Book Of Abstracts

30th International Student Congress Of (bio-)Medical Sciences

university of
groningen

ISCOMS
science beyond borders

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Preface
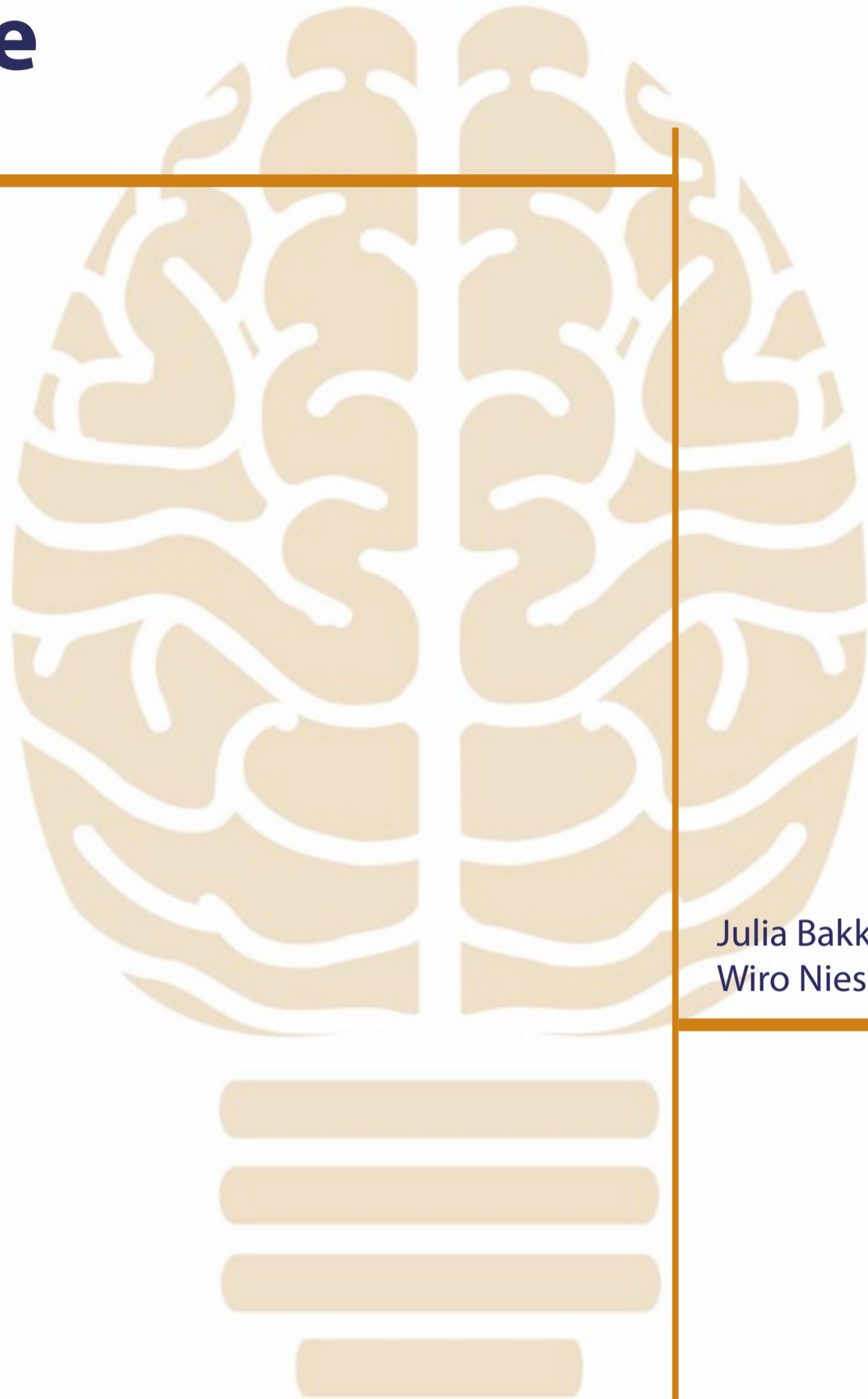
Julia Bakker
Wiro Niessen

Julia Bakker
President ISCOMS 2023

Dear participants,

With great pleasure, I welcome you to the full physical version of the 30th edition of the International Student Congress of (bio)Medical Sciences (ISCOMS).

After several editions of being either partly or fully online due to COVID-19, I am excited ISCOMS 2023 will entirely take place in physical form again. Although these online editions were very successful, I believe that attending ISCOMS in person is the best way to experience our congress.

Hopefully, ISCOMS 2023 can be a great example of how perseverance and creativity can lead to adaptability and ingenuity. 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.

During our programme, participants are able to attend three full days of inspiring lectures and student presentations. Furthermore, on Monday the 5th of June, we will start with the pre-course, a day in which enthusiastic students can improve their research skills by attending informative masterclasses. During the following three congress days, we will welcome Prof. Michael N. Hall, Maybritt Kuypers MD, Prof. Maria Yazdanbakhsh PhD, Prof. Robert Langer ScD, and Prof. Samuel Achilefu MD PhD.

On Tuesday, Prof. Michael N. Hall will talk about his research on TOR signalling and cell growth control. In addition, Maybritt Kuypers will give a lecture about her position as a flight surgeon for the ESA and discuss the medical challenges in space. On Wednesday, Prof. Maria Yazdanbakhsh will give a lecture about how microorganisms and parasites affect our immune system. Also, Prof. Robert Langer, one of the most cited scientists and co-founder of the Moderna-vaccine, will speak on 'controlled drug delivery and tissue engineering'.

On Friday, keynote speaker Prof. Samuel Achilefu will give a lecture about his groundbreaking invention, the cancer goggles, to identify cancer cells during surgery. This lecture fits perfectly within this year's theme; 'Hi-Tech Health', which will be reflected in various ways during the congress. There will be an interactive surgery where endometriosis is removed using the DaVinci robot. In addition, you will discover the theme in our hands-on workshops.

After the congress, around twenty-five 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 the Research Institutes of the UMCG.

On behalf of the entire Organising Committee, I wish you all a wonderful time and I hope you will enjoy ISCOMS 2023 as much as I did organising it.

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

Dear participants,

I would like to wish you a warm welcome to the International Student Congress Of bio(Medical) Sciences (ISCOMS) in the beautiful city of Groningen. ISCOMS is special: it is one of the world's leading student congresses in the biomedical sciences, and as such, it is not a regular congress. ISCOMS is run by a non-profit student organisation, active in the promotion of student research and its international exchange. This year marks the 30th edition and in Groningen, we are proud of it!

Who makes ISCOMS special? First, the Organising Committee, which has worked tirelessly to create a wonderful conference programme. This programme includes world-renowned speakers, among them the cofounder of Moderna, Prof. Robert Langer, Lasker Award winner Prof. Michael N Hall PhD, Maybritt Kuypers MD, Prof. Maria Yazdanbakhsh PhD, and Prof. Samuel Achilefu MD PhD. In addition, it will also provide students with the chance to observe a surgical operation, attend a patient lecture, and participate in interactive workshops. I would like to take this opportunity to thank the Organising Committee for their hard work and congratulate them on the exciting programme.

Second, you, as a participant, make it special. Out of the approximately 800 students, from all over the world, about 300 will present their own research and results. By engaging in workshops, discussions, and exchanging research ideas and views about research throughout the conference, you are all contributing to what this conference is meant for: establishing international contacts and collaborations that are at the heart of scientific progress and jointly, as a scientific community, making a societal impact. At the UMCG and University of Groningen, we foster this international collaboration, with ISCOMS being a flagship by bringing together students from a great variety of countries.

I would like to wish you an excellent stay and very pleasant days in Groningen. Enjoy the scientific discussions and interactions. I remember from my own time as a student, how I thoroughly enjoyed the first conferences that I attended, and in which I made friends, some of whom are now very close friends and will probably stay so for life.

Organisation

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

Executive Board

The ISCOMS Executive Board consists of nine (bio)medical students of the University of Groningen and is working together with 23 members of the different committees to give you the best possible experience at ISCOMS. Our goal is to provide students with the opportunity to present their research on an international platform, acquire knowledge by attending the scientific programme, and expand their network by interacting with other participants. After the Executive Board was formed in June 2022, 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 the 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 30th edition of the International Student Congress Of (bio) Medical Sciences! We wish you an extraordinary time!

Julia Bakker
Coco Wiegersma
Emiel van Woensel
Daniëlle Lieverse
Jochem Hendriksz
Stephanie Braunius
Maxim Keuper
Silke Kramer
Marijke Boskma

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

The main task of the president, **Julia Bakker**, 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, **Coco Wiegersma**, 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, **Emiel van Woensel**, 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 2023!

Emiel van Woensel, Julia Bakker, Coco Wiegersma

Scientific Programme

The Scientific Programme committee consists of six young and enthusiastic (bio)medical students. It is their responsibility to organise the scientific part of ISCOMS 2023. They are in charge of the keynote lectures, workshops, pre-course, interactive operation and the ISCOMS Research Fellowships (IRF). Their aim is to make the scientific programme of ISCOMS challenging and diverse. Besides this, they also supervise the abstract selection and ensure that students can present their research in a plenary, oral or poster session.

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

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

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

We 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 2023 a lot and we are looking forward to meeting you all!

Daniëlle Lieverse
Pia van Zon
Tijn Bartels
Luca van der Tuin
Nina van de Schepop
Estelle Achtereekte

Sponsors & Fundraising

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

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

Being a sponsor of ISCOMS allows extensive prospects for both large and small companies to create more awareness for the company, subsequently acquiring new business opportunities. Our purpose is to establish an agreement of mutual benefits. Companies can present themselves with an appearance of their logo on for example our website or our congress bag, a stand or giving interesting workshops. The sponsor program is available on the website under the heading 'supporters'.

Apart from contacting potential sponsors, the committee will also subscribe several funds to support ISCOMS. Besides that, one of the committee members is going to assist the treasurer with the finances during the congress. They are also responsible for the journal subscriptions which the presenting participants can win during the congress. And last but not least, they carry the responsibility to provide the participants with a full congress bag which contains gadgets, journals and information and will be online from this year. So bring your own bag!

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

Jochem Hendriksz
Roos Schoenmakers
Adrian Naguib
Susanne Bakker
Britte Resink

International contacts

The International Contacts committee takes care of the international part of ISCOMS. Their daily responsibilities include the worldwide promotion of the congress, and taking care of participants who encounter problems with their registration or experience other difficulties while preparing themselves for ISCOMS 2023.

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

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

As the International Contacts committee, we are constantly looking for new contacts around the world that would like to help us with promoting ISCOMS 2023. If you believe you can help, please send an email to iscoms@umcg.nl. If you have any other questions regarding promotion, Visas, ambassadors, Travel Grants, and so forth, please send us an email and we will be glad to help you!

We hope to see you at ISCOMS 2023!

Stephanie Braunius
Ali Eren Akkus
Leonie Thunissen
Tessa van Delden
Sascha Snoeck
Koen de Groot

Hosting & Logistics

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

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

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

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

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

We hope you are as excited as we are and we are looking forward to seeing you at ISCOMS 2023!

Maxim Keuper
Marit Poelsma
Arthur van der Vlis
Chloë van Haaren

Media & Branding

The Media & Branding committee is responsible for the appearance of ISCOMS and the online promotion of ISCOMS.

Their main task is to deliver 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. Furthermore, they 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 2023. Last but not least, the committee is responsible for the social media community of ISCOMS, including Facebook, Twitter, Instagram and LinkedIn.

Silke Kramer
Sam Plantinga
Milah Baumann
Frederique Schimmel

Research & Development

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

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

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

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

We would be delighted to welcome you to ISCOMS 2023!

Marijke Boskma
David Krijger
Max van Helsdingen
Jet Hilterman

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 was privileged to attend ISCOMS in 2022 for the first time and I learned so much through the keynote lectures, oral and poster presentations, laboratory tours, and many other educational and recreational activities. ISCOMS is a great platform for students to present their research, and learn from fellow students and researchers from all over the world on different types of research they are conducting in their respective fields." Alice Chimwemwe Mnyanga, a Master of Science student at the Kamuzu University of Health Sciences and a Research Assistant at Malawi Liverpool Welcome Trust.

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

If ISCOMS 2022 also excited you and makes you want to share your experience with others, you can apply to become an ambassador for ISCOMS 2024. 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.

Matheus Negri Boschiero

Brazil

Catherine Rejoice Nyirenda

Malawi

Ryan Gidda

United Kingdom
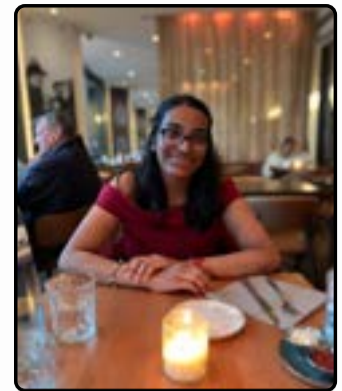
Mary-Pia Jeyarajasingham

United Kingdom

Gabryella C. Aquino

Brazil

Benson Oguttu

Uganda

Dev Patel

India

Rizana RIyaz

India

Kothari Arpit

India

Orsolya Kiss

Hungary

Mobin Azami

Iran

Iryna Sokolnyk

Ukraine

Adel Sadeghdoust

Iran

Seher ARI

Turkey

Dr. Camila Trillos

Colombia

Abhimanyu Agarwal

India

Alice Chimwemwe Mnyanga

Malawi

Kapilraj Ravendran

Bulgaria/UK

Mahsan Divanbeigi kermani

Iran

D.MOHAMMAD IBRAHIM

India

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Dr. Ashwini

India

Dr Yaa Owusuaa Offei Darko

Ghana

Bernard Annan

Ghana

Mayara

Brazil

Ruchi Jani

India

Nathalia R. Gimenes

Brazil

Ishika Mahajan

India / UK

Amogh Kadam

India

Kabarokole Annet

Uganda

Beyza Nur SU

Turkey

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Partners
AIMS

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

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.

Partners
AMSC

The Antwerp Medical Students' Congress is a project of the European Medical Students Association in Antwerp, Belgium. The AMSC has been organised yearly since 2006. Our congress is perfect for all students in the (para) medical field (medicine, pharmacy, dentistry, biomedical sciences and nursery) to share their knowledge with students from across the world. This year, AMSC will take place from the 12th to the 15th of September 2023. We will spend the first two days sharing all knowledge gathered by research conducted by medical students, using poster and oral presentations. Afterwards, we will inform you on the top medical practice, performed here in Antwerp and Belgium, through several interesting lectures and 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 last edition of BRAINCOMS took place in São Paulo, at UNIFESP - Universidade Federal de São Paulo, Brazil, from the 17th till the 19th of November. Stay tuned for our next edition!

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

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

EMSA

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

Our webpage: www.emsa-europe.org

Official BlueMist blog: www.bluemist.eu

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!

