of HDL-C when compared with the negative control. With a percentage serum lipid reduction of 45.11%TC, 48.23%TG, 63.39% LDL-C and 174.69% elevation of HDL-C, the group treated with the combination of 500mg/kg aframomum melegueta and 500mg/kg moringa oleifera produced the best hypolipidemic effect. This is closely followed by fraction MO4. Comparatively, moringa oleifera leave extract exerts a better antilipidemic effect than aframomum melegueta seed extract. The liver function test showed that both plants has no toxic effect on the liver cells at doses of 250mg/kg and 500mg/kg, hence confirming the hepatoprotective effects of both crude drugs at the doses administered.

Conclusion

In conclusion, results from this study suggests that ethanol extract of moringa oleifera leaves is more effective than ethanol extract of aframomum melegueta seeds as a hypolipidemic agent. However, combination of both crude drugs as lipid lowering agent has proved to be more effective and reliable when compared to each crude drug administered independently.

Structure-based virtual screening of selected Malaria Box compounds against a multi-staged protease, falstatin in Plasmodium falciparum

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Introduction

The multi-staged protease, falstatin, is a protein whose inhibition could lead to plasmodial cell death due to its significance in haem hydrolysis, erythrocytic invasion and rupture of schizont in Plasmodium falciparum. Therefore this study seeks to identify promising compounds that act as multiple stages of Plasmodium by screening falstatin against Malaria Box, a chemical library of antiplasmodial compounds by employing structure-based virtual screening, a technique that reduces the huge cost of clinical and preclinical drug development.

Materials & Methods

The three-dimensional structure of the protein (falstatin) was obtained by homology modelling on the Swiss Model server. Structure-based virtual screening (molecular docking) was conducted with the Molecular Operating Environment (MOE) software package. An antiplasmodial compound library was docked onto the falstatin's predicted binding site. Compounds with high binding energy were triaged based on their ADMET (absorption, distribution, metabolism, excretion and toxicity) properties. The top-ranked compound, based on a novel ligand scoring function, was subjected to molecular dynamics and redocking using a Generalized Born Solvation scoring function

Results

From the results, TCMDC 131646 had the highest ligand score which was computed based on binding energy and satisfactory pharmacokinetic properties. The compound contained no toxicophore and satisfied Lipinski, Egan as well as Muegge rules of medicinal chemistry. Analysis of the trajectories obtained from the molecular dynamics simulation revealed that TCMDC 131646 conferred stability on the protein model using the hydrogen bond analysis, root mean square deviation (RMSD), root mean square fluctuation (RMSF), dynamic cross-correlation matrix and principal component (PC) analysis tools. Similarly, the chemical diversity analysis revealed that TCMDC 131646 is structurally diverse from chloroquine, artemisinin, artemether and lumefantrine. This suggests that the compound may have a unique and novel mechanism of action.

Conclusion

Overall, TCMDC 131646 was predicted to be a drug-like and safe compound that can inhibit falstatin in Plasmodium falciparum. Chemical-disease co-occurrence analysis in literature revealed that this compound showed in-vitro antiplasmodial activity at an IC50 of 0.226MM and activity against neuralgia, hyperalgesia and arthritis. The research identified TCMDC 131646 as a potential antimalarial candidate that could yield novel analogues by hit expansion. However, confirmatory in-vitro and in-vivo studies are required to substantiate these predictions.

Relationship between placebo response and nocebo response in Attention-Deficit Hyperactivity Disorder: a meta-analysis and meta-regression of 57 randomized clinical trials

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Introduction

Placebo (clinical improvement with inert substances) and nocebo response (clinical worsening or the experiencing of treatment-emergent adverse events with inactive products) share mechanisms such as conditioning —imprinted memories of previous drug exposition could replicate such effects with an inert tablet— or expectancy —pre-existing beliefs could trigger a response to the inactive product in the expected direction—. In clinical research with drugs, placebo and nocebo response should be minimized to obtain clearer understanding of pharmacological efficacy and safety. This combined reduction would only be feasible if those phenomena were closely related, a fact that remains unknown in ADHD due to evidence lacking. For this reason, the aim of this study is to assess the relationship between placebo and nocebo response in randomized, double-blind, placebo-controlled trials (RCT) in patients with ADHD.

Materials & Methods

We conducted a systematic review of RCTs investigating the efficacy and safety of pharmacological interventions for ADHD patients. Data were extracted from Minerva Database® (www.minervadatabase.org: a comprehensive database of ADHD RCTs) and were combined using a random effects model. The relationship between placebo (mean change in ADHD symptoms severity in patients in placebo arms) and nocebo (proportion of patients receiving placebo that experienced adverse events) responses was studied by means of meta-regression.

Results

57 RCTs were included, involving 8,640 and 5,159 patients in drug and placebo arms, respectively. Pooled placebo response rate was 9.55 (median = 8.6; interquartile rang: 6.1 – 11.5). Pooled nocebo response rate was 60.19% (median = 58.06%; interquartile range: 49.58% – 68.05%), while the incidence of adverse events in drug arms was 74.68% (median = 77.24; interquartile range: 67.97% – 82.18%). Placebo response was not associated with nocebo response (coefficient = -0.0259; p = 0.1577).

Conclusion

This study found no evidence of association between placebo and nocebo response in RCTs with ADHD patients. In ADHD, strategies to reduce placebo or nocebo response should be tailor-made for only one of these scenarios, as their effects on the other one may be unrelated (even detrimental). Further studies are needed to determine which strategies are valid for diminishing either placebo or nocebo response.

Evaluation of anti-oxidant and hepatoprotective activity of Acacia jacquemontii in high-fat and CCl 4 induced liver injury in rats model

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Introduction

Liver fibrosis is characterized by the agglomeration of extracellular matrix and collagen proteins. Acute liver injury is initiated by increased expression of PAI-1, extracellular matrix (ECM), hemostasis and coagulation. Acute liver injury may potentiate the chronic liver injury by hepatic stellate cells (HSC) and reduction in matrix metalloproteinase (MMP) activity. The purpose of our study was to characterize the polyphenolic content present in Acacia jacquemontii stem and to evaluate its anti-oxidant and hepatoprotective activity.

Materials & Methods

The phenolic contents present in Acacia jacquemontii polyphenolic extract (AJPPE) were characterized using high performance liquid chromatography (HPLC). Hepatoprotective and anti-oxidant activity of AJPPE was determined through biochemical parameters (ALT, AST and ALP) lipid profile (TC, TG, HDL, LDL) antioxidant biomarkers (SOD, LPO, GSH and CAT) and histopathological analysis.

Results

HPLC analysis of AJPPE showed the presence of polyphenols including chlorogenic acid, P-coumeric acid, caffeic Acid and kampherol in remarkable therapeutic range. Results of in-vivo analysis have shown the significant decrease in the level of lipid profile including LDL (low-density-lipoprotein), TC (total cholesterol) and triglycerides; liver function markers (AST, ALT and ALP) and significantly increased the level of anti-oxidative biomarkers (CAT, SOD, LPO and GSH) by using AJPPE.

Conclusion

The above mentioned results have shown that AJPPE possess significant anti-oxidative and hepatoprotective effect. Furthermore, histopathological results also supported the antioxidant and hepatoprotective potential of AJPPE. While high-fat diet increased the TC, TG and LDL and AJPPE have potential to reverse the effects. Thus, AJPPE has anti-lipidemic effects.

Parental morphine exposure before gestation affects anxiety-like behavior in cocaine-induced sensitization in male rats

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Introduction

Opioid addiction is a devastating psychiatric disorder that affects both patients and families. Besides the genetic component, environmental factors such as low socioeconomic status, poor quality of parenting, drug availability, early social adversity, and many other factors play a significant role in the vulnerability to opioid abuse and addiction. It is hypothesized that a further critical risk factor is parental drug use before gestation that influences the vulnerability of opioid addiction in the offspring via epigenetic inheritance. The current study is designed to find the role of parental morphine exposure before gestation on anxiety-like behavior in cocaine sensitization.

Materials & Methods

In this experimental study, adult male (N=8) and female (N=8) Wistar rats were exposed to morphine for 10 days and let be drug-free for another 10 days. Then, they were prepared to mate. Each female rat just was allowed to mate with a male rat. A similar control group (8 male and 8 female rats) was received saline. Adult male offspring of the first parturition were used in this study. Cocaine sensitization was induced by cocaine injection (once daily for 3 days, 10 mg/kg) followed by 5 days free of the drug before the test. Ten minutes after the last exposure, the open field test was performed. The total locomotion and the total time in the center and corner were recorded.

Results

Cocaine psychomotor sensitization reduced total locomotor activity in morphine-exposed offspring compared with the drug-naïve offspring ($t_{14}=3.11$, $p=0.015$). In the morphine-exposed offspring, the total rearing (vertical movement) decreased compared with the drug naïve offspring ($t_{14}=2.26$, $p=0.049$). The total time in the center significantly reduced ($t_{14}=3.2$, $p=0.008$) in adult male offspring of morphine-exposed parents. Indeed, the spending time in corners also significantly increased in the morphine-exposed offspring ($t_{14}=2.66$, $p=0.024$).

Conclusion

The current results showed that cocaine sensitization increased anxiety-like behavior in the offspring of morphine-exposed rats compared with the control group. In addition, cocaine psychomotor sensitization was reduced in morphine-abstinent offspring.

Drug safety analysis: no sex differences in denosumab

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Introduction

Advocacy groups claim that women are underrepresented in medical research, resulting in unsafe treatments. Osteoporosis is a chronic disease that causes bone fragility and fractures and occurs predominantly in women. Denosumab is investigated for osteoporosis treatment separately in men and women, resulting in much sex-specific data. Nevertheless, it remains unclear whether men and women tolerate the treatment equally well. The objective of this project is to evaluate sex differences in the safety profile of denosumab. In a broader scope, we aim to formulate a sex-specific methodology for safety analysis, transcending denosumab and becoming applicable to other medicines.

Materials & Methods

We compared 4 groups (men and women, each with denosumab and control (placebo) treatments). There is no golden standard on how to assess differences in safety of a medicine between the sexes because gender differences are known to occur in control treatment hampering the interpretation of denosumab data. Adverse event data from representative studies on denosumab were retrieved from public sources and the Dutch regulatory authority's database. Visual summaries were made for exploration of adverse events. Statistical analysis by Fisher's Exact test was done using R-studio.

Results

Publicly available data lacked detail for these analyses. The authority database provided workable data from 8558 females and 1927 males for analysis. Serious adverse event incidence under denosumab and control treatment did not show significant sex differences (±11% female, ±15% male reports, p>0.05), neither did analyses per organ system. The biggest sex-effect was observed in the musculoskeletal system (relative risk male/female=0.43, confidence interval=0.22-0.86), in both the active and control arms.

Conclusion

Statistical analysis of representative studies does not reveal important sex differences in the denosumab safety profile.

Publicly available safety data from e.g., literature, and national and European assessment reports are insufficient for sex-specific safety assessment.

Visualization (as will be presented) aids in the exploration, comparison and comprehensible reporting of safety profiles, flagging organ systems of interest for subsequent statistical analysis. This method could be applied to assess other safety parameters such as discontinuations, or other medicines.

Copper containing organic complexes as a novel scaffold for further PDE4 inhibitors development: in vitro and in silico studies

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Introduction

Metal-containing drugs, such as cisplatin, are promising bioactive compounds in modern medicinal chemistry. Although platinum-containing compounds are the most potent anticancer agents used in clinical practice until now, however, their usage in the clinic has several side effects.

Based on the above expected, drugs containing endogenous metals are less toxic than platinum-based analogs. Previously, we synthesized the Cu(II)-salen complex. Based on the Tanimoto similarity score of the synthesized complex and already known inhibitors of the phosphodiesterase4 (PDE4) family enzymes, it has been suggested that the complex can show high inhibition activity.PDE4 family enzymes are responsible for the degradation of the cAMP. The cAMP has been known to play a role in regulating the cell cycle for many years.In many cell types, cAMP inhibits proliferation by preventing cells from entering the S phase, arresting them in G1. This study aims at a cytostatic effect determination and in silico evaluation of the binding affinity of the synthesized complex.

Materials & Methods

GAMESS-US tool was used for quantum calculations. Geometry optimization of the complex was carried out with a 6-31(d)/B3LYP method. Optimized geometry of complex was used for further ligand configuration for molecular dynamics(MD) and docking. 4MYQ structure in the protein bank was used as a protein model and reference molecule.
For MD simulations GROMACS package was used. Docking was done via AutoDock Vina, which shows high accuracy in many benchmark studies.

Cytostatic effect determination was done with MTT assay on HELLA and A549 (lung cancer) standard cell lines using solutions with different concentrations (5,10,15 and 20 uM) of complex in DMEM (0.25% DMSO).

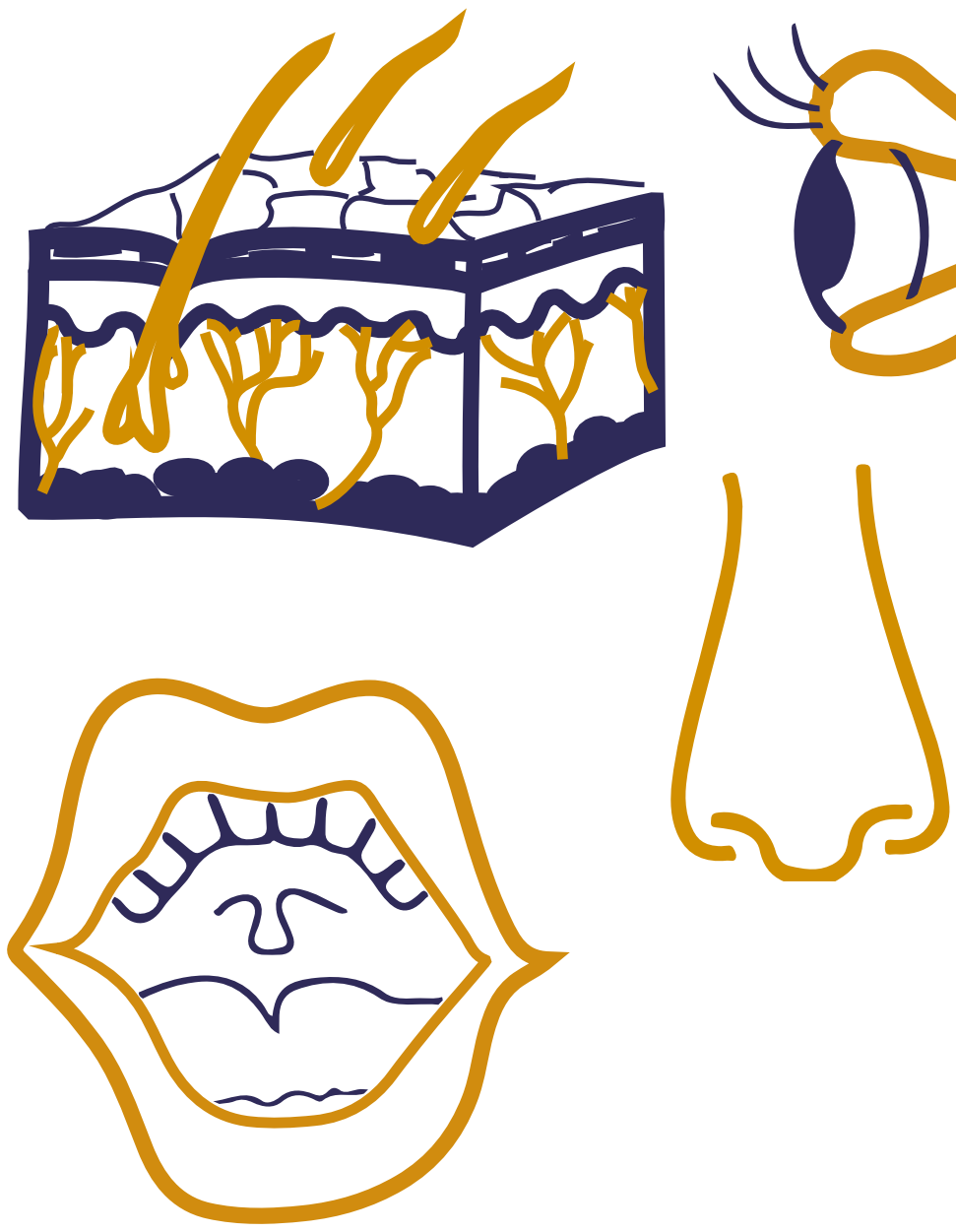
Results

In silico simulations shows the high stability of the ligand-protein complex and ligand's higher binding affinity (-11.2kcal/mol) than the reference compound (-9.8kcal/mol). MTT assay shows that in cases of both cell lines, the viability of cells doesn't decrease starting from 10 uM concentration. The viability of HELLA cells keeps stable at about 55% and for A549 77% against control.

Conclusion

This study demonstrates the studied Cu-containing complex's low cytotoxic and high cytostatic activity.We can say what illustrated Cu-containing scaffold can open new chemical space for further designing novel and high-efficient PDE4 inhibitors.

Ophtalmology and Otorhinolaryngology



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3D Measurement of Cystoid Macular Edema in Macular Hole based on Convolutional Neural Network Algorithm

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Introduction

Cystoid macular edema (CME) is common seen around the macular hole on optical coherence tomography (OCT). However, the pathogenesis and role of CME in MH is still less known. This study is to investigate the correlation of CME volume and morphological metrics of MH with visual outcome using a customized 3D algorithm based on convolutional neural network.

Materials & Methods

A retrospective case series study of 133 MH eyes/133 patients, which had undergone OCT scan before surgery. All OCT images was analyzed using new custom algorithm based on convolutional neural network, which can automatically compute MH volume, base diameter /area, minimal diameter /area, inner opening diameter /area, MH height, height from minimal area, and CME volume. Combined with clinical data, Spearman's correlation and stepwise multiple regression are used for correlation analysis.

Results

Spearman's correlation showed MH Volume were moderately correlated with CME Volume and postoperative visual outcome (r=0.50, 0.51 respectively, both p<0.05). MH Volume was strongly correlated with linear diameters and their corresponding plane areas (r=0.76~0.93, p<0.05) rather than height (r=0.38, p<0.05). CME volume was strongly correlated with macular base diameter and height (r=0.50, 0.78, p<0.05), but not visual outcome. Stepwise multiple regression showed minimal diameter and outer nasal retinal thickness were correlated with visual outcome.

Conclusion

CME volume is correlated with MH volume, base diameter and height, but little with visual outcome.

Diagnostic Accuracy of Imaging Devices in Glaucoma

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Introduction

Different devices have diverse accuracy in diagnosing glaucoma, and therefore choosing the best device is challenging. Thereby, this study was conducted to evaluate the diagnostic sensitivity and specificity of imaging devices in glaucoma.

Materials & Methods

In this systematic review and meta-analysis, electronic databases were searched for articles published between January 2004 and December 2020.

Results

Twenty-eight cross-sectional studies were included for meta-analysis. Devices were divided into two groups, based optic nerve area and macular area. For nerve area, the pooled sensitivity was 77% (CI 95%: 70-83%) and the pooled specificity was 89% (CI 95%: 84-92%), and for macular area, the pooled sensitivity was 87% (CI 95%: 80-92%) and the pooled specificity was 90% (CI 95%: 84-94%). Besides, we analyzed each device separately; For optical coherence tomography(OCT), the pooled sensitivity was 85% (CI 95%: 81-89%) and the pooled specificity was 89% (CI 95%: 85-92%), for Heidelberg retinal tomography (HRT) the pooled sensitivity was 72% (CI 95%: 57-83%) and the pooled specificity was 79% (CI 95%: 62-90%), and for optical coherence tomography angiography (OCTA) the pooled sensitivity was 82% (CI 95%: 66-91%) and the pooled specificity was 93% (CI 95%: 87-96%).

Conclusion

Macular area was more sensitive and specific than optic nerve head. Furthermore, OCT had higher sensitivity, and OCTA had higher specificity when compared to other imaging devices.

Involvment of Hmga2 in the reprogramming and cell fate determination of Müller cells in Retinitis Pigmentosa mice model

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Introduction

Retinitis Pigmentosa(RP) is a degenerative disease characterized by photoreceptor and retinal pigment epithelium (RPE) impairment, resulting in irreversible visual loss.Müller glia(MG) act as endogenous stem cells in retina are able to regenerate a damaged retina in zebrafish,However,MG are activated transiently and form glial scar eventually during the retinal degeneration in mammals.Recently, MG reprogramming has been realized in mice through gene editing and Adreno-Associated Virus(AAV) mediated transcriptor delivery technologies, while its efficiency was extremely low and the restoration of the visual function was limited.Therefore, we hypothesized that MG might be heterogeneous and some novel transcriptors may be involved in MG reprogramming and cell fate determination in mice.

Materials & Methods

Müller lineage tracing mice were used to establish a RP model by sodium iodate injection(SI), the heterogeneity of MG was analyzed according to the division pattern and single-cell RNA sequencing.After confirming the critical time window of MG fate determination with immunohistochemistry,Bulk-RNA and single-cell RNA sequencing were applied to screen transcriptors which determined the MG gliosis or reprogramming fate conversion.Then, the candidate transcriptor was delivered by AAV to MG specifically in the RP mice model. electroretinogram(ERG) and light/dark transition test were performed to test the function of retina.

Results

MG were characterized with heterogeneity after SI treatment and could be divided into four subpopulations according to the morphological changes,cell division patterns and sc-RNA sequencing cluster analysis. The time window of activated MG determined whether their cell fate was gliosis or reprogramming mainly is 3day after injury. Hmga2 was screened as the most potential transcriptor involved in the MG reprogramming.Over-expressing Hmga2 in MG cells significantly decreased the expression of GFAP (gliosis marker) by ~30%, and increased the ratio of CCND1+MG (proliferation maker) approximately 80% at 4 week post injury.Moreover, it also reduced the loss of photoreceptor by ~50%, increased the amplitude of b-wave by ~50%,and prolonged the residence time of mice in the dark chamber at the same time point.

Conclusion

MG heterogeneously response to injury;Hmga2 promotes the conversion of MG from gliosis to reprogramming fate; Hmga2 overexpression restores the visual function in RP mice model.

Association of nutritional deficiencies in the development of oral submucous fibrosis

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Introduction

Oral submucous fibrosis is a chronic condition causing progressive scarring and fibrosis of the buccal mucosa. This eventually results in rigidity, trismus and malignant conversion in long-standing cases. The cases of OSF have witnessed an 85% surge under the age of 35years. Chewing of areaca nut and tobacco consumption have been the main contributors as previously established by research. But other possible agents playing a role in the etiopathogenesis of OSF are yet to be studied thoroughly. Nutritional deficiencies of vitamin B complex, folic acid and iron, more common in vegetarian diets could accelerate the disease process. This research aims to study a possible association with nutritional deficiency and the development of oral submucous fibrosis.

Materials & Methods

A retrospective cohort study was performed with data collected from the blood reports and clinical histories of 250 patients, grouped into three categories of early, moderate and severe using the Madhuri and Jha System of classification. To establish a correlation between different factors, the chi-square test and p-values were used. A null hypothesis was devised with no association taken into consideration and chi-square and p-values were calculated to find probable association between the considered factors. The CI for p-value was taken at 95% with a 0.05 level of significance.

Results

Statistically significant results were found between nutritional deficiencies of vitamin B12 (chi-square value=15.7751, p-value=0.000375); folic acid (chi-square value=7.1417, p-value=0.028132); vegetarian diet (chi-square=12.9972, p-value=0.001506); low socioeconomic status (chi- square=6.8565, p-value=0.032444); Microcytic anemia with MCV <80fl (chi-square value=7.861,p-value=0.019634) and low serum iron levels<65mcg/dL (chi-square value=9.7447, p- value=0.007655) associated with the severity of oral submucous fibrosis cases.

Conclusion

Our study has highlighted a very critical and prevalent public health illness which has been on an escalated surge.The risk of cancer of the disease makes it very important to break the cycle of progression. Vegetarian diets with inadequate levels of vitamin B12, folic acid and iron are additional contributors towards the progression of oral submucous fibrosis. Therefore, encouraging balanced food habits along with awareness about the downsides of tobacco and areca nut consumption can lower the incidence of this debilitating condition.

GLAUCOMA CARE IN HEALTHCARE FACILITIES DURING THE COVID-19 PANDEMIC: THE PATIENT'S PERSPECTIVE

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Introduction

COVID-19 pandemic has made a major challenge for healthcare centers including ophthalmic services. Glaucoma is a fairly common disease in the elderly and patients diagnosed with glaucoma need regular ophthalmologist consultation and ongoing treatment to prevent progressive optic nerve damage. We conducted a study to assess how glaucoma care in personal healthcare facilities has changed during the COVID-19 pandemic in Lithuania from the patient's point of view.

Materials & Methods

The study was conducted using an original anonymous questionnaire to find out the data about how glaucoma care has changed due to restrictions on normal activities in health care settings before and during COVID-19 lockdown. In total 68 patients were interviewed at the Eye Diseases Center of Vilnius University Hospital Santaros Klinikos in February – March 2021. Descriptive statistical analysis was performed using MS Excel.

Results

The frequency of visits to an ophthalmologist was consistent in 54.4% of respondents, 23.5% visited less frequently. 66.2% of respondents were satisfied with the health care,10.3% were not. 72.1% of respondents indicated that registration to an ophthalmologist was no more complicated than usual, while 23.5% found it more difficult. The waiting time for a visit was the same for 75% of patients, 20.6% said it has prolonged. 14.7% of respondents postponed or canceled their visit. 8.8% of patients were incapable of seeing an ophthalmologist for an acute condition, 13.2% for a routine visit. Some of respondents had to change an institution: 17.7% chose another public healthcare institution, 10.3% chose a private. The duration of consultations remained unchanged in 82.3% of respondents, for 10.3% it became shorter. 92.7% of respondents felt that communication with the ophthalmologist remained unchanged, while 4.4% felt deterioration. 29.4% of the respondents had to use remote consultations.

Conclusion

More than one-fifth of the patients visited an ophthalmologist less frequently than usual, struggled to get an appointment, and had to refer for glaucoma to other facilities. One-fifth of patients could not see an ophthalmologist when needed. For more than a quarter of patients, part of the consultations became remote.

Use of electroretinogram(ERG) in the early diagnosis of diabetic retinopathy(DR) while there is no significance of visual evoked potential(VEP)

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Introduction

Diabetic retinopathy is a systemic disease, which affects up to 80% of all patients who have had diabetes. After 5 and 10years, approximately 25% and 60% have retinopathy respectively. The longer a person has diabetes, the higher are the chances. Diabetic Retinopathy is one of the main cause of blindness in the population aged 20 to 64 years. Despite the statistics, research indicates that at least 90% of the new cases could be reduced if there were early diagnosis, vigilant treatment and monitoring of the eyes. So screening for diabetic retinopathy can detect the early changes when preventive therapy is still possible.

Materials & Methods

Its an observational and cross-sectional study with 32 diabetic patients, out of which 12 are fundoscopic positive whereas 20 are fundoscopically normal(negative) long-standing diabetic patients ranging from 4 to 25 years. The method used for the analysis of data fall in generic group of General linear model like ANOVA or Regression analysis. In the present study Binary logistic regression analysis method was used to pick the data with fundoscopic status as the dichotomous variable and predictor variable used were P100, b/a ratio, OSP1_amplitude and OSP1_latency.

Results

The two groups analyzed were diabetics with fundoscopically positive retinopathy and diabetics without any changes on fundoscopy. The parameters recorded were latencies of P100 (VEP) and the b/a ratio, oscillatory potential amplitudes and latencies of P1wave (ERG) and were subjected to Binary Logistic Regression models. The analysis revealed that OSP1_amp was a statistically significant predictor of fundoscopic status while other parameters are not found to contribute significantly to the model prediction. To assess multicollinearity in the model, Pearson correlation coefficients were calculated between pairs of predictor variables and their statistical significance was assessed. P-value for OSP1 amplitude is 0.011 and odds ratio is 0.0856 indicating that the probability of fundoscopic positivity significantly increases with a decline in the amplitude of OSP1. Of the 20 fundoscopically negative diabetics, 5 have been predicted by the model to have diabetic retinopathy.

Conclusion

The results of the study lend evidence to the hypothesis that Electrophysiological methods have the potential for early diagnosis of Diabetic retinopathy. They are more specific and more sensitive than the standard fundoscopy examination. The amplitude of oscillatory potentials especially P1-wave is significantly predictive of incipient Diabetic retinopathy in fundoscopically negative patients.

Multiplex immunohistochemistry elucidates the role of inner ear macrophages in Cisplatin-induced hearing loss

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Introduction

The inner ear was previously thought to be immune-free due to the blood-labyrinth barrier. However, recent studies have discovered macrophages within the cochlea. Tissue macrophages are classically categorized into pro-inflammatory (M1) and anti-inflammatory (M2) macrophages. However, precise information about the types and role of macrophages in the inner ear remains unclear. Therefore, the objective of this study was to clarify the diversity of inner ear macrophages both in the normal state and following exposure to an external stimulant, such as cisplatin (CDDP), an ototoxic chemotherapeutic drug.

Materials & Methods

Mice were injected with 5mg/kg/day of CDDP intraperitoneally for six consecutive days. Mice cochleae were collected at day 0 prior to CDDP exposure and on days 8 and 15 following CDDP exposure and fixed in formalin and paraffin sections prior to immunostaining with a multiplex immune histochemistry (mIHC) technique, which can stain different markers within the same paraffin section.

Results

CDDP exposed mice developed a hearing threshold shift at day 8 post-CDDP, and this shift started to recover at day 15 post-CDDP. Additionally, there was an increase in the expression of markers for both pro-and anti-inflammatory macrophages ratio in the auditory nerve area on day 8 and started to resolve on day 15, suggesting a new subcategory of mixed macrophages in the inner ear. Furthermore, the Iba1ɣ macrophages ratio was increased at day 8 post-CDDP, suggesting microglial activation in the auditory nerve. These results suggest that CDDP exposure causes a state of acute auditory nerve inflammation that triggers macrophages polarization towards a new subcategory of macrophages with M1, M2, and microglia in the same macrophage.

Conclusion

Inner ear macrophages are a new subtype of macrophages, and they are not exclusively M1 or M2 macrophages. Furthermore, an increased Iba1 expression ratio following CDDP exposure suggests that the auditory nerve undergoes neuronal inflammation. Thus, inner ear macrophages play a significant role in understanding the mechanism of hearing loss onset following CDDP exposure.

Miscelleanous I

Presenters:
Asgharzadeh, F.A (Fereshteh) Dr
Sadeghdoust, A.S (Adel) Dr.
Masoud, F.M. Dr. (Farid)
Khayrulloh, Kh.M.M. (Mukhammad Amir)
Telesh, Ms (Anna) PhD student
Kasiak, P.S.K. Mr. (Przemysław) Student
Aligolighasemabadi, F. (Farnaz) Dr.
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Therapeutic effects of Cerium oxide nanoparticles containing sulfasalazine on DSS-induced colitis model

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Introduction

Cerium (IV) oxide (CeO2) exhibit anti-inflammatory activity via scavenge free radicals and decreasing the oxygen species (ROS) production. Here we aimed to exhibit the therapeutic effect of this nanoparticle in experimental colitis models.

Materials & Methods

Cerium oxide nanoparticles (CeONPs) were synthesized via using UiO-66 as a precursor. We used dextran sodium sulfate (DSS) to induce colitis in experimental models to investigate the anti-inflammatory effect of CeONPs. Colitis models are divided into four groups to receive the treatment, including control, colitis, cerium oxide, and sulfasalazine. We evaluated the therapeutic effects of CeONPs for the increased colitis clinical symptoms and attenuated the histological damage to colon tissue in colitis.

Results

This nanoparticle was significantly able to reduce the clinical symptoms of colitis. Moreover, CeONPs can enhance the disease activity index such as body lose weight, diarrhea, rectal bleeding, colon length, and spleen weight. Moreover, CeONPs showed a significant reduction in the histological characteristics of the colitis models.

Conclusion

These results suggest that CeONPs can be considered as promising therapeutic agents in treating the ulcerative colitis.

moringa stenopetala Leaves Extract Ameliorates Heat stress Induced Renal Biochemical and Histological Alteration in Swiss Albino Mice

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Introduction

Recently high prevalence of kidney disease of unknown cause in the hottest region of world has led to the initiation of "heat stress hypothesis" as etiology of acute kidney injury. In another way Moringa plant species have numerous physiological and pharmacological activities including Renin Angiotensin system modulation, potent anti-inflammatory and anti-oxidant properties. This study evaluated reno-protective effect of moringa stenopetala leaves extract in mice model of heat stress. Acute kidney injury (AKI) was induced by exposing to high ambient temperature. Prior to heat exposure Moringa stenopetala leaves 500mg/kg and 1000mg/kg of ethanol extract was administered orally. The biochemical and histological results showed that Moringa extract reduced kidney damage. The administration of Moringa leaves extract ameliorated heat stress induced elevation of serum creatinine and Blood urea nitrogen level.

Materials & Methods

The mice were randomly categorized into 4 groups; Normal control, Heat stress control, 500mg per Kg and 1000mg per Kg of moringa stenopetala treated heat stress groups. Moringa treated groups received ethanol extract of moringa stenopetala for 28 days and exposed to heat stress on the final day. Then all mice were anesthetized and blood samples were collected. Serum creatinine and BUN were analyzed. Renal tissue samples were also taken and histopathological changes were examined under optical microscope.

Results

There was significant increase in serum creatinine and blood urea nitrogen in heat stress exposed groups (P < 0.05) when compared with control. Moringa treated heat stress groups have shown significant amelioration of those biochemical parameters. 1000mg/kg Moringa treated heat stress group has shown significant reduction (P< 0.05) of serum creatinine and BUN when compared with Heat stress group. Loss of proximal tubules, infiltration of macrophages and interstitial collagen deposition by heat stress were slightly improved in moringa treated group.

Conclusion

Heat stress exposure has elevated renal damage biomarkers. It also distorted the renal tissues. Treatment with moringa stenopetala extract decreased both functional and structural insult to kidney. Furthermore the mechanisms and active ingredient(s) responsible for renal protective effects should also be identified.

Visual diagnostics methods including ASL MR perfusion in patients with diffuse liver disease and new coronavirus infection COVID-19

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Introduction

Diffuse liver disease is a widespread disease all over the world. Approximately 29 million persons in the European Union suffer from a chronic liver condition. Covid-19 infection is dangerous for this group of patients because of risk of SARS-CoV-2 infection in liver cells, drug-induced liver injury and systemic inflammation.

Materials & Methods

The aim of the study was to analyze possibilities of visual diagnostics methods including ASL MR perfusion in patients with diffuse liver disease and new coronavirus infection COVID-19. The study involved 54 inpatients hospitalized in June – December, 2021. Clinical and laboratory data, severity of lung involvement on the computer tomography (CT) were estimated in all of patients. We conducted ultrasound examination with compression elastography of the liver (n=54). Magnetic resonance imaging (MRI) with ASL MR of the liver was conducted for 48 (89%) patients after discharging from hospital and during dynamic observation. CT of the abdomen was conducted for 15 (28%) patients for the purpose of detection of another disease.

Results

Ultrasound examination shows efficiency as the first step of examination. Inflammatory changes in the liver were reasons of false positive results of compression elastography in the acute period of the coronavirus disease and in the beginning of recovery period. There was decrease of volumetric hepatic blood flow according to ASL MR perfusion (n=48). There was increase of volumetric hepatic blood flow in 3-6 month.

Conclusion

Ultrasound examination is recommended can be beneficial in patients with diffuse liver disease and new coronavirus infection COVID-19, when they are admitted to a hospital. Compression elastography is recommended to use 3 months after the onset of the coronavirus disease. MRI with ASL MR of the liver is recommended to use in patients with diffuse liver diseases, who have suffered from coronavirus infection, 15 days and 3 and/or 6 months after discharging from hospital.

Cardiometabolic syndrome in HIV-positive and HIV-negative patients at Zewditu Memorial Hospital, Addis Ababa, Ethiopia: an observational comparative cohort study.

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Introduction

Cardiometabolic syndrome (CMetS) has become a major health threat recently, especially for people living with chronic diseases. CMetS is most prevalent in ambulatory patients with chronic infections such as HIV and affects the quality of life of patients. The present study aimed at determining the comparative incidence and prevalence of CMetS, biomarkers, and predictors among HIV-infected and HIV-uninfected patients.

Materials & Methods

From January 25, 2019, through February 25, 2021, a hospital-based observational cohort study was conducted. Using logistic regression analysis, the associations of predictors with outcome variables at different dates were determined. The incidence and prevalence of CMetS were calculated using the National Cholesterol Education Program (NCEP) and the International Diabetes Federation (IDF) methods. The biomarkers and burden of CMetS were determined using Friedman ANOVA and Cochran's Q test, respectively. Except for the posthoc analysis, a 95 percent confidence interval and a p-value of 0.05 were considered statistically significant.

Results

HIV-positive people tended to be younger (under 45 years old) than HIV-negative people. At baseline, the point prevalence of CMetS was 285 per 1000 in HIV+ persons and 437 per 1000 in HIV-negative people, as per NCEP; it was 437 per 1000 in HIV+ people and 527 per 1000 in HIV-negative people, as per IDF. Based on the NCEP, obesity was found to be less likely to induce CMetS in HIV+ people (p=.003), while the IDF failed to indicate a meaningful link. Using both tools, hyperglycemia (p=.017) and hypertension (p<.001) were found to be less likely to trigger CMetS in HIV+ persons. After controlling for other factors, those with a positive family history, a higher age than 45, and a feminine gender were more likely to have CMetS. Freidman ANOVA revealed a significant impact of all the biomarkers in the outcome variable, and Cochran's Q test revealed the significant burden of CMetS in the population studied, the NCEP (ɣ2 (2) = 57.571, p<.001) and the IDF (ɣ2 (2) = 57.571, p=.033).

Conclusion

The study found significant evidence of CMetS prevalence, incidence, and biomarkers in HIV-positive and HIV-negative people in Ethiopia.

Impact of diet on the severity of COVID-19 and duration of recovery process among elite endurance athletes

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Introduction

COVID-19 could lead to significant negative health consequences. Diet has a wide effect on overall health. Elite endurance athletes (EEA) are at a high risk of harmful long-term COVID-19 effects on their fitness level (FL). The aims of this study were (1) to evaluate the impact of past infection on health status, FL, and diet among the EEA and (2) assessment of potential links between these factors on the recovery process.

Materials & Methods

A questionnaire consisting of 44 questions was fulfilled by the EEA at the tertiary care sports medicine clinic in Warsaw, Poland between 15th July-15th September 2021. Inclusion criteria were: (1) COVID-19 infection in a period <6 months, (2) age ≥18 years, (3) training experience ≥1 year. The survey conveys areas of (1) anthropometric characteristics, (2) health status and FL, (3) details of infection, (4) diet according to the recommendations of the Polish National Center for Nutritional Education (PNCNE).

Results

46 EEA (85% male) met the inclusion criteria. Sports disciplines were: running (n=22; 48%), cycling (n=17; 37%), triathlon (n=7; 15%). 93% (n=43) did not require hospitalization during infection. 78% (n=36) suffer from at least one of the most common complications of COVID-19 for >2 weeks. 50% (n=23) significantly modified their training program and observed a reduction in their FL. 67% (n=31) did not fulfill diet recommendations of the PNCNE (score <15 points). The EEA, who saw more positive changes in their diet during the pandemic, suffered from a lower number of long-term complications due to the COVID-19 (p=0.03). Moreover, EEA, who more often reported the positive impact of the pandemic on their eating habits, rated their health higher after infection (p=0.04).

Conclusion

Positive dietary modifications were associated with a less severe course of COVID-19 and a lower number of long-lasting complications. Proper diet is crucial for EEA during recovery after COVID-19. The personalized dietary approach for EEAs post-COVID-19 is an essential part of the comprehensive therapeutic approach. Healthcare professionals should be aware of the current situation and apply proper treatment strategies.

The novel topical herbal gel might be an alternative treatment in patients with acne vulgaris: a randomized, double-blind controlled study

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Introduction

Acne Vulgaris (AV) is one of the most prevalent skin disorders evolving in pre and post-adolescent periods. Conventional therapies indicate many adverse events and limitations; nonetheless, botanical agents are proposed for minimal side effects and faster action. This study aimed to assess the clinical efficacy of novel topical herbal gel and clindamycin/benzoyl peroxide in patients with AV.

Materials & Methods

In this randomized, double-blind, clinical trial study, fifty healthy subjects (42 females, 8 males) with mild to moderate AV were randomly assigned (1:1) into two groups, clindamycin and benzoyl peroxide gel 1%/5% (group A), and topical herbal gel (group B). They received a thin layer of topical gels on the affected area twice daily for twelve weeks. A total number of inflammatory lesions (TIL), total number of comedones (TC), and pustules and papules at baseline, weeks 4, 8, and 12 were measured as primary outcomes. Secondary outcomes included the DLQI questionnaire, and adverse events were also recorded. A p-value below 0.05 was considered to indicate a statistically significant difference.

Results

After 12 weeks of therapy, TIL, TC, the number of pustules and papules declined in both groups; however, only group B indicated significant differences at weeks 4, 8, and 12 (p<0.05). Moreover, TIL and TC diminished more rapidly in group B. Even though all adverse events vanished within the first week of the study, their incidence exhibited significant variations (p<0.05).

Conclusion

This study revealed that the novel topical herbal gel significantly improved the healing of AV symptoms with a high degree of patient satisfaction, and it might be utilized as a potential agent for treating AV.

Comparing clinical and laboratory findings in COVID-19 pediatric patients with gastrointestinal manifestations: a cross-sectional study

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Introduction

Despite the increase in vaccination rates, the world still facing a challenging healthcare crisis caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV2). As of October 2021, almost 5.7 million children in the United States have tested positive for COVID-19. Children are more likely to exhibit GI symptoms. This report aimed to compare clinical and laboratory findings in outpatients versus hospitalized COVID-19 pediatric patients with GI manifestations.

Materials & Methods

This research was a cross-sectional multicenter study to compare clinical and laboratory findings in COVID-19 outpatients (n=71) and hospitalized (n=38) pediatric patients with gastrointestinal manifestations. One month to 18 years old subjects who were diagnosed with COVID-19 based on positive polymerase chain test (PCR) for SARS-CoV-2 in nasopharyngeal swab, and had at least one GI symptom been included. Demographic data, symptoms, signs, laboratory, and radiologic findings on admission were recorded.

Results

The frequency of diarrhea and GI bleeding were significantly higher among hospitalized patients (both p<0.05). Forty-eight patients had GI symptoms in the absence of respiratory symptoms. Laboratory data analysis revealed that the white blood cells (WBC) and lymphocytes count were significantly higher in hospitalized patients (both p <0.05). The number of patients with elevated transaminases (AST or alanine aminotransferase [ALT]) in the hospitalized group (42.2%) was significantly more than the outpatient group (22.2%, p=0.039).

Conclusion

GI symptoms could appear in early stages of COVID-19 course of illness, even without or before the initiation of respiratory presentations. Moreover, the severe diseases are usually associated with higher rates of liver dysfunction. So, liver aminotransferase enzymes need to be considered and monitored in hospitalized patients. Because the elevation of these enzymes, especially AST, is highly associated with the mortality risk.

ART Outcomes After Hysteroscopic Proximal Tubal Occlusion Versus Laparoscopic Salpingectomy for Hydrosalpinx Management in Endometriosis Patients

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Introduction

The objective of this paper is to compare assisted reproductive technology (ART) cumulative live birth rates after hysteroscopic proximal tubal occlusion and laparoscopic salpingectomy in endometriosis patients, for management of hydrosalpinx.

Materials & Methods

This is an observational cohort study at a university hospital, including all endometriosis patients with hydrosalpinges undergoing ART, between January 2013 and December 2018. The patients underwent either laparoscopic salpingectomy or hysteroscopic proximal tubal occlusion with Essure® when laparoscopy was not an option (extensive pelvic adhesions at exploratory laparoscopy or a history of multiple abdominal surgeries with frozen pelvis). The diagnosis of endometriosis was based on published imaging criteria using transvaginal sonography (TVUS) and magnetic resonance imaging (MRI). Endometriosis patients with hydrosalpinges diagnosed by hysterosalpingography and/or TVUS and/or MRI were included. The primary outcome was the cumulative live birth rate.

Results

A total of 104 patients were included in the study; 74 underwent laparoscopic salpingectomy and 30 underwent proximal tubal occlusion with Essure®. The Essure® group had longer infertility durations (58.9 ± 30.0 months vs. 39.5 ± 19.1 months, p = 0.002) and a higher incidence of associated adenomyosis (76.7% vs. 39.1%, p < 0.001) than the salpingectomy group. The cumulative live birth rate was 56.6% after 44 ART cycles in the Essure® group and 40.5% after 99 ART cycles in the salpingectomy group (p = 0.13).

Conclusion

In a population of endometriosis patients undergoing ART, women treated by Essure® for management of hydrosalpinx have similar cumulative live birth rates as women treated by laparoscopic salpingectomy.

Spirometry findings in Patients with Allergic Rhinitis and Diagnosis of Silent Asthma

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Introduction

Allergic rhinitis is a chronic inflammatory disease of nasal mucosa induced by type I hypersensitivity response and affects up to 40% of worldwide population with an increasing prevalence over the past 20 years. Due to the high prevalence of Allergic rhinitis and asymptomatic cases of asthma, we performed this research to study spirometric parameters in allergic rhinitis patients without pulmonary symptoms.

Materials & Methods

This cross-sectional study included all patients with allergic rhinitis who referred to Gangavian hospital, a tertiary hospital in Dezful city (Iran), from August to December 2021. Patients with asthma, chronic cough, active respiratory infection, and smoker subjects and also those who recently used corticosteroids or anti- histamine were excluded from the study. Spirometry with and without bronchodilators was performed for all patients and FEV1, FVC, FEF25-75, were recorded. The spirometry test was considered positive if: (a) the difference in FEV1 before and after spirometry is more than 12; (b) The difference between FEF25-75 and FEV1 more than 20; (c) The difference in FEF25-75 before and after the spirometry test more than 20. Data were analyzed by SPSS software version 22 and P value ≤0.05 was considered significant.

Results

After initial recruitment of 459 patients with allergic rhinitis and careful consideration of the exclusion criteria, a total of 120 patients were included in this study. Fifty-five(45.8%) were female and 65 (54.1%) were male and the mean age was 32±12.32. According to spirometry study, FEV1 before-after in 24 of patients (20%) were more than 12, the difference between FEF25-75 and FEV1 in 33 of patients (28%) were more than 20, and FEF25-75 before-after in 30 patients (25%) were more than 20. There was no statistically significant relationship between spiromery parameters and age, gender, or duration of disease (p>0.05 for all).

Conclusion

According to the results, in patients with allergic rhinitis, spirometry can be helpful in early diagnosis of the asthma. It especially important in patients with new asthma treatment methods such as immunotherapy.

ANALYSIS OF THE EFFICIENCY OF SPECIALIZED SIMULATORS FOR PELVIC ORGANS PROLAPSE IN WOMEN OF REPRODUCTIVE AGE

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Introduction

According to studies in the structure of gynecological pathologies, prolapse of the uterus and vagina ranks third after benign diseases of the female genital organs and endometriosis. In view of the increase in the number of complaints, the manifestation of clinical manifestations in patients with pelvic organ prolapse, it was decided to develop the main preventive methods of combined correction.

Materials & Methods

40 women aged 25-50 years old with mild and moderate degree of prolapse were analyzed, which were divided into 2 groups: 1 - group that had loads on the muscles of the pelvic organs with simulators; 2 – operational group, before the operation, they received physical activity with simulators before surgery for 3-6 months. The comparison group consisted of 40 patients without pelvic organ prolapse. In the study group, the pelvic floor muscles were trained using specialized simulators for women who refused surgical treatment. When assessing the quality of life of patients with pelvic organ prolapse, a complex of specialized questionnaires PFIQ-7, PEDI-20, Wexner score, PISQ-12 was used.

Results

It was found that performing exercises on a regular basis improves tissue trophism, which contributes to restoring the tone of the pelvic floor muscles, reducing complaints such as improving the functioning of the gastrointestinal tract in 40%, due to the technique of proper breathing during exercise, and reducing pain in the hip joint in 60%. We found that in the group of surgical treatment prepared by specialized simulators, the time of surgical treatment decreased by 15 minutes, blood loss by 20%, rehabilitation in the postoperative period decreased due to a decrease in the pain factor in 60% compared with the control group.

Conclusion

In this work, we have shown the role of specialized simulators in improving the quality of life both in the surgical group and in the group without surgical intervention. Thus, for mild to moderate prolapses, the use of vaginal simulators is recommended in order to improve the course of the operation and the postoperative period.

Poster Session II

Oncology II

Presenters:
Asgharzadeh, F.A (Fereshteh)
Masoud, F.M. Dr. (Farid)
Shantha Kumar, Ms (Radhe)
Vanbraband, J. (Joren)
Farrokhi, P. (Pegah)
Brennan, A.K.B (Anna) Ms
Mühlbrand, A.S. (Alicia)

A Screening Tool for the Morphometric Analysis of Bladder Cancer

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Introduction

Bladder cancer (BC) has an incidence rate of 9.6/100,000 among men and 2.4/100,000 among women worldwide. Based on their shape, the two most common forms of BC can be broadly categorized into: i) papillary tumors with finger-like protrusions that project into the bladder lumen and ii) flat carcinoma in situ (CSI) which do not grow toward the bladder lumen but are limited to the inner layer of bladder cells.

Papillary tumors often have a low risk of tumor progression and since these tumors can be surgically removed, they tend to have favorable treatment outcomes. In contrast, CIS are at higher risk of developing into muscle-invasive cancers which tend to have a high propensity for distant metastasis. Computationally distinguishing flat and papillary tumors in mice can enable studies on the underlying mechanisms driving these two cancer phenotypes. However, tools are lacking. The aim of this project was to build and implement a machine learning algorithm which can automatically measure the thickness of the tumor epithelium and in turn distinguish between the two cancer phenotypes.

Materials & Methods

3D microscopy images of mouse bladders treated with the BC inducing drug N-butyl-N-(4-hydroxybutyl) nitrosamine (BBN) were processed to extract mesh surfaces of the epithelium-lumen and the epithelium-connective tissue interfaces. Two approaches were explored to measure the thickness of the epithelium i) Normal ray approach: which involves shooting normal rays from the epithelium-lumen interface to the epithelium-connective tissue interface, and ii) Closest points approach: which involves finding the closest points from a vertex on the epithelium-lumen interface to the epithelium-connective tissue interface. Moreover, the tool uses mean curvature values to categorize papillary vs flat tumors and z-scores to enable phenotype detection.

Results

Using the Normal ray approach, the epithelium of control and BC samples had a mean thickness of 63.75 ± 32.19um and 99.95 ± 25.63um respectively. Using the Closest Points Approach, the bladder epithelium of control and BC samples had a mean thickness of 57.02 ± 14.73um and 99.93 ± 23.02um respectively.

Conclusion

Our preliminary data indicate promising results in the automatic assessment of tumor epithelium thickness and phenotype detection in BC mice.

Valsartan enhances the anticancer activity of 5-FU in mouse model of colorectal cancer

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Introduction

Overexpression of the angiotensin-II receptor and renin–angiotensin system (RAS) is being reported in several malignancies, including colorectal-cancer (CRC), indicating its potential therapeutic target in the treatment of CRC. Here we explored the therapeutic-impact of targeting RAS using angiotensin II receptor blocker, valsartan, in CRC and studied its pharmacological-interaction with Fluorouracil (5-FU) in in vitro and in vivo models.

Materials & Methods

Anti-proliferative activity of valsartan was evaluated in 2-/3-dimensional cells and in vivo CRC models. Anti-migratory of this agent was assessed by wound-healing test, while apoptosis was studied using 4ɣ,6-diamidino-2-phenylindole or DAPI staining, Annexin-V–fluorescein isothiocyanate, and propidium iodide. Gene-expression was determined at mRNA/protein levels. By histological analysis and measuring of oxidative/antioxidant markers, we evaluated the anti-inflammatory properties of valsartan. Gelatin zymography was used to measure matrix metalloproteinase 2 and 9 activity (MMP-2 and 9).

Results

Valsartan suppressed cell-growth and synergistically enhanced the anti-tumor-activities of 5-FU by induction of apoptosis. Valsartan inhibited the cell migration by perturbation of MMP2/9. Furthermore, valsartan inhibited tumor-growth and metastasis, and this was more pronounce in valsartan/5-FU combination. The mechanism was plausible to be via the induction of ROS and down-regulation of SOD, thiol/catalase as well as VEGF. Valsartan may protect cells against intestinal fibrosis by modulation of pro-fibrotic and pro-inflammatory components include Interleukin, Col1A1/A2.

Conclusion

Our findings demonstrated that Valsartan interferes with cell-proliferation, induced apoptosis, reduced migration and synergistically interact with 5-FU, supporting further studies on this novel therapeutic approach for colorectal cancer

Long-term platinum treatment induces chemoresistance more effectively in PC-3 cells than in DU145 prostate cancer cells

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Introduction

As the second most frequent tumor disease in men worldwide, prostate cancer (PCa) challenges curative medicine due to the acquisition of resistances in progressed stages. Platinum-based drugs are used to treat the neuroendocrine PCa and are limited by cancer drug tolerance. We therefore compared the response of two PCa cell lines to platinum exposition aiming to characterize differences between specific cell types on a way toward developing individually optimized PCa therapy strategies.

Materials & Methods

The PCa cell lines DU145 and PC-3 were cultivated with cisplatin-containing medium (DU145: 0.05 µg/ml, PC3: 0.025 µg/ml) for a period of 42 days. After five weeks of treatment, the platinum tolerance of these cells was tested and compared to platinum-naive cells via a serial dilution of cisplatin and subsequent crystal violet and WST-1 viability assays. Furthermore, the migratory capacity was analyzed by scratch assay.

Results

After five weeks of platinum treatment, all cell lines exhibited elevated cisplatin tolerance based on IC50 values. However, there was a significant difference in the response between DU145 and PC-3 cell lines. Based on WST-1 and crystal violet assays, cisplatin resistance was increased 3- and 1.9-fold in PC 3, but only 1.6- and 1.1-fold in DU145 cells, respectively. In PC-3 cells, the increased cisplatin-tolerance was associated with a strongly increased migratory capacity, whereas migration was not altered in DU145 cells, as the scratch assay showed. Platinum-treated PC-3 cells closed 50% of the scratch wound twice as fast as untreated cells, while no significant reduction in time was observed for the DU145 cells.

Conclusion

According to the more effective acquisition of platinum resistance in PC-3 cells in contrast to DU145 cells, there are differences in the intrinsic capacity for platinum tolerance of the two PCa cell lines. However, the underlying mechanisms remain to be elucidated. As cellular processes traditionally associated with drug resistance, epithelial mesenchymal transition and neuroendocrine differentiation might play a role in the response to cisplatin exposure. We aim to unravel underlying molecular mechanisms by RNA-sequencing and to identify future therapeutic targets to tackle platinum-resistance.

The Role of Factor V Expression in Ovarian Cancer - An In Vivo and In Vitro Study

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Introduction

Ovarian cancer is one of the most fatal cancers with one third of women dying within one year of their diagnosis. Ovarian cancer has been shown to have a significant incidence rate of venous thromboembolism compared to other cancers and proteins involved in thrombosis are thought to play a role in the pathogenesis of this disease. Recent preliminary studies have shown that coagulation Factor V (FV) may play a role in ovarian tumorigenesis however the mechanisms are unknown.

Aim of the study: To determine the role of FV in ovarian cancer in vitro using a cell model and in vivo by comparing FV expression in ovarian tumours compared with controls.

Materials & Methods

FV mRNA was analysed by RT-PCR in ovarian cell lines (SKOV3,OVCAR3) and breast cancer cell lines (MCF-7, MDA-231). FV over-expression plasmid was transfected into ovarian cancer cell lines. Factor V protein expression in vivo was compared between ovarian (n=13) and benign (n=9) tumour samples using ELISA assay.

Results

FV was not expressed in SKOV3 and OVCAR cell lines. Following transfection, FV mRNA levels were detected in the OVCAR cell line. Following addition of platelets, FV mRNA expression was detected in SKOV3 cell line. FV mRNA expression was observed in both MCF-7 and MDA-231 cells. A 2-fold increase in FV mRNA expression was observed when platelets were pre-incubated with MCF-7 cells. FV antigen were detected in the ovarian cancer tumour samples however, there was no significant difference between malignant and benign samples (P=0.220).

Conclusion

FV protein levels do not appear to be increased in tumours from ovarian cancer patients however the results from our in vitro work suggest that platelets in the tumour micro-environment can modify tumour FV expression. Further work is required to determine the mechanisms involved. The use of advancing personalised medicine will allow us to open up more treatment opportunities and avenues for ovarian cancer patients. This study allows for continued research by improving healthcare practice through the delivery of a prognostic marker for ovarian cancer thus enabling evidence-based decision-making.

Completeness and selection bias of a Belgian multidisciplinary, registration-based study on the EFFectiveness and quality of Endometrial Cancer Treatment (EFFECT)

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Introduction

With the objective of achieving more uniformity and quality in the clinical management of corpus uteri cancer in Belgium, the EFFECT-project has prospectively collected detailed information on the real-world clinical care offered to 4063 Belgian women diagnosed with primary corpus uteri cancer between 2012 and 2016. However, as data was collected on a voluntary basis, a selection bias may be present. Therefore, this study aimed to assess the completeness and potential selection bias of the EFFECT-database.

Materials & Methods

Five databases were deterministically coupled by use of the patient's national social security number as unique identifier. Participation bias was assessed by identifying hospital characteristics associated with hospital participation, if any. Registration bias was studied by identifying patient, tumor and treatment characteristics associated with patient registration, if any. Uni- and multivariable logistic regression was applied.

Results

The EFFECT-database covers 56% of all Belgian women diagnosed with primary corpus uteri cancer between 2012 and 2016. These women were registered by 54% of hospitals, who submitted a median of 86% of their patients. Participation of hospitals was biased: low-volume and Walloon-region centers were less likely to participate in EFFECT. Registration of patients was also biased: patients with a less favorable risk profile and missing data, that did not undergo curative surgery, and were not discussed in a multidisciplinary tumor board were less likely to be registered for EFFECT.

Conclusion

The EFFECT-database is a valuable and unique data source covering detailed information on the real-world clinical care offered to 56% of Belgian women diagnosed with corpus uteri cancer between 2012 and 2016. However, due to its voluntary nature, the database suffers from a selection bias. This study, therefore, demonstrates the importance of assessing the selection bias that is potentially present in any registration-based study that voluntarily collects information that is not otherwise routinely collected. Indeed, having characterized this selection bias will now allow us to analyze and interpret EFFECT-data more accurately.

Dexamethasone and Citicoline mitigate Cisplatin-induced peripheral neuropathy: a novel experimental study in mice

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Introduction

Given the rising prevalence of Cisplatin-induced peripheral neuropathy (CisIPN), investigations for alleviating its adverse effects are required. Oxidative stress and free radical development are essential pathways of CisIPN. Specifically, dexamethasone and citicoline are characterized by anti-inflammatory and antioxidant activities that might reduce CisIPN incidence and severity. The current study assessed the possible impacts of novel interventions, dexamethasone, and citicoline, on CisIPN.

Materials & Methods

Seventy-two male mice were randomly allocated into nine groups (n=8/each group). Different doses of dexamethasone (7.5, 15, 30 mg/kg, i.p.), citicoline (10, 20, 40 mg/kg, i.p.) and the combined (dexamethasone 7.5 mg/kg + citicoline 10 mg/kg, i.p.) were injected in the first three days and one day before receiving cisplatin (2 mg/kg, i.p.). The tail flick method was used for the assessment of nociception. Furthermore, malondialdehyde (MDA), interleukin-1beta (IL-1β), tumor necrosis factor-α (TNF-α), total antioxidant capacity (TAC), and mice weight differences (ΔW) were measured. A p<0.05 value was assumed to demonstrate a statistically significant difference.

Results

Different doses of dexamethasone and citicoline enhanced latency time (p<0.05). Moreover, dexamethasone 15 mg/kg diminished the level of MDA and increased TAC (p<0.05), and in 30 mg/kg, MDA was reduced (p<0.05). Additionally, 20 and 40 mg/kg of citicoline reduced MDA and elevated TAC (p<0.05), and 10 mg/kg merely reduced MDA (p<0.05). Dexamethasone in all doses declined IL-1β and TNF-α levels, and citicoline only at 40 mg/kg lessened their levels (p<0.05). Interestingly, ΔW declined more in the dexamethasone and citicoline groups than the Cisplatin group (p<0.05).

Conclusion

Dexamethasone and citicoline attenuate CisIPN through enhancing anti-inflammatory effects, improving antioxidant capacity, and inhibiting lipid peroxidation.

Comparison perioperative FLOT chemotherapy regimen vs surgery as frontline treatment in patients with signet-ring cell carcinoma gastric cancer

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Introduction

SRCC is an aggressive type of gastric cancer that has a poor prognosis and is resistant to chemotherapy. Despite the low survival rate of SRCC gastric cancer, perioperative chemotherapy has been shown to have advantages for overall survival and progression-free survival. However, there is no consensus regarding the best chemotherapy approach in this setting. The purpose of this study is to determine the efficacy of FLOT perioperative chemotherapy in enhancing survival over surgery.

Materials & Methods

This retrospective study enrolled 63 patients between July 2015 and 2021. These patients had documented evidence of signet-ring cell carcinoma gastric cancer and were treated with perioperative chemotherapy regimens (n=32) or surgery alone (n=31). Patients received 4 cycles FLOT regimen before and after surgery. Each cycle comprised 50 mg/m2 docetaxel intravenous (iv) on day 1, 85 mg/m2 oxaliplatin iv on day 1, 200 mg/m2 leucovorin iv on day 1 and 2,600 mg/m2 5-fluorouracil iv in a 24-hour infusion on day 1, every 2 weeks.The primary endpoints were overall survival and progression-free survival which was estimated by Kaplan-Meier curves. Toxicity was considered as a secondary endpoint. Toxicity was evaluated according to CTCAE v4.0 criteria

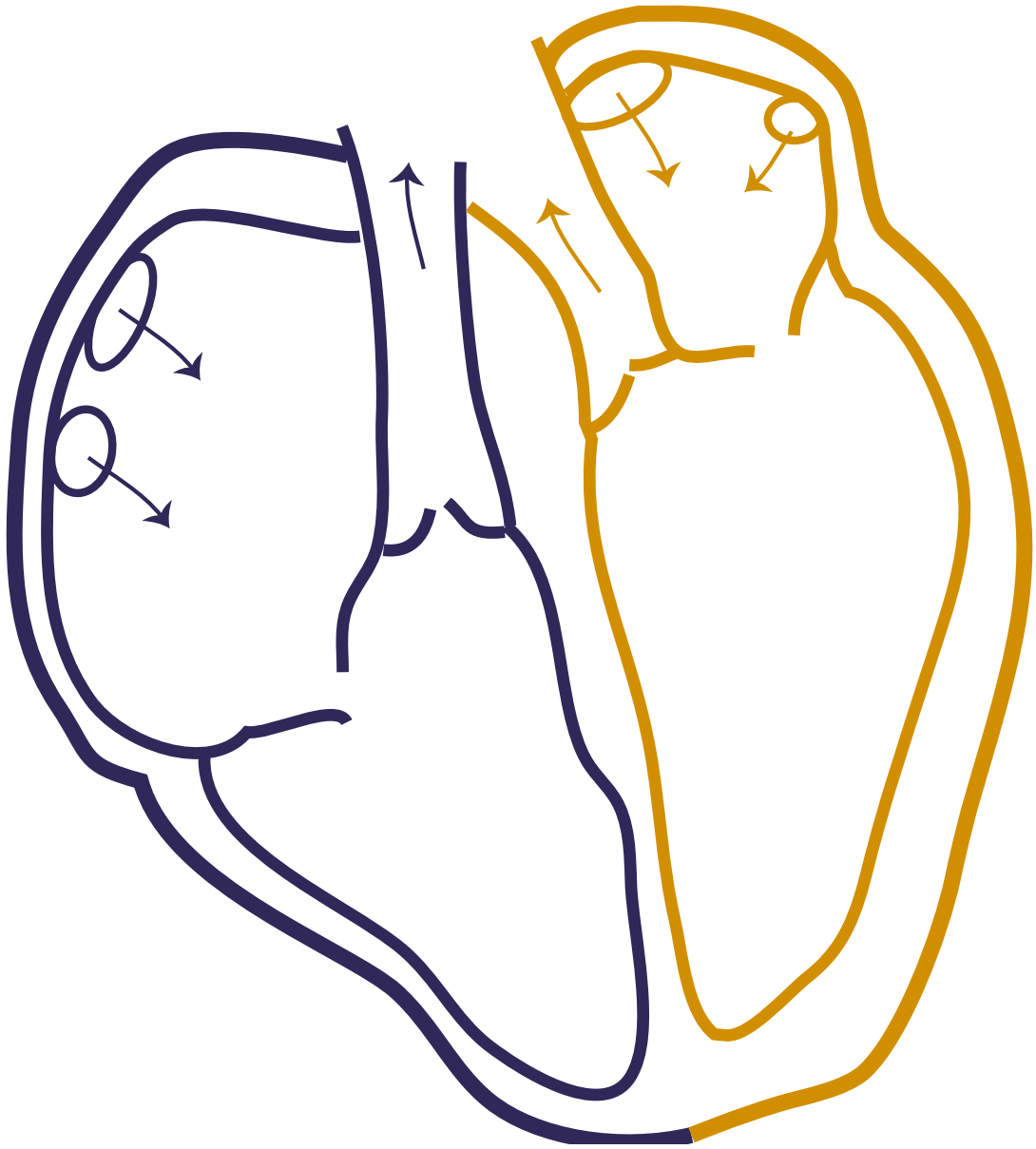
Results

The mean age of patients was 56.41±11.64. According to the KM curve, the median PFS in the surgery group was 12 months and the FLOT group was 14 months (log-rank = 0.26). There was a median overall survival of 21 months for the surgery and 23 months for the FLOTregimen (log-rank=0.23). There was acceptable toxicity associated with FLOT. Grade 3-4 neutropenia were 14.3% and mucositis were 8.3% in FLOT groups.

Conclusion

Despite the fact that FLOT treatment extends progression-free and overall survival in patients with gastric cancer with signet ring cells, these outcomes are not statistically significant when compared to surgery. As such, perioperative chemotherapy using the FLOT regimen should be carefully considered and outweighed by its efficacy and toxicity in comparison to surgery alone.

Cardiology II



Presenters:
Weber, B. (Bennet)
Sadeghdoust, A.S (Adel) Dr.
Bantel, A. (Amelie)
Momot, KM (Karol)
Bhatt, A. (Aarohi)
Gomez-Ruiz, R.P.G.R (Roxana Paola)
Fallahzadeh, A.F (Aida)

Comparison of percutaneous approaches used in invasive cardiology: traditional transradial (TRA) and distal transradial (dTRA)

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Introduction

Recently, distal transradial access (dTRA) has been proposed as an alternative to traditional transradial access (TRA) in cardiac catheterization. The aim of the study was to compare these two approaches in terms of patient comfort, time of gaining the access, need for conversion and local complications. Additionally, circulating endothelial injury markers were assessed.