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).
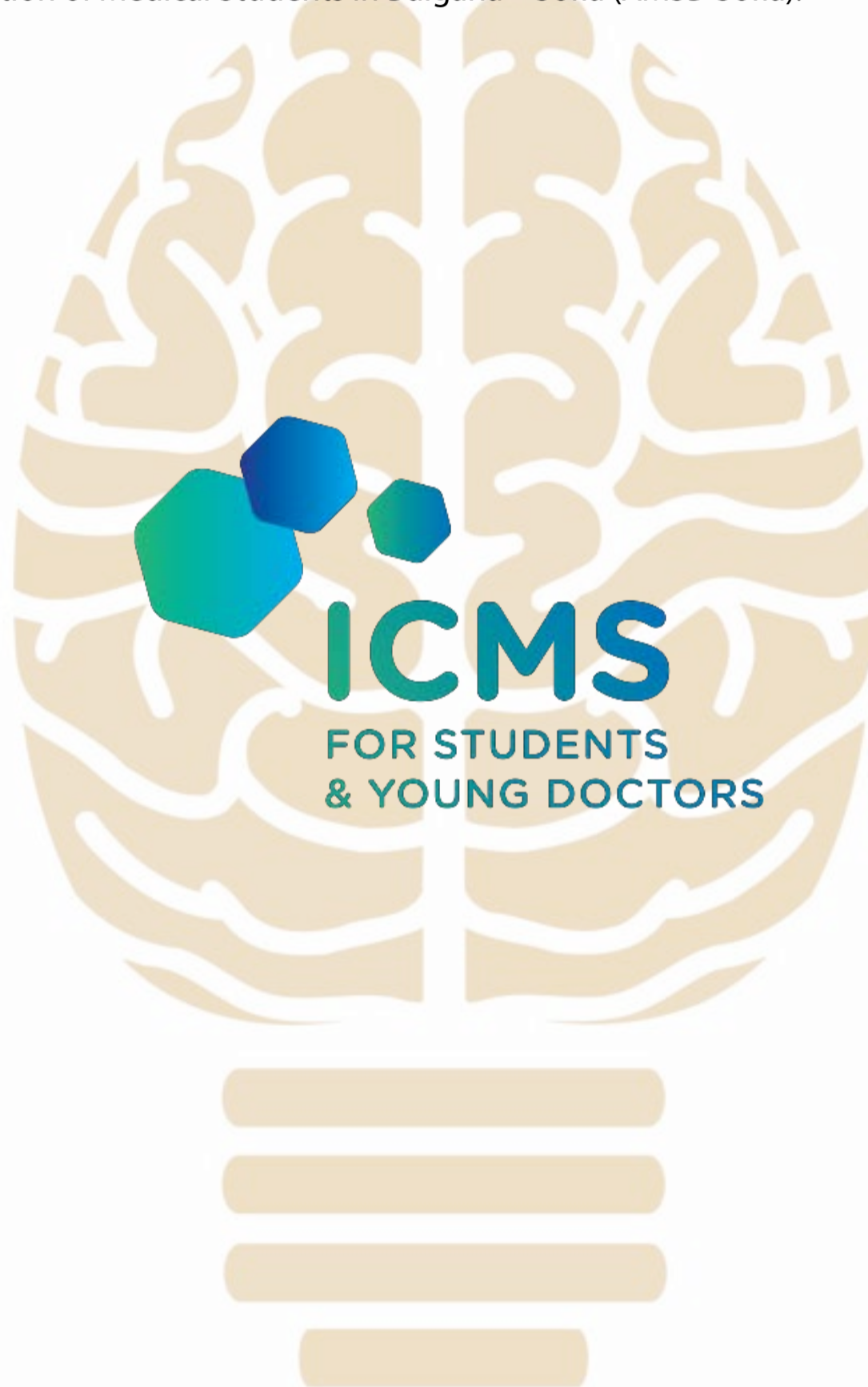
IFMSA

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/

LIMSC

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

WIMC

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

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

YES Meeting

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

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.

Organisation
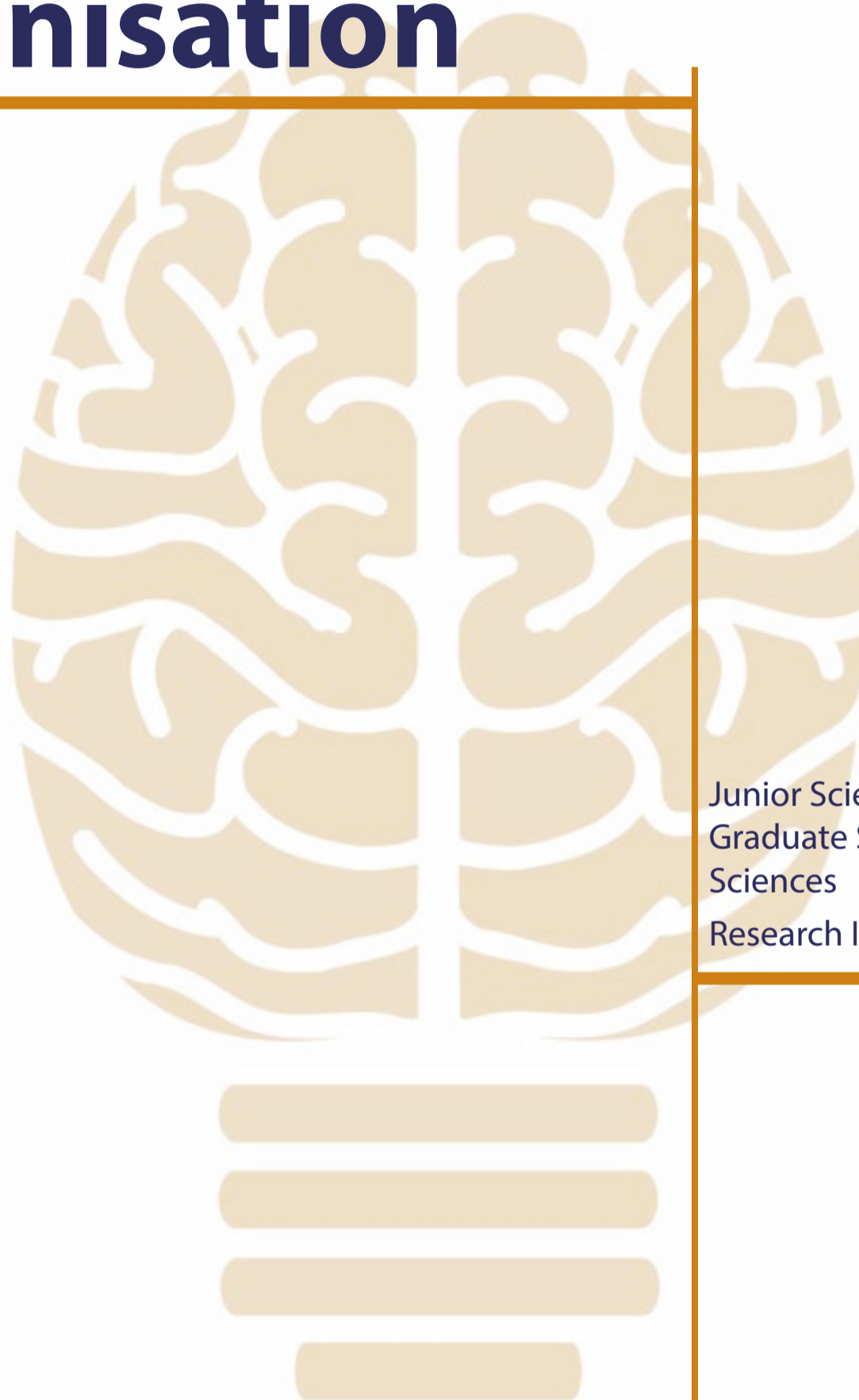
Junior Scientific Masterclass
Graduate School of Medical Sciences
Research Institute

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.

Personalised 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

Master programmes

The Graduate School of Medical Sciences administrates two master programmes:

1.   MSc Clinical and Psychosocial Epidemiology (research master)

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 scientists who are leading experts in their field. Mental and physical health, and the reciprocal relationship between these two form 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.

More information: rug.nl/cpe

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.

More information: rug.nl/cpehsp

2.   MSc Molecular Medicine and Innovative Treatment
The selective two-year master programme Molecular Medicine and Innovative Treatment (MMIT) 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.

The MMIT programme really allows you to dive into your topic of interest, by either choosing a specialization (Oncology, Neuroscience, Infection and Immunity, Nutrition and Metabolism, Systems Medicine and Drug Innovation) or follow a broad(er) programme. Either way, you decide on the content. You will be introduced to each of the specializations to help you decide.

More information: rug.nl/mmit

 How to apply
If you are interested in applying for one of these programmes, please consult the following link: https://www.rug.nl/research/gradschool-medical-sciences/master-programmes/how-to-apply/

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 Brain & Cognition
Director: prof. Iris E.C. Sommer MD PhD
Central theme: Behavioural and Cognitive Neurosciences

The Research Institute Brain & Cognition was established in 2005 and is part of the Graduate School of Medical Sciences (GSMS) and of the Research School of Behavioural and Cognitive Neurosciences (BCN). Brain & Cognition 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. More information can be found at https://umcgresearch.org/w/brain.

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. Marcel van Vugt, PhD
Central theme: Cancer Research

The Cancer Research Center Groningen (CRCG) organises 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 level. Integration of research activities is organised in a coherent and effective manner in several research programmes, to achieve fundamental, clinical and societal relevant research output. Ultimately, we aim to achieve personalised cancer therapy, by improving treatment effects and reducing 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.

W.J. Kolff Institute
Director: prof. Yijin Ren, DMD, MSc, PhD, MBA
Central theme: Biomedical Engineering, Materials Science and Digital Healthcare
The primary objective of the W.J. Kolff Institute is to bring together pre-clinical and clinical researchers and to foster a center of expertise for Biomedical Engineering, Materials Science and Digital Healthcare. It wants to stimulate clinical application and evaluation of biomaterial implants, extra-corporal support systems, sensing and monitoring systems, and data science and AI-based eHealth applications to contribute to the long-lasting well-being of patients in need.
Research is conducted within seven research programmes each with their own specific theme:

Basic and Translational Research and Imaging Methodology Development
Man, Biomaterials, Microbes
Nanotechnology & Biophysics in Medicine
Personalized Healthcare Technology
Regenerative medicine
Robotics and Image-Guided Minimally-Invasive surgery
… and new; Digital Healthcare

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 2023
- Day chairs
- Jury chair + members
- Awards
- Focus: Hi-Tech Health
- Keynote lectures
- Interactive Operation
- Workshops
- ISCOMS corporate member
  meeting

Monday 5th 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

Tuesday 6th of June - Congress day 1

07:45-08:30	Registration
08:30-09:00	Opening ceremony
09:00-10:00	Keynote lecture: Micheal N. Hall
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: Maybritt Kuypers
17:15-17:30	Closing ceremony
19:00-22:30	Formal Dinner

Programme ISCOMS 2022

Wednesday 7ᵗʰ of June - Congress day 2

08:30-09:00	Registration
09:00-09:15	Opening ceremony
09:15-10:15	Keynote lecture: Maria Yazdanbakhsh
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	Plenary session I
16:20 – 17:20	Keynote Lecture: Robert Langer
17:20-17:35	Closing ceremony
19:30-23:30	Recreational Evening

Thursday 8ᵗʰ of June - Congress day 3

08:30 - 09:00	Registration
09:00 - 09:15	Opening ceremony
09:15 - 10:35	Keynote lecture: Samuel Achilefu
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 Session II
15:45 – 16:15	Break
16:15 – 17:15	Operation: Endometriosis Removal by the DaVinci Robot
17:15 - 18:00	Award & Closing ceremony
19:00 - 22:00	Buffet
22:00 - 02:00	World Wide ISCOMS Night

Friday 9ᵗʰ of June – Post Congress Tour

08:30-20:30	Post Congress Tour

Day chairs

Monday the 5th of June
Otto van Leeuwen MD PhD

Otto van Leeuwen works as a postdoctoral researcher at the University Medical Center Groningen and as a surgical resident at the Martini Hospital Groningen. He started performing research in the group of prof. R.J. Porte in 2014, exploring the use of dynamic preservation techniques of donor livers prior to transplantation. In recent years, 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. Since 2016, van Leeuwen performed many of these clinical cases of machine perfusion of donor livers, enabling successful transplantation of these discarded donor livers. Over the last decade, the University Medical Center Groningen has grown to become one of the worldwide pioneering centers in the field of liver transplantation, with very high rates of donor liver acceptance and minimal waiting list mortality.

Prof. Esther Consten is a gastrointestinal and oncological surgeon and professor of robot- and computer-assisted surgery. She graduated as a surgeon at the University of Amsterdam in 2002. She was fellow in minimally invasive surgery at Mt Sinai Hospital and Weill Cornell University Hospital in New York, USA in 2003. She was the teaching professor of general surgery in Meander Medical Center, affiliated to University Medical Center Utrecht region, from 2007-2020. She started as a professor of robot-assisted surgery at the UMCG in 2019. Prof. Consten performs research on (minimally invasive and robot techniques) treatment of colorectal cancer at an (inter)national level resulting in numerous international scientific collaborations. As (former) chair of the Dutch Society for Endoscopic Surgery (NVEC), Working Group Innovation, Working Group Endoscopic Surgery (WIEC), and Working Group ColoProctology (WCP), she is explicitly involved in all developments of colorectal cancer treatment in the Netherlands. She is a board member of the Dutch Surgical Research Group and of the Robotics Research at KOLFF institute at UMCG. As board member of the Dutch Snapshot Research Group she helped write, review and coordinate many national cohort studies (https://snapshotresearch.nl/). Prof. Consten was involved in the development of many guidelines for the treatment of gastro-intestinal and colorectal pathology, including colorectal carcinoma. As chairman of the WCP prof. Consten assesses all new guidelines in this area. The WCP is a Dutch association dedicated to the development of coloproctology, acts at the request of the Dutch Association for Gastrointestinal Surgery (NVGIC) and the Dutch Association for Surgical Oncology, and is administratively represented in managing the NVGIC, NVCO and the Dutch Colorectal Audit (DCRA).

Regarding the dissemination of her research, prof. Consten disseminated results of robot-assisted treatment of rectal cancer throughout the Netherlands and Europe as she presents regularly at colorectal cancer conferences and symposia.

Currently, prof. Consten coordinates several (inter)national prospective clinical studies regarding innovative robot assisted surgical techniques for colorectal cancer treatment and complex pelvic floor disorders. Advanced immunofluorescence technology with targeted tracers, artificial intelligence development and peroperative image fusion will be the basis for the peroperative decision platform project. This project is expanded with digital twin technology, smart robot systems and multisensory feedback systems. This is the basis for digitalizing the operation room.

Frederike Bensch is a specialist in training in respiratory medicine and a postdoctoral researcher in pulmonary oncology at the University Medical Center Groningen (UMCG). Inspired by ISCOMS 2008 and the Summer School Transplantation Medicine, Frederike started a research project at the University of Groningen in collaboration with her home base, Heidelberg University, Germany. After finalizing medical school by the end of 2011, Frederike moved to Groningen to start her PhD program at the Department of Medical Oncology. Her research focussed on the role of PET imaging with radiolabeled antibodies to assess amongst others whole body distribution, drug target saturation, and early response prediction, which she defended in early 2019 (with honors). After a research internship in Cambridge, UK, Frederike continued her specialist training in respiratory medicine together with her research introducing molecular imaging, fluorescence, and PET, in pulmonary oncology. By July 2023, Frederike will join the Department of Pulmonary Diseases and specifically the Pulmonary Oncology team of the UMCG as a medical specialist.

In the area of early diagnosis of lung cancer, she envisions fluorescent molecular imaging to be a tool to improve the diagnostic yield of biopsy procedures and to help with the diagnosis in situ. Here, drug targets could be assessed in vivo, enabling informed local treatment in the same session to either boost already available treatment strategies or to directly treat single lesions by ablation techniques. In advanced or metastatic lung cancer, she imagines molecular PET imaging to be of additional value to amongst others assess target heterogeneity across the body which might be used for response prediction and patient selection. Furthermore, in the fast-advancing field of immunotherapy, molecular imaging in general, may help to assess the dynamics of effector cells after e.g., vaccination, and/or CAR-T cell treatment which again can help in selecting patients for the best available therapy.

"Dear participants of ISCOMS 2023, enjoy the rich program of the congress, the vibes of the city of Groningen, and foremost have fun talking science with speakers and other attendees. ISCOMS inspired me to pursue the path into research, and I hope you all will have the same great experience I had back in 2008.

Kees Poelstra is one of the founders of ISCOMS and works as a spinal surgeon. His own curiosity was stimulated after finishing Medicine in 1997 in Groningen, and he received a NUFFIC grant to take his research endeavours to the United States of America (USA). He completed his biomedical engineering PhD in 2000, and did his Orthopaedic residency in Charlottesville, Virginia. This was followed by a combined Orthopaedics/Neurology Spine fellowship at The Rothman Institute and Thomas Jefferson University in Philadelphia.

After four years of assistant professorship at Shock Trauma and the University of Maryland, he started his own Spine Institute in Destin, Florida. In addition, he helped develop various spinal implant systems, Robotic Surgery systems, and Augmented Reality surgical systems with much clinical success.

After developing Robotic Spine Institutes in Silicon Valley and Las Vegas, he is now back at The Rothman Institute heading up Orthopaedics and Spine as Systems Chief for CarePoint Health in Hoboken / Jersey City in New Jersey. He still works with the same enthusiasm as he did three decades ago on next-generation surgical implant- and robotic systems while teaching next-generation spine surgeons about enabling technology in the OR. The careful introduction of procedural automation into the operating room will allow many more surgeons to perform more accurate- and predictable surgeries with greater skill than they could have ever trained in his own theatre.

And all of that is only possible by staying curious and humble about the things that are

out there and ready to be discovered.

"Congratulations on 30 years of ISCOMS and enjoy this fantastic conference!"