Materials & Methods

Two hundred adult patients qualified for elective coronary angiography or angioplasty were included in the study. The patients were randomized into the two approaches. Time needed to gain vascular access was assessed. After the procedure, a pressure dressing was applied for 120 minutes. Next, the puncture site was assessed for the presence of hematoma and pulse. In forty patients (twenty from the dTRA and twenty from the TRA group) after the dressing removal, blood from cephalic vein was collected and plasma concentrations of Endothelin-1 (ET-1), Interleukin-8 (IL-8) and Soluble Vascular Cell Adhesion Molecule-1 (sVCAM-1) were determined using ELISA method. All of the subjects received 11-point Visual-Analogue-Scale (VAS) to assess the level of pain firstly at the time of gaining vascular approach (VAS-1) and secondly during the maintenance of the pressure dressing (VAS-2).

Results

Successful cannulation was obtained in 84 subjects (100%) in the TRA group and in 98 (84%) subjects in the dTRA. In 18 dTRA subjects (16%) operators failed to gain the access; they were in 100% successfully converted to TRA and included in the third group named “conversion”. There were no differences between dTRA and TRA in local endothelial injury measured by biochemical markers. TRA was associated with lower levels of pain perceived at the time of gaining vascular approach than dTRA and conversion (VAS-1 respectively: 2 vs. 4 vs. 4, p<0.05). dTRA was connected with a longer time needed to gain the access compared to TRA (81±8 vs. 50±4, seconds, p<0.05). Number of complications after procedures does not differ between these approaches.

Conclusion

We suppose that dTRA requires experience and practice, although considering its advantages, for example smaller area of local ischemia than in TRA in case of radial artery occlusion, it may be safely and widely used in percutaneous interventions in cardiology, radiology and neurology.

Outcome of percutaneous coronary intervention in old patients presenting with acute coronary syndrome

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Introduction

Octogenarians (age ≥80 years) with coronary artery disease constitute a high-risk group and elderly undergoing percutaneous coronary intervention (PCI) are at higher risk of adverse outcomes compared to young patients. In this study we aimed to describe the outcomes of the elderly with acute coronary syndrome who underwent PCI and also to identify the predictors of short-term major adverse cerebrocardiovascular events (MACCE) in octogenarians.

Materials & Methods

In this registry-based cohort study, we reviewed the data of patients (aged ≥65 years) who underwent PCI. Univariate Cox-regression model used to assess the univariate effects of covariates on mortality and MACCE. Covariates with P values less than 0.1 in the univariate Cox regression analyses were entered multivariate Cox-regression analysis model. Backward elimination method applied for multivariate Cox-regression analysis to discover MACCE predictors.

Results

We reviewed the data of 3332 patients (2722 elderly [65 to 79 years], and 610 octogenarians [≥80 years]). The cumulative hazard of MACCE was significantly higher in the octogenarian group compared with the younger group (P<0.001). MACCE in octogenarians presented with ST-elevation myocardial infarction (STEMI) was significantly higher than those with non-ST-elevation myocardial infarction/Unstable angina (NSTEMI/UA) (p<0.001); however, the cumulative hazard of mortality was not significantly different between two groups (P=0.270). Successful PCI and left main stenosis were independent predictors of MACCE in octogenarians with acute coronary syndrome.

Conclusion

In this registry-based study we found that MACCE and mortality were higher in octogenarians who underwent PCI, compared to younger adults. Moreover, in our octogenarian patient cohort, the risk of MACCE was higher in those presented with STEMI compared to NSTEMI/UA and the mortality trend was similar in first 6 months; however, the 1-year trend was in favor of STEMI subgroup. Our data also provided insights into the independent predictors of MACCE in octogenarians after 1-year follow-up.

Comparison between carotid endarterectomy and carotid stenting outcomes for patients with carotid artery stenosis: A meta-analysis

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Introduction

Since 1980s, treatment strategies for carotid artery stenosis have been well studied with several multicentre randomized trials. Compared to medical therapy alone, the superiority of carotid endarterectomy(CEA) has been well established. However, the era of carotid artery stenting(CAS) offered another treatment option. Numerous randomized control trials have been conducted to compare CEA and CAS. Consequently, large number of trials has resulted in inconsistent results. Hence, this meta-analysis compares the trials for better management of carotid artery stenosis.

Materials & Methods

A database search of the MEDLINE, Embase and Cochrane Central Register till 30th, December, 2020 was conducted. Controlled Trial and RCTs were included following PRISMA guidelines after being matched with inclusion and exclusion criteria. 13 RCTs were included with 3682 patients undergoing CEA and 3720 patients undergoing CAS. MESH strings such as “Carotid endarterectomy”, “Carotid artery stenting”, “Carotid artery stenosis”, “revascularization”.

RevMan 5.3 was used for appropriate statistical analysis.

P<0.05 was considered statistically significant

Results

CEA was associated with significant decrease in incidence of short-term (RR= 0.652, 95% CI=0.531 to 0.800, p<0.001) and long-term (RR= 0.754, 95% CI= 0.645 to 0.882, p<0.001) “stroke” compared to CAS. Decrease in incidence of “stroke or death” in CEA was more significant than CEA within 30 days (RR= 0.655, 95% CI= 0.542 to 0.791, p<0.001) compared to >1 year (RR= 0.851, 95% CI= 0.762 to 0.951, p=0.05) of intervention. Within 30 days of intervention, incidence of “all-cause-mortality, stroke or MI” (RR= 0.802, 95% CI= 0.658 to 0.976, p= 0.028) was less and of “MI” (RR= 2.145, 95% CI= 1.326 to 3.471, p= 0.002) and “Cranial nerve injury” (RR= 15.118, 95% CI= 8.226 to 27.784, p<0.001) was more than CAS. There was no significant difference in incidence of short- and long-term “all-cause mortality” and “all-cause mortality or disabling stroke” associated with both approaches.

Conclusion

CEA was found to significantly decrease the incidence of “stroke”, “all-cause-mortality or stroke” and short term “all-cause-mortality, MI or stroke”. However, it was associated with increased incidence of “MI” and “Cranial nerve injury” within 30 days of intervention.

Phosphodiesterase 2 reduces arrhythmic calcium waves in atrial cardiomyocytes induced by inflammatory cytokines

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Introduction

Atrial fibrillation (AF) is one of the most frequent cardiac arrhythmia increasing cardiovascular mortality. AF is associated with cardiac inflammation promoting electrical and structural remodeling. Inflammatory cytokines, such as TNFα and IL-1β, mediate abnormal intracellular calcium handling. Arrhythmogenic calcium release from the SR occurs via ryanodine receptors due to increased phosphorylation from cAMP-dependent kinases. Phosphodiesterases (PDEs) are hydrolyzing enzymes that degrade cAMP. PDE2 was shown to reduce pro-arrhythmic triggers in ventricular cells mediating cardioprotective effects. Here, we aim to investigate the role of PDE2 on cytokine-induced calcium release in atrial cardiomyocytes.

Materials & Methods

PDE2 expression was detected in human atrial tissues from patients with AF compared to controls (SR). Atrial Cardiomyocytes were isolated from mice with cardiac-specific PDE2 knockout (PDE2 KO) and control mice. After incubation with either IL-1β (1 ng/ml and 40 ng/ml) or TNF-α (0,05 ng/ml), intracellular calcium transients and spontaneous calcium waves (SCW) were detected by fluorescence microscopy in Fura-2 loaded cells.

Results

In AF patients PDE2 protein expression was significantly upregulated compared to SR. In murine atrial cardiomyocytes, intracellular calcium transient amplitudes were not significantly affected by IL-1β or TNF-α incubation. In cells from control mice, IL-1 only induced pro-arrhythmic SCW at high concentrations. In contrast, low concentration of IL-1β significantly increased the number of SCW in PDE2 KO cells. After incubation with TNF-α, a tendency to higher SCW was observed in both cardiomyocytes from control and PDE2 KO mice.

Conclusion

PDE2 might play a significant role in inflammatory processes in atrial cardiomyocytes. The genetic PDE2 deletion increased proarrhythmic spontaneous calcium waves induced by IL-1β. Thus, the stimulation of PDE2 might be a new therapeutic strategy in atrial fibrillation. To confirm the data, we will investigate the occurrence of SCW in cells from mice with PDE2 overexpression and from a pathophysiological mouse model, displaying heart failure.

Characterization of Delay to Treatment in Patients with Myocardial Infarction

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Introduction

In México, 47.4% of patients with acute ST-elevation myocardial infarction (STMEI) do not receive reperfusion therapy, an intervention that has consistently been demonstrated to improve survival. Furthermore, delay to the onset of treatment has been reported to be up to 10.8 hours, which precludes potential benefits of early reperfusion. However, the reasons behind these important delays are not fully understood.

The objective of the present study was to characterize the components of treatment delay in Mexican patients with STEMI.

Materials & Methods

A prospective observational study including consecutive hospitalized patients with the final diagnosis of STEMI. A 5-section, 39 item questionnaire was prospectively acquired in order to assess the timing and actions after the onset of symptoms, first and subsequent medical contact, approximate time of diagnosis, and logistic actions (including transfer and treatment).

Results

Data was collected from 95 patients of which 80(%) were male. 52.6% of the patients sought medical attention immediately after the chest pain, while 32.6% self-medicate themselves mainly with non-steroidal anti-inflammatory medications or proton pump inhibitors.

37.9% of patients had the first medical contact by a private office, 28.4% went to the emergency room a second-level hospital and only 14.7% looked for help directly at a PCI capable center. Out of these patients, only 75.8% receive the diagnosis of a STEMI during the first medical contact and out of them only 56.9% receive treatment for their condition, and 23.6% were transferred to the National Institute of Cardiology- Ignacio Chavez. Only 32.6% look for medical attention within the first hour since the start of the symptoms, the rest of the patients took an average of 678.90 min.

Conclusion

In Mexico, only 32.6% of patients with STEMI seek medical attention promptly (<60') when having chest pain, and 2.1% are diagnosed within the time recommended by the guidelines (<10'). On average, patients' time to ask for help and medical attention is 678.90 minutes from the start of the symptoms when they are having a myocardial infarction. This exploratory study denotes the highly important need for education about chest pain and myocardial infarction, and urgent public health actions are needed.

Moderate treatment adherence in patients with hypertension referred to a cardiologist in Kashan County: a cross-sectional study

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Introduction

Medication is a key method to long-term blood pressure control. The World Health Organization estimated that half of the patients suffering from hypertension do not comply with the prescribed drug regimen. Therefore, this study was designed to assess the treatment adherence in patients with hypertension.

Materials & Methods

This was a cross-sectional study and 18- to 85-year-old hypertensive patients were included in this research. Patients with secondary hypertension or disabilities were excluded. In order to increase the reliability and accuracy of the results, the adherence was assessed by two methods including Eight-Item Morisky Medication Adherence Scale (MMAS-8) and the Pill Count method. Patients who scored 8 points on the MMAS-8 were considered to have high adherence, patients who scored >6 and <8 points were considered to have medium adherence, and those who scored ≤6 points were regarded as having low adherence. The data were analyzed by SPSS software version 22 and p value <0.05 was considered significant.

Results

One hundred patients were included in this research. Treatment adherence score was high in 10% of patients, medium in 77% and low in 13% according to MMAS-8. Adherence to treatment did not differ significantly in gender (P=0.721) and marital status (P=0.161) but medication adherence decreased with age (P<0.001) and increased with higher level of education (P=0.016). Higher adherence to treatment score was associated with higher SBP (P=0.024); but was not significantly related to diastolic blood pressure (P=0.063) or body mass index (P= 0.713).

Conclusion

For successful pharmacotherapy, healthcare professionals should use available methods within their limits of practice to improve medication adherence. To ensure better blood pressure control, we need to separate the patients into high, medium, low adherence to treatment instead of using one-approach-fits-all model.

Antidiabetic Rosiglitazone does not aggravate ischemia/ reperfusion or interfere with cardioprotection in the absence of diabetes

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Introduction

An increased risk of myocardial infarction and mortality was first attributed to rosiglitazone, a thiazolidinedione-type antidiabetic, in a meta-analysis from 2007. These findings and following clinical observations lead to temporary marketing restrictions by the FDA, whereas the EMA´s prohibition of the marketing of rosiglitazone is still in place. The controversy in clinical observations leading to these differences could be attributed to cardiotoxic properties of rosiglitazone undiscovered until its use in comorbid populations. This implicates the need to investigate adverse cardiac events in the presence of cardiac risks as early as in the preclinical phases. Therefore, we aimed to assess whether hidden cardiotoxicity of rosiglitazone can be identified in models of ischemia/reperfusion (I/R) injury and cardioprotective ischemic preconditioning (IPC).

Materials & Methods

Adult rat cardiomyocytes (ARCM), AC16 and differentiated AC16 (diffAC16) human cardiac cell lines were treated with different concentrations of rosiglitazone and were subjected to simulated I/R. Viability was assessed by calcein staining. In a separate experiment, rats were treated with either 0.8 mg/kg/day rosiglitazone or vehicle for four weeks and were subjected to 30 min coronary artery occlusion and 120 min reperfusion with or without IPC. Arrhythmia analysis was performed and infarct size was measured.

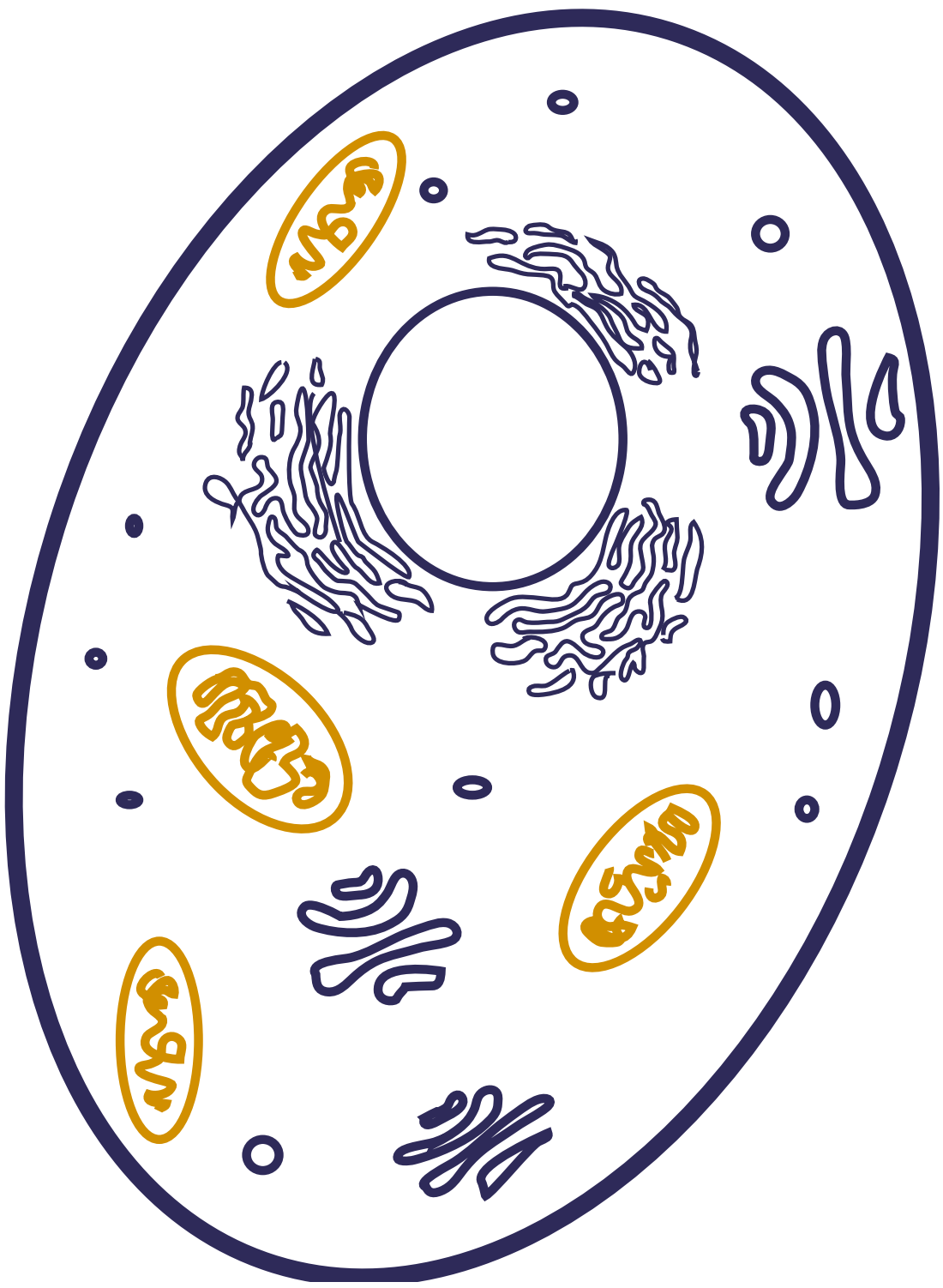
Results

Application of rosiglitazone at concentrations (0.1 - 1uM) improved the survival of AC16 cells but not of ARCMs or diffAC16s. In rats, rosiglitazone did not exacerbate I/R injury and did not deteriorate the cardioprotective effects of IPC which is indicated by unaffected rate of arrhythmias and infarct sizes.

Conclusion

This is the first demonstration that chronic administration of rosiglitazone does not interfere with cardioprotection in preclinical small animal and cell culture models. Our finding, that I/R injury was not aggravated by rosiglitazone, supports previous preclinical- and clinical observations where no increase in mortality and myocardial infarction was observed. These results suggest that the potential detrimental effects of rosiglitazone may only be observed in models reflecting the hyperglycemic/hyper-insulinemic conditions of the patient population treated with rosiglitazone. Therefore, further investigations are needed to identify preclinical models suitable for uncovering hidden cardiotoxicity of rosiglitazone.

Cell Biology



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Identification of chromatin interactome changes and regulators of H2AK119ub upon cellular stress ubiquitination using the miniTurboID system

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Introduction

The Polycomb repressive complexes (PRC) 1 and 2 play a vital role in cell lineage specification and stem cell self-renewal by epigenetic regulation. PRC1 ubiquitinates H2AK119 and PRC2 methylates H3K27, leading to gene silencing. It is of utmost importance to maintain this repressed state to avoid inappropriate expression of lineage markers, even under cellular stress, since misexpression of genes can lead to cancer development. Strikingly, it was recently found that heat shock (HS), a basic form of cell stress, leads to loss of PRC1/2 chromatin binding, temporary relocalization of these proteins to the nucleolus, and a concomitant reduction of PRC1/2-induced epigenetic marks (Azkanaz et al. eLife, 2019). The fast kinetics of H2AK119ub reduction suggest that this process may be enzymatically driven. Within this project we aim to investigate how the chromatin interactome is changed after HS and identify potential HS-specific regulators of H2AK119ub levels.

Materials & Methods

To this purpose, we employ the miniTurboID system, allowing proximity-dependent biotinylation of nearby proteins. We expressed a histone H2A-miniTurboID fusion protein in K562 cells and screened for changes in the chromatin interactome after HS using streptavidin-mediated purification of biotinylated proteins and subsequent LC-MS/MS analysis.

Results

Initial experiments show that the H2A-miniTurboID fusion protein is stably incorporated and can be ubiquitinated at H2AK119 suggesting the fusion proteins is fully functional. HS experiments show that miniTurboID remains functional during HS, and streptavidin pull outs show that chromatin-associated proteins (EZH2, CBX8) are efficiently biotinylated. Fluorescent microscopy analysis shows that biotinylated proteins are localized to the nucleus as expected.

Conclusion

Taken together, our preliminary data show that our H2A-miniTurboID approach works to identify chromatin associated proteins under normothermic and hyperthermic conditions. Next, we will identify changes in the chromatin interactome during cellular stress (heat shock, low oxygen conditions, and proteasome inhibition) by large-scale isolation of biotinylated proteins followed by LC-MS/MS analysis.

Elucidating the role of p62 in Salmonella Typhimurium infections

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Introduction

p62 is a crucial component of the autophagy pathway, linking ubiquitinated intracellular targets to LC3 and thus the autophagosome, and this includes intracellular bacterial targets. What has become clear over time is the many additional roles p62 can play in host defence against certain bacterial infections, however what is currently understood is far from conclusive. Using p62 depleted macrophages we have confirmed that the absence of p62 increases intracellular bacterial survival of Salmonella spp. and have begun to understand the mechanisms by which it does so.

Materials & Methods

Control and p62 depleted macrophages were infected with S. Typhimurium and a Gentamicin protection assay was done to discern intracellular bacteria. Immunofluorescent microscopy was performed to calculate p62 and Rubicon recruitment to the Salmonella. Transmission Electron Microscopy was also conducted.

Results

At 24 hours post infection p62 depleted macrophages showed significantly more intracellular Salmonella Typhimurium than the control. Transmission Electron Microscopy surprisingly revealed these macrophages to be in large single membraned vacuoles rather than in double-membraned vacuoles or the cytosol. This difference was then found to be independent of SPI-1 encoded genes that are essential for Salmonella invasion. Immunofluorescent microscopy revealed 10% of all Salmonella Containing Vacuoles (SCVs) were p62 positive at 1 hour post infection, a proportion that decreased to 2% by 10 hours. Staining for Rubicon, a crucial component of LC3-associated phagocytosis, was found to be co-localised to the SCV at 15 minutes post-infection, significantly more than later time points, with no difference between cell types.

Conclusion

Our results clearly show a role for p62 in controlling a Salmonella Typhimurium infection in macrophages, and this role is independent of SPI-1 induced damaged to the SCV, a mechanism of p62-interaction that has previously been suggested suggested in other cell types and for other intracellular bacteria. The results of the electron micrographs, in conjunction with the Rubicon positive SCVs ordained by immunofluorescence, suggests that the mechanism of action could be LC3-associated phagocytosis, a mechanism that shares characteristics of both autophagy and phagocytosis. It is this, and other potential avenues, that our work is currently trying to understand.

Aggregation of the protein TRIOBP-1, involved in schizophrenia, depends on two of its structural regions

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Introduction

Schizophrenia is a severe mental illness, characterized by life-long cognitive and behavioural changes. Its development is caused by genetic and environmental factors whose complexity has made it difficult to invent new treatment methods. It has recently been suggested that aberrant proteostasis may also impact the progression of schizophrenia. If certain misfolded proteins, caused by the disruption in proteostasis, are not degraded by the cell, aggregation occurs and the protein forms large insoluble structures known as aggregates. TRIO and F-actin-binding protein (TRIOBP-1) is one such protein which aggregates in a subgroup of patients. It has previously been shown that aggregation of TRIOBP-1 may depend on a region in the centre of the protein, but this has only been shown using plasmids encoding parts of the protein.

Materials & Methods

PCR was used to clone different plasmid constructs, encoding full length or partial TRIOBP-1, fused with FLAG-tag, which were then propagated in NEB5α bacteria. Purified plasmids were transfected in HEK239 human kidney cells and expression confirmed by Western blotting. Constructs were then overexpressed in SH-SY5Y neuroblastoma cells to visualise aggregation using immunofluorescent microscopy. All experiments and results were repeated 3 times and verified using negative controls.

Results

Constructs encoding TRIOBP-1 lacking different versions of the aggregation-critical region still aggregated when overexpressed in SH-SY5Y, suggesting that another structural part is also involved in TRIOBP-1's aggregation propensity. Based on previous results and research, we hypothesised that the optionally translated N-terminus of TRIOBP-1 might also influence aggregation. We confirmed this by truncating the full-length construct further, to exclude the N-terminal unstructured region. All these results lead to generating a non-aggregating TRIOBP-1 mutant (60-652, Δ333-340).

Conclusion

We have shown two regions to be responsible for the aggregation propensity of TRIOBP-1: the optionally translated N-terminus and amino acids 333-340 in the central section of the protein. By generating mutant TRIOBP-1 with the minimal number of mutations required to prevent aggregation we will be able to generate model systems for studying TRIOBP-1 aggregation, and allow us to better understand its role in the progression of schizophrenia.

This work was funded by the Croatian Science Foundation (IP-2018-01-9494).

Aggregation of NPAS3, involved in schizophrenia, is based on stress

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Introduction

Bipolar disorder, major depression disorder and schizophrenia are neuropsychiatric conditions categorized as chronic mental illness (CMI) and are some of the leading causes of disabilities worldwide. They are characterized by both genetic and environmental elements, with underlying complexity that remains relatively unknown. Over the past several years, a number of studies have proposed aggregation of specific proteins as one potential pathological cause of CMI. Proteins seen to misassemble and aggregating in brain samples of distinct subgroups of psychiatric patients include TRIOBP-1, DISC1, CRMP1 and NPAS3. It still remains unclear if this aggregation arises from genetic factors, environmental risk factors (stresses), or a combination of the two. We are investigating how stress factors affect the aggregation of these proteins in cells.

Materials & Methods

Each of the four proteins were expressed in the neuroblastoma cell line, SHSY5Y, transfected with plasmids encoding them. After this expression, we applied stress factors for 3 hours to the cell culture medium. Stress factors that are used for this procedure are sodium arsenite (50 μM), iron (II) chloride (1mM), calcium chloride (1mM), zinc acetate (1mM) and MG132 (10 μM). The cells underwent an immunocytochemistry staining technique and were visualised with fluorescence microscope.

Results

Out of the four proteins that have been tested, NPAS3 had the most interesting effect. After application of certain stress factors, it was shown to go out of the nucleus into cytoplasm, often forming visible aggregates. Sodium arsenite and iron (II) chloride had the clearest effect with a higher rate of aggregation occurring when compared to other stress factor treatments and control group. We are now analysing the dynamics and mechanisms behind these effects in more detail.

Conclusion

These results suggest that NPAS3 aggregation can be driven by stress depending on the stress factors used in the research, suggesting that NPAS3 aggregation in the brain may also be inducible by stress. We are hoping that the results of our research will contribute to understanding how does the stress affect CMI and provide the information to further research on generating suitable drugs that could effectively treat patients with these aggregated proteins.

Investigations into the Paracrine regenerative effect of Mesenchymal Stem cells and dermal fibroblasts

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Introduction

Along the spectrum of cardiovascular diseases, coronary heart disease (CHD), is a life-threatening disorder with an increasing burden worldwide. Current conventional treatment modalities do not replace the damaged ischaemic myocardium following an infarct. A promising alternative to replace the damaged ischemic myocardium lies in the potential of regenerative medicine. Mesenchymal stem cells (MSC) have been extensively investigated as a potential regenerative agent for the infarcted heart. Initial studies suggested that MSC were able to differentiate not only into the accepted adipose, bone, and cartilage lineages but even into neurons and cardiomyocytes. However, with opposing evidence of poor homing and engraftment of administered stem cells into infarcted heart models, the recent growing consensus is that MSC mediate their effects through the release of a plethora of bioactive molecules that carry out its paracrine effect on neighboring cells. As there are ongoing discussions in literature on whether mesenchymal stem cells and fibroblasts are possibly one cell type, this study aimed to investigate into the regenerative potential of conditioned media generated from bone marrow-derived mesenchymal stem cells and dermal fibroblasts isolated from the same rat host.

Materials & Methods

Establishment of primary stem cells lines from the same rat hosts and verify their functionality through stem cell differentiation into adipocytes and osteoblasts. Generation of conditioned media from both cell types and compare the strengths of their paracrine effect on human endothelial cells in in vitro cell migration, 3-day proliferation, and 3D spheroid angiogenesis. Lastly, compare the regenerative effects of isolated extracellular vesicles from each cell type.

Results

This is an ongoing study. Thus far, this study confirmed that BM-derived MSCs and dermal fibroblasts are phenotypically indistinguishable and were functionally verified through osteoblast differentiation. The cultured stem cells did indeed have a paracrine effect with the MSC having more reproducible effects across the different rat hosts.

Conclusion

Based on the different in vitro assays performed using the generated conditioned media, mesenchymal stem cells had a generally greater effect than their corresponding dermal fibroblasts with some variations. Future works need to further evaluate the effects of the MSC conditioned media in comparison to dermal fibroblasts in an in vivo or ex vivo CAM assay

Gestational and Breastfeeding Low-Protein Intake on Blood Pressure, Kidney Structure, and Renal Function in Male Rat Offspring in Adulthood

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Introduction

Our previous studies demonstrated that maternal protein-restricted (low-protein, LP) 16-week-old offspring had pronounced nephron number reduction and arterial hypertension associated with an unchanged glomerular filtration rate (GFR). An enhanced gomerular area may be related to increased glomerular filtration and overflow, which accounts for glomerular filtration barrier breakdown and early glomerulosclerosis. The effect of protein restriction during gestational and breastfeeding periods is unknown.

Materials & Methods

Method: The functional e-structural kidney evaluation was obtained using lithium and creatinine clearance, kidney morphometry, immunoblotting, and immunostaining analysis in 16 and 24-week-old LP offspring compared to age-matched NP progeny.

All data are reported as mean ± SD. Data obtained over time were analyzed using one-way ANOVA. Post hoc comparisons between means were performed using Bonferroni's contrast test when one-way ANOVA analysis indicated statistical differences between groups.

Results

Low protein rats' progeny had significantly reduced birth weight, without previous catch-up growth phenomena, in parallel with a decreased adiposity index. Transforming growth factor-beta 1 (TGF-β1) glomerular expression was significantly enhanced in the LP group. Also, the LP offspring had a 38% lower nephron number and an increased glomerular volume. They also presented with a higher cardiac index and arterial blood pressure compared with age-matched NP offspring. The LP rats exhibited augmented Na+/K+-ATPase in the proximal segments, and NOS1 immunoreactivity in whole renal tissue was associated with sodium retention in the proximal nephron segments. We also found significantly enhanced collagen content associated with increased TGFβ1 and ZEB1/2 renal immunoreactivity in LP offspring compared with NP offspring. Increased hypertrophy markers in LP podocytes were associated with an amplified IL-6/STAT3 pathway activity.

Conclusion

To our knowledge, these are the first data demonstrating renal functional and structural changes in protein restriction during gestation and lactation model of fetal programming. The fetal-programmed adult offspring showed pronounced structural glomerular disorders with an accentuated and advanced fibrosis stage, without a change in the GFR. These findings suggest that the glomerular enhanced TGF-β1 action may induce ZEB1/2 expression that may cause glomeruli epithelial-to-mesenchymal transition. Besides, decreased nephron number in the LP offspring with preserved glomerular function may be related to protective or even attenuate the activated IL-6/STAT3 pathway.

Multiple independent seeding of typical human G3 rotavirus strains on a DS-1-like and Wa-like genetic backbone between 2017-2019 in Blantyre, Malawi

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Introduction

Genotype G3 rotaviruses have emerged and spread globally the last decade with a majority being equine-like strains in the rotavirus vaccine era. Long-term rotavirus surveillance has detected re-emergence of G3 strains in November 2017, almost two decades after they were previously detected in Malawi. G3P[4] strains emerged first, followed by G3P[6] and G3P[8] strains. By 2019, G3 strains had completely replaced G1 and G2 rotaviruses as the most predominant strains in Malawi. To understand the re-emergence of G3 strains in Malawi, we undertook whole-genome sequencing and analysis of the re-emergent, previously circulating, and globally sampled G3 strains.

Materials & Methods

We selected at least one strain per month from November 2017 to December 2019 for sequencing. In total, G3P[4] (n=20), G3P[6] (n=1) and G3P[8] (n=6) strains were sequenced. Segment genotypes were assigned using ViPR, an online tool. Lineages were determined by constructing Maximum Likelihood trees with reference sequences in MEGAX.

Results

Whole genome analysis revealed G3P[4] and G3P[6] strains had a DS-1-like while G3P[8] strains had a Wa-like genetic backbone. G3P[4] strains (n=4) had a reassortant NSP1, N1. The VP7 genome segment of re-emergent Malawian G3 strains were typical human G3 strains showing high genetic similarity with strains from Pakistan in lineage 3. The DS-1-like backbone genome segments (VP1-VP3, VP6, NSP1-NSP5/6) were genetically similar to previously circulating local strains and those isolated from Pakistan. However, the Wa-like genome segments were only genetically similar to previously circulating local strains. Bayesian analysis revealed multiple independent introductions of G3 strains at different time points between 2017 and 2019.

Conclusion

Typical human G3 rotavirus strains have re-emerged post-rotavirus vaccine introduction in Malawi after two decades. The earlyG3P[4] strains seem to have been imported from Pakistan while the later reassortant G3P[4] and G3P[8] strains seem to have been imported from an

unsampled setting. The strains seem to have evolved independently once they were seeded in Malawi. Further genomic surveillance is required to monitor the dynamics and evolution of the emergent G3 strains in Malawi.

Immunological assessment of HIV-1 Nef-MPER-V3 harboring LDP12 penetrating peptide in BALB/c mice

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Introduction

In spite of the improvements in developing antiretroviral treatments, there are no approved HIV vaccines. To achieve an effective vaccine against HIV-1 requires induction of strong humoral and cellular immune responses. The objective of this study was the immunological assessments of HIV-1 Nef-MPER-V3 harboring LDP12 penetrating peptide in BALB/c mice in order to induce effective immune responses.

Materials & Methods

In the current study, presenting 55 female mice were utilized for immunization with LDP12-Nef-MPER-V3. The mice were divided into 11 groups of 5. Immunizations were performed three times at three week intervals and subcutaneously in a volume of 100 µl per mouse. Two weeks after final injection, humoral and cellular immune responses were evaluated in blood serum and splenocytes respectively, by using different types of ELISA method. Finally, the data analysis was performed, using Mann-Whitney U test.

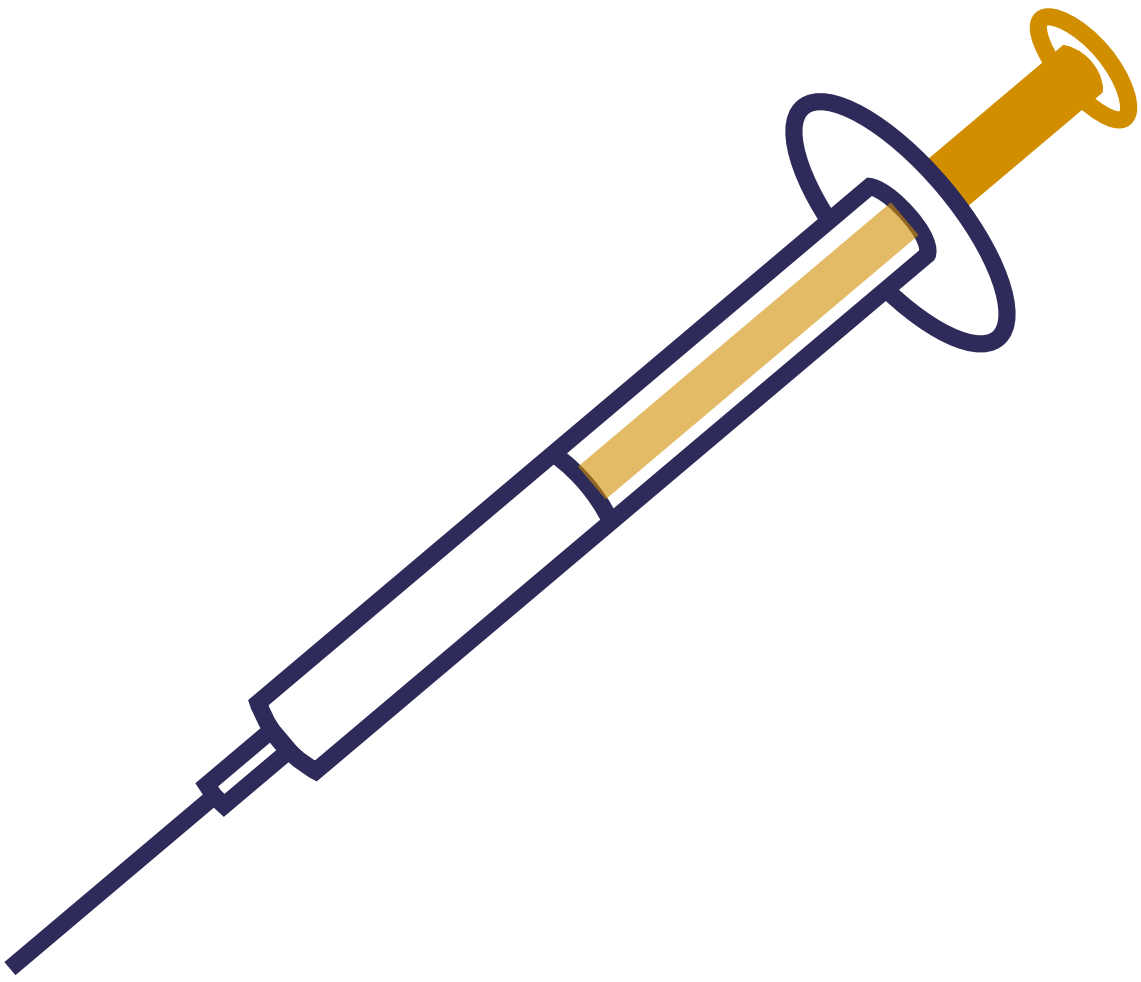
Results

Although the level of total antibody production was observed in all main groups with different titrations, but the total antibody level was higher in the mice group that injected with the LDP12 antigen with Hp91 adjuvant immunity than in the control group ($p=0.042$). Also, IgG2a was the predominant isotype (Th1-based response) in mice immunized group that had LDP12 antigen with Hsp27 adjuvant. On the other hand, significant increase in IFN-ɣ (Th1-based response) was observed in the groups which immunized with LDP12 antigen and mentioned adjuvants. But an increase of approximately 1100 pg/ml which showed a difference of $p=0.005$ to control group was determined in the mice group immunized with the LDP12 antigen and Hp91 adjuvant simultaneously, that the ratio of IFN-γ/IL-10 in this group was 11 ($p = 0.006$). Alongside, by evaluation of Granzyme B secretion and cell proliferation ELISA BrdU, the highest cellular immune responses were observed in LDP12-Hp91 immunized groups.

Conclusion

The data indicated LDP12-Nef-MPER-V3 antigen could stimulate humoral and cellular immune responses either alone or formulated with adjuvants. Also in Various formulations, utilizing of Hp91 adjuvant was effective in increasing cellular immune stimulation in mice, and it is hoped through using other formulations and more extensive studies in other animal models could achieve an effective vaccine against HIV.

Public Health II



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EVALUATION OF PRACTICE, ATTITUDE AND KNOWLEDGE ABOUT IRRATIONAL USE OF ANTIBIOTICS FOR COMMON COLD INFECTION IN SUDAN

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Introduction

Background:

As the majority of upper respiratory tract infections have a viral origin, antibiotics prescription for the common cold has become a common practice in medicine. The prescription of inappropriate and unnecessary antibiotics is the main cause of the development and increase of antibiotic resistance.

Objective: The main objective of this study was set out to evaluate practice, attitude, and knowledge about the irrational use of antibiotics for common cold infection.

Materials & Methods

Methodology: This cross-sectional study was conducted in Sudan from November 2020 to June 2021 comprised a random population of different age groups who had a common cold infection before. A well-established, self-administrated 100 questionnaires were randomly distributed to the population.

Results

Of the 100 participants 49 were males 51 were famles.74% of them were highly educated. (15-25 years) age group comprised the majority 44%. All participants had a common cold before 100% and 76% used antibiotics to treat this infection. 51% improved after taking antibiotics while 62% agreed that "Antibiotics cure common cold faster ".76% of participants mentioned they know the difference between cold and flu while the main reason behind using antibiotics for cold was physician prescriptions 48%. The majority 56% described antibiotics as the best treatment for a common cold.

Conclusion

A low level of knowledge about the nature of common cold infection and high levels of arbitrarily use of antibiotics for the common cold in this study makes it necessary to provide educational programs to raise awareness about the common cold and antibiotic resistance.

Inadequate health activities to prevent osteoporosis among Iraqi pharmacy students: a cross-sectional study.

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Introduction

One of the most determinants for lifelong bone health is skeletal growth during adolescence. The current pharmacy students are the future pharmacists; therefore, it is necessary that they have a good awareness of health issues, including osteoporosis. This study aims to investigate osteoporosis awareness and practices among young pharmacy students in many Iraqi universities.

Materials & Methods

A cross-sectional self-administered questionnaire study was conducted among undergraduate pharmacy students in many public and private Iraqi universities. A total of 443 respondents were asked to evaluate osteoporosis awareness and practices that include dietary practices (cow's milk, caffeine, and carbonated drinks consumption), smoking, physical activities, and family history of fragility fracture.

Results

A total of 443 respondents, 113 (25.6%) male and 329 (74.4%) female, 53.9% were pre-pharmacy stages (first and second), 46.1% were pharmacy stages (third, fourth and fifth), (43.9%) cow milk drinker, (56.1%) nondrinker of cow milk, (60.7%) coffee drinker, (39.3%) non-coffee drinker, (87.6%) tea drinker, (12.4%) non-tea drinker, (73.5%) consume carbonated beverages, (26.5%) not consume carbonated beverages, (92.3%) nonsmoker, (7.7%) smoker, (22.1%) have a family history of fragility fracture, (77.9%) no fragility fractures family history, (7.4%) regular physical exercise, (96.6%) not regularly exercise. There was a significant difference between genders in osteoporosis awareness and practice (P< 0.05). Different student stages and fracture family history showed no statistical differences in osteoporosis awareness and practice (P> 0.05).

Conclusion

Iraqi pharmacy students have insufficient health activities to avoid osteoporosis. Male pharmacy students showed a higher level of awareness compared with females. For successful osteoporosis prevention, educational programs to improve pharmacy students' awareness and knowledge are required.

Burnout and general health during COVID-19 pandemic among medical students in algeria

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Introduction

Burnout syndrome is caused by a high level of workplace stress, it is defined by a major triad: Emotional exhaustion, depersonalization, and reduced personal satisfaction. Medical schools are notorious for being a demanding environment, The unprecedented COVID-19 pandemic has resulted in a high level of physical and social stress. Therefore, this study aims to estimate the prevalence of symptoms of burnout and its relation to the general health state during the COVID-19 pandemic, among medical students.

Materials & Methods

This is a cross-sectional study, 167 participants in this study were recruited from the faculty of Medicine of Annaba Algeria, The survey consisted of four parts; general questionnaire, burnout assessment, general health assessment, and finally the Impact of COVID-19 pandemic and E-learning on the mental health of the students.

Learning burnout was evaluated by the French version of the Maslach Burnout Inventory-Student Survey (MBI-SS), General health (GH) was assessed using the GH domain of the 36-item health survey, The data were analyzed using t-test and comparison of mean was done with ANOVA, The Pearson correlation coefficient "r" and the regression line for the comparison of two quantitative variables (SPSS 21 version). The significance level was fixed in all cases at 0.05.

Results

Burnout was present in 82 participant (49.1%) of the students, there was a statistically significant difference in high burnout risk with year of education (P = 0.0461), a significant effect was found (P=0.035) implying that students with burnout had a worse general health state, also women were more likely to have poor general health than men, 60% of the participants reported an impact of the COVID-19 pandemic and E-learning on their health, no significant effect was found (P=0.15) in relation to an association of Burnout and COVID-19 pandemic impact.

Conclusion

The prevalence of burnout among medical students in Algeria was 49.1%, our study shows that general health status was also affected during the COVID-19 pandemic, with a special mention for higher years students who struggled more.

Preventing burnout is a must and early identification and resolution of the phenomenon, especially during the current pandemic, can help improve the health outcomes of students.

Investigation of COVID-19 lockdown impact on sleep quality in University students, Mongolia

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Introduction

The COVID-19 pandemic has led to significant changes in daily routines and lifestyle, therefore mental health issues have emerged as a consequence. In Mongolia, COVID-19 lockdown started on Nov 11th, 2020 and partially ended on Jan 3rd, 2021. We aimed to assess the presence of sleep disturbances during the lockdown in the medical students of Mongolia and correlation between depression and sleep issues.

Materials & Methods

A cross-sectional, online survey-based study on 402 undergraduate medical students from Mongolian National University of Medical Sciences, who are living through the COVID-19 pandemic, Dec 28th, 2020 to Jan 25th, 2021. Participants completed an online survey, which included Patient Health Questionnaire II to screen depression and specific questions assessing sleep pattern, bedtime hour, sleep latency, and sleep quality. All data were analyzed by STATA-13.0.

Results

Participants' mean age was 21.3±2.5 (range 19-24yrs). Of the 402 students, 46.4% indicated having depression during a lockdown. 79.8% (n=402) had delayed bedtime, 267 (66%) slept after 1am, 112 (27.9%) students mostly slept 4-6 hours.

We studied a comparison between participants' PHQ-2 score and sleep quality. Disturbance of regular sleep time is more observed in the depression group(p=0.42). The feeling of not being able to rest happens always or often, even after a full night of adequate sleep had a high prevalence in the depressed group(p=0.002). Regular sleep deprivation increases the risk of depression by 4%(OR = 1.04, 95% CI = 0.56-1.92). Feelings of not being able to rest after a full night of sleep often increase the risk of depression by 1.5 times, and the feeling of being constantly present increases the risk by 1.48 times (OR = 1.51, 95% CI = 0.54-4.24; OR = 1.48, 95% CI). = 0.45-4.90). However, there was no correlation between depression and sleep duration or bedtime.

Conclusion

Lockdown due to the COVID-19 pandemic, depression was noticed in one-half of medical students in our research. The lifestyle changes associated with the COVID-19 pandemic have also led to some changes in sleep patterns, which increase the risk of psychological problems. The results of our study may provide support for the implementation of some interventions for well-being in pandemic conditions.

Association Between Cultural Health Beliefs and Health-Seeking Behaviors with Quality of Life Across Generations Among Adult Filipinos in the National Capital Region (NCR), Philippines: An Analytical Cross-Sectional Study

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Introduction

The Philippines is a multicultural country with diverse beliefs that affect health practices and behaviors, and impact the quality of life (QoL) of Filipinos. The study aims to determine the association between cultural health beliefs (CHBs) and health seeking behaviors (HSBs) with QoL among adult Filipinos across generations from the National Capital Region of the Philippines. This would be significant in improving cultural sensitivity among healthcare providers, and allow Filipino physicians to incorporate Philippine traditional medicine with Western medicine, preventing cultural barriers between the physician and patient.

Materials & Methods

An analytical cross-sectional study was employed using non-probability convenience sampling. Two hundred and twenty-six (226) participants were recruited to answer an expert-validated and pre-tested Filipino questionnaire. It gathered data on CHBs and HSBs, and was integrated with WHOQOL-BREF questionnaire. SPSS-version-19 and chi-square test (95% CI, p=0.05) was used for statistical analysis.

Results

Participants who had positive CHBs and HSBs were 54.4% and 50.9% respectively. Majority had high (>50%) QoL scores in all domains of the WHOQOL-BREF. Those with high HSBs scores had an association with higher QoL in the physical, social, and environmental domains (p<0.05, 95% CI, 1.120 to 3.272; 1.506 to 4.938l; and 1.440 to 4.223, respectively). Through subgroup analysis, Generation X had an association between CHBs and HSBs with the environmental domain (p<0.05, 95% CI, 1.168 to 13.281 for CHBs and 1.026 to 11.476 for HSBs). On the other hand, Generation Y had an association between CHBs and the social domain as well as between HSBs and the physical, social, and environmental domain (p<0.05, 95% CI, 0.998 to 4.995; 0.502 to 16.477; and 1.208 to 6.156, respectively). Lastly, in Generation Z, an association was found only between HSBs and the social domain (p<0.05, 95% CI, 0.694 to 4.976).

Conclusion

High scores in a specific QoL domain are unique to a certain generation. They may have adapted differently in terms of health and approach to life, as most of their priorities and goals differ according to generations. Future research could explore other confounding variables (e.g. educational attainment, employment status, etc.) for analysis and find comparison in urban against rural communities.

Pre mature ovarian failure and its association with perceived stress after chronic kidney disease diagnosis: A challenge in all chronic kidney disease stages.

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Introduction

Chronic kidney disease is an emerging public health problem in Pakistan with an asymptomatic population suffering undiagnosed and untreated in urban and rural areas, the prevalence of chronic kidney disease has been on upsurge from past few decades, Asian countries have encountered the incidences in childbearing aged females, and premature ovarian failure is one of the prime reproductive concerns in our chronic kidney disease population, the aim of the study is to assess the frequency of premature ovarian failure in chronic kidney disease stage.

Materials & Methods

sample size is 384, where confidence level was 95% and Margin of error was 05%.

This technique will be Purposive, non-probability sampling, detailed medical history including age of menarche, menstrual cycles regularity, oligomenorrhea or sudden amenorrhea were differentiated.

The descriptive statistical tests were performed for independent variables including subject's age, years of chronic kidney disease diagnosis, parity, weight of subjects. While for dependent variables, frequencies were measured. The measure of association was analyzed with the help of Paired sample T Test, Compare means test and for validity of data chi-square test was performed. P-Value of < 0.05 was considered significant.

Results

The mean age of participated subjects was 41.31 ± 7.7,The pre-mature ovarian failure was described as menopause within the age of 40 years. indicated the measure of association of menopause after chronic kidney disease diagnosis into all CKD stage from Stage I to stage IV and End stage renal disease. The results showed almost equal number of study subjects indicating premature ovarian failure (menopause before the age of 40 years) with 19% (73/384) in CKD stage IV and 21.3% (82/384) In ESRD. While successful conception was reported by chronic kidney disease stage I and II patients only with 8.5% (33/384) and 4.6% (18/384) frequency respectively

Conclusion

we conclude that incidences of menstrual disturbances and pre mature ovarian failure is excessively reported in patients with chronic kidney disease stage III, IV and end stage renal disease. Psychological consultation is necessity for all patients regularly to maintain better mental health as well as understanding of coping mechanism and accepting the disease prognosis.

Effect of University Closure on Undergraduate Students in Egypt during COVID-19 Lockdown

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Introduction

The pandemic of COVID-19 has forced societies and governments to close schools and universities for the sake of preventing the potential spread of infection among the population. Since then, there was a global shift to more online education and interaction. Study objectives: To assess and explore the effects of lockdown and university closures on student learning abilities, depression, anxiety, and learning approaches.

Materials & Methods

A cross-sectional study was conducted on 864 university students from 15 faculties (88.2 % governmental &11.2 % private universities). Study subjects responded to an Arabic self-administered online questionnaire (through google form) that was distributed on social media groups of university students in Egypt. The questionnaire included demographical data for each student, 18 questions about the academic and learning abilities and experiences during the lockdown, 20-questions of Revised Two Factor Study Process Questionnaire (SPQ 2F) to measure learning approaches of students during university closures, patient health questionnaire (PHQ9) to scale depression, and finally GAD-7 to scale anxiety.

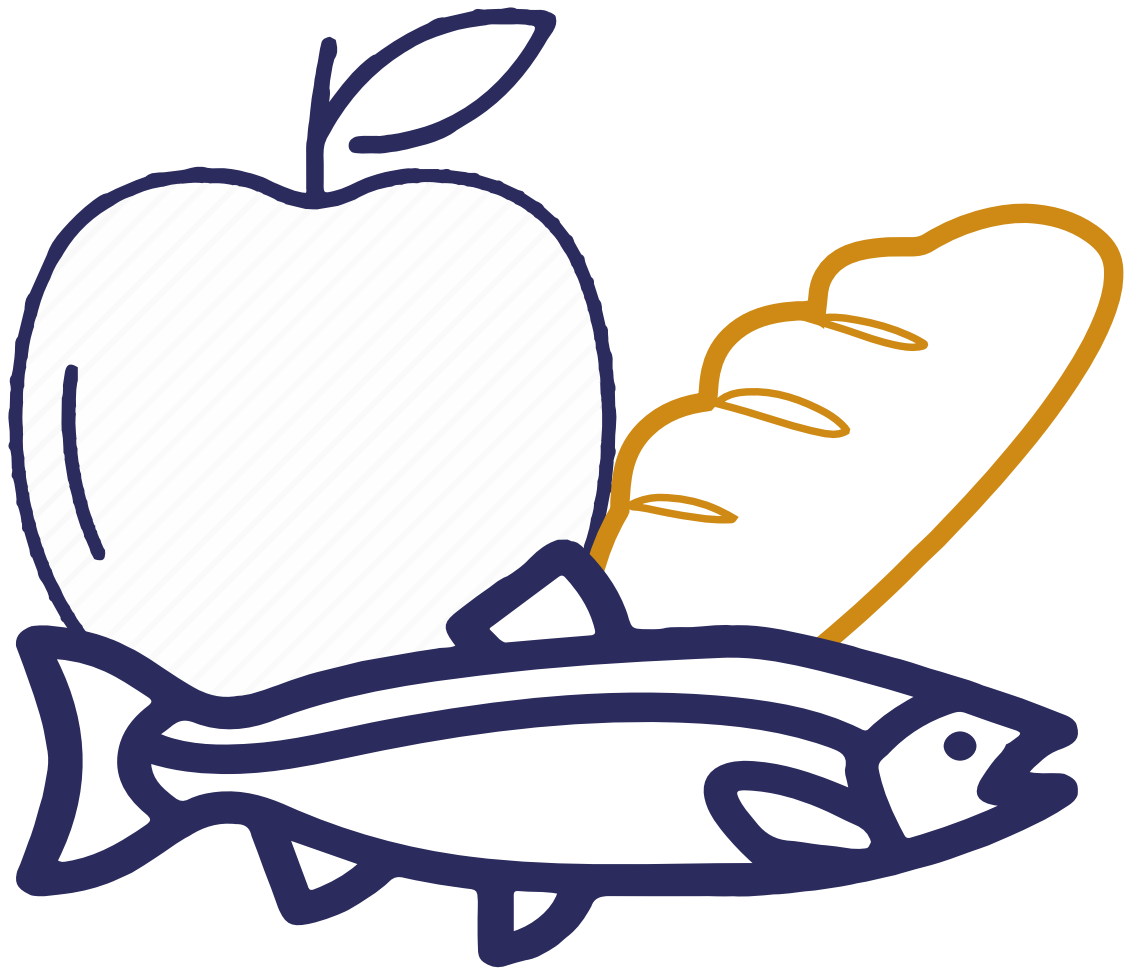
Results

Students who had onsite exams had more anxiety scores than those of students who had their assessments as research or online exams (mean=12.7, compared to 11.8, 11.5). Mean PHQ and GAD-7 scores were significantly higher among females than males during the pandemic lockdown. As regards R-SPQ, mean score for surface approach was significantly higher than deep approach during lockdown, opposite to before lockdown. While 64% had more frequent negative thoughts, 71.1% felt helpless due to lack of interaction, and 73.5% had increased social media time, only 17.8% of students reported increased number of study hours, 21.3% had better concentration, and 14.6% memorized easier. In contrast, 41.9% read more; 40.7% exercised more; 61% used more time for reevaluating their thoughts and lives and beliefs.

Conclusion

Lockdown has affected students' studying experiences in adverse ways as study hours, concentration, memorization, helplessness, negative thoughts, and social media. It had beneficial effects as well in sleep, exercise, reevaluating life, and reading. Surface approaches were significantly higher than deep approaches during lockdown. Psychological effects varied according to gender and the type of assessment students had during lockdown.

Nutrition



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Pandemic Triggered Food Consumption and Life Style Changes

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Introduction

Novel coronavirus (COVID-19) is an issue of concern throughout the world. Lockdown, confinement to home and social distancing have led to a drastic change in the daily activity, food purchase, sedentary lifestyle, over or under eating, increased on-screen time, impaired sleep and so on. The likelihood of the disease to recur in waves has created an additional threat and fear for mankind. We aimed to assess effect of pandemic on food consumption, lifestyle and financial security of respondents.

Materials & Methods

A pretested questionnaire including questions relating to personal information, dietary habits, change in body weight, work/job, income, household and daily activities, feeling of hopelessness and financial security was circulated online through Whatsapp, Facebook and email using snow-ball technique. The collected data was analyzed and chi-square test of independence used to find association between various categorical variables.

Results

A total of 286 people responded. Findings included increase in time spent on doing household activities (72.4%), impact on work/job (72.7%), decrease in feeling of financial security (30.42%), feeling of hopelessness (50.3%), loss of interest in daily activities (56.3%), increase in household conflicts (17.5%), and gain in body weight (29.7%). A significant association was observed between increased food consumption and decreased feeling of hopelessness (p<.001), enjoyment of happy moments happening in life (p<.001), increase in body weight (p<.001), interest in daily activities (p<.01), feeling of being financially secure (p<.01) and increase in time spent in household activity (p<.05).

Conclusion

Food is the basis of health, both of individual as well as the society. Disaster like coronavirus pandemic has changed the way people accessed their food, where they ate, food stocking and how their food was prepared. Number of meals per day and snacking between the meals has increased for many thus leading to a gain in weight. Financial insecurity, loss of job, shift in time spent on household activities, feeling of hopelessness, loss of interest have further forced people to vary their food consumption and a clear association was seen between these variables.

The influence of childhood trauma to uncontrolled eating

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Introduction

Emotional eating, binge eating, food addiction and other conditions related to overeating are becoming more and more prevalent in the Western world. Studies suggest that there could be a relationship between childhood trauma and binge eating. This study aimed to explore if there is an influence between childhood trauma and other variables which describe uncontrolled eating.

Materials & Methods

We used data collected from 254 patients who were evaluated in Montpellier hospital eating disorders unit for various eating disorder related symptomatologies. The mean respondents age was 28.12 ± 1.4, 91.7% of them were female. Data collected included BMI, body muscle mass, fat mass and questionnaires - YFAS (Yale food addiction scale), EMAQ (Emotional Appetite Questionnaire), CTQ (Childhood Trauma Questionnaire). The statistical analysis was done using SPSS, correlation was calculated using Kendall's Tau non-parametric test.

Results

A positive relationship between CTQ score and BMI was found (p<0.001, correlation coefficient was 0.296). Statistically significant positive correlation was found between childhood trauma and body fat mass (p<0.001, correlation coefficient 0.267) while correlation with muscle mass was negative (p<0.001, correlation coefficient -0.268). The strongest association was between YFAS and emotional abuse during childhood (p<0.001, correlation coefficient 0.300), while it was less pronounced between YFAS and physical neglect (p<0.001, correlation coefficient 0.231). Association between YFAS and sexual abuse during childhood was the weakest (p<0.001, correlation coefficient 0.145). Our results show correlation between childhood trauma and emotional eating as well (p<0.001, correlation coefficient 0.165).

Conclusion

Childhood trauma influences uncontrolled eating behaviours. Statistically significant correlations were found between CTQ and BMI, body muscle and fat mass, YFAS and EMAQ. Results emphasize importance of addressing emotional problems stemming from childhood in people with food addiction, emotional eating and other uncontrolled eating behaviours.

The Relation of the Serum 25-Hydroxyvitamin D Level with the BMI of the Children Over 2 Years Old among the Patients referred to Javaheri Hospital During 2017

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Introduction

Regarding the high prevalence of vitamin D deficiency and obesity , there are evidences which show that there are inverse relations between serum 25-hydroxyvitamin D level and the Body mass index (BMI) of children; concerning the limited studies in this field and the paradoxical information, this study has been planned and performed with the aim of analyzing the relation between serum 25-hydroxyvitamin D level with the BMI of the children over two years old among patients referred to Javaheri Hospital during 2017.

Materials & Methods

In this descriptive and cross-sectional study, 150 children over two years old have been examined by serum 25-hydroxyvitamin D level test, and the weight of each child has been measured and recorded. It will be considered either as the vitamin D deficiency when serum 25-hydroxyvitamin D level be less than 10 ng/ml and when its level is 10-30 ng/ml, like the Vitamin D insufficiency. Gathered data in SPSS software has been revised, and 25 inputs with recourse to the statistical tests like Kolmogorov-Smirnov, Shapiro-Wilk, chi-square, Mann-Whitney, and Kruskal –Wallis be evaluated in two quantitative and qualitative scales.

Results

According to the findings of this study, it is revealed that from the aggregate of 150 children with the demographic characteristics as mentioned-above, 6.7 percentages are afflicted with vitamin D deficiency, and 54.7 percent are afflicted with insufficient vitamin D level. Assuming 5 percent error of the Vitamin D deficiency and insufficiency prevalence in children respectively, are calculated as ɣCIɣ_(95%)=[3.6.-10.8] and ɣCIɣ_(95%)=[50.8.-58.8]. Also, no significant relations between serum vitamin D level of children with the BMI, and between age and gender have been observed (P-Value>0.05).

Conclusion

In our study, 61.4 percentages of children are afflicted with either deficiency or insufficiency of vitamin D. Concerning the undesirable Vitamin D status, it is recommended that further analysis be done for finding vitamin D deficiency causes and its prevention and treatment with vitamin supplements.

Lactuca breeding affects human intestinal biological efficacy: a comprehensive experimental and computational approach

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Introduction

The ever growing global population is accompanied by an increase in food demand. In combination with the decrease in available agricultural land, innovative solutions to increase crop production are required. Plant breeding is purposed as solution which focusses on enhancing yield and disease resilience of crops. However, the effect of genetic alteration of crops on the health of the end consumer is often neglected. The intestine plays an important role herein being the place where digested food enters the body. As lettuce is one of the most cultivated crops worldwide, a total of nine lettuce cultivars (at different domestication levels) were tested for human intestinal biological efficacy.

Materials & Methods

Nine lettuce cultivars, ranging from wild to domesticated, were exposed to a novel intestinal in vitro model, the bioengineered intestinal tubules. Various essential intestinal parameters were taken into consideration such as intestinal epithelial barrier integrity, cell viability, brush border enzyme activity, inflammation and oxidation. Data obtained were used for a comprehensive cluster analysis to evaluate distinct biological behaviour between cultivars.

Results

After confirmation of accurate recapitulation of physiological intestinal function, bioengineered intestinal tubules were exposed to the Lactuca cultivars. Wild lettuces induced detrimental effects on the intestinal epithelium as a tendency towards a disrupted barrier, a decrease in cell viability and brush border enzyme activity were shown. In addition, wild type lettuce exposure promoted cell detachment from the basement membrane. As cultivars became more domesticated, this detrimental effect disappeared with a maintained intestinal epithelial barrier and physiological levels of cell viability and brush border enzyme activity. The comprehensive cluster analysis revealed distinct intestinal biological behaviour based on different levels of domestication as wild and domesticated cultivars clustered together.

Conclusion

In this research it was shown that wild lettuces induced detrimental effects on the intestinal epithelium which gradually decreased as lettuces became more domesticated. It is thought that alterations in phytochemical composition play a central role in the induction of biological effects. This research underlines the effect plant breeding can have for the end consumer. Therefore, it is suggested to include biological evaluations in plant breeding, which consequently could aid in breeding towards health promoting crops.

Knowledge and awareness about aggravating factors of the peptic ulcer disease: a cross-sectional study

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Introduction

Peptic ulcer disease is a gastrointestinal disorder due to the imbalance between the defense mechanism and gastric acid secretion. It affects 5-10% of the population worldwide and induces eight million deaths every year globally. In Sudan, this disease represents as one of the major health problems. Limited studies have shown the knowledge level of Sudanese about aggravating factors of Peptic ulcer disease, which lead to more prevalent complications. Therefore, this study aimed to assess awareness about aggravating factors of peptic ulcer disease among the population at Khartoum state, Sudan.

Materials & Methods

A descriptive cross-sectional study targeted the general population in Khartoum state during the period from August to December 2021. We used an online survey form to collect data from the study population. The distribution of the questionnaire was done via social media tools. We analyzed the data using SPSS Software version 26.

Results

The study included 398 participants, 40.7% of them were male and 59.3% were female, with mean age equal 24.9 (SD=8.9), and range between (18-64). Most of the participants (77.1%) were unmarried and (89.2%) were educated. The type of food was the most known risk factor (79.1%) and the weather changes were the least known risk factor (8.5%) that have effects on peptic ulcers. There also was a significant difference between educated and non-educated people based on the awareness of peptic ulcer risk factors, as the second was higher (p>0.000). Furthermore, people with peptic ulcers and people who have one or more members of their family with peptic ulcers had scored more than nonpatients and those who did not have (p>0.000, p= 0.04; respectively).

Conclusion

In conclusion, awareness about aggravating factors of peptic ulcers was variable among the population in Khartoum state. Our study findings revealed a high knowledge effect of type of food, helicobacter pylori, analgesic medications, drinking coffee, smoking, and social stress of majority population. As for other factors, the weather changes, genetic factors, and body weight were associated with a poor level of awareness. Therefore, these results need to be affirmed by furthermore research with a large sample among the general population in different regions in Sudan.

Technology-Assisted Personalized Nutrition Therapy Reduces Malnutrition Problems and Improves Healthy Diet Among Obese Adults: A Meta-analysis

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Introduction

Overweight and obesity have long been known to significantly raise the risk of developing diabetes and other metabolic diseases worldwide, but the COVID-19 pandemic has put more challenges to its management. The novel concept of personalized nutrition therapy (PN) is believed to be much more effective than the conventional population-based intervention. PN therapy uses personal phenotypic and genotypic data from each patient to design a comprehensive diet plan and healthy lifestyle advice. Aided with technology, PN is a novel potential solution to be adapted especially during this pandemic era. Through this meta-analysis, we aim to quantitatively evaluate the effectiveness of technology-assisted PN therapy in managing malnutrition problems among obese adults.

Materials & Methods

We conducted a literature search through databases including PubMed, Scopus, Cochrane, ScienceDirect, EBSCOHost, and Google Scholar, searching for clinical trials implementing technology-assisted PN up to October 2021. The quality of studies was evaluated using the Cochrane Risk of Bias 2.0 tool and converted to AHRQ standards. We conducted qualitative extraction and quantitative analysis of mean differences using Review Manager 5.4 in inverse variance, random-effects model and whenever possible, subgroup and sensitivity analyses were performed.

Results

Our search yielded 9 studies with 5,173 participants. Technology-assisted PN is proven effective in improving anthropometric outcomes including weight (pooled MD: -0.82; 95%CI:-1.30-(-0.35); p=0.0007), BMI (pooled MD: 1.30; 95%CI:-1.97-(-0.62); p<0.00001), and intakes of fruits and vegetables (pooled MD: 0.86; 95%CI:0.18-1.53; p=0.01). The quality assessment revealed that most studies in this review have a low risk of bias. Technology-assisted PN delivered through web, mobile, or telephone-based approaches, utilizes each individual's characteristics and information to create specialized nutritional advice. This intervention provides a more effective and convenient way for patients to manage their condition, through promoting weight change and intake of nutritious foods, reduction of saturated fat and sweetened beverages, as well as general diet scores.

Conclusion

Technology-assisted PN is proven to be more effective in improving overweight problems and increasing fruits and vegetable intake compared to previous population-based intervention, thus supporting its potential use in clinical settings especially during this pandemic era.

Anti-tuberculosis Drugs Significantly Affect the Body Mass Index of Tuberculosis Patients.

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Introduction

Tuberculosis is one of the most common and lethal infections. Several studies conclude malnutrition is critical in the development of pulmonary tuberculosis and linked with the relapse risk and treatment response rate of pulmonary tuberculosis. Thus, Malnutrition is meticulously linked with tuberculosis yet changes before and after treatment remain undistinguishable. The study was aimed to investigate the longitudinal changes in BMI in patients receiving anti-tuberculosis treatment.

Materials & Methods

A State government NTEP funded, retrospective cohort analysis of protocol-based collective data from the Tuberculosis units located in south Gujarat, India was conducted. 4 tuberculosis units were selected based on the annual case finding rate of tuberculosis. Treatment cards of 826 patients from Tb units were evaluated, followed by the trend of BMI between the start and end of treatment. Next, comparison of BMI in different age groups from (i) baseline to end of intensive phase BMI, (ii) baseline BMI to end of continuous phase BMI and (iii) end of intensive to end of continuous phase BMI was done along with the difference of BMI with demographic and clinical variables. Data is presented as means and standard deviations (SD) for continuous variables. Longitudinal changes in BMI were analyzed by the Anova test using IBM SPSS Statistics , version 20.