Jury Chair
Prof. An Reyners MD PhD
Consultant medical oncologist and professor of palliative medicine at the UMCG

Prof. An Reyners is a consultant medical oncologist at the University Medical Centre Groningen (UMCG) and a professor of palliative medicine at the University of Groningen.

Her clinical duties include the care of patients with malignancies. She is specialized in the treatment of gynaecological malignancies and sarcoma. Prof. Reyners is the director of the medical oncology residency program at the UMCG. As a specialist in palliative care, she is chair of the palliative care team of the UMCG.

Prof. Reyners's research focuses on diagnosing and treating gynaecological malignancies and sarcomas. Her research's main scientific aim is to improve patients' quality of life. She has received numerous ZonMw and KWF grants in the field of palliative care and oncology. So far, she has published over 140 peer-reviewed articles. Her work is embedded in national and international research consortia. She supervises a team of ten PhD students, one post-doc, one research analyst, and many students. She is co-chair of the European Society of Medical Oncology (ESMO) working group, consisting of Designated Centers of Integrated Oncology and Palliative Care services. She is (co-)Principal Investigator of several multicentre clinical trials, including GALLOP (clinicaltrials.gov NCT02331914) and GALLOP-11 study (NCT05178030).

"When I was a medical student, ISCOMS did not exist. I remember my first congress: I was one of the only medical students that attended! I think it is something to be proud of that the UMCG hosts one of the congresses for medical students. It gives you opportunities to present and discuss your work with peers. Moreover, you can build a network and it can help you in your future as a clinical researcher. I hope to meet you at ISCOMS!"

EmProf. Cees Th. Smit Sibinga MD PhD
Expert Advisor World Health Organisation

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

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

Prof. J. Marc C. van Dijk MD PhD
Professor and chair of the department of Neurosurgery at the UMCG

J. Marc C. van Dijk is professor and chair of the department of Neurosurgery at the University Medical Center Groningen (UMCG),The Netherlands. His main surgical specialties are Neuromodulation,Neurovascular Surgery, and Skull Base Surgery. Marc van Dijk started his neurosurgical training with Raph Thomeer in Leiden in 1994. After graduation in 2000, Marc was admitted to do a prestigious clinical and research fellowship in Toronto, Canada. As such, he had the opportunity to work closely with world-leading neurovascular specialists, a.o. Karel Ter Brugge and Chris Wallace, in The Western Hospital. During the Toronto experience, Marc was fascinated by the dural arteriovenous fistula, a rare and peculiar neurovascular disorder, of which he collected a large database that resulted in several hallmark papers and ultimately in a PhD thesis. Once returned to The Netherlands in 2002, prof. van Dijk was appointed as staff neurosurgeon and clinical director in the Leiden University Medical Center. Despite this demanding position, he managed to obtain an additional master's degree (MSc) in neurovascular diseases at the Université de Paris-Sud under the guidance of Pierre Lasjaunias. In 2006, prof. van Dijk was invited to join the neurosurgical staff at the UMCG. This appointment brought to him the unique opportunity to further broaden his experience as a teacher on the European platform (EANS), as well as to learn the fine arts of neuromodulation covering the full spectrum from the deep brain stimulation to the microvascular decompression of cranial nerves in the cerebello-pontine angle. Because of his multifaceted academic profile, Marc was offered a tenure-track position that resulted in the appointment as a university tenuretrack professor on the topic 'Ageing Brain'. Besides the fact that this topic is closely related to the motto 'Heathy Ageing' of the University of Groningen, the focus on the ageing brain also gives rise to the unique opportunity to bundle the efforts of multiple clinical and preclinical academic disciplines, instead of the traditional monodisciplinary research. Being a true bridgebuilder, Marc's firm belief is that by merging skilled knowledge and efforts a range of new and groundbreaking indications for neuromodulation is ready to be identified, by which treatment or at least modulation of societal issues such as epilepsy, dementia, arterial hypertension, morbid obesity, tinnitus, and psychiatric disorders might be well within reach.

Marijn Hendriksz MSc
PhD candidate at the Experimental Internal Medicine department of the Radboud University Medical Center, Nijmegen

Marijn Hendriksz MSc Marijn was the secretary of the organising committee of ISCOMS in 2019. She has aspired a scientific career since the beginning of her bachelor's Life Science & Technology, and this aspiration has only been enhanced by ISCOMS. She recently received her master's degree in Molecular Nutrition & Toxicology from the Wageningen University and Research. During her master's, she developed a particular interest in the interplay between metabolism and immunity, especially in the development of obesity-induced adipose tissue inflammation. Since the 1st of September, she has started as a PhD candidate at the Experimental Internal Medicine department of the Radboud University Medical Center, Nijmegen. During her PhD, she will study factors that drive inflammation upon hypoglycaemia in people with diabetes, with the aim to identify a drug target that can mitigate hypoglycaemia-induced inflammation. "Dear participants, I am looking forward to meeting you all during ISCOMS in Groningen. Every year, it is extraordinary to see how many of you come from all over the world to visit ISCOMS. Ever since I organised ISCOMS, it has been truly special to be surrounded by fellow students who have the same interests and ambitions. From my own experience, I can only encourage you to talk to your fellow-students and share your aspirations with the experts that are present. I would like to wish you all a wonderful time at ISCOMS 2023!"

Tessa de Bruin was the president of the Organising Committee of ISCOMS in 2021. She is currently finishing her Research Master's in Biomedical Sciences with a track in Science, Business, and Policy at the University Medical Center Groningen (UMCG). Being the president of ISCOMS inspired her to do research herself as well. After ISCOMS 2021 she started her research at the Department of Surgery at the UMCG, focussing on long-term perfusions of porcine iliac arteries. For the past months she was an intern at VRelax, a company that uses their Virtual Reality technology in healthcare. As president of ISCOMS 2021, I am honoured to be a jury member of the 30th edition of ISCOMS this year! It must be mentioned that the 30th edition is a special one. After 30 years of experience, ISCOMS has grown to become the leading student congress in (bio)medical sciences. I am very glad to see that the Organising Committee of ISCOMS 2023 managed to finally organise the congress in a completely physical manner again. They have been working very hard the past year to fill the programme with interesting Keynotes, workshops, and Plenary- Oral- and Poster sessions. I am looking forward to welcoming you all at the UMCG. I am sure that all the participants will become inspired by each other's research and will be able to start lifelong collaborations and friendships at this year's congress. ISCOMS offers a unique platform to do so. Furthermore, I want to encourage you to also sign up for the social programme. Which I am sure you will enjoy too!
I would like to wish you all a great time at ISCOMS 2023.

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 (bio)medical congresses of your choice. All these winners will also receive a one-year online subscription to the 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 and the First Year Crew. Despite not having much research experience, the First Year Crew will also judge the plenary sessions as part of the audience with great care. The plenary presenter most appreciated by the audience will receive a cheque of €150, - to spend on visiting a (bio)medical congress of his or her choice, and a one-year online subscription to the world's leading multidisciplinary science journal 'the New England Journal of Medicine' (NEJM).

The Founder's award
Since this marks the 30th edition of ISCOMS, a special award will be given to one of the presenters. The winner of this award will be determined by ISCOMS's founders Eric Maarsingh and Kees Poelstra. The prize of this award is yet to be determined and will be handed out by one of the founders themselves.

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 either an abstract award for the Clinical Sciences, the Basic Sciences or Public Health. Our official jury will select three winners out of all the different oral topics. Winners will receive a cheque of €100,- to spend on visiting a (bio)medical 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 30th 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.

Hi-Tech Health

As medical practices become more and more automated among patients and doctors, the role of technology in healthcare has become critical for effective patient care. Technology helps to reduce errors, prevent adverse drug reactions, protect patient privacy, and improve overall care. Nowadays, technology plays a major role in every aspect of health care. One of these aspects is the development of treatment methods that result in better patient outcomes. Therefore it is crucial that future doctors gain knowledge of the increasing number of technical innovations in health care. ISCOMS 2023 will give you an exclusive insight into the world of Hi-Tech Health.

Different aspects of Hi-Tech Health will be displayed at ISCOMS 2023. For instance, the operation will be about the removal of endometriosis using the cutting-edge Da Vinci robot. Furthermore prof. Samuel Achilefu MD PhD will give an interesting lecture about his invention of the so-called 'Cancer Vision Goggles' which allows a surgeon to see cancer cells during an operation. Moreover, Hi-Tech Health will be demonstrated in several workshops.
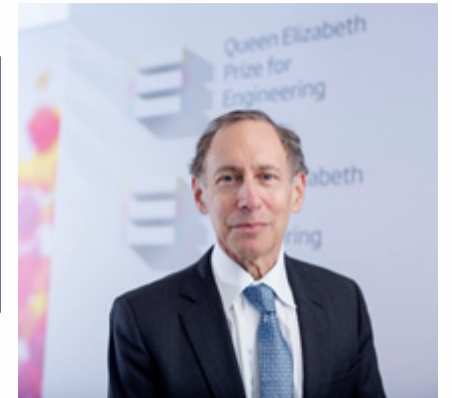
Below, you see the logo for Hi-Tech Health. Workshops or lectures that are Hi-Tech Health-related can be recognised via this logo.

Keynotes

Dr. Robert Langer
From nanotechnology to mRNA therapies, and what's to come: How overcoming scepticism and barriers led to new cancer and heart disease treatments, vaccines, and ways to tackle global health challenges'.

Robert Langer Sc.D. is currently one of the 12 Institute Professors at the Massachusetts Institute of Technology (MIT). He is a chemical engineer, scientist, entrepreneur, inventor and cofounder of a number of companies including 'Moderna'. Dr. Langer served as Chairman of the FDA's Science Board from 1999-2002. He has written over 1.500 articles, which have been cited over 374,000 times, he has the highest h-index of any engineer in history and the 2nd highest of any individual in any field. The main focus of dr. Langer's research is developing controlled release systems for macromolecules. He will also discuss how that led to the isolation of the first angiogenesis inhibitors which then led to nanoparticle-based drug delivery. An important example is the rapid development of nanoparticles for delivering the Covid-19 mRNA vaccine. His research is also on novel oral delivery systems for macromolecules such as insulin and their potential impact. Finally dr. Langer will discuss ways to develop organs and tissues from scratch and how that led to the field of tissue engineering and organs on a chip. Dr. Langer's lecture is called: 'From nanotechnology to mRNA therapies, and what's to come: How overcoming scepticism and barriers led to new cancer and heart disease treatments, vaccines, and ways to tackle global health challenges'.

Prof. Michael N. Hall PhD
"mTOR signaling in growth and metabolism"
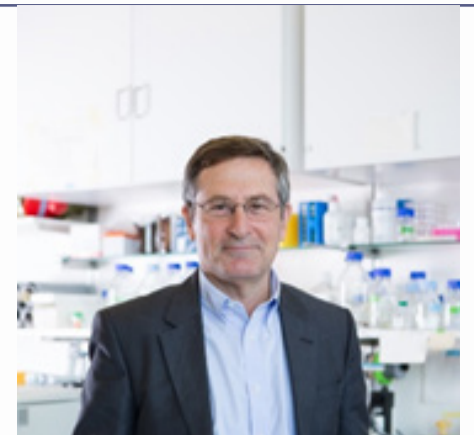
Prof. Michael N. Hall PhD is professor and former Chair of Biochemistry at the Biozentrum of the University of Basel. He is a member of the US National Academy of Sciences and has received numerous awards, including the Albert Lasker Award for Basic Medical Research (2017). Professor Hall is a pioneer in the fields of TOR (Target of Rapamycin) signaling and cell growth control. In 1991, Hall and colleagues discovered TOR and subsequently elucidated its role as a central controller of cell growth and metabolism. TOR is a highly conserved serine/threonine kinase, which controls cell growth and metabolism in response to nutrients, growth factors and cellular energy. The discovery of TOR led to a fundamental change in how one thinks of cell growth. TOR was originally discovered in yeast, but is conserved in all eukaryotes including plants, worms, flies and mammals. TOR is found in two structurally and functionally distinct multiprotein complexes termed TORC1 and TORC2. Thus, the two TOR complexes constitute an ancestral signaling network conserved throughout eukaryotic evolution to control the fundamental process of cell growth. As a central controller of cell growth, TOR plays a key role in development and aging, and is implicated in disorders such as cancer, cardiovascular disease, obesity, and diabetes. The challenge now is to understand the role of TOR signaling in disease and in coordinating and integrating overall body growth and metabolism in multicellular organisms.

Prof. Maria Yazdanbakhsh PhD
'The immunological footprints generated by different environmental factors and their importance in vaccine research.'

Prof. Maria Yazdanbakhsh Phd is head of the department of parasitology and board member at the Leiden University Center of Infectious Diseases. She is also a member of the Scientific research board of LUMC and advisor at the Indonesia Medical Education and Research Institute (IMERI). The department of parasitology engages in basic and clinical research. The department also employs an interdisciplinary group of basic and clinical scientists who focus on understanding host-parasite interactions at the molecular, cellular and population level.

There is increasing evidence for tremendous variation in the immune system geographically, which is unlikely to be accounted for by genetics, implicating that environmental factors are important players in shaping the immune system. An altered immune system might have serious consequences for immunogenicity and efficacy of vaccines. Vaccines are made and first tested in high income regions of the world and when results are promising they are marketed. However, when tested in low and middle income countries (LMIC), some vaccines have shown poor immunogenicity and/or efficacy. To start understanding the link between altered immune system and vaccine hypo-responsiveness, mass cytometry has been used for in depth characterization of peripheral blood mononuclear cells from different populations and environments. By ensuring that we understand the immune system and pathways involved in populations living not only in high income regions, but also in low income regions of the world, we might be more successful in developing better vaccines.

Professor Maria Yazdanbakhsh's lecture is called: 'The immunological footprints generated by different environmental factors and their importance in vaccine research.'

Prof. Samuel Achilefu PhD
"Convergence of light, devices, and molecules to detect and treat cancer"

Professor Samuel Achilefu is inaugural chair and professor of the Department of Biomedical Engineering at the University of Texas Southwestern (UTSW) in Dallas. He is the Lyda Hill Distinguished University Chair and a professor of radiology at the Simmons Comprehensive Cancer Center. Professor Achilefu is an inventor of 69 U.S. patents. He published over 300 scientific papers, and received over 30 local, national and international honors. Furthermore professor Achilefu received multiple awards for research excellence.

Professor Samuel Achilefu is an expert in the molecular imaging of human diseases, utilizing multimodal imaging methods to address imaging challenges, focusing on optical imaging platforms. His current research interests include image-guided cancer surgery, portable imaging devices, and nanotechnology. Through a multidisciplinary team of investigators, he has guided multiple research endeavors from concept to clinic.

Recently he conceived and led the development of Cancer Viewing Glasses (CVGs) that can provide real-time intraoperative visualization of tumors and sentinel lymph nodes without disrupting the surgical workflow. The CVGs were designed to detect near-infrared fluorescence (NIRF) from molecular probes targeting cancer cells. Both NIRF and normal visible light used in the operating room are projected onto a head-mounted display. The optical see-through CVGs prototype allows direct visual access to the surgical field while projecting NIRF to the eyes under normal operating room light conditions. Aided by a new tumor-targeted NIR fluorescent molecular probe capable of accumulating in most solid tumors, CVGs provided real-time image guidance for complete tumor resection in subcutaneous and metastatic mouse models and cancer patients.

Professor Achilefu's lecture is called: 'Convergence of light, devices, and molecules to detect and treat cancer'.

Maybritt Kuypers MD FAWM
"Human Spaceflight Medical Operations -Challenges and Opportunities in Space"

Maybritt Kuypers MD FAWM, completed her master's degree at the Rijksuniversiteit Groningen, The Netherlands. After completing her MD, Maybritt Kuypers trained as an emergency medicine physician at the Onze Lieve Vrouwe Gasthuis, Amsterdam. In 2010 she was accepted to the Fellowship Program, Fellow of the Academy of Wilderness Medicine (FAWM), in Austin, Texas. Two years later (2012) Maybritt Kuypers was trained at the University of Texas Medical Branch (UTMB) in the field of Aerospace Medicine.

M. Kuypers is co-founder of Outdoor Medicine. This is a company that provides expedition and wilderness medicine courses and conferences, custom training and medical guidance on expeditions. Since 2016 she is a PhD Candidate in Emergency Medicine at the University Medical Centre UvA, Amsterdam. In 2012 she received the NVSHA (Netherlands Society of Emergency Physicians) award for the best initiative in emergency medicine.