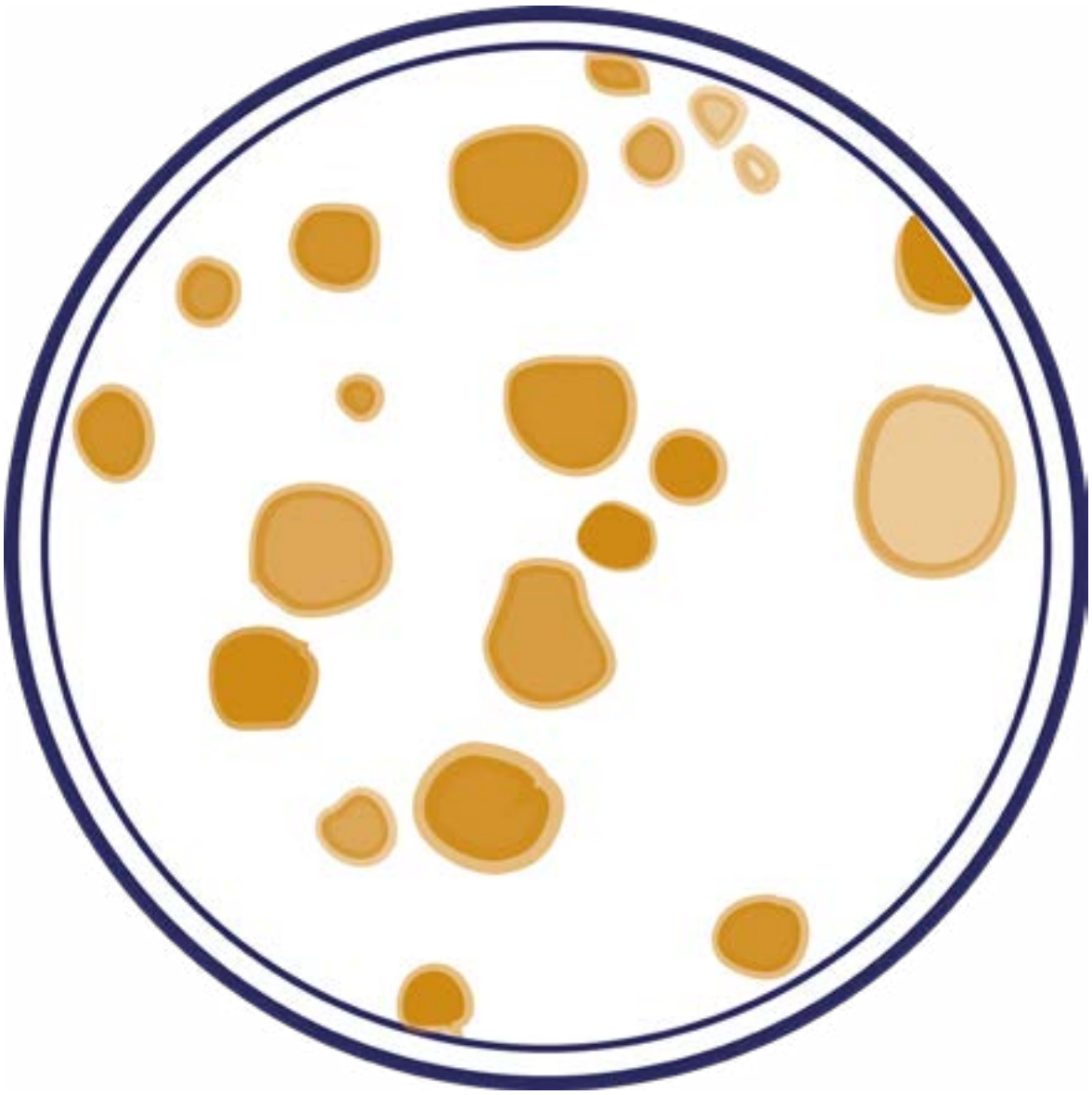
Results

A statistically Significant rise between baseline BMI 19.08 ± 4.32 and at the end of continuous phase, was observed 19.79± 4.38 , along with rise in BMI at the end of the intensive phase being 19.30± 4.33 which was statistically significant (p-value ɣ 0.001). Among demographic variables only socioeconomic status showed statistical significance, with improvement in mean of above poverty line TB patients being 0.76 and below poverty line patients being 0.59. Other clinical variables did not show any significant change .

Conclusion

BMI variation during tuberculosis therapy predicts treatment outcome and therefore its evaluation should be incorporated into routine clinical management. Patients losing BMI during TB treatment are at risk of failure or death. BMI gain ɣ 5% at the end of treatment, high bacterial load and lack of sputum conversion correlate with unsuccessful treatment outcome.

Medical Microbiology



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PREVALENCE OF MRSA COLONISATION AMONG PATIENTS ADMITTED WITH INJURIES AT MACHINGA DISTRICT HOSPITAL

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Introduction

MRSA is a major challenge to the treatment of S.A infections. People colonized with MRSA are at risk of developing a subsequent infection and present an important MRSA reservoir for further transmission.

Objectives: The main objective of this study was to determine the prevalence of MRSA colonization among patients admitted with open wound injuries at Machinga District Hospital.

Materials & Methods

A longitudinal research design was used. Participants between 5 to 65 years old with a wound sustained from an injury consented to take part in the study. Samples from both anterior nares and site of the wound were collected. Samples were cultured to identify individuals with MRSA colonisation at admission and within their hospital stay. Antimicrobial susceptibility testing was performed for S.A positive samples by disc diffusion method. An interview guide was used to acquire demographic data and ascertain the exposure to risk factors for MRSA carriage.

Data analysis was done using statistical package STATA 15. The prevalence of MRSA among patients admitted with injuries was estimated with 95% CI.

Results

A total of 232 individuals participated in the study. 116 had a wound and 116 had no wound. Nasal colonisation with S.A was seen in 42/232 (18.1%) individuals but only 7/232 (3%) were confirmed to be MRSA by Oxacillin disk diffusion method. 2/7 (28.6%) of MRSA isolates were from the community. Prevalence of MRSA colonisation among patients admitted with injuries was 6/116 (5.17%) in our study. Antibiotic resistant to Penicillin was 85.71%, Erythromycin 42.86%, and Ciprofloxacin 30.95%. All isolates were 100% sensitive to Vancomycin and Rifampicin regardless of their Methicillin status.

Conclusion

We found prevalence of MRSA colonisation among patients admitted with injuries to be at 5.17% in this study and 28.6% of MRSA isolates were from the community suggesting that there is a considerable reservoir in the community for possible transmission.

We recommend screening of MRSA colonisation to patients admitted with injuries as a measure of combating transmission and avoid subsequent infection.

Prevalence and risk factors of Hantavirus infection in patients undergoing hemodialysis in Khartoum, Sudan, in 2019: a cross-sectional study

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Introduction

Hantaviruses are enveloped negative sense RNA viruses that cause hemorrhagic fever with renal syndrome (HFRS). The risk of Hantavirus infection increases with exposure to the excreta of rodents, either at home or in the workplace. Chronic renal failure and hypertension as the long-term sequel to HFRS has been reported in follow-up studies. Worldwide, multiple studies have showed variable results regarding the presence of Hantavirus antibodies in chronic kidney disease (CKD) patient. It is worth noting that a high percentage (10.7%) of end-stage renal disease (ESRD) cases were due to unknown causes in a study that included 1583 hemodialysis patients in Sudan. Hence, other causes that are not usually considered may play a role in the etiology of ESRD among Sudanese patients. Thus, this study aimed to identify the prevalence of Hantavirus IgG antibodies and possible risk factors for Hantaviruses infections among end-stage renal disease (ESRD) patients attending the Dr Salma dialysis center in Sudan.

Materials & Methods

This was a cross-sectional study in which 91 ESRD patients and 30 healthy plasma samples were screened for Hantavirus IgG antibodies using ELISA. A questionnaire containing socio-demographics, history of rat exposure and clinical data information was filled in by each ESRD patient. : The study protocol was ethically approved by the Central Laboratory of Ministry of Higher Education and Scientific Research, Sudan. Written consent was obtained from respondents after informing them about the objectives and benefits of the research.

Results

In this study, 9 out of 91 ESRD patients (9.9%) tested positive for Hantaviruses antibodies (IgG) while none of the 30 healthy plasma samples showed sero-positivity. There was no statistically significant association between age, gender, educational level or rat exposure and Hantavirus infection in ESRD patients (p>0.05).

Conclusion

This study is the first to be conducted in Sudan regarding Hantaviruses and ESRD. The prevalence of Hantavirus antibodies among ESRD patients is high compared with findings reported in the literature from studies conducted on the same group of patients. It points to an interesting question as to whether Hantaviruses have an association with ESRD but further studies are needed before drawing any conclusions.

Analysis of Antiquorum-Sensing and Antibiofilm Activity by Pomelo Peel Extract (Citrus maxima) on Multidrug-Resistance Pseudomonas aeruginosa

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Introduction

Pseudomonas aeruginosa is gram-negative bacteria with high adaptability by forming biofilms and quorum-sensing mechanisms to avoid immune responses and antimicrobial agents which tend to develop into Multidrug Resistance (MDR) related to Healthcare-Associated Infection (HAI) with mortality rate up to 69%. Polyphenol compounds found in pomelo peels (Citrus maxima) have been shown to have antibiofilm and antiquorum-sensing effects but are less investigated. Therefore, this study aimed to investigate those effects on MDR P. aeruginosa.

Materials & Methods

In vitro study design is performed to evaluate the inhibition effect of ethanolic extract on bacterial growth (Kirby-Bauer test), biofilm formation (biofilm assay), and quorum-sensing activity (pyocyanin and pyoverdine assay) on clinical isolates of MDR and ATCC strain as comparator. Furthermore, we employed computational methods using docking protein analysis.

Results

Biofilm formation was significantly inhibited by 71.1%±4.4% in MDR (p<0.001) and 47.1%±25.6% in ATCC (p<0.001) with extract concentration of 15 mg/mL. Antiquorum-sensing activity in MDR through inhibition of pyocyanin and pyoverdine production was found significant by 44.9%±22.2% (p<0.001) and 53.9%±22.9% (p<0.001) respectively at concentration of 5 mg/mL. This finding may occur due to inhibition of gene regulators (LasR and LasI) by active compounds of Citrus maxima. Molecular docking was used to further strengthen this hypothesis, showing no significant differences in bonding energy of polyphenol compounds found in pomelo peel with LasR and LasI compared to the native ligand and inhibitors.

Conclusion

Pomelo peel extract can be considered as a potential therapy for MDR P. aeruginosa infection mediated based on its antibiofilm and antiquorum-sensing effects.

Microbial analysis and chemical composition and associated factors of raw cow milk in the dairy farms of South Gondar zone, Ethiopia, 2021

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Introduction

Milk is one of the most valuable and regularly consumed food by millions of people. However raw milk is a highly perishable food and serves as a good growth medium for pathogenic micro-organisms because of its neutral pH, high water, and nutrient content. The main purpose of this study is to evaluate the microbial analysis and chemical compositions of raw cow milk and associated factors among dairy farmers in South Gondar Zone, Ethiopia, 2021.

Materials & Methods

A laboratory-based cross-sectional study was conducted from April to May 2020. A total of 160 randomly selected milk samples were collected to analyze milk microbes; Coliform, S aureus, Molds and Yeast, and milk quality; Total solid, and Specific gravity. Water, utensil, and hand swab samples were analyzed using standard laboratory techniques. While knowledge, attitude, and practice of milk handlers were also assessed using a pretested structured questionnaire. Descriptive statistics and multiple linear regression models were used to analyze the data.

Results

The mean Total coliform count of raw cow milk was 14.96±0.34 logs CFU/10ml. while the mean S aureus count was 8.29±0.19 log CFU/100ml and the mean Mold and Yeast count at dairy farms was 4.25±0.14 logs CFU/100ml and 8.90±1.20 logs CFU/100ml respectively. The mean total coliform count of water, milking utensil and hand swab samples were 4.04±0.34, 4.32±0.57, and 3.58±0.55 log CFU/100ml or Cm2 respectively. The mean total soluble varied from 9.3%-12.1%, while the mean Specific gravity was between 1.013-1.029. In the final model poor personnel hygiene, poor water quality, poor utensil quality; poor attitude, low sanitation practices, and lack of sufficient knowledge of the milkers were associated with higher milk microbes.

Conclusion

Almost all milk samples analyzed were contaminated by one or all microbes above the limit set by European Union. Many easily manageable and preventable factors were associated with higher microbial contamination, which suggests continuous monitoring of milk and milk products is necessary.

A study of prevalence of pathogenic bacteria, particularly, fecal coliforms and their antibiotic resistance pattern in environmental water samples of a tertiary-care hospital, Ahmedabad

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Introduction

The antibiotic-resistant bacteria (ARB) are creating a major public health issue, globally, owing to their presence and spread, especially in aquatic ecosystems that are known for the ARB and antibiotic resistance genes (ARGs). There is a scarce knowledge regarding the effects of ARGs in the drinking water bodies, in which recently, they were found to be the emerging contaminants. Escherichia coli are a part of the normal flora of human and animal fecal matters, which may contaminate the soil and water. By far, no study is done in our region to know the prevalence of antibiotic resistance in environmental bacteria.

Materials & Methods

50 water samples consisting of drinking water, water from the drainage pipes, and water from the leaking pipes of General Hospital, Sola, Ahmedabad, India, were studied for the determination of the prevalence of antibiotic- resistant coliforms. Water samples were collected for analysis of fecal contamination and to detect the most probable number (MPN) of fecal coliforms by multiple-tube fermentation technique. Antibiotic resistance of the E. coli isolates and Klebsiella were determined by Kirby–Bauer disc diffusion method using Clinical and Laboratory Standards Institute (CLSI) guidelines.

Results

Of the 50 samples collected from the civil hospital, 22 samples (44%) showed contamination with fecal coliform. Of the 22 positive samples, E. coli was isolated from 12 water samples; Klebsiella was isolated from 10 samples. Majority of the isolates from the drinking water were sensitive to cotrimoxazole, quinolones, chloramphenicol, aminoglycosides, third- generation cephalosporins, and tetracyclins. However, all the E. coli isolated from drainage water were resistant to cotrimoxazole, third-generation cephalosporins, and gentamicin. About 50% isolates from the drainage supplies showed resistance to quinolones and tetracyclins. Isolates from tap water and leaking pipe lines were sensitive to majority of the drugs.

Conclusion

A comparison of isolates from drinking water with drainage water revealed that antibiotic resistance is widespread in environmental bacteria.It can be correlated with an extensive and sometimes over use of antibiotics, along with use of higher antibiotics only ,even for the treatment of mild infections spillage of resistant bacteria from patients to the environment.This study alarms for an appropriate and judicious antibiotic usage.

Oral microbiota in hypertension in Mexico

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Introduction

Hypertension is one of the most prevalent diseases worldwide. Since its development is multifactorial, resulting from endogenous and environmental factors (e.g., diet), the role of the microbiota in cardiovascular disease (CVD) has been evaluated recently. In hypertensive patients, there is a significant decrease in the diversity and abundance of the gut microbiota. Although few reports exist on oral microbiota, oral dysbiosis has been associated with high blood pressure (HBP).

Materials & Methods

The present study characterized the oral microbiota of 22 patients, 18 with and 4 without HBP. After taking dental bacterial plaque samples, the V3-V4 region of the 16s rRNA gene was sequenced on Novaseq6000 Illumina PE250 platform. Data analysis and interpretation was performed with Qiime2 and rstudio. Alpha-diversity was measured with Chao1 and Shannon index and beta-diversity was visualized using principal coordinate analysis based on the Bray–Curtis distances.The nonparametric Mann-Whitney U test was applied for statistical analysis, considering significance at $p \leq 0.05$.

Results

The most abundant phyla observed in all patients were Firmicutes, Bacteroidetes, Proteobacteria, Actinobacteria and Fusobacteria. Only Fusobacteria was statistically different between groups, being less frequent in the patients with versus without HBP (11.41% vs 16.70%, respectively). Of the 15 main genera identified in the sample, the most abundant were Veillonella, Streptococcus, Neisseria, Fusobacterium, Porphyromonas, and Prevotella. Only Fusobacterium and Porphyromonas were statistically different between groups, being less frequent in patients with versus without HBP (7.82% vs 12.37% and 4.39% vs 8.95%, respectively). Analysis of alpha and beta diversity did not show significant differences, although slightly greater diversity was exhibited in the group without versus with HBP.

Conclusion

No difference in microbiota diversity was found between patients with versus without HBP. However, the abundance of the phylum Fusobacteria and the genera fusobacterium and Porphyromonas was different between the two groups. The current results are provided with the hope of stimulating further research on the characterization of the oral microbiota in CVD.

Search and analysis of CRISPR / Cas system loci and structures in the genome of Streptococcus mutans NG8 strain and phages detected by them by bioinformatics methods

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Introduction

Streptococcus mutans is a type of gram-positive, facultatively anaerobic bacteria that is detected in the human oral cavity, being the main cause of the development of caries. They can also enter the bloodstream and cause systemic infections, such as infectious endocarditis. Antibiotics can no longer cope with bacterial pathogens due to the development of resistance to them and phage therapy is becoming relevant again. Structures of CRISPR/Cas systems, which are the mechanism of their adaptive immunity against phages, have been identified in the genomes of bacteria. Bioinformatics methods make it possible to detect these systems and identify through the spacers of their CRISPR cassettes the spectrum of phage races that this bacterium has encountered and developed resistance to them. The aim of the work was to search and analyze the loci and structures of CRISPR/Cas systems in the genome of the S. mutans strain and to identify the spectrum of phage races through spacers in the CRISPR cassette using bioinformatics methods.

Materials & Methods

The genome of the S. mutans strain was taken from the GenBank database (no. NZ_CP013237). The search for CRISPR/Cas system structures and phage profiles in it was carried out using the algorithm of the following programs: MacSyFinder (ver. 1.0.2); makeblastdb (ver.2.2.28); HMMER (ver.3.0); PILER-CR: fast and accurate identification of CRISPR repeats; CRISPI: a CRISPR Interactive database; CRISPRFinder; CRT: CRISPR recognition tool; CRISPRDetect; BLASTn; CRISPRTarget; Mycobacteriophage Database; Phages database.

Results

The revealed structure of the CRISPR/Cas system of S. mutans was assigned to type II. The CRISPR cassette contained 5 spacers up to 31 nucleotides long, separated by 6 repeats 36 nucleotides long. The CRISPR cassette locus in the genome occupied positions between 1327915 and 1328241 sequences. Through spacers complementary to protospacers of phage genomes, phages were identified whose hosts are bacteria from genera: Mycobacterium, Gordonia, Rhodococcus.

Conclusion

Thanks to the use of the algorithm of bioinformatics software methods, information was obtained about the structure of the CRISPR/Cas system in the genome of the S. mutans strain. Through spacers, complementary phage protospacers were identified and the spectrum of phage races to which it is resistant was determined. This approach makes it possible in the future to develop a technology for targeted phage therapy of infections caused by pathogenic bacteria.

Comparison the efficacy of semi-nested PCR with PCR/HRM in detection/identification of mucormycosis from fresh clinical specimens using Mucorales specific primers

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Introduction

Mucormycosis is a fungal emergency featured by its angioinvasion, aggressive tendency for progression particularly if not timely diagnosed and managed. We investigated the utility of high-resolution melt analysis (HRMA) and semi-nested PCR using Mucorales-specific primers targeting a 180 bp region of the 18S region of rDNA for detection and identification of Mucorales DNA from fresh specimens in comparison with diagnostic value of culture, direct and histopathological examinations.

Materials & Methods

Specimens from patients with suspicion of invasive fungal infections were prospectively chased up for mucormycosis diagnosis through histopathology and direct microscopy. Identification of Mucorales culture was performed using PCR with pan-fungal ITS primers. For molecular diagnosis of those specimens showed broad aspetate hyphae suggestive of mucormycosis, HRM analysis and semi-nested PCR using Mucorales-specific primers were attempted. The amplicons of PCRs were sequenced to identify the agents. Identification via PCR/HRM was assessed according to the similarity of melting curve to each of reference melting curve generated by the mucormycete strains.

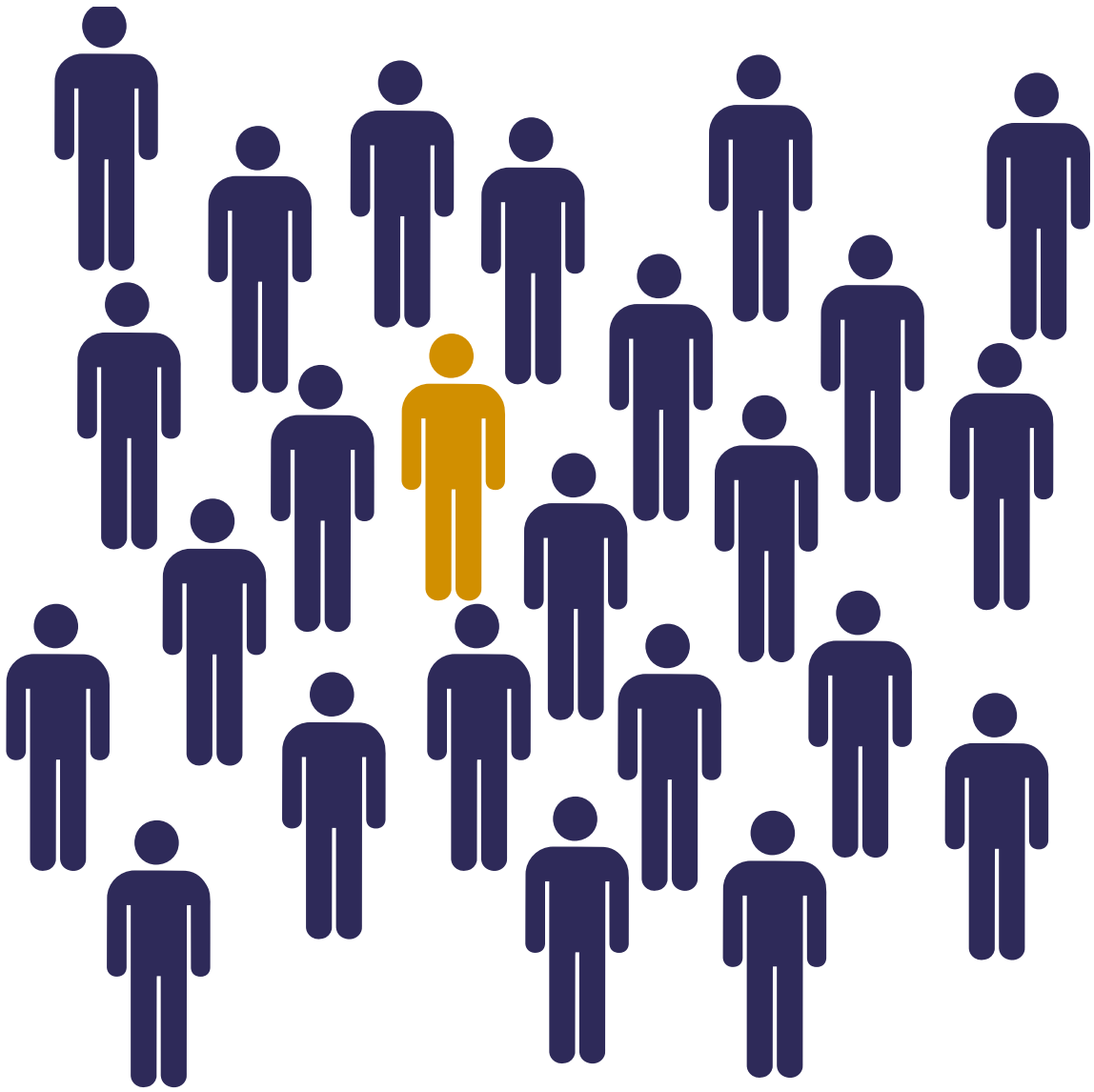
Results

Overall, 31 cases (30 proven and 1 probable cases) of mucormycosis out of 341 investigated specimens were diagnosed. Rhino-orbito-cerebral mucormycosis (45%) was the most common presentation. Isolation was possible in 22/29 (~76 %) specimens. Regarding molecular diagnosis, the semi-nested PCR enabled detection and identification of Mucorales in 26/29 (90%) cases with a turnaround time of <9 h (regarding DNA extraction step) while using PCR/HRM, the detection and identification of Mucorales in all of the cases (100 %) with a turnaround time of <5 h (regarding DNA extraction step) was achieved. R. oryzae (22/29, 76%) was predominantly identified. The sensitivity, specificity, negative and positive predictive value of PCR/HRMA was all 100%.

Conclusion

Through direct molecular diagnosis, the deficiency of conventional diagnosis is overcome, the necessity for culture based molecular identification will be eliminated and turnaround time to establish the diagnosis is reduced. Using semi-nested PCR, the detection rate of mucormycosis in a shorter time increased in comparison with culture. PCR/HRM is novel technique showed superiority over the semi-nested PCR, histopathology, culture and ITS sequencing in terms of cost-effectiveness, rapidness and sensitivity for diagnosis and identification to species level when a sequencing facility is not available.

Epidemiology



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Coronavirus antibodies demonstrate early childhood onset of exposure: a Nicaraguan pediatric cohort study

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Introduction

Despite certain pathogenetic, epidemiological, and clinical anomalies, SARS-CoV-2 relates to four other human coronaviruses (hCoVs): hCoV-229E, hCoV-NL63, hCoV-OC43, hCoV-HKU1. The latter group contributes to 15%-30% of cases of common colds in adults globally. A more robust understanding of endemic coronaviruses will aid scientists as they face this global threat. This project uses samples from a longitudinal pediatric prospective cohort study in Managua, Nicaragua, an urban area within the tropical middle-income country. Participants' exposure trends gave rise to the question: when is the expected age of earliest exposure to human coronaviruses (hCoVs)? We hypothesized that by age 5, a majority of children would have seasonal hCoV antibodies from prior exposure.

Materials & Methods

Enzyme-linked immunosorbent assays (ELISAs) were performed on 1,346 blood serum or plasma samples from children aged ≥ 6 months to five years, collected annually in 2019 and 2020. Screening ELISAs were performed using antigens to the four endemic hCoVs. Participant samples were paired when applicable. An antibody control (anti-HKU1) and serum control were used. Replicates were conducted on 10% of samples. Samples with optical density greater than 0.700 were determined to be positive. Statistics were performed in RStudio Version 1.4.1717.

Results

Sex was evenly distributed across all ages (p=0.65 | p=0.26; 2019 | 2020, respectively). All those positive for a strain in 2019 were also positive in 2020. In 2020, 391 participants (47.68%) had antibodies against all four hCoVs, with 772 participants (94.15%) demonstrating exposure to at least one of the hCoVs. Chi-squared testing demonstrated that the number of hCoVs detected increased significantly with age (p<<0.001). For every year increase in age, the odds of being positive for at least one of the hCoVs increased 1.56 times. Females were more likely to demonstrate antibodies against all hCoVs (p=0.034), as well as both beta coronaviruses–hCoV-OC43 and hCoV-HKU1– simultaneously (p<0.001).

Conclusion

This study concludes that participants demonstrate immune response to at least one hCoV by age 5, with fairly ubiquitous exposure. Future studies should include titering of samples positive for hCoVs, to better quantify antibodies exhibited by participants. Establishing immunity patterns to endemic coronaviruses can help scientists identify possible cross-reactivity with SARS-CoV-2, and design preventative interventions.

No influence of non-modifiable factors on the risk of catheter-associated urinary tract infections in burn and urological patients

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Introduction

Females and patients over 60 years, exposed to a urethral catheterization, are known to have a risk of catheter-associated urinary tract infection (CA-UTI) can be higher. However, these data have been obtained as a rule based on studies of urological patients. Furthermore, patients of other clinical profiles were underrepresented in those studies. We assessed the independent influence of certain non-modifiable factors (gender and age) on the morbidity rate of CA-UTI in urological and burn patients, and modeled the statistical interactions of these factors.

Materials & Methods

To determine the occurrence relation between CA-UTI and age as well as gender, we followed a cohort of 309 urological patients with a urethral catheter and 113 burn patients (all the individuals were met our pre-defined inclusion criteria). With Kaplan-Meier curves, Cox proportional hazards regression were performed, checking residuals (Martingale, scaled Schoenfeld, df-beta), and the proportional hazards assumption.

Results

The probability of CA-UTI was higher in patients with burns (B=2.158, SE=10.59, p=0.001): HR=8.65 (95% CI 2.36-31.74). We obtained inconclusive evidence on the impact of non-modifiable factors on the risk of CA-UTI: for the age over 60 years HR= 0.99 (95% CI 0.96-1.02); females HR=0.86 (95% CI 0.41-1.79). Modeling of statistical interactions showed that the contribution of the duration of bladder catheterization to the risk of infection also did not significantly depend on either age (B=-0.001, SE=0.019, p=0.947) or gender of the patient (B=0.622, SE=0.626, p =0.32).

Conclusion

Assessment of the risk of UTI during bladder catheterization in adult burn and urological patients allowed us to conclude the following: the age and gender of a patient did not influence the risk of CA-UTI. When modeling statistical interactions of known risk factors, we pointed out that the effect of long-term catheterization on the risk of developing an infectious complication did not largely depend on either the patient's age or gender. Of note, we are currently expanding our database for further more profound analysis.

Effectiveness and Safety of an integrated self-monitoring strategy and health education for hypertensive patents in rural area, Thailand: A pre-post intervention study

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Introduction

Hypertension has been a major concern of national health policy in many developing countries for decades. Despite various health interventions, the proportion of well-controlled hypertension is still limited. Thus, the objective of this study was to identify the effectiveness and safety of an integrated self-monitoring strategy and health education.

Materials & Methods

A triple-arm pre-post study was conducted. The three programs included only self-monitoring strategy, only health education, and self-monitoring strategy with health education. Three separated areas were randomly selected for each program, then participants were randomly allocated into it. For the self-monitoring strategy, participants were given a walking promotion and recorded data into their personal logbook with local health volunteers to regularly visited. The health education group would be provided with monthly conferences related to hypertension for four consecutive months. Systolic blood pressure (SBP), diastolic blood pressure (DBP), body mass index (BMI), daily walking steps, and over health score were collected pre/post sessions. Comparisons were performed using Kruskal-Wallis test and Fisher's exact test. The protocol of this study was reviewed and approved by the IRB of the royal Thai army, medical department.

Results

A total of 61 participants was enrolled in the study. The demographic and the baseline characteristics were collected at the beginning of the study. Due to a preliminary result after 8-week-intervention, there was a significant drop in SBP (ρ=0.032). On the other hand, there was a minimal change of DBP at week 8 (ρ=0.358). While it was not different from post-intervention daily walking steps among groups.

Conclusion

A synergistic effect of an integrated health intervention can reduce systolic blood pressure. We can exemplify to other rural communities to conduct this intervention for better controlled hypertension.

Does the COVID-19 period Modify the Effect of Shift Work on Fasting Blood Sugar Over Time in Hospital Staff? A Result from Multilevel Analysis

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Introduction

Previous studies have reported that shift work potentially affects circadian rhythm and hormone dysregulation that leads to a wide range of health effects from sleep disturbance to diabetes risk. Evidence showed that shift work is associated with increased fasting blood sugar (FBS) level. During the COVID-19, hospital staff's health behavior, lifestyle and work-life balance have changed. We hypothesized that this period may modify the effect of shift work on FBS levels. The present study aims to examine the effect of shift work on FBS for 4 years compared to non-shift work and to investigate whether the COVID-19 period modifies the effect of this association.

Materials & Methods

We conducted a retrospective cohort study which included 86 hospital staff whose initial FBS level was between 100-125 mg/dL from January to December 2018 at Phrae hospital. We defined term shift work as staff who have any work schedule that falls outside the hours of 8.00-16.00, and non-shift work (the reference group) as those with work schedule of 8.00-16.00. FBS was measured repeatedly at 4 time points by consecutive years (2018-2021). Potential confounders from previous studies were set at priori. We performed a multilevel regression analysis to assess the exposure-outcome association and reported beta-coefficients (β) and 95% confidence interval. We tested an interaction term of shift work and the COVID-19 period (dichotomous, cut by the year of 2019). AIC was used to compare the models.

Results

Shift work staff was about 56% (n=49), non-shift work about 44% (n=37). At baseline, sex, age, BMI, waist circumference, and biomarker profiles such as FBS and lipid were not different between the two groups. The fixed effect (β) of shift work on FBS over time was 2.4 (95%CI: -4.3, 9.1) in crude analysis. After adjusted for all potential confounders, the adjusted effect changed in direction -1.1 (95%CI: -4.9, 2.6), but not statistically significant. The interaction term was also not statistically significant (β = -3.8, 95%CI: -8.7, 1.2).

Conclusion

There was no difference in FBS change over 4 years of observation between hospital staff with shift and non-shift work. In addition, the COVID-19 period did not modify the effect of this association.

Risk of Hip Fracture and Type 2 Diabetes Mellitus in the Elderly: A case-control study

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Introduction

Diabetes incidence remains high in Thai population. With an aging society, diabetes even becomes more important since it is evidently associated with a wide range of long-term complications including hip fracture which potentially causes disabilities in the elderly and gives burdens to caregivers. Previous research has shown conflicting results of the association between diabetes and risk of hip fracture and the mechanism remains unclear. The present study aims to examine the association of diabetes and the risk of hip fracture in the elderly

Materials & Methods

We conducted a retrospective case-control study that included elderly people between October 1st 2019, and September 30th 2020 at Phrae hospital, Thailand. The elderly aged > 60 years and being hospitalized due to falling were enrolled in the study. Cases (n=76) refer to the elderly who were diagnosed with hip fracture and were confirmed by radiographic imaging. Controls (n=304) refer to those without hip fracture. We used calendar timing of density sampling to match the controls with the cases. Data on the exposure variable (presence of diabetes type 2) and covariates such as comorbidities, alcohol drinking and smoking were collected from hospital registry 2 years prior to case definition. The ratio of cases-to-controls was 1:4. Multivariable logistic regression was used to explain the effect of diabetes on the risk of hip fracture and adjusted odds ratio (ORs) with 95% confidence intervals were reported.