Currently, Maybritt Kuypers works as an emergency physician at the St. Antonius Hospital, Nieuwegein, The Netherlands, and as flight surgeon for the European Space Agency (ESA) at the European Astronaut Centre, in Cologne, Germany. As a flight surgeon she determines whether an astronaut is in the right health state to go into space on a mission through an extensive medical examination. She is also responsible for the medical training of astronauts. As a flight surgeon she provides medical support during landing and upon return. Together with the medical team, she oversees the entire process after the flight. This includes an assessment of physical and mental well-being, scientific examination and intensive rehabilitation so that the astronaut can return to the same level of health he or she had before spaceflight.

During her keynote lecture, Maybritt Kuypers will mainly focus on discussing her position as a flight surgeon for the ESA. It also discusses the medical challenges in space and several highlights on human research topics.

Interactive Operation

The operating theatre of the future:
ROBOTIC ENDOMETRIOSIS SURGERY
Dr. Froukje Hoogenboom MD PhD and Dr. Ellen Klinkert MD PhD

During ISCOMS 2023, we will show video fragments of a robotic multidisciplinary surgery for endometriosis. Endometriosis is a chronic disease affecting 1 in 10 women during their reproductive years. It has a great impact on the quality of life and can cause chronic pain and fertility problems in these women. Froukje Hoogenboom, colorectal surgeon, and Ellen Klinkert, gynaecologist and head of the Endometriosis Expert Center in the University Medical Centre Groningen (UMCG), will guide us through the surgery and show you deep infiltrating endometriosis and the value of the DaVinci robot during this complex surgery.

The UMCG is an Endometriosis Expert Center for the treatment of deep infiltrating endometriosis and a referral centre for the northeast of the Netherlands. Yearly 50-70 patients with deep endometriosis undergo radical laparoscopic surgery in a multidisciplinary team consisting of a gynaecologist, a colorectal surgeon, and in some cases a urologist. During these procedures all endometriosis is removed, including the organs involved, for example the uterus, ovaries, rectosigmoid or appendix. The main goal of this surgery is improving the quality of life by removing all endometriosis with as little collateral damage as possible and if desired retaining or improving fertility. These are long and complex surgeries, taking 4-8 hours per procedure.

Since 2018 half of the procedures are performed with the DaVinci Xi robot. The main advantage of using the DaVinci robot is the surgeon's ergonomics. The image is enlarged with a 3D view, which is especially useful during suturing. Also, the instruments are articulated, which makes it easier to reach difficult angles. In the UMCG we have 2 robot consoles, making it possible to perform the surgery together and assist and coach each other, which has added value, especially in complex cases.

Dr. Froukje Hoogenboom MD PhD   Dr. Ellen Klinkert MD PhD

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

Department: Wenckebach Institute for Education and Training.
Supervisor(s): Monique Timmer, Instructor ERC / NRR CPR-Instructor
Date(s): Tuesday June 6th, Wednesday June 7th, Thursday June 8th

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: Lab on a chip

Department: Research Institute of Pharmacy
Supervisor: Drs. Ing. P.P.M.F.A (Patty) Mulder
Days: Wednesday June 7th, Thursday June 8th

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: 3D lab Groningen

Department: 3D-lab / Orthopedic Surgery / Trauma Surgery
Supervisor(s): Peter Pijpker, Anne Meesters en Nick Assink (Technical Physicians and 3D specialists)
Date(s): Wednesday June 7th , Thursday June 8th

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.

Nick Assink   Anne Meesters   Peter Pijpker

Workshop: An introduction in life threatening situations in the ICU

Department: Department of Critical Care, UMCG
Supervisor(s): A. (Annalies) de Bont-Prins and M. (Marije) Smit MD
Date(s): Tuesday June 6th, Thursday June 8th

Implementation of interdisciplinary teams in the Intensive Care Unit (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 centre, 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.

M. (Marije) Smit MD

Workshop: Boundaries

Department: Health psychology
Supervisor(s): Margreet Smit ,Miranda Trippenzee
Date(s): Wednesday June 7th

Inappropriate behaviour comes in all shapes and sizes. From the innocent 'I know you don't have time, but can you still...', to situations in which people (including patients) demand or require things from you that you do not support and which you can experience as crossing your boundaries. Not only do others cross our boundaries, we also regularly cross our own. Before someone else crosses your boundary, you have often already crossed many boundaries within yourself. During this workshop we will work on these kind of situations Therefore, we will not concentrate on serious physical or verbal boundary crossing behaviour. For example, we will work on not saying no to requests that do not fit at the time or asking too much of you.

In this workshop you will become more aware of your signals (in your body, thoughts and feelings) when you or someone crosses your boundaries. Also, we will reflect upon that in situations where there is boundary crossing behaviour often one of your values is ignored. We will end the workshop with practising with a communication method to respond to inappropriate/boundary crossing situations.

Note: this workshop has already been taught to third year medical students of the UG.

Margreet Smit   Miranda Trippenzee

Masterclass strategy consulting: hoe maken we de zorg duurzamer?

Date(s): Woensdag 7 juni

De Nederlandse gezondheidszorg is verantwoordelijk voor ongeveer zeven procent van de Nederlandse CO_2-uitstoot. In de Green Deal duurzame zorg hebben stakeholders vanuit het hele zorgstelsel afgesproken de CO_2-uitstoot met 49 procent te verlagen. (Academische) ziekenhuizen kunnen hier een grote impact op maken. Een van de academische ziekenhuizen heeft ons gevraagd een inschatting van de grootste bronnen van uitstoot te maken.

Gupta Strategists helpt klanten van het hele zorgstelsel met het oplossen van dit soort strategische vraagstukken. In deze workshop geven we jullie een beeld van strategy consulting in de gezondheidszorg. We zullen oefenen met het structureren en oplossen van complexe problemen en geven een inkijkje in ons werk en de impact die we maken voor onze klanten.

Note: Dutch Only

Workshop: Dental implants in the aesthetic zone

Department: Oral Maxillofacial Surgery, UMCG Prosthetic Dentistry, UMCG
Supervisor(s): Prof. Henny J.A. Meijer DMD PhD, Prof. Gerry M. Raghoebar DMD PhD, Wim J.W.A. Slot DMD PhD, Charlotte Jensen DMD PhD
Date(s): Thursday June 8th

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

Wim J.W.A. Slot DMD PhD

Workshop: Dissection of the Human Brain

Department: Anatomy & Medical Physiology, Biomedical Sciences of Cells & Systems, UMCG
Supervisor(s): Gerben Ruesink, MSc., Janniko Georgiadis, PhD
Date(s): Thursday June 8th

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

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

Gerben Ruesink MSc   Janniko Georgiadis, PhD

Workshop: Plastic Surgery: How do tissue expanders work?

Department: Plastic Surgery, University Medical Center Groningen
Supervisor(s): Vera van Aalst MD
Date(s): Thursday June 8th

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

What is the aim of this workshop?
The main goal of this workshop is to familiarise participants with different treatment options available for breast reconstruction. Specifically, they will learn how to use tissue expanders for use in breast reconstruction.

Vera van Aalst MD

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

Department: Radiotherapy
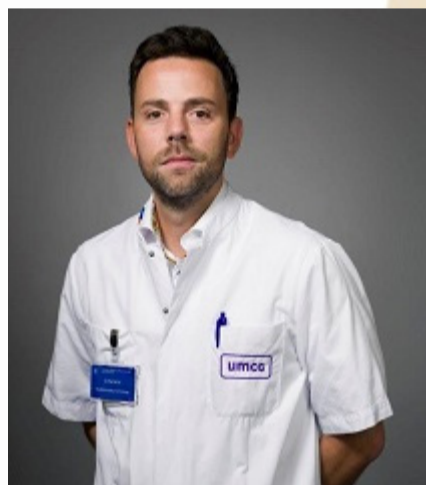**Supervisor(s):** Christian Hammer MD
Date(s): Tuesday June 6th

Radiotherapy is one of the pillars of the treatment of oncologic patients, next to surgery and systemic therapy. In the Netherlands, this specialty is developing very fast, resulting in the treatment of new indications with state-of-the-art techniques to optimally treat cancer with minimal side effects.
One of the most important innovations is proton therapy. The UMCG was the first institute that started this new technique in the Netherlands, back in 2018.
Proton therapy is a relatively new method to treat patients with radiation, as protons have special characteristics to inflict DNA damage without further passing through the body, as photons do.
This makes it possible to inflict less damage to the healthy organs surrounding the tumor. The workshop entails an interactive presentation, where input from the audience is asked in a number of clinical urological cases in which new techniques are applied, and will also provide basic insights in the treatment principles of cancer.

Christian Hammer MD

Workshop: Measure my Physiology! An Educational Journey to determine Pulmonary Function.

Department: Biomedical Sciences of Cells and Systems, section Anatomy and Medical Physiology
Supervisor(s): E. Sietsema, H.H. van der Wal
Date(s): Tuesday June 6th, Wednesday June 7th, Thursday June 8th

Pulmonary function tests, including spirometry, play an important role in the detection of asthma and Chronic Obstructive Pulmonary Disease (COPD). Measurements of pulmonary function help to chart the course of the disease and assess the risk of complications. As a doctor and clinical researcher, it is important to accurately interpret and analyse spirometry testing results. Therefore, practicals in performing these spirometry tests are an important part of the education provided by the medical faculty to its students. When attending this workshop, you will experience one of the informative medical physiology laboratories about lung function testing as it is given to students of the University of Groningen Medical Faculty. Students learn to do lung function tests on their fellow students and generate their own physiology data. In addition, students gain skills in performing lung function testing and learn to analyse and interpret their personalised data. Lastly, students get a chance to learn what these physiological concepts actually mean. In conclusion, just come and join this workshop in our newly modernized High Tech Laboratory. You might even get a tour through our lab with all new instruments in measuring one's physiology.

E.Sietsema

H.H. van der Wal

Workshop: PULSE Racing – We stimulate to cycle

Department: Pulse racing
Supervisor(s): Jace Ravenburg, Kristel den Engelsman and Tijn van Rietschoten
Date(s): Tuesday June 6th, Wednesday June 7th

PULSE Racing was founded to advance functional electrostimulation (FES) for people with spinal cord injuries. Having a spinal cord injury causes several physical problems. Besides the inability to walk and reduced mobility, people with paraplegia (inability to voluntarily move the lower parts of the body) also have a reduced condition, disturbed blood circulation and a high risk of pressure sores. This has a negative impact on their quality of life and personal well-being. FES has a proven positive influence on the physical condition of people with spinal cord injury. The active movements induced by FES have positive effects on the condition, blood circulation and psychological state. In this workshop, you will get the chance to get a deeper understanding of how electrostimulation works and get the ability to talk to paralympic athletes who used this technology to cycle. Perhaps you even have the possibility to try the bike for yourself!

Burn injuries globally – an introduction to the diagnosis of burn wounds

Department: Burn Centre, Groningen
Supervisor(s): M.E. van Eck MD
Date(s): Tuesday June 6th , Wednesday June 7th

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

M.E. van Eck MD

Workshop: Inside the psychotic experience

Department: Psychiatry, UMCG
Supervisor(s): F. D. van Es MD
Date(s): Tuesday June 6th

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

F. D. van Es MD

Fix a mandibular fracture yourself

Department: Oral and Maxillofacial Surgery, UMCG
Supervisor(s): Prof. Ruud R.M. Bos DMD PhD, Baucke van Minnen MD
Date(s): Thursday June 8th

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

Prof. Ruud R.M. Bos DMD PhD   Baucke van Minnen MD

Workshop: Gut anastomosis

Department: Surgery, UMCG
Supervisor(s): Vincent Meyer MD PhD
Date(s): Wednesday June 7th

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

Vincent Meyer MD PhD

Workshop: Transgender debate

Department: Genderteam UMCG
Supervisor(s): A. G. Schuringa
Date(s): Wednesday June 7th

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

Since the late '70s the University Medical Center Groningen (UMCG) in the Netherlands offers a treatment programme for transgenders, according to the professional standards of the World Professional Association of Transgender Health (WPATH). Once patients have been diagnosed with gender dysphoria by the psychiatrist, the 'real life phase' starts. This 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, a lifelong continuation of cross-sex hormone therapy is needed to maintain secondary sex characteristics of the desired gender.

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

A.G. Schuringa

Workshop: Positive Energy

Department: Radiation Oncology, UMCG
Supervisor(s): Prof. Stefan Both MD PhD
Date(s): Wednesday June 7th

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 a significant reduction of radiation exposure to normal tissues. In certain patients, this may lead to fewer 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 a discussion on patient selection including ethical issues and cost-effectiveness, and ongoing scientific investigations to compare PBS to other radiation therapy technique

Prof. Stefan Both MD PhD

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

Department: Cardiothoracic Surgery, UMCG
Supervisor(s): M. Kuijpers MD PhD, W. Bouma MD PhD
Date(s): Thursday June 8th

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

W. Bouma MD PhD   M. Kuijpers MD PhD

Workshop: Light up the tissue and brighten your patients odds

Department: Gastroenterology & Endocrine Surgery, UMCG
Supervisor(s): Andrea Sterkenburg TP PhD candidate, Eline Feitsma MD PhD candidate
Date(s): Tuesday June 6th, Thursday June 8th

The ultimate surgical goal in surgical oncology is the resection of all tumour tissue, while preserving adjacent healthy tissue. The presence of tumour-positive surgical margins significantly decreases survival in a variety of solid tumours. However, intraoperative tumour delineation is performed with ancient techniques: human vision and tactile information.

Although conventional imaging techniques, such as CT and MRI, support the surgeon by providing preoperative information, reliable imaging techniques that can provide information on the resection margins during surgery are lacking. In the University Medical Center Groningen (UMCG), we have one of the world's pioneering research groups in fluorescence-guided surgery. Here, we lighten up the tumour with the use of targeted fluorescent tracers and enhance the contrast between tumour and adjacent tissue. The main goal is to improve tumour visualization where it is needed most: the surgical theatre. Before surgery, patients are administered with the tracer and, with dedicated fluorescence camera systems, we can directly visualize these tumour-specific tracers intra-operatively and provide direct surgical margin evaluation.

During this workshop, you will be able to track tumors in a phantom model and to try to resect all of these with the aid of our dedicated fluorescence camera systems.

Andrea Sterkenburg
TP PhD candidate

Eline Feitsma
MD PhD candidate

Workshop: Organ perfusion

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.

Kirsten Francis Ma PhD   Stein van der Heide MSc

Workshop: Lab visit with PhD students

Date(s): Wednesday June 7th

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.

Speed keynotes

Dr. Jasper van Praagh MD PhD
"Anastomic leakage"

Colorectal cancer is one of the most common cancers in the world. Annually, more than a million new colorectal tumours are diagnosed worldwide, making it the fourth most common cancer.

Surgery is the cornerstone in the treatment of these gastrointestinal cancers; in advanced cases this is combined with neoadjuvant chemotherapy and/or radiation therapy. Tumour resection with the reconstruction of the gastrointestinal continuity is the standard of care. The anastomosis, a surgical wound to restore the continuity of the gastrointestinal tract, often does not heal well, leading to anastomotic leakages (AL) in up to 20% in lower colorectal anastomoses. This causes luminal content
to leak into the abdominal cavity, leading to a high morbidity and mortality rate. Despite new techniques and much research, the mechanisms behind the development of AL are not yet fully
understood. Dr. Van Praagh and his team are interested in how the billions of microbiota near the anastomosis influence the development of AL. Details of their experimental studies and newly obtained, non-published results will be shared in this Speed Keynote Lecture.

Dr. Linda Vriend, PhD
'Adipose tissue-derived components –
treatment modalities to treat dermal damage'

Linda Vriend studied Medicine at the Erasmus University of Rotterdam and did her PhD at the UMCG (Universitair Medisch Centrum Groningen). Linda her thesis discussed the regenerative effects of the components of adipose tissue and explored the possibility of a therapeutically functional scaffold of these components. The purpose of this was to treat dermal damage and augment fat graft retention, while enhancing understanding of their effect in tissue. A clinical trial was designed to objectify the changes as a result of tSVF-enriched fat grafting for adherent scars. A systematic literature review regarding the effect of supplementation strategies on graft retention resulted in a list of requirements for effective research in this area. Rodent studies and a systematic review were conducted to investigate the currently used decellularization procedures to obtain ECM hydrogel scaffolds, and to test their feasibility to treat dermal damage. The findings of my thesis provide substantial direction for future translational research and may accelerate the development and adoption of adipose tissue derived scaffolds and ultimately improve patient's quality of life

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.