Results

Cases were more female (n=63, 82.9%) than controls (n=175, 57.6%). Mean age of cases and controls were 77.8 years (SD=7.5) and 73.9 years (SD=7.2) respectively (p<0.001). Body mass index (BMI), smoking, alcohol drinking and other comorbidities were not different between cases and controls. Diabetes was more frequent in cases (n=22, 28.9%) than in control (n=59, 19.4%). After adjustment for age and sex, the adjusted ORs of the association of diabetes and the risk of hip fracture was 1.78 (95%CI: 0.97-3.24). In the fully adjusted multivariable logistic model after additional adjustment for BMI and comorbidities, the adjusted OR was 1.91 (95%CI: 0.88-4.08).

Conclusion

There was no evidence from our study that diabetes increased risk of hip fracture from falling in the elderly.

Clinical Prediction Rules to Predict 1-year Mortality in Newly Diagnosed Pulmonary Tuberculosis Patients: A Developmental Phase

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Introduction

Tuberculosis (TB) is one of the main ten causes of death by infection diseases in Thailand. In our TB clinic, newly diagnosed cases were found dead more than 15% during one year of follow-up. Therefore, to develop a prediction tool could help a physician to classify patients with different risk groups and to plan further management.

Materials & Methods

We conducted a prognostic prediction research and used a retrospective cohort study as the design the data collection. A cohort of 791 newly diagnosed cases of pulmonary TB in Phrae Hospital, Thailand was formed between October 1st, 2013 to June 30th, 2020. The 11 candidate predictors were reviewed from previous studies and were collected from hospital database at the date of TB diagnosis such as age, body mass index (BMI), hospitalization, sputum test result, and co-morbidities such as HIV infection, chronic obstructive pulmonary disease, and cancer. We measured the outcome status (death or censored) at one-year follow up after diagnosis. The CPR was developed under the Cox proportional hazard model and the strength of association was reported by hazard ratio (HR) and 95% confidence interval. The C-statistic was performed as to assess discriminative ability of the final prediction model. The likelihood ratio positive (LR+) of each level of risk scores was reported.

Results

Five potential prognostic factors associated with one-year mortality included being hospitalized after first diagnosis (HR=8.50, 95%CI: 5.16-14.03), having cancer (HR=4.83, 95%CI: 2.12-10.98), age > 60 years old (HR=2.77, 95%CI: 1.92-4.00), BMI < 18.5 kg/m2 (HR=2.11, 95%CI: 1.39-3.20), and positive sputum test (HR=1.44, 95%CI: 0.98-2.10). The C-statistic of the final Cox model including these five predictors was 0.82. The risk scores ranged from 0 to 13 and classified into 3 levels: low risk (0-3), moderate risk (4-7), and high risk (8-13). The LR+ for each level were 1.00 (95% CI: 0.63-1.60), 2.22 (95%CI: 1.84-2.67), and 5.59 (95%CI: 4.30-7.28) respectively.

Conclusion

Clinical prediction rules including five predictors was developed. However, the validation of the prediction tool must be performed in further research.

COVID-19 Vaccination: The Greater Manila Experience

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Introduction

The emergency use of COVID-19 vaccines is being promoted worldwide to protect the public from severe symptoms. Vaccine confidence is an issue in the Philippines since it dropped between 2015-2018, triggered by the Dengvaxia scare. With almost half of adult Filipinos unwilling to receive the COVID-19 vaccination in early 2021, this study aims to describe the COVID-19 vaccination experience in the Greater Manila Area.

Materials & Methods

Using an analytical cross-sectional study design, 1,248 Filipinos aged 18-60 years old residing in Greater Manila Area answered a validated four-part questionnaire given through Google Forms. A sample size of 361 was computed using OpenEpi with an assumed 62.5% anticipated percent frequency and a 95% confidence level. The study focused on clinico-sociodemographic characteristics as the independent variable and a subject's willingness or refusal to get vaccinated against COVID-19 as the dependent variable. IBM SPSS 25.0 and MedCalc were used to analyze the data. A Fisher's exact test was used to compute the p-values for the association between the willingness or refusal to get vaccinated and five clinico-sociodemographic characteristics. A two-sided p-value of <0.05 was used as the significance threshold. The relative risk and 95% confidence intervals were also computed.

Results

Results show that 97.92% are willing to get vaccinated against COVID-19. Among those who are willing, majority of the participants strongly agree that the COVID-19 vaccines outweigh the risk of harm (47.5%) and are a societal responsibility (47.9%). Majority of participants who refused to be vaccinated strongly agreed that the vaccine might cause immediate serious side effects (46.2%) and unforeseen side effects in the future (34.6%). Most of the participants are willing to get vaccinated with CoronaVac, while the least preferred is Bharat BioTech. Those who are more likely willing to get vaccinated are males, college graduates, above Php10,000.00 monthly income earners, and those with co-morbidities and a family history of COVID-19. Educational attainment, monthly income, and family history of COVID-19 have a p-value of <0.05.

Conclusion

There are more Filipinos willing to get vaccinated and there is a significant association between educational attainment, monthly income, and history of COVID-19 in the family with vaccine willingness or refusal.

Assessment of Diabetes Mellitus Risk among Medical Students: A Cross Sectional Study

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Introduction

About 422 million adults globally suffer from diabetes mellitus, of which 90% have Type2 diabetes mellitus (T2DM). T2DM shows an alarming shift from adulthood to obese young adult population. The resultant prolonged exposure to hyperglycemic states can result in numerous complications leading to early morbidity and poor quality of life. Medical students owing to their rigorous academic needs, their susceptible psychosocial pattern, stressful and sedentary lifestyle are an especially high risk group. This study aimed to screen and assess the prevalence of high-risk population for T2DM using Indian diabetic Risk Score (IDRS) among medical students.

Materials & Methods

This cross-sectional study was conducted on 200 students from medical college attached to a tertiary care hospital.Students already diagnosed with T2DM, on hypoglycemic drugs or those not giving consent to participate were excluded. A pretested semi-structured questionnaire having three sections consisting of socio-demographic profile, IDRS questionnaire and anthropometric measurements was used to collect the information. IDRS scores consist of non-modifiable risk factors (age and family history) and modifiable risk factors (abdominal obesity and physical activity). The data was entered and analyzed using MS Excel and SPSS version 28.

Results

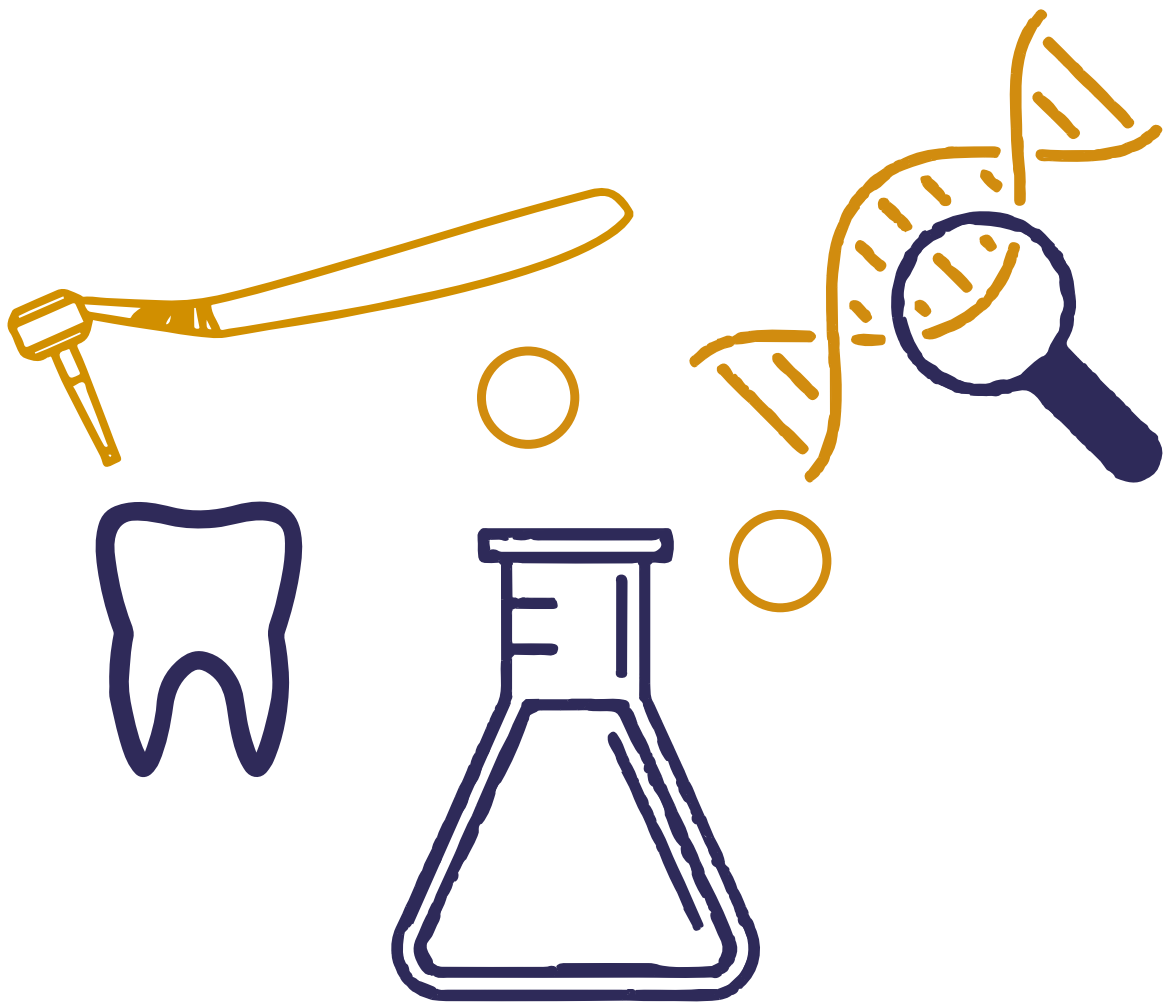
Total 200 students participated in the study. As per IDRS 34% had low risk, 60.5% had medium risk and 5.5% had high risk of developing T2DM. Significant association was found between IDRS and physical activity, BMI and family history using odd's ratio (p<0.05). With IDRS of ≥30, sensitivity and specificity was 83.3% and 35.2% respectively. Whereas, with an IDRS score ≥60 the sensitivity and specificity became 8.3% and 94.7% respectively.

Conclusion

The results of the study reflected that 66% of the students according to IDRS had medium to high risk of developing T2DM.

A statistically significant association between IDRS and physical activity, BMI and family history was found .There is an urgent need to initiate tactful awareness, preventive measures and interventions targeted towards the young adult population who are at risk for developing T2DM. This will help decreasing the burden of the health care system.

Biomaterials



Presenters:

He, Y. (Yuwei) Student
Sheikhlou, M Ghareh (Maryam)
Kargar, M. (Mahshid)
Suleimanov, Sh. (Shakir)
Firoozbahr, M (Meysam)
Presniakova, V. (Victoria)
Ehsanifard, S.E (Sara)
Menshikh, K.M. (Ksenia)

fabrication of a 3D biosensor scaffold using electrospinning of starch nanofibers for pathogenic bacteria detection

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Introduction

Electrospun starch nanofibers are promising to be used as biosensor scaffolds due to mimicking the structure of the natural extracellular matrix. However, the hydrophilic property limits diverse biomedical applications. Therefore, it was blended with a chemical hydrophobic synthetic polymer, to improve the water-resistance property of nanofibers. Since the addition of a crosslinking agent in the electrospinning solution could affect the electrospinning process, we investigated a starch nanofiber scaffold fabrication approach compatible with biosensor development.

Materials & Methods

The starch solution was prepared by dispersing starch in DMSO. The starch-DMSO solution was transferred to a syringe and the electromagnetic field was applied. The feeding rate, collector distance, and the temperature range of the electrospinning chamber were optimized. The electrospun starch nanofibers were placed in a desiccator containing glutaraldehyde as the crosslinking agent and incubated Subsequently, the nanofibers were vacuum dried. Polyacrylonitrile (PAN) was chosen as the second electrospun layer to support the scaffold and stabilize the whole structure. Likewise, in the PAN electrospinning process, the mixture was stirred and transferred into a syringe, and a 23kV voltage was applied to the syringe tip.

Results

The fabricated scaffold was imaged using SEM/FE-SEM and the average size of starch and PAN electrospun nanofibers were 400 nm and 122 µm, respectively. It was shown that after the starch crosslinking process, nanofibers swelled, fused, and resulted in a larger size.

Conclusion

With the hydroxyl functional groups on the surface, the scaffold serves as a potent framework for biosensing applications using nucleic acid biomarkers for detecting pathogenic bacteria, including a nosocomial infection agent, Burkholderia Cepacia.

An Electric-Field Control Strategy to Precisely Assemble Staggered Nanofiber Scaffolds for Bone Tissue Regeneration

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Introduction

Electrospun nanofibers are considered as promising scaffolds similar to natural extracellular matrix for tissue engineering. However, traditional electrospinning technology is difficult to control the alignment of nanofibers, resulting in chaotic architecture and poor mechanical properties. Here, a novel electrospinning device is developed which utilizes auxiliary electrodes to regulate electric field distribution and small-diameter rods to collect nanofibers with controllable alignment. The application of this technique was demonstrated by the fabrication of: 1) an inner vascular-like channel including parallel-aligned nanofibers; and 2) an outer osteon-like structure composed of staggered nanofibers.

Materials & Methods

Polycaprolactone (PCL), gelatin (Gel) and nano-hydroxyapatite (n-HA, synthesized in our lab) were used to prepare mixed solutions for electrospinning. The electrostatic field distribution in the apparatus was simulated and analyzed by Ansys Maxwell16.0. Characterization of electrospun nanofibers including SEM observation, tensile strength test, surface wettability, in vitro degradation behavior and protein adsorption capacity were studied. HUVECs and MG63 cells were chosen for cell experiments, and SEM, immunofluorescent staining and qRT-PCR were also used to evaluate the effect of aligned topography of electrospun nanofiber scaffolds on cell morphology and functions like angiogenesis and osteogenesis.

Results

Electrospun nanofibers with controllable alignment could be fabricated through the originally designed electrospinning device. Physio-chemical characterization demonstrates that the specially aligned scaffolds possess enhanced mechanical properties, suitable hydrophilicities and long-term biological stabilities. In vitro bioassessment indicates that the topography of nanofiber scaffolds does exert an influence on cell morphology. It also reveals that parallel arrangement of nanofibers can induce angiogenic differentiation of HUVECs, and staggered-aligned topography can enhance the expression of osteogenesis-related proteins and marker genes in MG63 cells.

Conclusion

In this study, we developed an electrospinning device composed of auxiliary electrodes and rotating mandrel to control nanofiber orientation and assemble them into an osteon-mimetic structure. The topographically well-defined electrospun scaffolds had good mechanical properties, suitable hydrophilicities and long-term biological stabilities. Biocompatible components and biomimetic hierarchical topography of nanofibers synergistically regulate cell fate and functions. The prepared osteon-mimetic nanofiber scaffolds combining angiogenic ability and osteoinductivity could be a promising candidate for vascularized bone regeneration.

Fabrication and characterization of Pep-1-BoNT/A nanoparticulate complex delivery system

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Introduction

Botulinum Toxin, widely used in cosmetic procedures, can result in side effects due to the injection as the only available route of administration. Since the interval between two injections is relatively short, it may affect patient adherence and cause discomfort. Furthermore, other side effects are related to botulinum toxin intrinsic characteristics leading to unwanted paralysis in different parts aside from the injection site. Cell-Penetrating Peptides (CPPs) such as Pep-1 can be used to address these side effects by transporting the toxin as cargo to the other side of the cellular membrane more efficiently. CPPs enhance the botulinum toxin penetration into cells, reducing the amount of toxin per injection. Moreover, it prolongs the toxin release from its carrier, increasing the interval between injections.

Materials & Methods

Pep-1 was used as a carrier to prepare Pep-1-BoNT/A nanoparticles with manufacturing differences (e.g. homogenization, solvents, pH and incubation time) and different Pep-1 to BoNT/A concentration range. We employed the self assemble polyelectrolyte complexing method to produce the nanoparticles. We also assessed the particle sizes and morphology of each nanoparticle formulation using DLS and SEM techniques. Furthermore, Pep-1-BonT/A nanoparticles' penetration into cells and their toxicity on the NIH-3T3 cell line were assessed by confocal imaging reader and MTT assay, respectively. Statistical analyses were performed using Sigma Plot version 14.0, A three-way ANOVA.

Results

Ideal condition(e.g. manufacturing factors and concentration ratio) for the production of PEP-1-BoNT/A nanoparticles with the smallest size, low polydispersity and desired morphology were determined. MTT assay indicated that Pep-1/BoNT/A nanoparticles has more toxicity on NIH-3T3 cells compared to BoNT/A alone. Furthermore, Images from confocal imaging reader showed more accumulation of BoNT/A in cells treated with Pep-1-BoNT/A nanoparticles than free BoNT/A treated group .

Conclusion

BoNT/A from its negatively charged parts can bind to the positively charged lysin rich domains of PEP-1 molecules by self-assemble polyelectrolyte complexation. The physiochemical characteristics of Pep-1-BoNT/A nanoparticles(size and morphology) can be affected by various manufacturing factors and concentration ratio of Pep-1 and BoNT/A. Pep-1-BoNT/A nanoparticles can be used as a new formulation for BoNT/A which deliver the toxin into cells more efficiently and reduce the injection frequency.

Scaffolds activate neutrophils to increase generation of oxidants capable to degrade materials

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Introduction

Implantation of biomaterials causes the local inflammatory response. Neutrophils are the first immune cells recruited at the site of tissue damage and activated to generate reactive oxygen species (ROS) and oxidants. The subject of this research was to study neutrophil activation in whole blood by two different types of scaffolds (natural and synthetic materials) and evaluate the degradation of the biomaterial by oxidizing agents released by activated neutrophils.

Materials & Methods

Decellularized bovine pericardium crosslinked with genipin (DBPG) and branched polylactide functionalized with methacrylate groups (3-PLA-2ph) were chosen as scaffolds. Activation of neutrophils was demonstrated by luminol-dependent chemiluminescence (CL) and by flow cytometry with the intracellular marker of ROS – dihydrorhodamine 123. The level of neutrophil-specific enzyme myeloperoxidase (MPO) and marker of inflammation tumor necrosis factor-α (TNF-α) were measured by ELISA. Confocal microscopy was used to visualize neutrophils and platelets in the blood. Fluorescence lifetime imaging microscopy was employed to study the oxidation of DBPG.

Results

Incubation of blood with both DBPG or 3-PLA-2ph increased the CL amplitude and shortened the time of reaching the maximal CL response. In addition, a shift of fluorescence intensity of dihydrorhodamine 123 was observed. These results indicate the increased ROS-generating activity of neutrophils. In plasma of blood samples incubated with DBPG or 3-PLA-2ph, a significant increase in the amount of MPO and TNF-α vs. controls was observed. In blood incubated with DBPG, the formation of neutrophil extracellular traps (NETs)-like structures and platelets aggregates were detected, platelets likely participated in the NET formation. For DBPG, we revealed the oxidative degradation of the biomaterial by the major product of activated neutrophils - hypochlorous acid.

Conclusion

DBPG and 3-PLA-2ph scaffolds activate neutrophils in whole blood causing respiratory burst, NET formation, MPO, and TNF-α secretion. Platelets play an important role in scaffold-induced activation of neutrophils. Reactive agents released by activated neutrophils oxidatively modify the biomaterial surface.

This study was supported by the RFBR (project no. 20-015-00480). Research at Sechenov University in the part of phagocyte redox activity measurements was funded by the Ministry of Science and Higher Education of the Russian Federation under the grant agreement (No. 075-15-2021-596).

Preparation, physicochemical evaluation and in vivo studies of berberine nanofibrous mats for recurrent aphthous ulcer treatment

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Introduction

Berberine is an isoquinoline alkaloids compound with highly potent antioxidant, anti-inflammatory and antibacterial properties. Taking into consideration the promising therapeutic properties of berberine and the remarkable advantages of gelatin/chitosan-based nanofibers including biocompatibility, biodegradability, ease of manufacturing process and scale up capability, we investigated the nanofibers' potential effectiveness to treat oral aphthous following local delivery to the injury site. The main objectives of this study were optimal formulation and physicochemical investigation of berberine nanofiber, in order to treat oral aphthous and promote quality of life in patients.

Materials & Methods

For optimization of berberine nanofibers, various mass ratios of gelatin-blended-chitosan (100:0, 70:30, 50:50, 30:70) were prepared and electrospinning parameters (such as voltage and flow rate) were investigated. The fiber morphology and structure were determined by SEM, XRD and AFM analyses. Dispersion of berberine chloride in nanofibers was confirmed by functional groups investigated by FT-IR. Drug content and in vitro release behavior were assessed by UV spectroscopy. In vivo studies were performed to assess aphthous treatment with berberine-loaded electrospun nanofibrous mats.

Results

SEM and AFM experiments showed blended ratio of gelatin/chitosan (70:30) fabricated smooth, beadless fibers with average diameter between 240 to 300 nm. Other blended nanofibers showed beads in the fibers. FT-IR indicated absence of interaction between ingredients and blended-polymers. Content of loaded drug was about 85% and the formulation presented approximately 97% drug release from nanofibers within 24 h in a controlled manner. Base on these finding and histopathology observations berberine loaded complex composite nanofibers significantly accelerate healing process in comparison to other groups.

Conclusion

Based on this results, gelatin-chitosan nanofiber was successfully fabricated. Due to physicochemical characterization, control release and in vivo experimental results; this electrospun nanofibrous mats indicated excellent ability for aphthous healing.

Endophytic fungi solvent extracts as a novel source of bioactive compounds in electrospun polycaprolactone wound dressing

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Introduction

Although there are more than 3000 dressing types in the wound management market, still wound care is a global health issue with a financial burden equating up to US$96.8 billion annually just in the USA. Especially Chronic non-healing wounds, which show delayed and incomplete healing process. Developing efficient wound dressings requires embedding antibacterial additives against microbial infections. The lack of novel antibacterial agents and misusing the previous antibiotics have caused an increase in antimicrobial resistance (AMR) affecting ten million lives by 2050 worldwide. These ongoing challenges clearly indicate an urgent need for developing new antibacterial additives in wound dressings targeting reported microbial infections. Natural products and their derivatives have long been a significant source of pharmaceuticals against AMR. In this study, endophyte as a novel natural source of bioactive compounds is considered as a sustainable source for therapeutic applications resulting in an anti-AMR efficient antibacterial additive for chronic wound dressing.

Materials & Methods

In this study, 27 types of endophytic fungi originated from 12 Australian native plants studied for their antibacterial activity against targeted wound bacteria Staphylococcus aureus using two extraction methods of freeze-drying and solvent extraction. The most active sample was identified and used as an additive in processing Polycaprolactone electrospun fibers. FTIR and disc diffusion tests data were used to investigate the presence of additives in the fiber and its antibacterial activity consecutively.

Results

Among all the 27 purified cultures, Eremophila Longifolia 19 showed the best antibacterial activity with an inhibition zone of 17mm and a minimum inhibitory concentration of 0.156 mg/ml. Utilization of this extract as an additive was performed successfully and the FTIR test approved the existence of antibacterial additive in electrospun fibers. In the final step, disk diffusion tests showed the antibacterial property of the fibers

Conclusion

After admitting the antibacterial activity of the selected endophytes, their utilization for the first time in electrospun fibers targeted for wound dressing was proved successfully. This sustainable source has a great potential to be used as a novel antibacterial additive for medical purposes.

Electrospun thermoresponsive polymers as a platform to produce scaffold-free constructs for articular cartilage tissue engineering

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Introduction

Hyaline cartilage injuries due to traumas and osteoarthritis are the prevalent cause of impaired mobility and loss in quality of life. Tissue engineering offers a promising alternative to existing pharmacological and surgical treatment strategies. Currently available techniques (scaffold implantation, cell suspension or pellet injection) face complications such as improper integration, rejection etc. Furthermore, the use of the most popular cell material – autologous chondrocytes, is associated with donor-site morbidity and in vitro dedifferentiation. Our study aimed to develop a new approach to obtaining scaffold-free tissue-engineered constructs using autologous multipotent mesenchymal stromal cells (MMSC) for hyaline cartilage restoration.

Materials & Methods

The ethanol solution of thermoresponsive polymer poly-N-isopropylacrylamide-co-N-tert-butylacrylamide was electrospun to obtain fibrous matrices 200-300 μm-thick, with a parallel orientation of fibers (2-2.5 μm in diameter). The matrices were seeded with human bone marrow-derived MMSC (150000 cells per cm^2) and cultivated in a chondrocyte differentiation medium for 7, 14 or 21 days. At these time points, the constructs were immersed into cold Hank's solution (4°C, 5 min) to dissolve the matrices. The obtained cell sheets were washed to remove the residual polymer and collected for analysis (histology, immunocytochemical staining, atomic force microscopy (AFM)). 2-week cell sheets were also multi-layered (3 sheets in one) and cultured for three additional weeks to increase construct thickness.

Results

Dense 50-100 μm-thick tissue engineering constructs with parallel-oriented collagen fibrils formed by day 21. Safranin O staining showed that the glycosaminoglycans were predominantly accumulated in the periphery of constructs. Confocal microscopy of stained cells sheets showed that the amount of collagen type I decreased while collagen type II increased during the cultivation process. Cartilage-specific proteoglycan aggrecan and transcription factor Sox9 were widely represented in 21-day cell sheets. The preliminary AFM analysis showed that cell sheets' Young's modulus was about 100 kPa. Cell sheet layering allowed for increasing construct thickness to 400 μm.

Conclusion

The proposed technique allows producing the scaffold-free cell-based constructs with abundant oriented extracellular matrix specific to cartilage tissue. This makes it a promising technology for the regeneration of articular cartilage injuries.

This work was supported by the Russian Science Foundation grant № 21-15-00349.

Alginate-Bioglass Scaffold as an Engineered Environment for the Osteosarcoma Model

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Introduction

Nowadays in the field of tumour engineering, there is a lack of robust in vitro models for hard tissue cancers such as osteosarcoma. The aim of this work was to provide osteosarcoma cell spheroids with the proper environment mimicking biomechanical conditions of primary bone cancer needed for adequate cell behaviour and, thus, reliable response to antitumour treatments.

Materials & Methods

Human osteosarcoma cells (U2OS) were cultured in an agarose-coated multiwell plate in standard conditions to obtain stable cell aggregates. The dynamics of cell metabolic activity in spheroids and their morphology were monitored by resazurin reduction assay, as well as light and fluorescent microscopy.

Alginate and bioglass were the components of choice for producing the bone-like scaffold due to their reputation as biomaterials. Bioglass particles differing in size were tested along with alginate in different ratios, volumes and gelation periods. After the onset of polymerization via soaking in calcium chloride (CaCl2), samples were frozen overnight and freeze-dried. The optimal parameters were chosen based on the analysis with scanning electron microscopy (SEM) and element mapping. Osteosarcoma cell spheroids were then arranged inside the sterilized and pre-soaked in culture media porous scaffolds.

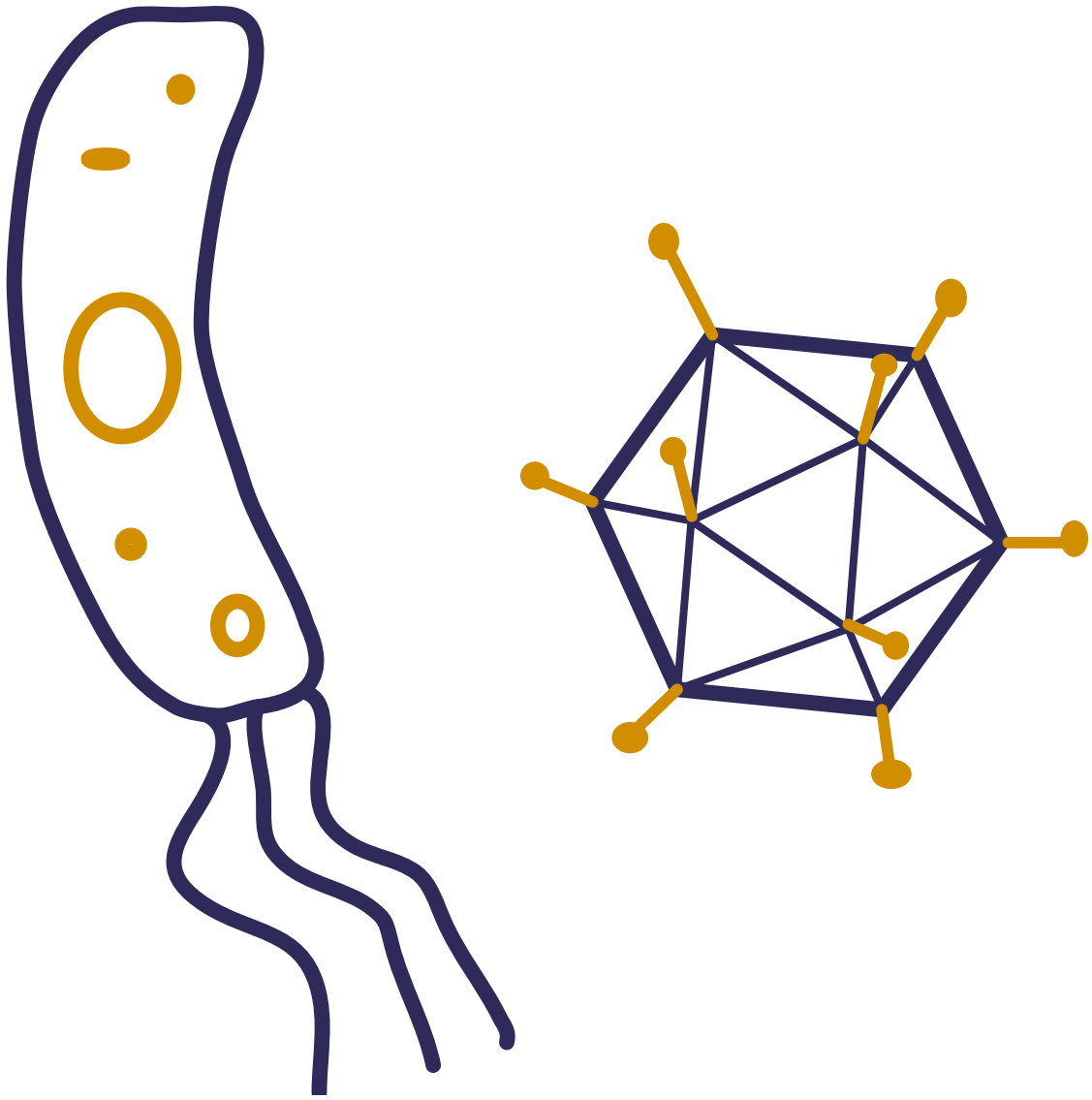
Results

Throughout the experiment, the optimal parameters and content for obtaining the scaffolds were established. Mechanical characteristics were sufficient, and morphology resembled trabecular bone tissue. The bioglass particles were shown to be evenly distributed with the maintenance of the initial morphology. The viability of spheroids, estimated by resazurin reduction assay, as well as morphological analysis conducted with the help of histological methods, allowed us to conclude that the obtained scaffolds are suitable as an environment for 3D in vitro culture.

Conclusion

The described approach for creating a proper engineered environment for the osteosarcoma model can be admitted as promising in terms of developing antitumor drug test systems and studying peculiarities of primary bone cancer of an individual, getting closer to personalized medicine. Moreover, the proposed system is tuneable, which offers the possibility of introducing various cell lines, such as endothelial cells, and setting up dynamic conditions for further experiments.

Infectious Disease



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Community-based sero-prevalence of chikungunya and yellow fever in the South Omo Valley of Southern Ethiopia

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Introduction

Chikungunya (CHIK) and yellow fever (YF) are becoming major public health threats in East African countries including Ethiopia. In Ethiopia, there is no reliable information about the epidemiology of CHIK. This study aimed to assess a community-based sero-prevalence of CHIK and YF in the South Omo Valley, an endemic area for YF.

Materials & Methods

Between February and June 2018, blood samples were collected from study participants and screened for IgG antibody against CHIK virus (CHIKV) and YF virus (YFV) infections using ELISA. Data were computerized using Epi Data Software v.3.1 and analyzed using SPSS

Results

A total of 360 participants (51.7% males, age range from 6 to 80, mean age ± SD = 31.95 ± 14.05 years) participated in this study. The overall sero-prevalence of IgG antibody was 43.6% (157/360) against CHIKV, while it was 49.5% (155/313) against YFV. Out of 155 samples which were positive for IgG antibody to YFV, 93 (60.0%) were positive for IgG antibody to CHIKV. Out of 158 samples which were negative for IgG antibody to YFV, 64 (40.5%) were positive for IgG antibody to CHIKV. There was a significant positive correlation between IgG antibodies to CHIKV and YFV (sr = 0.82; P<0.01). Residency in the Debub Ari district (AOR = 8.47; 95% CI: 1.50, 47.74) and travel history to sylvatic areas (AOR = 2.21; 95% CI: 1.02, 4.81) were significantly and positively associated with high sero-prevalence of IgG antibody to CHIKV and YFV, respectively.

Conclusion

High sero-prevalence of IgG antibody to CHIKV shows the circulation of the virus in the present study area. A low sero-prevalence of IgG antibody to YFV in YF vaccine received individuals is highly concerning from a public health point of view as waning of immune response to YFV infection could result in a periodic outbreaks of YF in endemic areas. Nevertheless, the present study has not investigated for possible cross-reactivity of antibody to CHIKV with other alphaviruses like O'nyong-nyong virus and antibody to YFV with other flaviviruses like Dengue fever virus and this warrants further studies in the present study area.