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.

Stress corresponding to PhD research
Prof. Dr. J. Fleer en dr. ir. S. Scholtens

Do I see myself as a PhD student?

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

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.

Poster Presentation - Stand out from the crowd
Prof. Dr. T.S. Van der Werf

Imagine making your first scientific mark, when your work is accepted for a poster presentation at a scientific meeting. How can you avoid the pitfall of writing a dense full article, instead of drafting a well-designed poster that reads easily? And that helps you to attract curious conference attendees, and have helpful and challenging discussions about your work?
In this course, we will discuss the challenges of reaching out to colleagues in the field, and attract the attention of colleagues. By presenting in a condense, attractive, and easily accessible fashion, using real-life examples, in an interactive course.

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.
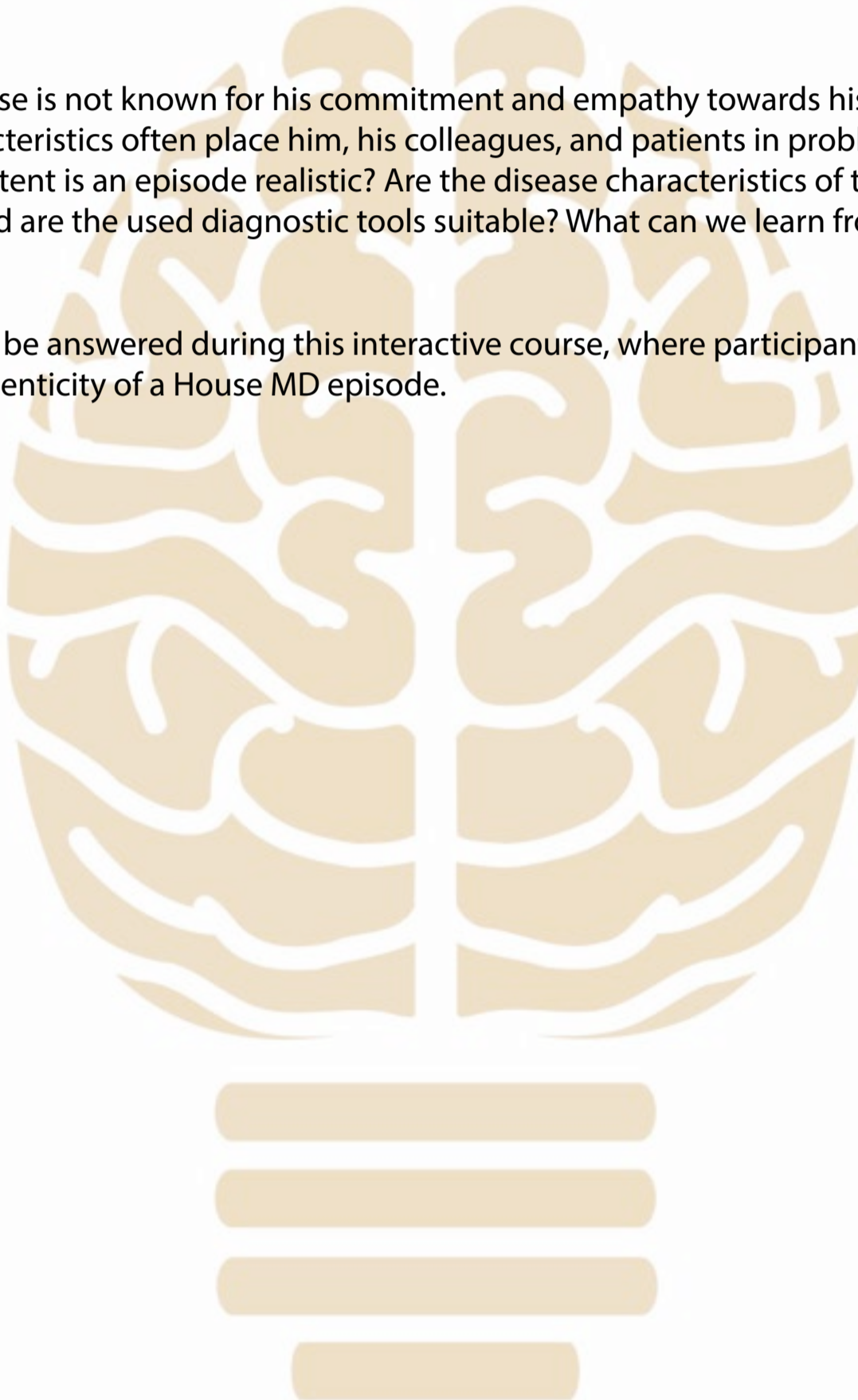
Patient Lecture: Deep Brain Stimulation in patients with Obsessive Compulsive Disorder (OCD)

Kamini Ho Pian

In this Science Elective the illusive mechanisms of our brain and its psychological phenomena will be explored. Star Trek was not far off displaying new scientific devices and techniques which we now are so accustomed to, like computers, touch screens and mobile phones. New technology allowed us to investigate our brains further, and generated new treatment possibilities for our patients.

Obsessive-compulsive disorder (i.e. fear of contamination or checking compulsion) is one of those new areas in which technological intervention can bring a solution in heavily affected patients.

Now, what is our current understanding of obsessive-compulsive symptoms and the involved neuronal circuitry? Which technological interventions do we have at our disposal? And how does a patient experience these hightech possibilities?

Live at ISCOMS, a patient expert can answer your questions. So, travel with worp nine to this elective!

Social Programme

Sunday 4ᵗʰ of June: Welcoming night: City tour & pub quiz

During the welcoming night, those of you who are already present in Groningen will have the possibility to walk through the city together with the ISCOMS Organising Committee and our First Year Crew. The city tour, which will last for about one hour, will end at a local pub in the centre of Groningen. In this pub, the welcoming night and our ISCOMS pub quiz will take place. The city tour and welcoming night will allow you to socialize with one another and meet the ISCOMS organizing committee. You are always welcome to join the welcoming night, regardless of your participation in the city tour.

Monday 5ᵗʰ of June: Dancing workshop
Most of you will arrive in Groningen on Monday. Monday will be our pre-course after which a social activity will follow. For those of you who have registered for the pre-course, the social programme for this day will be included.
During the social activity on our pre-course day, you will be guided to a location at which a dancing class will take place. On arrival, a buffet will be served, and we will have dinner together. After the intensive day, you have the opportunity to blow off some steam and show everyone your dancing skills at the dancing workshop!

Tuesday 6ᵗʰ of June: Formal Dinner
The first official congress day will be followed by our 'Formal Dinner'. This year, the Formal Dinner will take place at one of Groningen's most beautiful venues: 'het Prinsenhof'. During this dinner, all present participants have the chance to dress up fancy while enjoying a six-course walking dinner! Besides enjoying a delicious dinner, this event provides the perfect opportunity for socialising with other ISCOMS participants.

Wednesday 7ᵗʰ of June: Recreational evening
After our second congress day our 'recreational evening' will take place. This evening will start off by having dinner with the entire group. Once dinner is finished, you will get the option to choose between a selected number of fun activities. Some examples of activities we organized last year are a biking tour of Groningen, a yoga workshop, bowling, and many more!

Thursday 8ᵗʰ of June: World Wide ISCOMS Night
After our final congress day and the official closing ceremony, we will relocate to 'Huize Maas' where the World Wide ISCOMS Night will take place! This evening will start off with a delicious buffet with many different dishes from around the world. Afterwards, the great party will begin. During this night, the end of a successful and joyful congress will be celebrated. During this night, the traditions of the different countries will be central. Dress up in traditional clothing and bring a traditional snack or dish from 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!

Social Programme

Friday 9th of June: Post Congress Tour

Unfortunately, all good things come to an end. After three days of congress and the World Wide ISCOMS Night, ISCOMS 2023 will have reached its end. But don't worry, because we have one last activity for you: the Post Congress Tour! During this day we will be visiting another Dutch city. This year we will be traveling to the capital of Friesland, Leeuwarden. Leeuwarden is also proclaimed the cultural city of Europe in 2018. Two buses will be arranged which will take us to Leeuwarden. When arrived in Leeuwarden, we will start off with lunch. During our lunch, we will visit a typical Dutch restaurant called 'pannenkoekenschip', where we will have real Dutch pancakes. After this, a few activities will be organized throughout the city. This will give you the opportunity to get to know more about Leeuwarden, the Frisian culture, and visit some nice sites in the city.

After a day full of activities, we will finish off with a dinner in one of the many restaurants in Leeuwarden. Afterwards, the buses will take us back to Groningen. Upon arrival back in Groningen, ISCOMS 2023 will be officially over.

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.

THEORY OF MIND AND EMOTION RECOGNITION OF CHILDREN AND ADOLESCENTS WITH BILATERAL DEAFNESS

Nathalia Rodrigues Gimenes
Brazil

Introduction

The ability of social cognition is established at the interface of socio-cognitive and communicative development, consolidating itself at 5 or 6 years of age. The development in Brazilian deaf children is still unknown. Theoretical models identify important domains in social cognition, such as theory of mind, and emotion recognition. Studies with hearing children indicate intrinsic relationships between social cognition and language, a relationship still unknown in Brazilian deaf children. This pioneering, cross-sectional and exploratory study aimed to investigate aspects of the development of social cognition in deaf children and adolescents, focusing on theory of mind and emotion recognition, as well as investigating associations with language through vocabulary.

Material & Methods

The study included 15 children and adolescents, with bilateral deafness, from 7 to 14 years old, with different communicative models, with hearing parents. Also participating were 20 hearing children and adolescents, in the same age, also with hearing parents. All participants were evaluated in an emotion recognition test, a theory of mind task, and their subdomains, and expressive and receptive vocabulary tests, adaptable or validated for the deaf children. The applications were carried out by video call, due to the pandemic, by the main researcher, a clinical psychologist qualified in Brazilian Signal Language, Libras. In the data analysis, generalized linear models were used for quantitative variables and chi-square tests for categorical variables.

Results

As expected, the results revealed that the deaf participants performed worse in theory of mind compared to the hearing ones. Low performance predominated in the subdomains of diverse desires, access to knowledge and false belief in the Brazilian sample. Deaf participants from 10 years of age performed better than younger ones, denoting an important effect of age. In emotion recognition, it was also observed, in general, inferior performance, except for the recognition of fear and disgust emotions. No associations were observed between social cognition and language skills, through receptive and expressive vocabularies, not even associations between social cognition skills and the participants' communicative models, such as use of cochlear implant or communicative pattern, Libras or Portuguese.

Conclusion

The results suggested a possible influence of late communicative model consolidation in the sample of Brazilian deaf children with hearing parents, on lower performance. Further studies are suggested with comparisons only between deaf people and their communicative models. The pioneering nature of the online application suggests the need to develop and adapt neuropsychological tests to be applied to deaf children.

Dynamics of mitochondrial DNA heteroplasmy during the development of reconstructed mouse embryos after pronuclear transfer.

Elena Korchivaia
The Netherlands

Introduction

Pathogenic mutations in the mitochondrial genome result in mitochondrial diseases, which often prove fatal for affected children. In recent years, nuclear transfer technology has gained popularity as a means to prevent disease inheritance by transferring the mother's genome - which carries the mutant mtDNA - into an enucleated donor oocyte. However, this method remains risky. During pronuclear transfer (PNT), some of the maternal mtDNA is transferred to the donor oocyte, leading to heteroplasmy - the simultaneous presence of different mtDNA haplotypes in a single cell. Over time, the mother's mitochondria can displace the healthy donor mitochondria and result in disease development. Previous studies have not accurately assessed the impact of this technology on heteroplasmy levels. Our goal is to evaluate the efficiency of PNT and assess the mtDNA heteroplasmy rates after PNT and further embryo development.

Material & Methods

Fresh zygotes were obtained from C57bl/6 and Balb/c mice lines with sequenced mitochondrial genomes. Using cytoskeleton inhibitors, we performed PNT between C57bl/6 and Balb/c zygotes. The reconstructed embryos were cultured to the blastocyst stage, then either transferred to a mouse, or to a special implantation medium in highly-adhesive cups. Estimation of mtDNA heteroplasmy in embryo cells and cell populations was performed at the stages of 1-6 cells, implantation in vitro, gastrulation, and neurulation, by digital PCR.

Results

The efficiency of the PNT was above 70%, according to the number of 2 cells per number of PNT. Further development from the moment of successful procedure to the morula stage for the reconstructed embryos was 70% (n=131) compared with the intact control (80%, n=91). The reconstructed embryos were capable of in vitro (n=5, 100%) and in vivo implantation (29%, n=7 compared to 28%, n=16 in control). MtDNA heteroplasmy detected by dPCR was absent in controls and varied within and between reconstructed embryos from 5% to 37%.

Conclusion

Our findings indicate the need for further research on PNT as a means to address mitochondrial diseases, as well as the risk of mtDNA heteroplasmy. These heteroplasmy dynamics can serve as a guide for predicting the PNT impact on embryos and keep the state of the developing fetus under control.
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Mutational analysis of HPV-induced and HPV- independent penile squamous cell carcinomas

Mikhail Ermakov
Austria

Introduction

Penile squamous cell carcinoma (SCC) is a rare, but lethal malignancy, that arises after transforming human papillomavirus (HPV) infection or independent of HPV in the background of lichenoid dermatoses. Genetic events accompanying penile carcinogenesis are poorly understood. We performed a comparative study of genetic alterations in HPV-induced and HPV-independent penile SCC in a large cohort of 133 patients from a low incidence country.

Material & Methods

DNA was extracted from micro-dissected, formalin-fixed and paraffin-embedded tumor tissues, and analyzed for the presence of 32 HPV genotype-specific DNA using the LCD-Array Kit (CHIPRON GmbH, Germany) and for mutations in hot spot regions of 50 cancer genes by Ion Torrent Next- Generation Sequencing. Immunohistochemical overexpression of p16INK4A in HPV-induced SCC served as a surrogate marker for a transforming HPV infection.

Results

48% (64/133) SCC were classified as HPV-induced, 52% (69/133) SCC arose independent of HPV. Only 20/64 (31%) of HPV-induced penile SCC, but 61/69 (88%) of HPV-independent SCC carried somatic mutations (Chi-square; $p< 0.001$). PIK3CA, FGFR3 and FBXW7 mutations occurred in both groups in similar numbers. Mutations in TP53 (41/69; 59%), CDKN2A (30/69; 43%) and HRAS (12/69; 17%) occurred exclusively in HPV-independent SCC, with a frequent co-occurrence of TP53 and CDKN2A mutation (25/69; 36%). More than one mutation per gene (multi hit) was characteristic for HPV-independent SCC in 14/69 (20%) compared to 3/64 (5%) HPV-induced SCC (Chi square; $p< 0.001$). The total number of mutations in HPV-induced penile SCC (38 mutations) was significantly lower than in HPV-independent (136 mutations; Welsh test; $p<0.001$). Gene mutations did not correlate with age or tumor stage of the primary SCC in neither etiologic group, suggesting that the acquisition of driver gene mutations are early events.

Conclusion

Somatic gene mutations significantly differ in HPV-induced and HPV-independent penile SCC. While mutations in tumor suppressor genes (TP53 and CDKN2A) drive HPV-independent penile carcinogenesis, the oncogenic action of HPV is sufficient for HPV-induced SCC.

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Fabrication of matrix-rich articular cartilage progenitor cells(ACPC)-derived cartilage organoids

Jeske Feenstra
Nerherlands

Introduction

To improve cartilage repair after injury, cartilage organoids can be created. Large-scale production of organoids can be achieved using chondrocytes supplemented with notochordal cell-derived matrix(NCM) in a spinner flask(SF) bioreactor. However, NCM is porcine-derived and its content is not yet fully known, making it less desirable for treatment. Moreover, obtaining a large quantity of chondrocytes is challenging due to the dedifferentiation in 2D expansion culture. A solution is to use articular cartilage progenitor cells(ACPCs), these can proliferate without losing their chondrogenic phenotype in 2D. The aim of this research is to create ACPC organoids with the use of the growth factor BMP-9 to increase matrix production, without the need for NCM.

Material & Methods

Experiments were performed using pre-aggregated cell pellets, and single cells combined with NCM, into SFs with or without one dose of BMP-9. Histology and biochemistry assays were performed to measure the GAGs/DNA content. A one-way ANOVA test was used to analyze the differences in matrix production. Furthermore, a parallel plate compression was conducted to measure the mechanical properties of the NCM and one-dosed BMP-9 organoids. The Young's modulus was calculated as the secant of the stress/strain curve up to 20% strain.