Study of antibacterial properties against E. coli using benzenesulfonamide compounds with various substitutes

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Introduction

Irrational use of antibiotics has led to the rise of resistance to the commonly used anti-infective drugs. One possible strategy to overcome antibiotic resistance, is the search for new chemical compounds and alternative targets. Few studies shown that enzymes of carbonic anhydrases could become a potential target for

antimicrobial drugs. In healthy GI, E. coli does not cause illness, but it can provoke meningitis, sepsis, inflammations in immunosupressed patients or infants. Since E. coli expresses two carbonic anhydrases important for their metabolism, we hypothesized that it could potentially become a new drug target.

Materials & Methods

In this study, we evaluated minimal inhibitory concentrations (MICs) and sensitivity of the commercial and newly synthesized benzenesulfonamide compounds, according to the Clinical and Laboratory Standards Institute (CLSA) and European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines against the E. coli ATCC 25922 by the agar broth microdilution method. Assay performed in the 96-well microplates, concentration of the compounds ranged from 0 µM to 200 µM, bacterial inoculum concentration was standardized to 10^5 CFU/ml, optical density was measured at 600 nm OD.

Results

A total number of 40 compounds were screened against the E. coli ATCC 25922 during this study in at least quadruple experiment repetition with a perspective of synthesizing a new and specific compound library according to the primary acquired MIC results. Of the commercially available carbonic anhydrase inhibitors (CAIs) ethoxzolamide had the strongest bacteriostatic or cell growth inhibiting properties with the MIC value of 200 µM. Other commercial compounds were not so efficient on inhibiting the cell growth. Prominent effect on the cell growth dynamic was also noticed with the compound of VD12-05 (laboratory name), p-, o-substituted trifluorinated benzenesulfonamide. Determined MIC value was 50 µM. It was also observed from the growth curves, that the cell cultures were sensitive for aliphatic substituted compound EA10-3 with the MIC 100 µM.

Conclusion

Results from this study indicate that there is a significant perspective on the further research for alternative antibiotic substitutes from thebenzenesulfonamide class. Our findings suggest, that expansion of the compound library and continuation of research could provide treatment option for E. coli caused infections.

Hepatitis B Virus and Hepatitis Delta Virus infection in Colombian indigenous communities

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Introduction

The World Health Organization estimates 296 million people with chronic Hepatitis B Virus (HBV) infection and 820,000 deaths/year related to this infection. Despite the universal vaccine program, there are regions with high Hepatitis B prevalence such as the Amazon Basin. Moreover, coinfection and superinfection with Hepatitis Delta Virus (HDV) are frequent in these regions inhabited by indigenous communities among other populations. This study aims to characterize the serological and molecular HBV and HDV infection markers in indigenous communities from four states in Colombia: Amazonas, Guaviare, Antioquia, and La Guajira.

Materials & Methods

Indigenous diagnosed with HBV infection and controls from the same communities were invited to participate in the study. The serum samples of the cases and controls were analyzed for serological and molecular markers of HBV and HDV infection. The S (422-758 nt) HBV genome region and the HDAg (887-1290 nt) HDV genome regions were amplified in the cases and samples HBsAg-/Anti-HBc Total+ obtained from controls to identify Occult hepatitis B infection (OBI).

Results

Up to date, 64 cases and 122 controls have been recruited. Among the cases, the mean age is 34.45 years old, and 79.69% are female. From 60 cases' samples analyzed for molecular markers, the HBV S (422-758 nt) region was amplified in 18/60; while the HDV HDAg (887-1290 nt) region was detected in 17/60 samples indicating an HBV/HDV co/superinfection rate of 28.33%. From the 47 cases' samples analyzed for serological markers, one case of acute infection (HBsAg+/Anti-HBc IgM+), 27 cases of chronic infections (HBsAg+/Anti-HBc IgM-/Anti-HBc total+), and three cases with resolution were identified. On the other hand, 21/90 samples from controls that were negative for HBsAg rapid test were positive for Anti-HBc. The analysis of these 21 samples revealed the detection of HBV DNA in three samples which could be OBI cases.

Conclusion

These preliminary results suggest that HBV and HDV infections are still public health issues in indigenous communities in Colombia. This study will allow us to analyze the epidemiological evidence on these infections in the indigenous population.

BIOINFORMATIC ANALYSIS OF THE CLOSTRIDIUM BOTULINUM CRISPR-CAS LOCI AND SCREENING OF PAGE WHICH CAN BE USED FOR PERSONALIZED PHAGE THERAPY AGAINST THIS PATHOGEN

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Introduction

The search for new ways to combat Clostridium botulinum infections remains relevant in current medicine. Antibiotic therapy becomes ineffective and often leads to the emergence of new highly pathogenic forms of bacteria. Therefore, new approaches are needed to create effective methods of treating Cl. botulinum infections. The aim of this study was to perform bioinformatic analysis of the CRISPR-cas loci in Cl. botulinum genomes and to perform phage screening through spacers of CRISPR arrays.

Materials & Methods

Materials and methods. The objects of the study were the CRISRP-cas loci in the genomic sequences of Cl. botulinum chromosomes downloaded from the NCBI GenBank database. ORF annotation was performed using GeneMarkS 4.28. Cas-genes were identified using MacSyFinder v.2. The search and analysis of CRISPR arrays was implemented with CRISPRFinder and PILER-CR. The study of consensus repeat sequence was performed using CRISPRmap web application. The investigation of protospacers was realized using BLASTn algorithm through database NCBI RefSeq-Viral.

Results

52 sequences of Cl. botulinum chromosomes were analyzed. Complete CRISPR-cas loci or CRISPR arrays without cas-gene locus were found in 48 sequences. 4 CRISPR-Cas system subtypes were identified. According to CRISPR-Cas classification these systems belong to class 1 type I (I-B subtype) and type III (III-A, III-B, III-D subtypes). One chromosome genome usually includes one CRISPR-cas locus but sometimes it contains two different subtypes together. The number of identified CRISPR arrays ranges from 1 to 13 in different genome. The number of spacers in CRISPR arrays varies from 1 to 72. 1277 unique spacers were detected but phage protospacers were identified only to 33 of them. Revealed through protospacers phages belong to Cellulophaga (19%), Aeromonas (12,5%), Bacillus (12,5%), Escerichia (10%), Lactococcus (9%), Clostridium (6%), Citobacter (6%). The identification of phages which are specific to bacteria allow to estimate the resistance of bacteria to them. This in the future can be used in the technology of targeted phage therapy of infections caused by pathogenic bacteria, including "superbacteria".

Conclusion

33 phages specific to Clostridium botulinum were revealed through spacers of CRISPR arrays. These phages can be used for development of personalized phage therapy against these pathogenic bacteria.

Human Papillomavirus (HPV) vaccination awareness, acceptability, and hesitancy among 22 states in the Arab World: a systematic review and meta-analysis

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Introduction

The Arab world stretches from Morocco across Northern Africa to the Persian Gulf. It is characterized by societies with a more conservative sexual behavior than others, which reflects a lower prevalence of sexually transmitted HPV infection in this region. The rapid changes in lifestyle, and sexual behavior affects this prevalence considerably. Given, the HPV infection causes cervical, oropharyngeal, and anogenital cancers, it can be prevented by the HPV vaccine, so we conducted this meta-analysis to assess rates of HPV vaccine awareness, acceptability, and factors correlated with vaccine hesitancy among the Arab population.

Materials & Methods

We searched English written studies in PubMed, Scopus, EBSCO, and Cochrane library using a strict searching strategy. We used Open-Meta analyst v.12 and applied the random-effect model in our analysis. In quantitative analysis, we pooled awareness, acceptability, and recommendation rate. The Awareness rate (AR) was stratified by gender, occupation, region, and sampling method.

Results

Of 1086 identified studies, 41 were included (n = 27,914) in this meta-analysis and published between 2006 and 2022. All articles were cross-sectional studies. The awareness, acceptability, and willingness to recommend rate of HPV vaccine were as follows: 42.6% (95% CI: 35.4%, 49.9%), 63.6% (95% CI: 54.7%, 72.5%), and 66.9% (95% CI: 54.4%, 79.4%) respectively. The main barriers to accept or recommend HPV vaccine were side effects, efficacy, cost, and inadequate information as follows: 35.4% (95% CI: 24.4%, 46.5%), 22.2% (95% CI: 15.7%, 28.6%), 25.9 (95% CI: 18.2%, 33.5%), and 46.4 (95% CI: 28.9%, 63.9%). The pooled AR of HPV vaccine among healthcare worker was as follows: 61.1% (95% CI: 39.5%, 82.7%), 51.5% (95% CI: 29.6%, 73.4%) for females and males. The pooled AR of HPV vaccine was as follows: 43.9% (95% CI: 35.8%, 52%), 33.9% (95% CI: 21.1%, 46.8%) for Asian and African regions, 43.3% (95% CI: 33.6%, 52.9%), 42.6 % (95% CI: 35.4%, 49.9%) for convenient and random sampling methods.

Conclusion

This meta-analysis indicates that awareness of the HPV vaccine among the Arab population remains relatively low despite licensing of HPV vaccine since 2006. Our findings may provide useful information to better understand the HPV vaccine awareness status among the regions.

Prevalence of Cytomegalovirus-DNA in the Patients' Serum with HIV using Real time PCR

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Introduction

HIV is known as one of the most important pathogens and mortality in all human societies, but unfortunately no definitive cure has been found for it. Due to its weakened immune system, this virus causes a variety of primary and secondary opportunistic infections. Cytomegalovirus (CMV) is one of the most relevant opportunistic viruses seen in HIV-positive people that cause various infections in HIV-positive people. This virus causes various infections in HIV-positive people, such as retinal infection (CMVR), gastro-intestinal infections, diarrhea, severe weight loss, and cerebrospinal fluid problems. These various infections make it important to evaluate the prevalence of CMV in HIV-positive people to diagnose it quickly and in a timely manner. This infection in HIV-positive people reduces life expectancy and causes serious harm to patients. However, a simple test in HIV-positive people can prevent the virus from progressing.

Materials & Methods

In this study, we collected 200 blood samples (including 147 men and 53 women) from HIV-positive individuals and examined the frequency of CMV-DNA in these cases by real-time PCR method. In the next step, the data was analyzed by SPSS software and then we obtained the relationship between age, sex and the frequency of CMV in HIV-positive individuals.

Results

The total frequency of CMV DNA was about 59%, which is a relatively high prevalence due to the age range of the subjects. The frequency in men was 61.2% and 52.8% in women. This frequency was also higher in males than females. We also observed more frequency in two age groups of 16 to 30 years and 31 to 45 years.

Conclusion

Due to the high prevalence of CMV in HIV-positive individuals and causing serious problems in this group of people, this study was shown that both the patients and the community should pay more attention to this issue. Ministry of Health as a stakeholder organization can make CMV DNA testing mandatory as soon as a person was HIV positive.

Diagnostic Performance of Xpert MTB Ultra on Pericardial, Pleural and Ascitic fluids for Diagnosis of Extrapulmonary Tuberculosis in Malawi.

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Introduction

Diagnosis of extrapulmonary Tuberculosis in hospitals in low- and middle-income countries is challenging. We investigated the diagnostic performance of Xpert MTB Ultra compared mycobacterial culture and compared to composite reference standard for diagnosis of extrapulmonary TB (pericardial, pleural and ascitic fluid) in adults at a Queen Elizabeth Central Hospital Malawi

Materials & Methods

Consecutive adults with extrapulmonary TB were screened for evidence of extrapulmonary fluid using FASH and tested for TB using Xpert MTB Ultra and mycobacterial culture. Diagnostic performance of the Xpert MTB Ultra was compared to culture and composite reference standard. Participants were followed up to eight weeks to assess vital status.

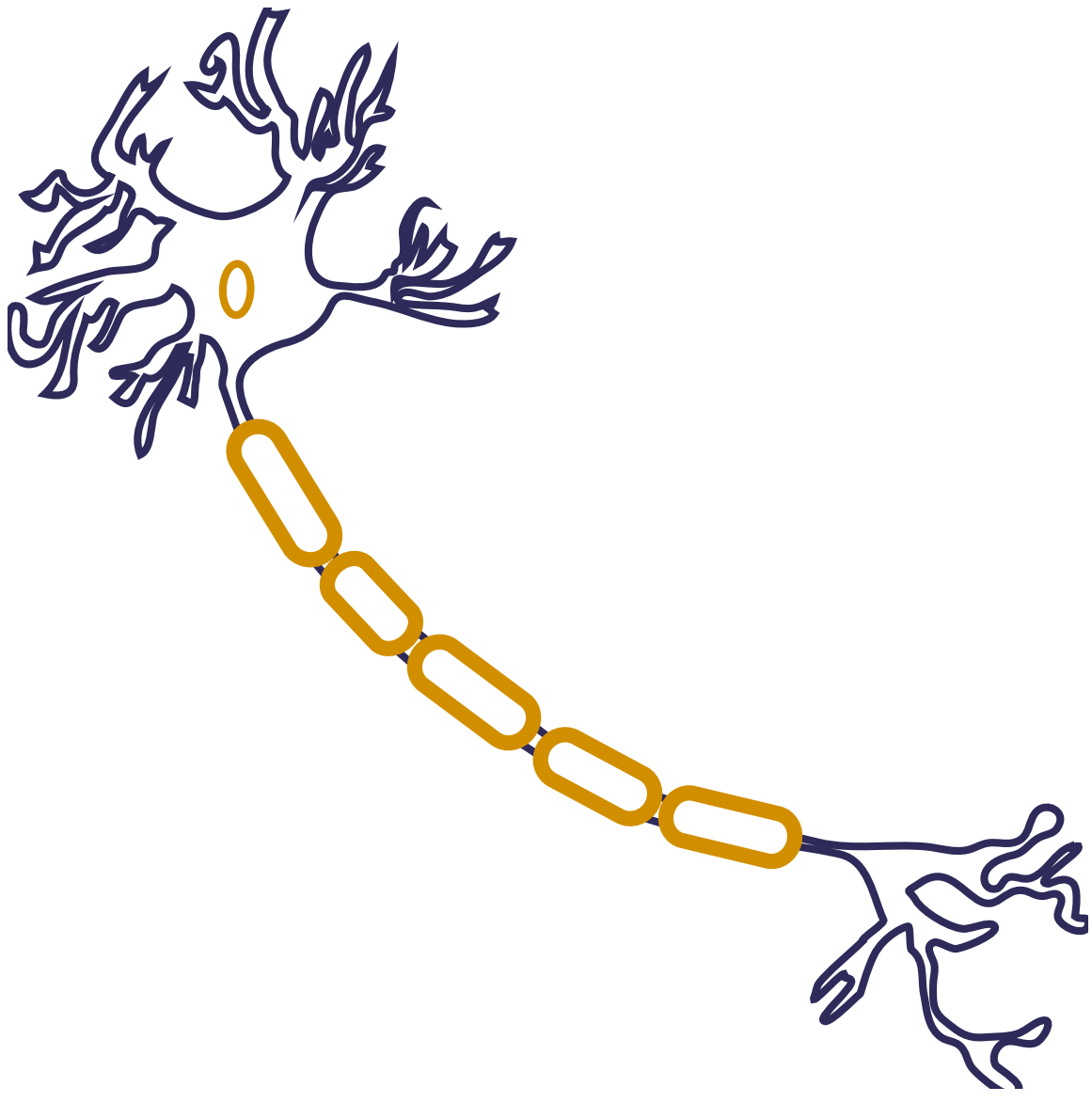
Results

There were 174 patients recruited: 99/174 (56.9%) pleural, 70/174 (40.2%) ascitic and 5/174 (2.9%) pericardial fluid. Overall, 10/174 (5.7%) had bacteriologically confirmed TB and 30/174 (17.2%) were started on TB treatment based on FASH or other clinical findings. The sensitivity and specificity of Xpert MTB Ultra compared to culture was 83.3% [n=5/6] (95%CI:35.9%-99.6%) and 97.6% [n=164/168] (95%CI:94.0%-99.3%) respectively. Compared to composite reference standard, the sensitivity of Xpert MTB Ultra was 17.1% [n=6/35] (95%CI:6.5%-33.7%) and specificity was 97.8% [n=134/137] (95%CI:93.7%-99.6%). There were 43/134 (32%) deaths among non-TB patients while 4/40 (10%) TB patients died, unadjusted OR 4.17 (95%CI:1.39-16.67, p-value=0.0058). All four deaths among TB patients were in people living with HIV; and three of these had severe immunosuppression and/or probable Immune Reconstitution Inflammatory Syndrome.

Conclusion

Xpert MTB/RIF Ultra provides good diagnostic performance on pleural, pericardial and ascitic fluid. FASH is useful in identifying patients with extrapulmonary TB that test negative on routine TB tests. Patients with TB or non-TB effusions have high mortality and further research must focus on role of good management of HIV infection and other co-morbidities in reducing mortality.

Neurology



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Collateral circulation status affects outcomes of endovascular treatment in patients with acute basilar artery occlusion

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Introduction

This study evaluated the effects of collateral status on the prognostic value of endovascular treatment (EVT) in patients with basilar artery occlusion (BAO).

Materials & Methods

The study included 646 patients who underwent EVT for acute BAO and for whom composite collateral scores were available. The effects of collateral status on EVT were evaluated based on categorical composite collateral score (0–2 vs. 3–5). The primary outcome was a modified Rankin Scale score of 0–3 at 90 days.

Results

The composite collateral score was 0–2 in 316 patients, 3–5 in 330. Good collateral status (composite collateral score 3–5) was associated with a favourable outcome (adjusted odds ratio [95% confidence interval]: 1.65 [95% CI, 1.09–2.50], P=0.018). A lower baseline National Institutes of Health Stroke Scale (NIHSS) score (adjusted OR, 0.92 [95% CI, 0.89–0.95]; P<0.001), distal BAO (adjusted OR, 2.67 [95% CI, 1.25–5.68]; P=0.011), and an onset-to-puncture time (OPT) ≤4 h (adjusted OR, 1.82 [95% CI, 1.00–3.29]; P=0.048) were independent predictors of favourable outcome in patients with poor collateral status. Among the single patent vessel of this score, multivariable logistic analysis revealed that posterior cerebellar artery (PICA)–superior cerebellar artery (SCA) anastomosis was significantly correlated with good outcomes (adjusted OR, 1.75 [95% CI, 1.16–2.65], P=0.007).

Conclusion

In conclusion, this study shows that a patent PICA-SCA anastomosis is significantly correlated with better outcomes in patients with BAO after EVT. Taking into account the PICA-SCA anastomosis may improve the prognostic accuracy of posterior circulation collateral scores.

Protective Effect of Nano Emulsions Containing Rosemary on Hippocampal CA1 Pyramidal Neurons in a Rat model of Cerebral Ischemia-Reperfusion

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Introduction

Stroke is an important cause of mortality and morbidity worldwide but effective therapeutic strategy for the prevention of brain injury in patients with cerebral ischemia is lacking. Rosemary is a plant that have strong antioxidant and anti-inflammatory effects that may be helpful. In this study, we aimed to investigate the effect of Rosemary on the expression of genes involved in apoptosis and percentage of viable neurons in the CA1 hippocampal region of rats following transient global I/R.

Materials & Methods

This study had two main parts: In vivo and in vitro. In in vivo part, we divided wistar rats into 8 groups (control, ischemia/reperfusion, 3 dose of aqueous-alcoholic extracts of rosemary and 3 dose of aqueous extracts of rosemary), after 21 days of rosemary administration the ischemia and reperfusion was done, finally apoptosis gene (by Annexin V assay, Flow cytometry, Real time PCR, and Western blot tests), and neurons death (by TUNEL and Nissl staining) were assayed in hippocampus and in in-vitro part, we cultured hippocampus neurons (in 7 groups: control, 3 dose of aqueous extracts of rosemary and 3 dose of aqueous-alcoholic extracts of rosemary) and then cell viability (by MTT Assay) was assayed.

Results

We demonstrated that 200 mg/kg aqueous extracts of rosemary decrease the apoptosis gene expression and increase the anti-apoptosis gene expression in compare to ischemia (p<0.05) and decrease the neuron death in Hippocampal CA1 pyramidal neurons (p<0.05).

Conclusion

Present study demonstrated that cerebral ischemic tolerance induced by rosemary extracts pretreatment, the aqueous-alcoholic extracts of rosemary in 200 mg/kg dose was more effective to protect of hippocampus.

Tranexamic Acid for Patients with Aneurysmal Subarachnoid Hemorrhage: A Systematic Review and Meta-analysis of 2991 Patients

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Introduction

The efficacy of tranexamic acid for subarachnoid hemorrhage remains controversial.We aimed to synthesize evidence from published clinical trials on the efficacy and safety of tranexamic acid (TXA) administration in patients with aneurysmal subarachnoid hemorrhage (aSAH).

Materials & Methods

We followed the standard methods of the Cochrane Handbook of Systematic Reviews for interventions and the PRISMA statement guidelines 2020 when conducting and reporting this study. A computer literature search of PubMed, Scopus, Web of Science, and Cochrane Central Register of Controlled Trials was conducted from inception until1 January 2021. We selected observational studies and clinical trials comparing TXA versus no TXA in aSAH patients. Data of all outcomes were pooled as the risk ratio (RR) with the corresponding 95% confidence intervals in the meta-analysis models.

Results

Thirteen studies with a total of 2991 patients were included in the analysis. TXA could significantly cut the risk of rebleeding (RR 0.56, 95% CI 0.44 to 0.72) and mortality from rebleeding (RR 0.60, 95% CI 0.39 to 0.92, P=0.02). However, TXA did not significantly improve the overall mortality, neurological outcome, delayed cerebral ischemia, or hydrocephalus (all P>0.05). In terms of safety, no significant adverse events were reported. No statistical heterogeneity or publication bias was found in all outcomes.

Conclusion

In patients with aSAH, TXA significantly reduces the incidence of rebleeding and mortality from rebleeding. However, current evidence does not support any benefits in overall mortality, neurological outcome, delayed cerebral ischemia, or hydrocephalus.

Accelerated Long-Term Forgetting in Multiple Sclerosis-Patients: Application of a Neuropsychological Test to Detect Everyday Memory Deficits in Early-Stage Multiple Sclerosis

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Introduction

Multiple Sclerosis (MS) is a chronic neurological disease. 40-65% of patients suffer from cognitive dysfunctions with a higher impact on quality of life than motor symptoms. Accelerated long-term forgetting (ALF) is not tested routinely in MS and is defined as extraordinarily information loss after a delay of days. We hypothesize, that MS-patients show ALF, and furthermore, ALF can be used to objectify subjective memory impairments (SMI).

Materials & Methods

In this prospective observational study, we included 30 early-stage MS-patients and 30 healthy matched controls (HC). Each participant was tested for ALF and with a standardized neuropsychological test-battery. The ALF-test (word list, geometrical figure, logical memory (LM)) was executed at baseline, 30 minutes and 7 days. SMI was evaluated with a score (0 – 100; higher score meaning greater SMI). Primary outcome (PO) was defined as the ratio of the 7 days to the 30 minutes ALF-score. We included self-questionnaires sensitive for fatigue and SMI.

Results

The demographic group characteristics showed no significant difference in mean age (years±SD; MS 28.56±3.83 vs. HC 29.3±6.38) or years of education (years±SD; MS 12.03±0.96 vs. HC 12.03±1.24). Analysis revealed a difference for the POword-list (MS 0.66±0.13 vs. HC 0.82±0.16; p=.000108) and the POLM (MS 0.88±0.15 vs. HC 1.01±0.12; p=0.02). However no significant results were found regarding POfigure (MS 0.84±0.22 vs. HC 0.88±0.17; p=0.439). Comparison of neuropsychological testing showed a difference for SMI (MS 35.67±15.9 vs. HC 24.67±9.73; p=0.004) and Fatigue Impact Scale (FIS) (MS 36.27±21.21 vs. HC 20.07±15.82; p=0.003), but not in routine cognitive tests, depression or processing speed. Regression analysis found FIS (coefficientB=0.003; p=0.034; 95%CI -0,005 – 0.0) and SMI (coefficientB=-0.004; p=0.01; 95%CI -0.008 - -0.001) to be correlated with POword-list, with significantly lower correlation for HC.

Conclusion

Three conclusions are made; first, early-stage MS-patients show ALF after 7 days compared to healthy participants, although initial acquisition and initial recall were comparable between both groups. Second, patients showed no signs of depression, a decline in cognitive function or processing speed as confounding factors. Third, SMI can be objectified using a test sensible for ALF. These results demonstrate the impact of ALF in MS-patients.

Modulation of explorative decision making via deep brain stimulation of the Globus pallidus interna

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Introduction

The Globus Pallidus interna (GPi) is commonly thought of as a basal ganglia motor output nucleus, however non-human primate and limited clinical evidence suggests a role in modulating action selection during reinforcement learning. We hypothesised that functional lesioning of the GPi via deep brain stimulation (DBS) will modify exploratory/exploitative choice behaviour during a probabilistic reward learning task.

Materials & Methods

19 patients with focal or segmental dystonia treated with bilateral chronically implanted GPi DBS electrodes performed a 2-armed bandit task incorporating a reward contingency reversal. Task data was fitted to a model of decision-making processes: the reinforcement learning drift diffusion model (RLDDM). Behavioural effects were correlated using individual DBS electrode contact coordinates and a group normative connectome.

Results

There was no effect of DBS on task performance ($F(1,17) = 0.9$, $p = 0.34$) or upon decision time ($F(1,17) = 0.01$, $p = 0.92$). Fitting the RLDDM model allows for identification of exploratory/exploitative choices, demonstrating behaviour was significantly more explorative in the DBS-on state ($F(1,17) = 4.64$, $p = 0.03$). Functional connectivity analysis enabled calculation of a whole-brain "R-Map" depicting correlations between individual connectivity and DBS-induced exploration. This spatial correlation significantly explained variance in DBS-induced exploration ($n = 14$, $R2 = 0.28$, $p=0.04$, Permutation test: $R = 0.53$, $p = 0.009$). Cortical regions identified by this R-map are consistent with previous functional imaging studies. Posterior predictive checks demonstrated that the increase in explorative behaviour in the DBS-on state is driven by reduced drift rate scaling and boundary parameters.

Conclusion

GPi DBS increases explorative behaviour in a 2-armed bandit task incorporating reward contingency reversal, implying the GPi plays a role in controlling the balance between explorative and exploitative behaviours. Future research may focus on the identification of ideal target lesions to treat impaired reward processing in neuropsychiatric disorders e.g. apathy in Parkinson's disease.

Deciphering gene expression patterns of peripheral mononuclear blood cells transcriptome between patients suffering from Alzheimer's and Parkinson's diseases

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Introduction

Dementia is a rapidly growing global concern and a target of intensive studies aiming to find an adequate and effective treatment as well as tools for early diagnosis. Alzheimer's disease (AD) and Parkinson's disease are the most common neurodegenerative diseases with some shared pathophysiological features. However, both PD and AD are lacking diagnostic strategies for early phase disease recognition. In this in silico study, we aim to explore the gene expression signature that differentiates between AD and PD based on peripheral mononuclear blood cells transcriptome.

Materials & Methods

RNA-seq dataset GSE161199 was acquired from NCBI Gene Expression Omnibus (GEO) database. Genes with read counts lower than 10 were removed and raw counts were transformed using variance stabilizing transformation. Principal component analysis (PCA) was performed to investigate sample clustering. The differentially expressed genes (DEGs) were identified with DESeq2. DEGs with Benjamini-Hochberg adjusted p-values < 0.05 and those with 2-fold change in expression were identified as significant. Functional enrichment analysis using clusterProfiler was performed for Reactome Pathways and Gene Ontology (GO), with redundant GO terms being removed with semantic similarity method.

Results

PCA identified that AD and PD samples were grouped in distinct clusters. Out of 15,079 genes analyzed, there were 1,183 (7.8%) down-regulated (expression higher in PD) and 2,386 (15.8%) up-regulated (expression higher in AD) DEGs. The most significant up-regulated DEGs were MTRNT2L6, GTF3C6, and RSRC1, whereas RPL28, AES, and SH2D2A were the most significantly down-regulated. GO enrichment analysis has detected significant downregulation in biological processes of ß-catenin/TCF complex assembly, lymphocyte differentiation, and internal protein acetylation, with up-regulated protein folding, and splicing processes. Reactome pathways enrichment uncovered significantly down-regulated interactions with transcription factor RUNX1 involved in normal hematopoiesis, while most up-regulated being RNA processing pathways.

Conclusion

This study revealed that almost one fourth of blood transcriptome is different between patients suffering from AD and PD, and since blood can be easily obtained clinical sample, top hits from this study could be investigated further to serve as potential biomarkers. On the molecular level, these results indicate a widespread deregulation of RNA metabolism in neurodegenerative diseases.

DISC1 and TRIOBP-1: co-aggregation partners in schizophrenia

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Introduction

Schizophrenia is one of the major chronic mental illnesses, and it presents with persistent disturbances in cognitive processes, social interaction, and emotional responsiveness. The treatments currently available are insufficient and mostly focused on diminishing the symptoms, rather than treating the cause. Recently, stemming from the research of neurodegenerative disorders, we and others proposed disrupted proteostasis and aggregate formation as a possible mechanism for non-genetic causes of schizophrenia onset. The proteins we studied, Disrupted in Schizophrenia 1 (DISC1), and TRIO-Binding Protein, splice variant 1 (TRIOBP-1), were previously seen to aggregate in a subgroup of schizophrenia patients. However, while they aggregate separately in patients, it is unclear if they co-aggregate together.

Materials & Methods

DISC1, wild type TRIOBP-1 and its non-aggregating mutant were fused with EGFP or FLAG-tag, and verified by Western blot. DISC1 was overexpressed in neuroblastoma cell line, SH-SY5Y, on its own and with either wild type or mutant TRIOBP-1. Presence of (co)-aggregates was determined using fluorescent microscopy and CellSens software. All of the results were repeatable (n=3), independent of tags/fusion proteins used and verified by using negative controls.

Results

Both DISC1 and TRIOBP-1 were confirmed to aggregate when overexpressed in the neuroblastoma cells on their own. Additionally, upon their co-expression, their aggregates were seen to co-localize in the cells, therefore implying these proteins co-aggregate. Experiments with wild type DISC1 and a non-aggregating TRIOBP-1 mutant (60-652, Δ333-340) suggest that mutant TRIOBP-1 stabilizes DISC1, hindering its aggregation, and in turn DISC1 induces TRIOBP-1 aggregation. These results propose that DISC1 and TRIOBP-1 might be interaction partners as well as co-aggregation partners.

Conclusion

One of the main issues surrounding early and reliable diagnosis of schizophrenia is the lack of biomarkers. These newly-discovered co-aggregates could potentially lead to advances in the research of disrupted proteostasis as a possible underlying biological cause of non-genetic schizophrenia causes. Further experiments are required to propose a possible mechanism by which the co-aggregation occurs, and eventually how to prevent it. Lastly, protein co-aggregates could possibly be detected in the bloodstream or cerebrospinal fluid of schizophrenia patients, and serve as diagnostic biomarker or even make a conceivable drug target for more effective schizophrenia treatment.

Psychiatry

Presenters:

Bakshi, S (Sanket) Student
AQUINO, I.M.M. (IRA MARIA MA.)
Djordjevic, M (Matej)
Prameyllawati, D.M.
Shah, T.V.S (Takshit) Dr
Rawee, P (Pien)
Gimenes, Rodrigues, N.R.G (Nathalia) Master's Student

Post-acute Covid-19 Syndrome: Psychological profiles in Indian multitude

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Introduction

Even after pragmatically treating the Covid infection, majority of the cases suffer from post-acute Covid-19 syndrome. Presentation of various overlapping symptoms causing psychological impact on their quality of life are being seen. Comparatively less reports accessible and precise incidence rate being unknown, it seems that advent of these chronic symptoms requires a structured response to acknowledge, treat and avert the diabolical after-effects.

Materials & Methods

This study was a cohort study, which included the Covid 19 infected cases who fully recovered after taking the treatment as per the WHO guidelines. The study population eventually underwent a systematic assessment 12-16 weeks after successful treatment. PCS was defined as persistence of at least one clinically relevant symptom or abnormalities in spirometry or chest radiology. Analysis done by multiple logistic regression (OR; 95%CI). Demographics, acute infection phase data, Charlson's index and COVID-GRAM score, were withdrawn utilizing medical records. A structured evaluation was performed using clinical frailty scale and with reference to PHQ2 and TSQ questionnaire. Data was analyzed using spss software.

Results

712 patients recovered from mild (16.3%) or severe (83.7%) forms of Covid infection were evaluated 96 days (IQR 91–108) after disease onset. 471 cases (66.15%; 95%CI 45.0–56.7%) were diagnosed suffering from PCS. Variations in spirometry seen in 9.3%, along with 30.3% having Charlson's index >3. The median decrease of 7 points on the EuroQol VAS depicted an abysmal presentation. 66.7% cases suffering from PCS were diagnosed to have anxiety associated depression, also 34.2% did suffer from insomnia induced temper outbursts, of whom 24% cases showed prognosis towards post-traumatic stress disorder.

Conclusion

Incidence of PCS among the recovered cases is significantly high. The psychological parameters are seen to be dramatically fluctuating. The impending psychological impact of the infection certainly hinders the satisfactory recovery aimed otherwise. Hence, psychosomatic therapeutic interventions in patients recovering from Covid turn out to be of outmost importance.

Efficacy and safety of ketamine in major depression: a systematic review and meta-analysis of randomized controlled trials.

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Introduction

Depression is a mood disorder causing a persistent feeling of sadness and loss of interest. Major depressive disorder or clinical depression affects how one feels, thinks, and behaves, leading to various emotional and physical problems. A substantial proportion of patients do not achieve a clinically meaningful benefit despite multiple antidepressant trials and augmentation strategies. This meta-analysis studies the efficacy and safety of the NMDA receptor antagonist Ketamine.