Results

Matrix production was increased when the cells are pre-aggregated and stimulated with BMP-9 when compared to using NCM and BMP-9 in the SFs. There was a significant difference in diameter 2085μm(95%CI 1947-2223μm), 404.2μm(95%CI 382.0-426.5μm), and in GAGs/DNA production 86.09(95%CI 40.76-131.4) and 19.73(95%CI 2.0-37.46), respectively. There was no significant difference in Young's modulus between organoids created with NCM combined with BMP-9 and just BMP-9, however, there was a trend for a higher modulus when there was more ECM present based on histology.

Conclusion

This preliminary study shows that the cell-cell contact achieved when pre-aggregating the ACPCs combined with one dose of BMP-9 synergizes in the SF. However, this pre-aggregation step is time-consuming, and the use of NCM in the SFs is no improvement since it has a decreased ECM content. Upcoming experiments will focus on further improving the SF culture to achieve large-scale production of matrix-rich ACPC organoids by optimizing growth factor supplementation.

Dynamics of mitochondrial DNA heteroplasmy during the development of reconstructed mouse embryos after pronuclear transfer.

Elena Korchivaia
The Netherlands

Introduction

Pathogenic mutations in the mitochondrial genome result in mitochondrial diseases, which often prove fatal for affected children. In recent years, nuclear transfer technology has gained popularity as a means to prevent disease inheritance by transferring the mother's genome - which carries the mutant mtDNA - into an enucleated donor oocyte. However, this method remains risky. During pronuclear transfer (PNT), some of the maternal mtDNA is transferred to the donor oocyte, leading to heteroplasmy - the simultaneous presence of different mtDNA haplotypes in a single cell. Over time, the mother's mitochondria can displace the healthy donor mitochondria and result in disease development. Previous studies have not accurately assessed the impact of this technology on heteroplasmy levels. Our goal is to evaluate the efficiency of PNT and assess the mtDNA heteroplasmy rates after PNT and further embryo development.

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Conclusion

Our findings indicate the need for further research on PNT as a means to address mitochondrial diseases, as well as the risk of mtDNA heteroplasmy. These heteroplasmy dynamics can serve as a guide for predicting the PNT impact on embryos and keep the state of the developing fetus under control.

THE IMPORTANCE OF VARUS ENTITY PROFILING BEFORE KNEE OSTEOTOMY: FINETUNING THE IDEAL LIMB FOR HIGH TIBIAL OSTEOTOMY.

Yannick Vanneste
Belgium

Introduction

Clinical medial open-wedge high tibial osteotomy (MOWHTO) studies often analyse a mixture of varus entities without differentiating for its primary varus-inducing component. The study wants to verify the most prevalent preoperative varus malalignment phenotypes with their respective radiological and clinical outcomes before and after MOWHTO. The hypothesis was that tibial bony varus deformities with or without a moderate intra-articular (IA) varus component have favourable clinical and radiological outcomes.

Material & Methods

Accurate MOWHTO (180-184°) cases with minimal 2-year clinical follow-up were retrospectively selected from a knee osteotomy database (2016-2019). Based on the preoperative medial proximal tibial angle (MPTA), lateral distal femoral angle (LDFA) and joint line convergence angle (JLCA), subjects were allocated to six predefined varus cohorts: (1) constitutional, (2) intra-articular, (3) tibial, (4) tibial with IA, (5) femoral, (6) femoral with IA. Clinical outcomes were NRS and KOOS at 1,2 and 4.5 years. Inter-observer correlation (IOC) and One-way ANOVA testing was performed for cross-cohort outcome comparison. Alpha was set at 0.05.

Results

A total of 119 cases (age 53.4 ± 9.3, female 32.8%) were selected. Excellent IOC (r≥0.85) was found for radiological data. Except for the postoperative mFTA (p=0.60), all radiological parameters were significantly different between at least 2 cohorts (p<0.001). For the postoperative MPTA, cohort 6 (95.7° ±2.2) differed significantly from cohort 1-4 (p<0.001) while cohort 3 (90.2 ±1.7°)
differed from cohort 2 (92.9° ±1.8) and 5 (93.5° ±2.2) (p<0.001). Cohort 6 (7.3° ± 1.9) had significantly higher postoperative JLO values than cohort 1-5 (mean <5°) (p<0.001). Clinically, no significant differences between varus cohorts were found from baseline up to 4.5 years follow-up (n.s.), however at 4.5y, large numerical differences were observed in favour of cohort 1, 3 and 5 and subgroup 2.3. the KOOS (p=0.03) and absolute KOOS improvement (p=0.04).

Conclusion

The most prevalent cohort was the intra-articular varus in which small malalignments with mild OA did significantly better than large malalignments with severe OA at minimal 2 year follow-up. Primary radiological and clinical indications for single-level MOWHTO are symptomatic constitutional varus and small intra-articular varus deformities with a preferable tibial bony varus component in combination with mild-moderate overall preoperative varus malalignment.

Effective low-cost pediatric vision screening by nonspecialized healthcare personnel using the Arclight device

Jenny Wang
United States

Introduction

Pediatric vision screening is essential to detecting visual pathologies early to prevent blindness. However, vision screening requires costly equipment and specialized skills that are limited in under- resourced areas. Our study explores whether the Arclight device, a low-cost, solar-powered, easy- to-use combination ophthalmoscope, anterior segment loupe, and otoscope, can be used effectively by non-ophthalmologists to screen for amblyopia and anatomical abnormalities.

Material & Methods

54 pediatric patients (108 eyes) were examined by five non-ophthalmologist healthcare personnel using the Arclight and by an ophthalmologist using the slit lamp and indirect ophthalmoscope. Both parties were blinded to the other's exam findings. Tests performed included the optic disc exam, estimation of the cup-to-disc ratio (CDR), corneal light reflex test (CRT), Bruckner's red reflex test (BRT), and evaluation of refractive error (emmetropia, hyperopia, myopia). Ease of use of the Arclight was also recorded. Statistical analyses were conducted to determine the sensitivity, specificity, positive predictive value, and negative predictive value of the Arclight exam compared to the gold standard exam of the ophthalmologist.

Results

Using the Arclight device, the optic nerve exam was successfully completed in 65% of patients. CDRs above and below 0.5 could be determined with 66.7% sensitivity and 84.4% specificity. Arclight CRT measurements were significant ($p < .00001$) predictors of strabismus diagnosed via gold standard, with 80% sensitivity, 95.1%, specificity, 80% positive predictive value, and 95.1% negative predictive value. Arclight BRT results were not significant predictors of amblyopia diagnosis, with a 34.6% sensitivity, 85.7% specificity, 69.2% positive predictive value, and 58.5% negative predictive value. Refractive error was estimated with a success rate of 81% for emmetropia, 38% for myopia, and 21% for hyperopia. Ease of use was rated on average as a 4.4 (SD=0.9) on a scale of 1 to 5, with 1 being the hardest and 5 being the easiest.

Conclusion

Our study demonstrates the Arclight to be a low-cost yet effective alternative to the traditional ophthalmoscope that is also easy to use. Widespread use of the device for the assessment of common pediatric vision disorders offers the opportunity to strengthen eye health services in many low-resourced regions of the world.

Effects of Dance on Memory Functioning in Multiple Sclerosis: Stable Functional Connectivity of the Hippocampus Within the Default-Mode Network

Brigitta Ramsaransing
Nederland

Introduction

Memory decline and altered functional connectivity in the default-mode network (DMN) have been widely reported in people with multiple sclerosis (PwMS). Dance has been suggested to induce neuroplasticity and memory improvement, yet it remains unclear whether dancing can serve as a tool to improve brain functioning and memory performance in PwMS. Therefore, our objectives are (a) to examine differences in resting-state functional connectivity between PwMS and healthy controls (HC) at baseline, and (b) to investigate the short-term effects of an 8-week dance intervention on functional connectivity of the hippocampus within the DMN and its association with changes in memory functioning in PwMS.

Material & Methods

19 PwMS and 38 matching HC took part in this study. Regarding PwMS (44.53 ± 8.52 years, 15:4 ratio of relapsing-remitting MS and secondary progressive MS, with 8.9 ± 8.8 disease duration in years), neuropsychological (Brief Repeatable Battery memory tests), psychological (Multiple Sclerosis Neuropsychological Questionnaire; MSNQ among other questionnaires), and functional MRI data were collected pre-/post-intervention. Data of matching HC (44.68 ± 8.47 years) was adopted from the Amsterdam MS cohort. All PwMS completed an 8-week dance intervention with 1-hour sessions being held twice a week. Repeated measures tests of variances (ANOVAs) and one-tailed Pearson correlations were conducted.

Results

Baseline hippocampal connectivity within the DMN was reduced in PwMS compared to HC (p= .036). Following the dance intervention, hippocampus-DMN connectivity remained stable (p= .252). While verbal learning memory improved (65.05 ± 8.38 total score, p= .001), visuospatial memory did not (p= .517). Additional analyses showed improved subjective cognitive functioning indicated by the MSNQ (24.84 ± 9.38 score, p= .035), but this was not associated with changes in objective cognitive functioning (r= -.331, p= .083) nor with changes in functional connectivity (r= -.355, p=.068).

Conclusion

Participation in dance can improve verbal learning memory and self-perceived cognitive abilities in PwMS. Either the duration of the intervention was too short to induce a change in hippocampus- DMN connectivity or stable functional connectivity may be regarded as a sign of neuroprotection. Future studies with longer intervention duration and follow-up are needed to further elucidate the benefits of dancing on cognition and brain functioning in PwMS.

Gut Biomarkers Associate with Congestion, Disease Severity and Nutritional status in Patients with Heart Failure: Analysis of the BIOSTAT-CHF Cohort

Mats Kutscher
Netherlands

Introduction

Heart failure (HF) is a major public health issue with a large disease burden on both individual and societal levels. Patients with HF have a plethora of comorbidities such as renal failure, pulmonary diseases, diabetes and cognitive dysfunction. Our current knowledge about gastro-intestinal involvement is relatively scarce, but bowel discomfort and nutritional deficiencies are common in patients with HF. Previous research has suggested that markers of gut dysfunction such as Trefoil factor 3 (TFF-3) and Trimethylamine N-oxide (TMAO) are associated with prognosis in patients with HF. Associates of gut dysfunction in patients with HF are currently unknown, therefore we sought to investigate clinical determinants of gut dysfunction markers.

Material & Methods

The BIOSTAT-CHF cohort is a European multicenter, prospective, observational study that was conducted from 2010–2014 across 69 centers in 11 European countries. The study included 2516 participants with worsening HF. We studied 2083 patients with known TFF-3 and TMAO levels.
Univariable and multivariable regression analyses were performed to establish determinants of TFF-3 and TMAO. Stepwise backward elimination method was used to establish the final multivariable linear regression models. To ensure reliability of the final models, a bootstrap analysis was conducted using 1000 repetitions, with variables selected more than 700 times considered as robust determinants.

Results

In univariable models, TFF-3 levels associated with higher age, disease severity (NYHA class, NT- proBNP), markers of congestion, renal disease and levels of TMAO; lower nutritional estimated protein intake, cholesterol, hemoglobin and iron parameters and female sex. TMAO levels associate with higher age, disease severity, congestion, renal disease, anemia, and levels of TFF-3. In multivariable analyses, TFF-3 associated with disease severity, renal disease, congestion, estimated protein intake, anemia and female sex (all P < 0.05). Independent determinants of TMAO were renal disease and higher levels of TFF-3 (all P < 0.05).

Conclusion

This study demonstrates that markers of gut dysfunction correlate with HF severity, renal disease and markers of volume and nutritional status in patients with HF. This suggests that the gut is yet another organ system involved in the pathophysiology of HF and its consequences and potential as treatment target should be further evaluated.

Oral Sessions I
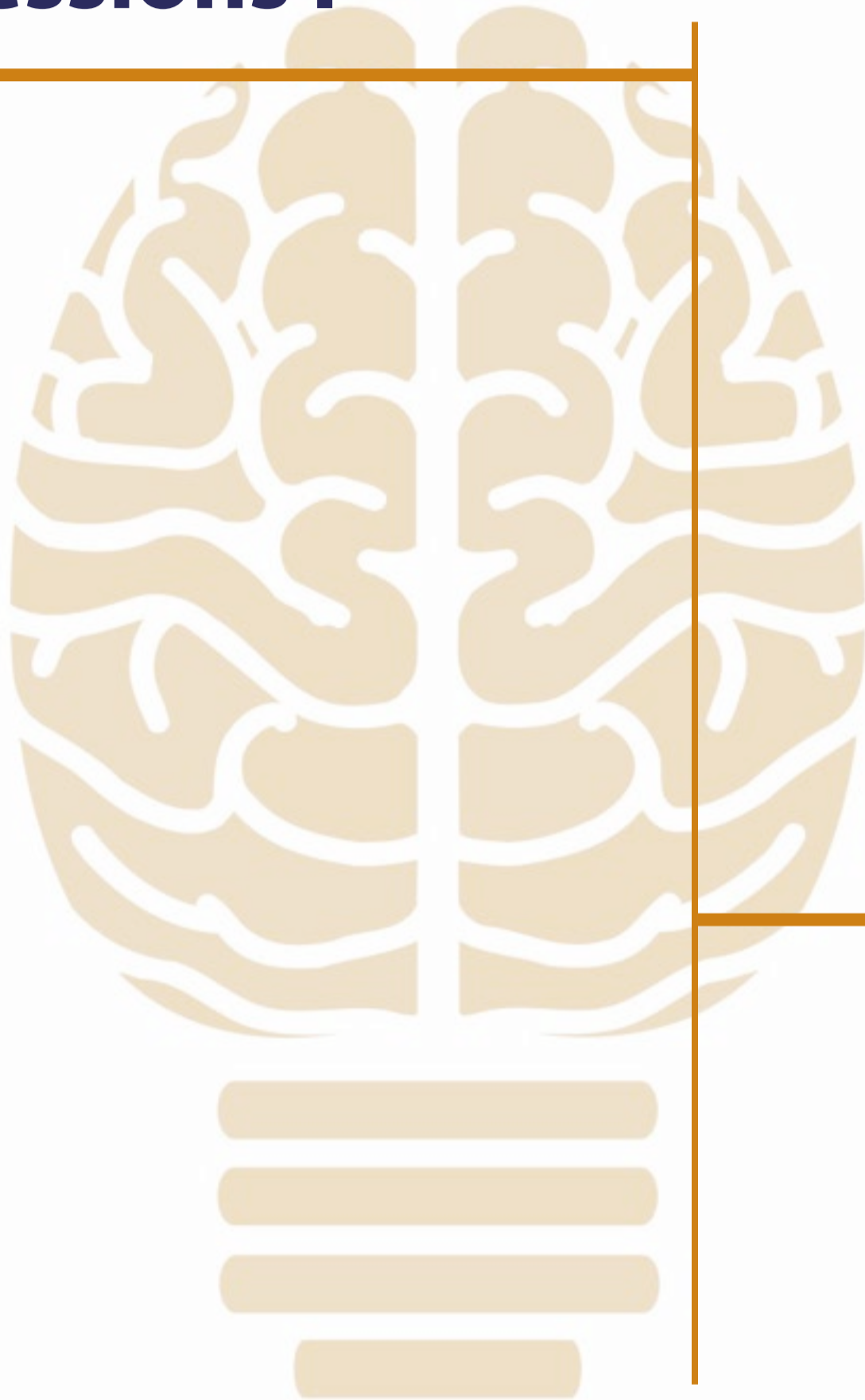
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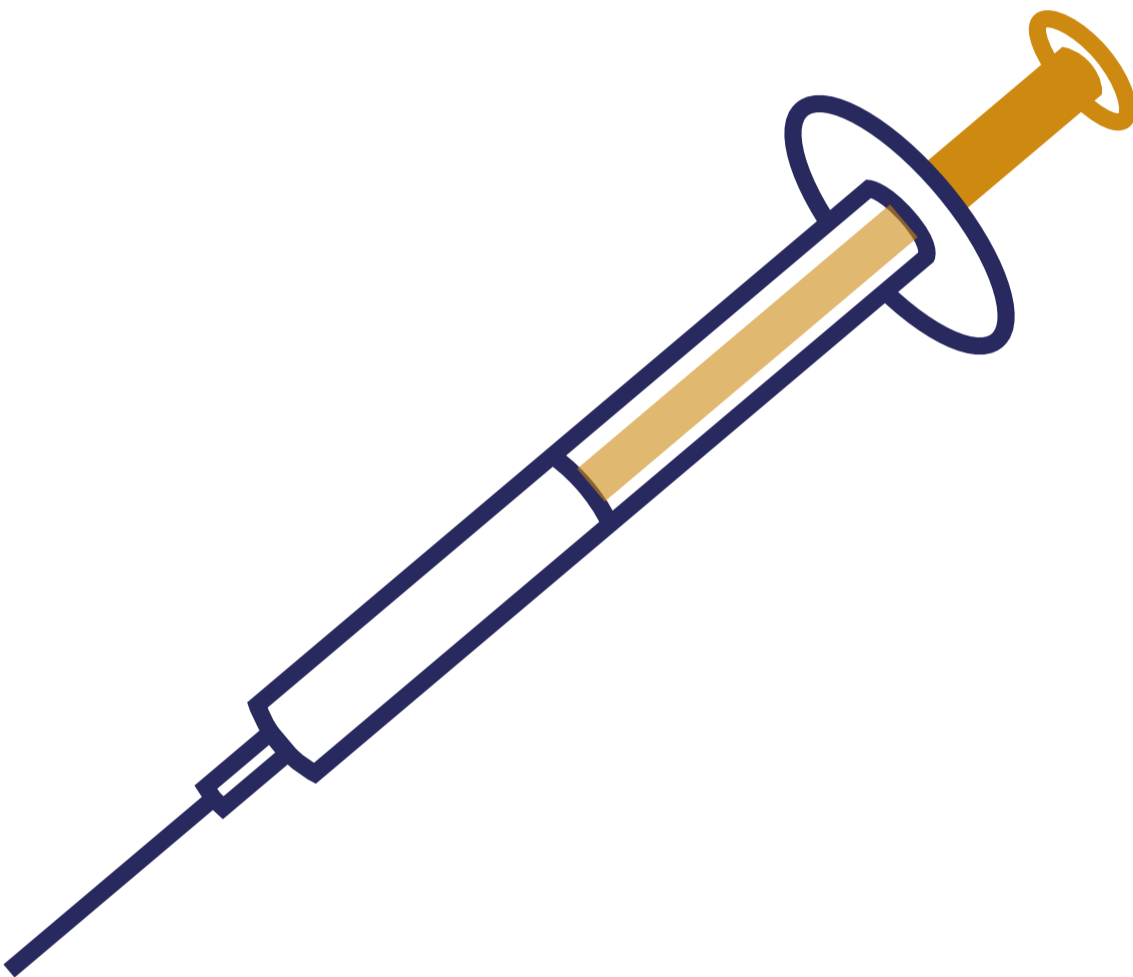
Presenters:
Fadia Hadi
Isa Tricht
Celina Oldag
Perminder Singh
Ehsan Majidi
Anna Dietze