Materials & Methods

We searched databases for randomized controlled studies evaluating the efficacy and safety of ketamine compared with supportive care in patients with major depression. The efficacy outcomes were depression severity 24 hours after drug administration, as assessed by the Montgomery-Åsberg Depression Rating Scale (MADRS). The safety outcomes were adverse events and serious adverse events. A meta-analytical summary was estimated using the random-effects model through the Mantle-Hanzle method. To assess heterogeneity an I2 test was used. RevMan 5.3 was used for appropriate statistical tests. P-value <0.05 was considered statistically significant.

Results

A total of 217 articles were identified, with 29 studies screened, yielding seven studies included in our systematic review. Four randomized controlled trials (N = 182, mean age 36.9 ± 8.1 years, 62% females) were included in the meta-analysis. Pooled analysis suggested a significant antidepressant effect of ketamine (SMD: -0.73; 95% CI: -1.08, -0.43; p<0.001; I2 = 0%) compared to placebo at the endpoint. There were no significant differences in the overall side-effects between ketamine and the placebo group (RR 1.26, 95% CI: 0.87-1.84; p = 0.23).

Conclusion

The moderate-quality evidence suggests the benefits of ketamine on major depressive disorder with minimal risk of adverse events.

Theory of Mind in Deaf Children and Adolescents: Contributions of Language and Social Cognition.

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Introduction

Theory of Mind (TOM) is understood as the ability to attribute mental states about yourself and others. It is believed that this ability develops during the preschool years, but the process of this development in Brazilian deaf children and adolescents is still unknown, since there are different guidelines on the prognosis for deafness, as well as the process of language acquisition.

Materials & Methods

The present research aims to understand how different factors such as language, intelligence, emotion recognition, social level, treatments and specialized schools, which are scarce in Brazil, contribute to this ability in deaf children and adolescents aged 9 to 14 years in the city of São Paulo. The parents of the volunteers answered a questionnaire to survey the history of the child or adolescent, and a video call was held, because of the pandemic due to the new COVID 19, with each volunteer, for the evaluation of the domains of language, intelligence, recognition of emotions in faces, and a TOM test adapted and provided by the University of Buenos Aires, all non-verbal instruments. The domains were evaluated in the experimental group of deaf people in LIBRAS (Brazilian Sign Language), or in Portuguese, depending on the proficiency of each volunteer, and in the control group of volunteers without hearing loss with the same age in Portuguese.

Results

Preliminary analyzes of our partial data when comparing performance between groups suggest significant differences in intelligence and especially in TOM of the experimental group. The observations even suggest a significant intra-domain variability of TOM in the same group, as language, and not another cognitive variable of Social Cognition, seems to predict the performance of this group in TOM.

Conclusion

The research is still in its course, yet so far the role of language in the development of deaf children and adolescents seems to be of extreme relevance. With this research, we intend to present guidelines for brazilian family members and specialists of any nationality.

Risk Factors of PTSD, Depression and Anxiety in Patients with Previous COVID-19 Infection: A Systematic Review and Meta-analysis

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Introduction

Since the start of the COVID-19 pandemic, several studies have found that those who tested positive for COVID-19 have a 65% risk for psychiatric disorder, while those undergoing isolation or quarantine puts the patient at risk for anxiety and depression. The objective of this study is to gather and appraise studies that determine these risk factors and their association with psychiatric disorder post-COVID-19 infection.

Materials & Methods

All cross-sectional and cohort studies from 2019 onwards that had COVID-19 survivors that developed anxiety, depression and/or PTSD, and reported in English language were included in the study. A number of databases including Medline, Cochrane Library and Clinical key were searched using meSH terms including "COVID-19", "depression", "anxiety", "post-traumatic stress disorder", and "risk factor". Risk of bias was assessed using the Newcastle-Ottawa scale. The data extracted from the studies were characteristics of the participants, risk factors, outcome measures and outcomes.

Results

Four cohort, and four cross-sectional studies were included with a total of 1438 COVID-19 survivors that developed depression, anxiety and/or depression. The risk factors that were statistically significant were (1) female sex [RR 1.86 (1.06, 2.04); Z=2.32; p=0.02] for depression, (2) having family members infected with COVID-19 [RR 1.56 (1.32, 1.85; Z= 5.17; p=<0.00001] for depression, (3) steroid administration during hospital admission [RR 1.62 (1.07, 2.47); Z=2.26; p=0.02] for anxiety and (4) female sex [RR 2.13 (1.16, 3.91); Z=2.45, p=0.01] for PTSD. Other risk factors had a positive association for their respective psychiatric outcomes but were statistically insignificant.

Conclusion

This meta-analysis shows that there are certain risk factors that can predict the incidence of depression, anxiety and PTSD in COVID-19 survivors. Female sex increases the risk of patients to have depression and PTSD. Having family members with COVID-19 is also predictive for the development of depression. Steroid administration during hospital admission is a risk factor for anxiety in post-discharge patients.

Personality Traits and Coping Strategies in Recent-onset Psychosis: Associations with Symptom Severity and Psychosocial Functioning

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Introduction

Personality traits and coping may be related to symptom severity and psychosocial functioning of patients with recent-onset psychosis. This study aimed to investigate associations of personality traits and coping strategies with concurrent and follow-up symptom severity and functioning in those patients, and to identify whether coping mediates relations between personality and symptom severity or functioning.

Materials & Methods

The Psychosis Recent Onset Groningen Survey (PROGR-S, 1998-2009) contains baseline data of 527 patients (73% male, mean age=28 years) on personality (Neuroticism-Extraversion-Openness – Five-Factor Inventory, NEO-FFI), coping (Utrecht Coping List, UCL), symptom severity (Positive And Negative Syndrome Scale, PANSS) and psychosocial functioning (Global Assessment of Functioning Scale, GAF). From 149 patients, follow-up symptom and functioning assessments after one to five years were available through the Pharmacotherapy Monitoring and Outcome Survey (PHAMOUS). Multivariable linear regression analyses were performed to assess cross-sectional associations of personality and coping with symptom severity and functioning at baseline. Next, longitudinal associations of baseline personality and coping with follow-up symptomatic remission and functioning were analyzed with multivariable linear regression and multivariable binary logistic regression analyses, respectively. Lastly, it was investigated whether coping mediated associations between personality and symptom severity or functioning.

Results

Higher baseline Agreeableness (B=-0.019, [95% CI: -0.031; -0.007]) and Neuroticism (B=-0.017, [95% CI: -0.028; -0.006]) were associated with lower concurrent symptom severity. The coping strategy Reassuring Thoughts was associated with better functioning at baseline (B=0.833, [95% CI: 0.272; 1.393]). Neither personality nor coping were associated with follow-up symptomatic remission or functioning. Coping did not act as a mediator of associations between personality and symptom severity or functioning.

Conclusion

Results indicate that only the coping strategy Reassuring Thoughts is associated with better baseline psychosocial functioning in patients with recent-onset psychosis. Personality traits seem to have limited clinically relevant relations with symptom severity or functioning at baseline and after one to five years.

The role of daily coping and general coping in predicting the outcome of psychotic experiences

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Introduction

Psychotic experiences (PEs) are relatively common in the general population and can signal risk for developing a clinical diagnosis of psychosis. This transition of PEs into psychotic disorders does not happen suddenly, but often more gradually. One factor with a potential protective role in this development is coping. Coping can be operationalized in two different ways, but it is not clear how these different operationalizations relate to one another or which operationalization has more clinical relevance (e.g., as predictor of outcome of PEs). As coping has been highlighted as a crucial target in (early) intervention, further investigation of both operationalizations is needed. Therefore, the present study aimed to compare two operationalizations of coping, namely "daily coping" – assessed with daily diary reports, and "general coping" – assessed with self-report questionnaires, in a sample of individuals at risk for psychosis.

Materials & Methods

We investigated (i) the correlation between two operationalizations of coping (i.e., daily coping and general coping) and (ii) the role of both operationalizations of coping in predicting the outcome of PEs over the course of one year. This project used data from the MIRORR study, which includes N=96 individuals with different levels of risk for psychosis. We distinguished 7 coping styles for each operationalization. First, we used Spearman correlation to examine the overlap between both operationalizations. Second, we used a series of multiple linear regressions to determine the role of coping in predicting PEs after one year while controlling for PEs at baseline.

Results

Preliminary results showed that out of the seven coping styles, two coping styles (i.e., passive reacting and expression of emotions) were correlated ($p \leq 0.05$). Analyses regarding the role of both operationalizations of coping in predicting the outcome of PEs are still ongoing.

Conclusion

Daily coping and general coping were largely uncorrelated. This implies that individuals' perception in how they cope in general does not reflect their daily life behavior; thus, the two operationalizations seem to tap into different aspects of coping.

Development of gender contentedness during adolescence and early adulthood

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Introduction

Adolescence is an important period for the development of several aspects of a person's identity, among which gender identity (e.g., male, female, non-binary, gender queer). Limited evidence exists about how prevalent gender non-contentedness (i.e., unhappiness with being the gender that is aligned with one's sex) is among adolescents in the general population. Also, its longitudinal development across adolescence has not yet been studied in detail. Earlier studies found that childhood gender non-contentedness (in clinical samples with a formal diagnosis of Gender Dysphoria), is more often seen in adolescent girls than boys and is associated with a negative self-concept and a homosexual orientation in adulthood. However, these associations have not been extensively studied in a population sample.

Materials & Methods

This project will fill these knowledge gaps by studying how gender (non-)contentedness, which is operationalized by the statement "Wishes to be of the opposite sex" with answer options 0-never, 1-sometimes/a little, 2-often/a lot (item 110 of the commonly used Youth Self Report), develops across adolescence and early adulthood. We will furthermore study the associations with sex, self-concept and sexual orientation. For this project, six data waves (age range 10 to 26 years) of the general population cohort Tracking Adolescents' Individual Lives Survey (TRAILS; n=2229) and the clinical cohort TRAILS-CC (n=543) are used. Subgroups will be defined based on the developmental trajectories of gender contentedness, using latent class growth analysis. Multinomial logistic regression is used to analyse how the factors self-concept, sex, and sexual orientation relate to the different trajectories of gender contentedness.

Results

Preliminary data analyses revealed that 11% of participants sometimes or often experience gender non-contentedness at the first assessment wave (age range 10-12 years). The described analyses will be conducted in the upcoming months.

Conclusion

New insights about the prevalence of gender non-contentedness in the general population and about trajectories of gender (non-)contentedness during an important developmental period can be valuable for school information campaigns and for clinicians providing counselling and treatment to youth who struggle with their gender identity.

Miscelleanous II

Presenters:
Qazi, M. (Mustafa)
Leão, gonçalves R., R. (Rômulo)
Jesus, de, G.E. (Gabriela)
Jaitly, R Dr. (Riya) Intern
Goel, A.G. (Akshita) Doctor
Shkaarupa, A.S. (Anastasiia)
Rashidiani, S.R (Shima) PhD student
Jani, R.J. (Ruchi)
Pajouhi, A. (Ali)
Dalal, Y. (Yagnya) Medical student

High prevalence of Schistosoma mansoni infection among adults with chronic non – communicable diseases in Malawi – a cross-sectional study at Mangochi district hospital

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Introduction

Schistosomiasis is associated with cardiovascular diseases and non-communicable diseases. Schistosoma haematobium is common in Malawi but limited data exist on other disease forms especially Schistosoma mansoni. In a sample of NCD patients, prevalence of S. mansoni was assessed and associated factors examined.

Materials & Methods

We conducted a cross-sectional study at Mangochi District Hospital. Adults over 18 years diagnosed with NCDs (n = 414), admitted or attending weekly outpatient clinics were recruited between August 2021 and January 2022. Data were collected on sociodemographic characteristics, medical history, body weight, blood pressure, and fasting blood glucose. Stool and midstream urine were collected for Kato Katz (KK) microscopy and urine circulating cathodic antigen (CCA) tests respectively. We computed prevalence of S. mansoni as number of positive KK and CCA tests, each divided by total submitted samples. Univariate and multivariable logistic regression were done to evaluate risk factors of NCDs and association between S. mansoni infection and NCDs.

Results

In preliminary data analysis of 343 participants, median age was 58 years (IQR 47 – 68) and 70% were female. 296 and 291 participants submitted urine and stool samples respectively. Prevalence of S. mansoni based on urine CCA was 14.9% (95% CI 11.0 – 19.4) and 0% on microscopy. In univariate analysis, S. mansoni was not statistically significantly associated with hypertension, diabetes or heart disease. But, age (OR 1.02, 95% CI 1.01 – 1.04, p-value 0.004), no education (OR 7.4, 95% 1.03 – 53.3, p-value 0.046) and household size (OR 1.17, 95% 1.02 – 1.33, p-value 0.021) were statistically significantly associated with hypertension. Age (OR 0.96, 95% 0.95 – 0.98, p-value <0.001) was statistically significantly associated with diabetes. Household size (OR 1.44, 95% CI 1.14 – 1.82, p-value 0.003) was statistically significantly associated with heart disease. In multivariable analysis, no education (OR 16.3, 95% CI 3.4 – 19.0, p-value <0.001) and household size (OR 1.17, 95% CI 1.02 – 1.34, p-value 0.030) were statistically significantly associated with hypertension.

Conclusion

In this preliminary analysis, we observed high prevalence of S. mansoni infection among adults in the study. This is within the range observed in children in Mangochi from 10 – 56.7%.

Identification of chromatin interactome changes and regulators of H2AK119ub upon cellular stress ubiquitination using the miniTurboID system

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Introduction

The Polycomb repressive complexes (PRC) 1 and 2 play a vital role in cell lineage specification and stem cell self-renewal by epigenetic regulation. PRC1 ubiquitinates H2AK119 and PRC2 methylates H3K27, leading to gene silencing. It is of utmost importance to maintain this repressed state to avoid inappropriate expression of lineage markers, even under cellular stress, since misexpression of genes can lead to cancer development. Strikingly, it was recently found that heat shock (HS), a basic form of cell stress, leads to loss of PRC1/2 chromatin binding, temporary relocalization of these proteins to the nucleolus, and a concomitant reduction of PRC1/2-induced epigenetic marks (Azkanaz et al. eLife, 2019). The fast kinetics of H2AK119ub reduction suggest that this process may be enzymatically driven. Within this project we aim to investigate how the chromatin interactome is changed after HS and identify potential HS-specific regulators of H2AK119ub levels.

Materials & Methods

To this purpose, we employ the miniTurboID system, allowing proximity-dependent biotinylation of nearby proteins. We expressed a histone H2A-miniTurboID fusion protein in K562 cells and screened for changes in the chromatin interactome after HS using streptavidin-mediated purification of biotinylated proteins and subsequent LC-MS/MS analysis.

Results

Initial experiments show that the H2A-miniTurboID fusion protein is stably incorporated and can be ubiquitinated at H2AK119 suggesting the fusion proteins is fully functional. HS experiments show that miniTurboID remains functional during HS, and streptavidin pull outs show that chromatin-associated proteins (EZH2, CBX8) are efficiently biotinylated. Fluorescent microscopy analysis shows that biotinylated proteins are localized to the nucleus as expected.

Conclusion

Taken together, our preliminary data show that our H2A-miniTurboID approach works to identify chromatin associated proteins under normothermic and hyperthermic conditions. Next, we will identify changes in the chromatin interactome during cellular stress (heat shock, low oxygen conditions, and proteasome inhibition) by large-scale isolation of biotinylated proteins followed by LC-MS/MS analysis.

Prevalence Of Pressure Ulcers In COVID-19 Patients: A Retrospective Study

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Introduction

Pressure ulcer (PU) can be defined as an ischemia, dead cell and tissue necrosis caused by circulatory disorder for prolonged periods usually over a bony prominence as a result of pressure. Nowadays, among the five most common causes of harm to patients and preventable patient safety problems worldwide, Pressure Ulcers are recognized as one. A Pressure Ulcer is a significant health problem which increases the risk for morbidity and mortality, prolongs hospital stay and augments treatment costs which may drastically increase if the patient is already being treated for COVID-19.

Materials & Methods

This retrospective study was conducted at North West General Hospital and Research Center, Peshawar.

The database was searched using the keywords "bed sore, pressure sore, and pressure ulcer". Data were collected on patient demographics, department, site of pressure ulcer, stage of pressure ulcer and length of stay at the hospital. All patients who acquired pressure ulcers during their stay at the hospital from 1st July 2020 to 30th June 2021 were included in the study.

Results

32 patients were documented to have acquired Pressure Ulcers during their stay at the hospital. 21 (65.6%) of the patients were males and 11 (34.4%) were females. Incidence of Pressure Ulcers was highest in adults of 51 to 70 years age group. The most common grades of Pressure Ulcers detected were Grade 1 and Grade 2, both of which were 43.8% of the total while the most common sites were Sacrum and Gluteal region.

Conclusion

COVID-19 patients are susceptible to PU if not properly cared for. Old age and longer durations of stay at the hospital amplify this risk, however prospective studies need to be conducted in collaboration with other hospitals and on a larger scale since none have been conducted so far to the best of the authors knowledge. COVID-19 patients as well as their families go through a lot and PU, which are easily preventable, add to their misery. The concerned patient safety authorities should provide awareness and training to focus on the prevention and early detection of PU to reduce or entirely eradicate the risk of complications.

Modified computed tomography severity index – a reliable predictor of clinical course and outcome in acute pancreatitis

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Introduction

Acute pancreatitis is a common yet one of the most complex and challenging abdominal conditions with unpredictable outcome. 1/5th of all acute pancreatitis patients develop complications. Several predictive scoring systems are used in the prognostication of acute pancreatitis (AP). The aim of our study was to evaluate the usefulness of modified CT severity index (MCTSI) to predict need for ICU stay, complications and mortality in acute pancreatitis.

Materials & Methods

An observational, prospective study was conducted for a period of one year in a tertiarty care teaching hospital. Fifty cases diagnosed as acute pancreatitis were included in this study. These patients underwent contrast enhanced computed tomography (CECT) of the abdomen and pelvis. The findings were recorded as per the modified CT severity index. Patients' demographic details, clinical findings, duration of hospital stay, complications, surgical interventions were recorded. SPSS version 26.0 was used statistical analysis.

Results

A total of 50 patients were enrolled in the study. Mean age was 43.34 years. Total hospital stay was 9.02±6.47 days, mean ward stay was 6.08±2.73 days, mean ICU stay was 2.94±4.7 days. Five deaths were reported in this study. There is significant correlation with age and ICU stay (r=0.344, p=0.014), age and ward stay (r=-0.340, p=0.016). There is a strong correlation with total hospital stay and MCTSI score (r=0.742, p=0.000), ward stay and MCTSI score (r=-0.442, p=0.001), ICU stay and MCTSI score (r=0.869, p=0.000). Higher MCTSI grade is significantly associated with presence of local and systemic complications and with death

(P =0.0001).

Conclusion

Grading by modified CT severity index in acute pancreatitis has a significant correlation with necessity of ICU admission, duration of ICU stay and total duration of hospital stay. Modified CT severity index can be used to predict the possibility of developing local and systemic complications, the need for interventions and necessity of ICU admission. Modified CTSI is reliable predictor of clinical course and outcome in cases of acute pancreatitis.

Association of veterans aging cohort study index with frailty among older people living with HIV in a tertiary setup.

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Introduction

In recent times, there is an increase in elderly individuals affected with HIV. These individuals are susceptible to geriatric problems like frailty earlier than the general population. We evaluated the HIV status of individuals aged 50 years and above using VACS score (veterans aging cohort study index) - a prognostic tool to predict mortality and other outcomes. Further, we assessed the patients for physical impairment and aimed to correlate the findings with their VACS score.

Materials & Methods

A cross sectional study was done and 100 elderly HIV outpatients were identified in a tertiary setup. Details about their demographics and HIV status such as duration of infection, ART regimen, CD4 count, comorbidities etc. were collected and VACS score was calculated. Furthermore, patients were assessed for frailty using Fried Frailty index. This includes- unintentional weight loss over one year, handgrip strength, exhaustion assessment, slow gait and physical activity. Patients who fulfilled none of the criteria were considered non-frail, those who fulfilled 1 or 2 criteria were considered prefrail and the rest were considered frail. Finally, association was drawn between frailty and VACS scores of patients using chi square test taking p value <0.05 as significant.

Results

Hundred patients were assessed during the study period. Mean age of the sample was 56.49 with a male to female ratio of 4:1. The VACS scores calculated for the study population ranged from 12-89 with a mean of 40.36 ± 18.0. An ROC curve was plotted and a VACS score of 28 and above was considered high. Out of the total, 13 patients were normal in fried frailty assessment, 79 patients were prefrail and the remaining were frail. Association between fried frailty phenotype and VACS index was found to be significant as higher VACS score were seen in patients who were frail (p value= 0.019).

Conclusion

We concluded that VACS index can be used effectively as a routine screening tool to analyze frailty of HIV affected geriatric population and enable doctors to provide prompt treatment.

Epigenetic profiling of the human chromosome 12 (p13.33) region reveals a novel promoter of the TEAD4 transcription factor

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Introduction

The TEAD4 transcription factor is involved in the regulation of a variety of cellular activities as a component of the Hippo signaling cascade. TEAD4 is an effector protein of the Hippo tumor suppressor pathway that determines the rate of cell proliferation and apoptosis, which may be of particular relevance in the context of tumorigenesis.

Materials & Methods

The analysis of active promoter-associated epigenetic profiles of human chromosome 12 was performed in databases (e.g. ENCODE, NCBI, and Ensembl). To detect the transcriptional start site(s) in the intragenic regions of the TEAD4 gene, the 5' rapid amplification method of cDNA ends was used. A novel alternative transcript starting from a new intragenic promoter was PCR amplified, cloned and Sanger sequenced. The subcellular localization of the novel TEAD4 isoform was investigated by transient expression assays. The expression pattern in cell lines and human tissues was examined by isoform-specific PCR. Western blotting was used to monitor protein expression in tissue samples. DNA methylation status of the alternative promoter was analyzed by quantitative methylation-specific PCR and bisulfite sequencing.

Results

ChIP-Seq data profile analyses on human chromosome 12 predicted an alternative promoter for the TEAD4 gene. The novel transcript originates from the intragenic (i.e., intronic) region of the TEAD4 gene and is expressed in a tissue-specific manner. The new TEAD4 transcript encodes a short isoform (TEAD4-ΔN) lacking the DNA-binding domain and localizing predominantly in the cytoplasm. Gene and protein expression studies combined with DNA methylation analyses demonstrated that cells and tissues expressing the TEAD4-ΔN isoform are hypomethylated in the intronic promoter region.

Conclusion

Epigenetic databases can be used to predict alternative promoters and corresponding transcripts. A truncated TEAD4 isoform lacking a DNA-binding domain of an unknown function. The promoter activity of the new isoform is epigenetically regulated. The DNA methylation-mediated regulation of the novel promoter may be of great importance in biological and pathological contexts where DNA methylation plays a crucial role through genetic reprogramming and the surveillance of cancer-specific gene expression.

Polypharmacy and oral health status of geriatric population

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Introduction

Better medical facilities have led to an increase in life expectancy. Senility leads to plethora of oral changes, most commonly being decreased salivation, tooth loss, dental caries, alveolar atrophy and temporomandibular problems. In a country like India, multimorbidity is an emerging problem. To treat this, patients undergo lengthy treatments with extensive drug regimes. It becomes a concern for geriatric patients because of its side effects. In this study, we aim to co-relate the association between Polypharmacy and oral health status among the elderly.

Materials & Methods

A self-made descriptive cross-sectional questionnaire pilot study including 50 patients was done. The questionnaire was made addressing the Polypharmacy status of the elderly in the region. It included the Polypharmacy status of the patient, the oral problems faced by them and their dental care. Geriatric Oral Health Assessment Index (GOHAI) and Oral Health Assessment Tool (OHAT) score was also included in the questionnaire. Categorical variables were reported as counts and percentages. The data was statistically analysed using chi square test.

Results

Out of 50 subjects, 34% showed polypharmacy status and 2% showed excessive polypharmacy status. 80-85 year age group showed 100% Polypharmacy status. Hypertension was the most commonly observed medical condition (40%) making amlodipine (26%) the most commonly used drug. Pain in mastication (46%) and xerostomia (34%) were the most common polypharmacy associated oral problem. From OHAT index poor oral health was found to be prevalent in elderly. In GOHAI score used to evaluate the physical, physiological and psychological aspect of the elderly, the oral health was found to be compromised. On statistical analysis, p value was found to be significant (0.004) for correlation between number of oral problems and Polypharmacy status.

Conclusion

Based on findings of the pilot study, it can be stated that the age group of 80-85 years old has the highest level of polypharmacy. The prevalence of polypharmacy was observed to increase with age. Patients with polypharmacy and oral issues were found to have a strong link. With increased polypharmacy, numbers of oral problems were found to be more prevalent.

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

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Introduction

Diabetes mellitus affects around 9.3% of the world population. Appoximately 30%-40% of diabetics develop diabetic kidney disease (DKD). Metabolic changes, such as glomerular hypertrophy, tubulointerstitial inflammation, and fibrosis are found in the DKD setting. Thus, mitigating the occurrence of these changes compounds the search for new therapeutic strategies. 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, in addition to an environment of lower oxidative stress. Another therapeutic approach comprises the mesenchymal stem cells (MSCs), whose reparative and immunomodulatory behavior combine 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 seek to establish their potential for recovery of damaged renal tissues.

Our aim was to verify whether MSC-based cell therapy or empagliflozin modulate ckit+ cell population in the kidney of diabetic and obese BTBR ob/ob mice.

Materials & Methods

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 MSCl 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 detection of ckit+ cells in distinct compartments after MSC and empagliflozin therapies, including Henle´s loop, distal tubules, collecting ducts, but not in proximal tubules. Strikingly, c-kit cells were found within the glomeruli.

Conclusion

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

Pretreatment administration of hydro-ethanolic extract of Syzygium aromaticum (HESA) prevents thioacetamide-induced liver injury in rat: a functional and molecular study

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Introduction

Liver injury is an important problem in health care. Thioacetamide (TAA) induced liver injury is an established model in experimental studies to evaluate the effect of different poisons and drugs on the liver. TAA exerts its deleterious effects through oxidative biomolecules generation. Oxidative stress then alters the functions of the liver, leading to changes in enzymatic activity of liver aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase (ALP). Liver fibrosis is another feature of TAA-induced liver injury, characterized by overexpression of collagen and α-smooth muscle actin (α-SMA). Syzygium aromaticum has profound antioxidative and anti-inflammatory effects. Also, it has been used in traditional medicine to treat liver disorders; hence in this study, we assessed the hepatoprotective effect of the hydroalcoholic extract of Syzygium aromaticum against TAA-induced liver injury.

Materials & Methods

Hepatotoxicity was induced by intraperitoneal injection of TAA (150mg /kg body weight, b.w, 3 days/week for 4 weeks) in wistar rats. Pretreatment usage of HESA (three doses of 50,150 and 300 mg/kg, b.w, orally) was started at 4 weeks before TAA administration and lasted for 8 weeks. The serum AST, ALT, and ALP activities and the activities of liver superoxide dismutase (SOD), glutathione peroxidase (GPX), catalase (CAT), and Malondialdehyde (MDA) were assessed. Histopathological studies were done by hematoxylin and eosin (H&E) and immunohistochemistry staining.

Results

The results showed that the pretreatment of HESA significantly lowered (P<0.01) the TAA-induced oxidative stress. Similarly, TAA significantly increased (P<0.01) serum levels of AST, ALT, and ALP while extract recovered corresponding values to control levels. H&E staining studies also showed that TAA marked structural liver injury. This histopathology finding was partially resolved in pretreatment extract groups. Finally, TAA significantly increased α-SMA expression in liver tissue while the extract significantly ameliorated the pre-fibrosis effect of TAA.

Conclusion

The results of this study support the antioxidant and anti-inflammatory effects of Syzygium aromaticum in the liver.

Off Label Use of Endobronchial Valves for Persistent Air leak is Safe and Effective

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Introduction

Persistent air leak (PAL) is a challenging clinical problem associated with prolonged hospital stay and increased morbidity. The primary diagnoses that place patients at higher risk for PAL also make management more challenging as invasive surgical interventions are frequently precluded. Historically, treatment options were limited to thoracostomy tube drainage, mechanical or chemical pleurodesis, and robotic or open surgical repairs. Endobronchial valves are a minimally invasive, well-tolerated treatment modality, and a viable alternative to invasive surgical interventions. We report our experience with endobronchial valves (EBVs) in the management of PAL at an academic center in Wisconsin, USA.

Materials & Methods

We performed a retrospective review of our single-center EBV experience. Data collected included demographics, primary pathology leading to PAL, comorbidities, time to chest tube removal, complications, mortality, need for any additional procedure, and time to EBV removal. Patients were divided into two groups based on the use of EBV: On-label (FDA-approved indications, e.g., Post lobectomy or segmentectomy) and off-label (non-FDA approved indications such as necrotizing pneumonia).

Results

During the study period, 15 patients underwent EBV insertion for PAL. The mean age was 57±17 years with 4 (26.7%) females. The on-label cohort contained three patients (PAL following lobectomy or segmentectomy). The off-label cohort had twelve patients. Four had secondary spontaneous pneumothorax, six had empyema, one had penetrating trauma, and one presented following percutaneous lung nodule biopsy. In the on-label cohort, all subjects had successful removal of the chest tube after a mean duration of 4±1 days. In the off-label cohort, 83.3% (10/12) of patients had successful chest tube removal 16.2±5.7 days ($p=0.396$) after EBV placement. One patient developed hypoxic respiratory failure shortly after EBV insertion, necessitating the removal of two out of five valves.

Conclusion

EBVs are a minimally invasive, well-tolerated treatment modality for patients with PAL. Procedure or valve-related complications are rare. Valves can be removed and do not preclude surgical intervention. Updated guidelines are necessary to formalize PAL management.

Does empagliflozin intervation promote a protective effect in rhabdomyolysis model? Analysis of functional and structure parameters in the kidney

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Introduction

Rhabdomyolysis is a term used to describe the rapid injury of striated muscle characterized by rupture and/or necrosis of muscle fibers, commonly associated with trauma events. Despite the knowledge of its pathophysiology, treatments are still incipient, leaving only intense fluid replacement and medical follow-up. Empagliflozin, a sodium-glucose-2 co-transporter (iSGLT2) inhibitor, has a protective factor for microalbuminuria, reduced progression of chronic kidney disease (CKD) and even decreased risk of end-stage CKD.However, these results come from cardiovascular studies, and studies focusing on AKI are needed. Thus, the feasibility of empagliflozin in accelerating the recovery of renal tissue after the rhabdomyolysis process or even mitigating its effects is studied.

Materials & Methods

The study is composed of 3 analysis groups with transgenic mice of the c-KitCre strain: control with rhabdomyolysis insult, population with rhabdomyolysis insult + empagliflozin and drug-free control. Each group will be monitored for up to 7 days, being divided according to their time-point (1, 3 or 7 days) of evaluation for renal tissue collection. After 24h water restriction, a dose of glycerol in sterile saline solution will be administered intramuscularly in the mouse to induce the rhabdomyolysis process. Empagliflozin will be administered through the gavage technique. After this process, the mice will be monitored for a period of up to 7 days, checking the following intravenous biomarkers: CPK, NGAL, KIM-1, BUN, IL-18, IL-1ß, TNF-alpha; in addition to the assessment of mRNA and protein markers of necroptosis (RIP1-RIP3-MLKL) and oxidative stress (4-HNE) and the assessment of preservation of the pool of c-Kit-positive stem cells in renal tissue. AKI score will also be quantified through renal histological analysis.

Results

It is expected to verify the efficacy of empagliflozin treatment in the attenuation of acute kidney injury induced by the rhabdomyolysis insult, both in structural improvement: decrease in acute tubular necrosis of the proximal renal tubules, fibrosis, oxidative stress and necroptosis; and functional improvement through the rates of CPK, urea and Creatinine levels and preservation of the pool of c-Kit-positive stem cells in the kidney.

Conclusion

Study in progress.

Intercellular distribution of aberrations as an indicator of chromosomal instability in the culture of lymphocytes of cancer patients

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Introduction

Recombinogenic DNA damage can give rise to chromosomal rearrangements. Many of these rearrangements will result in cell death, however, some stable rearrangements are postulated to give rise to a condition of transcriptional stress that results in a potentially self-perpetuating mutator/recombinator phenotype, may ultimately produce a cancerous cell. At the same time, disfunction genes of reparation, replications, recombinations, violation of the regulatory pathways of their expression which lead to transcriptional stress can lead to chromosomal instability.

We suggested that the chromosomal instability mediated by transcriptional stress can be considered as a common sign of the implementation of different pathways of carcinogenesis, and the occurrence of chromosomal rearrangements in this case is not random. Analysis of distribution of chromosomal aberrations in cells represents interesting approach to the understanding of mechanisms of chromosomal instability.

Materials & Methods

Statistical analysis of a cytogenetic study (culture of human peripheral blood lymphocytes) of thyroid cancer patients (42) and healthy donors (20), conducted at the National Research Center for Radiation Medicine of Ukraine. Therefore, we applied geometric (non-random nature of aberrations, one DNA damage leads to many DNA damages), Poisson (stochastic nature of aberrations) distributions and their compound to our data.

Results

The distribution of chromosome aberrations in in cells is best described by a compound Poisson and geometric distributions. The average group theoretically expected share of a subpopulation of cells with a geometric distribution in thyroid cancer patients - 18,9% (individual indicators only 12 patients - from 13 to 70%), control group - 5,8% (individual indicators only 3 donors – 0,6, 1, 21,7%). At the same time, the overall frequency of chromosome aberrations in cancer patients and in the control group did not differ (3,73±0,23 and 2,61±0,39, p >0,05). A very small number of publications have been found in which it is possible to verification the distribution of chromosome aberrations over cells.

Conclusion

In the peripheral blood lymphocytes of patients with thyroid cancer, the subpopulation of cells in which the occurrence of chromosome aberrations is not random (when one DNA damage leads to many damages) is significantly increased.

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