Therapeutic drug monitoring of the drug-drug interaction between tacrolimus and azoles in lung- and kindey recipients

Fadia Hadi
The Netherlands

Introduction

Tacrolimus (TAC) is an immunosuppressant used in solid organ transplant recipients (SOTR) to improve graft survival but increases the risk for fungal infections (FI). Treatment of FI with azole antifungal drugs is complex considering drug-drug-interactions. Therapeutic Drug Monitoring (TDM) of TAC is therefore important. It is unknown to what extent TDM should occur, how TDM is practiced, and what factors contribute to TAC ΔCmin/D ratio variability and adverse events occurrence.

Material & Methods

In this retrospective cohort study, characteristics of TDM of TAC were investigated when combined with azoles (voriconazole, fluconazole or posaconazole) in lung- (LTxR), kidney/pancreas-(KTR) and recently transplanted KTR (KTR-RT). Patients were selected with SlicerDicer in Epic electronic patient dossier (EPD). Data was collected from the EPD, extracted into REDCAP, an online database platform, and analyzed using SPSS. Primary outcome was the rate (%) of lung- and kidney recipients that had a TAC measurement within therapeutic range during and directly after azole discontinuation, and if dose adjustments were conform protocol. Correlations between relevant parameters and ΔCmin/D ratio were assessed with Pearson's correlation test. Influence of baseline variables on occurrence of adverse events was assessed with linear regression analysis.

Results

A total of 75 SOTR were included. 59 SOTR used TAC before the azole treatment from which 86.4% had a dose adjustment of TAC just before the treatment as a precaution for the interaction. 36% had a dose reduction less than required and 22% had a dose reduction more than required. At the first TAC measurement after azole start, 22% was within therapeutic range. However, 75% reached the therapeutic range of TAC within the azole treatment period (LTxR: 82%, KTR: 63%, KTR-RT: 46%). After azole discontinuation 61% reached therapeutic range within 6 measurements (LTxR: 65%, KTR: 57%, KTR-RT 54%), within a median 46.45 days (IQR 14.6-159.3). Change in albumin was correlated with ΔCmin/D ratio (-0.399, P=0.008). No significant parameters influenced adverse events occurrence.

Conclusion

While a total of 25% of SOTR did not reach therapeutic range during azole treatment, even a higher percentage, 39% does not reach therapeutic range directly after treatment. Change in albumin may affect the TAC ΔCmin/D ratio.

Diffusion weighted MRI for the assessment of functional differences between kidneys in vivo and during ex vivo normothermic machine perfusion

Isa Tricht
Netherlands

Introduction

Renal normothermic machine perfusion (NMP) is a method that rewarms a kidney on an ex vivo isolated perfusion machine in a near-physiological environment, providing a platform for optimal organ preservation and pre-transplant organ assessment. To increase our knowledge about ex vivo renal physiology, we combined non-invasive functional magnetic resonance imaging (MRI) with renal normothermic perfusion in a porcine model. This project aimed to determine the differences between in vivo and ex vivo regional water diffusion patterns by means of diffusion weighted imaging (DWI).

Material & Methods

Pigs (n=26) were anaesthetized and brought into a clinical grade MRI scanner. In vivo DWI scans were acquired to non-invasively quantify local water motion in the renal parenchyma. Subsequently, both kidneys were retrieved and randomized to be subjected to either no warm ischemia (WI) or 75 minutes of WI. Next, kidneys were connected to an MRI compatible NMP circuit and perfused for 6 hours. Every two hours, DWI images were acquired from both kidneys and regions of interest were drawn to calculate mean signal intensity.

Results

The in vivo cortical (2.09 ± 0.02 x 10-3 mm^2/s) and medullary apparent diffusion coefficient (ADC) values (2.34 ± 0.02 x 10-3 mm^2/s) were significantly higher compared to those in both ex vivo groups ($P<0.001$), indicating more water diffusion restriction ex vivo, compared to in vivo. During NMP, cortical ADC values decreased significantly in the group without WI, compared to the 75 min WI group ($P<0.001$). The medullary ADC value was initially higher in the group without WI, compared to the 75 min WI group ($P<0.003$), but decreased during the course of NMP and then became similar for both groups.

Conclusion

These results provide the first evidence for remarkable differences in regional water diffusion patterns between normal in vivo renal physiology and during ex vivo NMP. Especially the cortical ADC value decreased strongly during NMP in kidneys without WI, which probably implies better vascular integrity and preservation of vasomotor activity, compared to kidneys that sustained ischemic injury. Moreover, these results highlight profound differences between in vivo and ex vivo physiology, indicating that organ viability assessment during NMP should consider other parameters than those commonly used in vivo.

Validation of the erasmus polyneuropathy symptom score in kidney transplant recipients

Celina Oldag
The Netherlands

Introduction

Polyneuropathy is a common complaint in kidney transplant recipients (KTR) and affects quality of life of patients adversely. The current gold standard for the diagnosis of small and large fibre polyneuropathy are quantitative sensory testing (QST) and nerve conduction studies (NCS), respectively. Both NCS and QST are time consuming and require a specialist to perform the testing. Therefore, a convenient screening tool for polyneuropathy is needed to optimise the follow- up of KTR in daily clinical practice and to enable further research. The aim of this study was to validate the Erasmus Polyneuropathy Symptom Score (E-PSS), a questionnaire that might constitute such a screening tool.

Material & Methods

For this cross-sectional cohort study, 150 KTR were included and underwent QST of the foot and NCS. QST was performed according to the method of limits with the dorsal foot as the testing site. In NCS the sensory nerve action potential (SNAP) amplitudes of the sural and ulnar nerve were recorded. Prior to the study visit, participants filled in the E-PSS. To validate the E-PSS, negative binomial regression analyses were performed. With the dichotomous polyneuropathy outcomes, Cohen's Kappa was determined and Bland-Altman plots were produced.

Results

The E-PSS was associated with both the warm (IRR=1.09, $p<0.01$) and cold (IRR=0.96, p=0.01) threshold tests of the QST. The E-PSS was associated with the SNAP amplitude of the sural nerve (incidence rate ratio [IRR]= 0.894, p=0.02) and the ulnar nerve (IRR=0.97, p=0.02). Cohen's kappa showed fair agreement between the QST and E-PSS (K=0.24) and moderate agreement between NCS and E-PSS (K=0.53). The Bland-Altman plots showed good agreement between the E-PSS and both QST and NCS, no proportional bias was found (all $p>0.05$).

Conclusion

The E-PSS appears to be a useful tool for the screening of polyneuropathy in KTR, and may be used for both research purposes and the follow-up of polyneuropathy in KTR.

Anti-nociceptive effect of octreotide, a somatostatin analogue in acute inflammatory pain in rats and its comparison with morphine

Perminder Singh
India

Introduction

Opiates like morphine are used for the treatment of moderate to severe pain. However long-term use often leads to adverse effects like dependence and tolerance. Thus, newer analgesics with lesser side effects need to be identified. Somatostatin, an important neurotransmitter at spinal level, modulates the transmission of pain. Studies in our laboratory has shown somatostatin exerts significant antinociceptive effect when administered locally. Unfortunately, somatostatin has a short half-life. In this study, octreotide (a more stable synthetic analog of somatostatin) was given systemically to assess its antinociceptive property in an acute inflammatory pain model. Since octreotide dose not cross the blood brain barrier, its peripheral effect was analysed.

Material & Methods

Adult male Sprague-Dawley rats were divided into three equal groups (n=6/group). Acute inflammatory pain was induced by intraplantar administration of carrageenan in the right hind paw. Standardized dose of Octreotide (3µg) and morphine (10mg/kg) was administered subcutaneously 2 h after carrageenan on the same side flank. Mechanical allodynia was estimated by von Frey filaments at the site of inflammation after 1 and 2 h of drug administration. Paw odema due to carrageenan was evaluated by plethysmometer at 2 h. Open-field activity was also examined.

Expression of Somatostatin type 2 receptor (SSTR2) was observed at the lumbar region (L4-L5) of the spinal cord by immunohistochemistry.

Results

The dose of octreotide was standardized by administration of 3µg, 10µg ,30µg &100µg and measuring the corresponding anti-nociceptive effect. The 3µg dose was finally selected due to the optimum effect. Octreotide decreased allodynia compared to saline treated control group. However, paw odema was not affected by any of the drugs instead there was mild increase in odema within morphine treated group, which was not related to increased mobility in these rats. Importantly nociception returned to baseline values after administration of morphine. SST2A expression was present in superficial lamina of the spinal cord sections of naïve group which was increased in control group, whereas in morphine treated groups this expression was absent. However, Octreotide treated group show diffuse expression which was more on lateral part of superficial lamina of dorsal horn.

Conclusion

The results show that a low dose of octreotide is effective in reducing nociception, compared to higher doses. However, this anti-nociceptive was not as much as morphine which is considered to be the gold standard drug for pain relief. Our findings are supported by other studies which have also observed antinociception in rodents after octreotide. This information may have clinical relevance.

Comparison of the Effect of Gabapentin and Caffeine on post-Dural Puncture Headache after Cesarean Section Surgery

Ehsan Majidi
Iran

Introduction
Post-dural puncture headache is one of the main side effects of regional anesthesia in women undergoing a caesarean section. The aim of this study is to compare the effect of gabapentin with caffeine in the reduction of post-dural puncture headaches following spinal anesthesia.

Material & Methods
In this randomized, double blind clinical trial, 80 patients undergoing cesarean section with spinal anesthesia who had post-dural puncture headache were observed. Patients were randomly assigned to two groups receiving caffeine 100 mg every 12 hours and gabapentin 300 mg every 12 hours. Pain was measured and recorded in 3 times, 0, 24 and 48 hours after the start of treatment in patients using visual analog scale (VAS). Need additional pain killer and re-hospitalization was also recorded.

Results
There were no significant differences between the two study groups regarding the basic characteristics. Pain in both groups decreased in the first 24 and 48 hours after intervention, but the mean pain score in gabapentin group significantly lower than caffeine group after 48 hours (2.11 vs 5.29, $P<0.0001$). The need for painkiller in the gabapentin group was 5.6% of the patients and in the caffeine, group was 34.2% of the patients, which had a significant difference in the two groups ($P<0.0001$). Also, there was a need for re-visit in 13 patients of the caffeine group, while it was not observed in the patients of the gabapentin group ($P<0.0001$).

Conclusion
Based on the results of our study, it seems that the administration of 300 mg of gabapentin every 12 hours has reduced the occurrence of post-dural puncture headache and the need for additional painkillers as well as reduce hospitalizations.

Monitoring of unfractionated heparin in critical ill ICU patients: comparing aPTT and ClotPro® IN / HI ratio to anti-Xa

Anna Dietze
Germany

Introduction

Anticoagulation is indicated for the prevention or therapy of thromboembolic events, but remains highly challenging considering the high risk of bleeding events in critically ill patients. Unfractionated heparin (UFH) is widely used as preferred anticoagulation for patients on intensive care units (ICU) due to its beneficial short half time and fast elimination. For monitoring of UFH, activated partial thromboplastin time (aPTT) is mainly used but can be misleading in both directions. Anticoagulation monitoring using anti-Xa levels is an established alternative. Using point-of-care (POC) viscoelastic testing (VET) with a specific ratio between clotting time (CT) in intrinsic test (IN-test) compared to heparinase test (HI-test) – which includes the inactivation of heparin in the probe - might help to determine the UFH effect in critically ill patients.

Material & Methods

From 09/2020 to 07/2022, 467 samples from 120 adult ICU patients receiving UFH treatment were prospectively collected. Samples for aPTT, anti-Xa measurement and POC VET using ClotPro® were simultaneously collected. Measurement for aPTT (C.K. Prest) and anti-Xa (Liquid AntiXa) were performed using the STA R Max 3 device. Correlation was analyzed using Kruskal-Wallis test in SPSS version 27 and R version 3.2.4.

Results

467 samples under UFH treatment were included in this analysis. The majority of these patients were treated for COVID-19 associated acute distress syndrome. Anti-Xa targets were sat at 0.3-0.5 IE/ml for standard high risk prophylaxis and 0.5-0.7 IE/ml for therapeutic anticoagulation therapy. Anti-Xa targets were characterised in 1 (<0.3 IE/ml), 2 (0.3-0.5 IE/ml), 3 (0.5-0.7 IE/ml) and 4 (>0.7 IE/ml) categories. A correlation to anti-Xa levels is shown by using CT ratio. Lower values up to 0.5 IE/ml show a narrow distribution compared to higher categories (cat.1:1,46(1,17;1,83)). At a value of >0.5 IE/ml scattering is higher. (cat.4: 2,72(2,25;3,19) For aPTT, the median varies in a small range, 52s in both category 2 and category 3.

Conclusion

Whole blood POC VET using a specific heparinase-approach (IN/HI ratio) is superior to aPTT in detecting patients in or out of targeted anti-Xa levels. POC VET might help to guide anticoagulation management in critical ill patients, being faster and potentially more widely available than lab-based anti-Xa testing.

Biomaterials
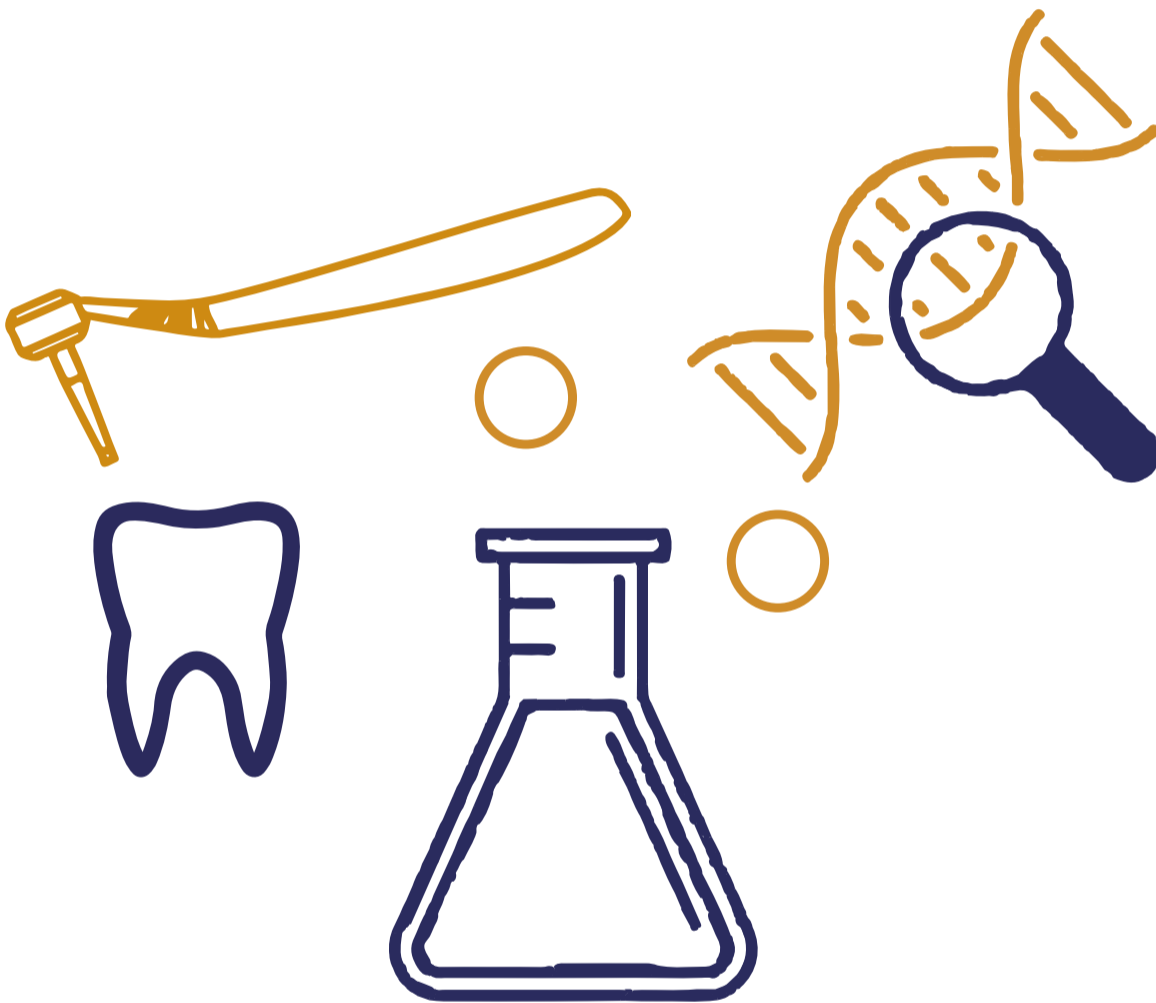
Presenters:
Nieshanth Parthiban
Branko Muskinja
Vahideh Nosrati-Siahmazgi
Mert Egemen Caliskan
Amber Beek
Samin Abbaszadeh

Iron levels are elevated in the wound bed of chronic pressure ulcers

Nieshanth Parthiban
India

Introduction

Pressure ulcers are chronic wounds that are a major health concern for patients with prolonged immobility due to spinal cord injury, degenerative nerve disorders, stroke, advanced age etc.

Though iron is required for normal wound healing process, iron-overload has been associated with the delayed wound healing in chronic non-healing ulcers. Evidence from animal studies demonstrated the beneficial effect of iron chelation on wound healing. Yet there is little information on the iron levels in the chronic wound in humans, especially pressure ulcers. In the present study, we attempted to address this lacuna, by estimating iron levels in wound biopsies collected during the surgical closure of pressure ulcers.

Material & Methods

This was a cross-sectional analytical study involving 24 patients with spinal cord injury, aged 18 to 60 years, with stage III or IV pressure ulcers, who were undergoing surgical wound closure as part of their routine treatment. Tissue samples from the wound bed and the normal skin surrounding the wound were obtained during surgery. Iron content in the samples was estimated using the bathophenanthroline dye-binding method. Demographic and laboratory data (including complete blood count, and liver and renal function tests) were recorded. The Mann-Whitney U test was used to look for significant differences in the iron content of the wound bed and normal skin. Spearman correlation was used to look for associations between iron content in these two sites. All statistical analysis were done using the SPSS 21.0 software.

Results

Iron content in the wound bed (median: 104.5 mg/g dry wt., IQR: 74.37) was significantly higher than that in the surrounding normal skin (median 91.75 mg/g dry wt., IQR: 39.13); $P = 0.032$).

Bivariate analysis showed a weak positive correlation between wound bed iron content and serum albumin levels ($r=0.349$, $p=0.056$).

Conclusion

The findings of the present study support the hypothesis that iron accumulates in the wound bed of pressure ulcers. It remains to be seen if this plays a role in impairment of the healing process, possibly by altering the wound microbiome or macrophage polarization. Ongoing work is attempting to elucidate the mechanism(s) involved.

Osteoimmunomodulatory effects of size and structure of xenogeneic bone particles on foreign body reaction as a pattern of biomaterial integration

Branko Muskinja
Serbia

Introduction

The use of bone substitutes may cause different degrees of inflammatory response which may be related to size and origin of these materials. In a whole cascade of events regarding the immune response, foreign body reaction remains the last step. Macrophages that certainly play the main role in a foreign body reaction can often merge leading to multinucleated giant cell (MNGC) formation. Considering that MNGCs have an effect on a biomaterial integration, the main objective of this study was to evaluate the intensity of a foreign body reaction.

Material & Methods

The study was conducted on an animal model featuring New Zealand rabbits. Four critical-sized defects were created on cranial vaults followed by xenogeneic bone particles filling. The tested materials were of bovine and equine origin available in two dimensions, small and large particles. Morphological features were examined using micro-CT analysis. After 4 and 8 weeks the animals were sacrificed and tissue samples were prepared for pathohistological analysis. Hematoxylin-Eosin and Masson's Trichrome stained sections were analyzed using descriptive histology and histomorphometric assessment. Furthermore, MNGCs were analyzed using histochemical and immunohistochemical methods.

Results

After 4 and 8 weeks of healing defects filled with equine derived particles showed higher number of MNGCs compared with bovine derived ones, regardless of their size. The highest number of MNGCs was present in case of small equine particles. During healing significant difference regarding decreased MNGC population was noticed between 4 and 8 weeks. In the multivariate regression analysis size of the bone substitute and healing duration were found to be significantly associated with number of MNGCs describing 77% variabilities (B=-7.38, 95CI=-13.01- -1.75, p=0.012 ; B= -4.62, 95CI = -7.65 - - 1.58, p=0.004, respectively).

Conclusion

Within the limits of the present study, it may be concluded that change in particles size can evoke a different extent of multinucleated giant cell response having decreasing tendency as healing progresses. In contrast to small particles, large ones evoke negligible nonspecific inflammatory reaction.

An Injectable Photothermal Hydrogel Incorporated with CuO Nanosheets for Skin- Tumor Therapy, and Multidrug-Resistant Infection-Induced Wound Healing

Vahideh Nosrati-Siahmazgi
Iran

Introduction

Melanoma, with more than one million patients diagnosed each year, results in significant morbidity and mortality. The conventional treatment process includes surgical excision followed by chemotherapy and radiotherapy. However, the multidrug-resistant bacteria infected-wound and severe side effects of chemotherapy and radiotherapy are still important challenges. Therefore, there is a high demand for the development of novel multifunctional biomaterials that can simultaneously treat cancer and infected wounds for efficient skin regeneration. In recent years, photothermal therapy has made significant breakthroughs as a promising strategy to treat cancers and heal created wounds by hyperthermia. Copper oxide (CuO) is an attractive candidate as a photoactive agent, which can show combined antimicrobial and photothermal effects for regenerative applications. Incorporating these nanoparticles along with regenerative drug molecules inside adhesive injectable hydrogels would allow the design of advanced formulations for skin-tumor therapy and tissue repair.

Material & Methods

CuO nanosheets were synthesized by precipitation method. Subsequently, PG hydrogel was prepared through the chemical crosslinking between poly (methyl vinyl ether maleic acid)-gelatin, followed by the incorporation of CuO and allantoin to form PGCA hydrogel. Physicochemical characterization, injectable property, and photothermal performance of the hydrogel was assessed. Furthermore, antibacterial activity, in vivo toxicity, wound healing assessment, and photothermal anti-cancer therapy of the hydrogel were evaluated.

Results

CuO nanosheets with lengths ranging from 100-400 nm were successfully synthesized. CuO nanosheets revealed good photothermal efficiency which could ablate cancer cells within 10 min at 1.5 W/cm2 power density at the concentration of 400 µg/ml. Moreover, by exploiting the intrinsic properties of CuO and Alla, the hydrogel supported angiogenesis and proliferation of cells, respectively, which resulted in wound healing acceleration after cancer ablation. In addition, the abscess model results demonstrated that CuO could effectively kill bacteria owing to the synergistic effect of hyperthermia and inherent antibacterial properties. Finally, the histopathological evaluation of the main organs of rats showed no organ damage, like necrosis and inflammation.

Conclusion

In this study, an injectable multifunctional hydrogel containing CuO and allantoin was prepared to simultaneously ablate melanoma cells and bacteria. Moreover, the hydrogel effectively promoted wound healing via stimulating fibroblast proliferation and enhancing angiogenesis.

PRP Laden Regenerative and Bioadhesive Hydrogel for Corneal Defects

Mert Egemen Caliskan
Turkey

Introduction
There have been various attempts for developing hydrogel-based biomaterials to fill in corneal defects. However, such biomaterials lack growth factors and hence are limited in promoting regeneration thereby only acting as a bioadhesive. We have therefore embarked on developing a composite PRP-laden hydrogel biomaterial with the aim of accomplishing simultaneous wound sealing and regeneration.

Material & Methods
GelMA with a prepolymer concentration of 10% was combined with varying concentrations of PRP (5% [GelMA-P5], 10% [GelMA-P10] and 20% [GelMA-P20]) and photopolymerized using a visible light crosslinking system (450-550 nm) under 100 mW/cm2 irradiation. To demonstrate wound sealing properties, a 3 mm full-thickness defect was created on bovine corneas using a dermal punch and the defects were sealed using GelMA, Tisseel Fibrin Sealant (Baxter, Deerfield, IL) and cyanoacrylate (Variclose, Biolas, TR). Corneas were mounted on an artificial anterior chamber (Coronet) and burst pressures were calculated (n= 3 for each adhesive) using a wireless pressure sensor (PASCO, Roseville, CA, USA). For assessing regenerative potential, in vitro scratch tests were performed using limbal stromal/mesenchymal stem cells (hLSSC). The wound area was monitored every 24 hours up to 3 days and the rate of wound healing was computed using the initial wound surface area as the benchmark via a software (Zen 2 Pro) integrated microscope (Carl Zeiss Axio Observer D1).

Results

Burst pressure of GelMA was 235±39.5 mmHg and improved with addition of 5% and 10% PRP (245±15.4 mmHg, 251±37.7 mmHg, respectively), while comparable values were obtained for fibrin-glue (296±27.1 mmHg) and cyanoacrylate (330±5.9 mmHg). Nonetheless, GelMA-P20 exhibited significant reductions in maximal burst pressure (134±14.7 mmHg). Wound closures rates of pristine GelMA, GelMA-P5, GelMA-P10 and GelMA-P20 at day 1 were 49%, 26%, 34% and 82%, respectively. At day 3, the most rapid wound closure was observed in GelMA-P20 (95%) followed by GelMA-P5 (87%), GelMA-P10 (80%) and pristine GelMA (74%).

Conclusion
Higher PRP concentrations up to 10% PRP showed comparable burst pressure results with conventional tissue adhesives. Furthermore, PRP-laden GelMA displayed improved regenerative effects compared to pristine GelMA, with 20% PRP demonstrating the fastest wound closure rate.

Inducing zonal distribution in a chondrocyte- laden construct by mechanical stimulation and an acellular top layer

Amber Beek
The Netherlands

Introduction
The lack of zonal distribution plays a role in the failure to treat cartilage defects. It is believed that the mechanical loading of cartilage, which is distributed by the top layer known as lamina splendens, contributes to the origin of this zonal distribution. Moreover, by using a strong biomaterial for mechanical strength, together with a hydrogel which is able to encapsulate chondrocytes, it is thought that mechanical stimulation and recreating such lamina splendens can
overcome the lack of zonal distribution in vitro. The aim of this project is therefore to induce zon-
al
distribution in a chondrocyte-laden construct, consisting of Gellan Gum (GG) and silk fibroin (SF), by dynamic mechanical stimulation together with an acellular top layer (AT).

Material & Methods
SF-GG scaffolds with varying pore sizes with or without AT were used for the preliminary experiments. Pore size was determined by obtaining the mechanical properties, soluble fraction, and visible damage. The thickness of the AT was determined by testing scaffolds without AT and with varying AT thickness by its mechanical properties. Mechanical properties were obtained for both by performing stress-relaxation tests. Here, a pre-load of 0.1N was applied with a strain of 15% for 10 minutes. Data were compared using a one-way ANOVA.

Results
The 355-425 µm pore size of the SF-GG scaffolds had a significantly lower sol-fraction compared to smaller pore sizes with 0.12(95%CI0.0004-0.2471). Larger pore sizes showed visible damage, but no differences in mechanical properties were observed (n=1). The AT layers which were 0.55 mm and thicker showed a significant difference in peak modulus, compared to scaffolds with no ATlayer with a mean difference of -140.0(95%CI-232.6—47.31). AT layers of 0.45 mm showed were not significant while the mean difference was -59.37(95%CI-1.52.0-33.29).

Conclusion
Optimized scaffolds can be achieved which can handle the mechanical load and have a high crosslinking rate. The AT layer of 0.55 mm is able to increase the mechanical properties significantly, but still be as thin as possible to be comparable to native lamina splendens. Upcom-
ing
experiments will focus on dynamically stimulating chondrocyte-laden SF-GG scaffolds for a peri-
od
of 28 days.

A Multi-functional Injectable Hydrogel for Photo-Chemo-Immunotherapy of Cancer

Samin Abbaszadeh
Iran

Introduction

Photothermal therapy (PTT) has attracted extensive attention in cancer therapy owing to the minimal damage to non-target tissues. Bi2S3 nanorods (NRs) are promising photothermal agents for cancer therapy due to their light-to-heat conversion ability to induce apoptosis in tumor cells. Combination of PTT with chemotherapy and immunotherapy has a high potential to increase the chance of cancer eradication without metastasis to other vital organs. In this work, cancer cell- membrane (CCM) and sorafenib (SFN) were loaded into a photoactive injectable hydrogel to render tumor-specific immunotherapeutic function and chemotherapy to the prepared hydrogel.

Material & Methods

Bi2S3 NRs were prepared using a simple chemical reaction and coated with hyaluronic acid to form BiH NRs. An injectable hydrogel of poly methyl vinyl ether-maleic acid (PMVE-MA) and gelatin was prepared via chemical crosslinking. BiH NRs, CCM, and SFN, were loaded within the hydrogel. The physicochemical characterization and photothermal performance of the NRs and hydrogels were assessed. Afterward, the in vivo toxicity, the antibacterial activity of the hydrogels, and its anti- cancer effect were evaluated on a 4T1 tumor-bearing mouse model.

Results

The rod shape nanoparticles, with an average particle size of about 57 nm were successfully loaded into the chemically crosslinked hydrogel, which had good injectability. BiH NRs demonstrated sufficient temperature elevation to kill cancer cells after 10 min of near infrared (NIR) irradiation. No abnormality was observed in the histopathological analysis of the main organs of treated groups. In addition, the BiH loaded hydrogel showed very potent antibacterial activity. The combined intratumoral photo-chemo-immunotherapy demonstrated more anticancer effect than the individual photo-, chemo- or immunotherapy alone.

Conclusion

In this study, an injectable hydrogel containing BiH NRs, CCM, and SFN is reported for cancer ablation via a synergistic effect. In addition, the injectable hydrogel had the capability to load drugs for sustained release at the cancer tissues over a long period.

Cardiology
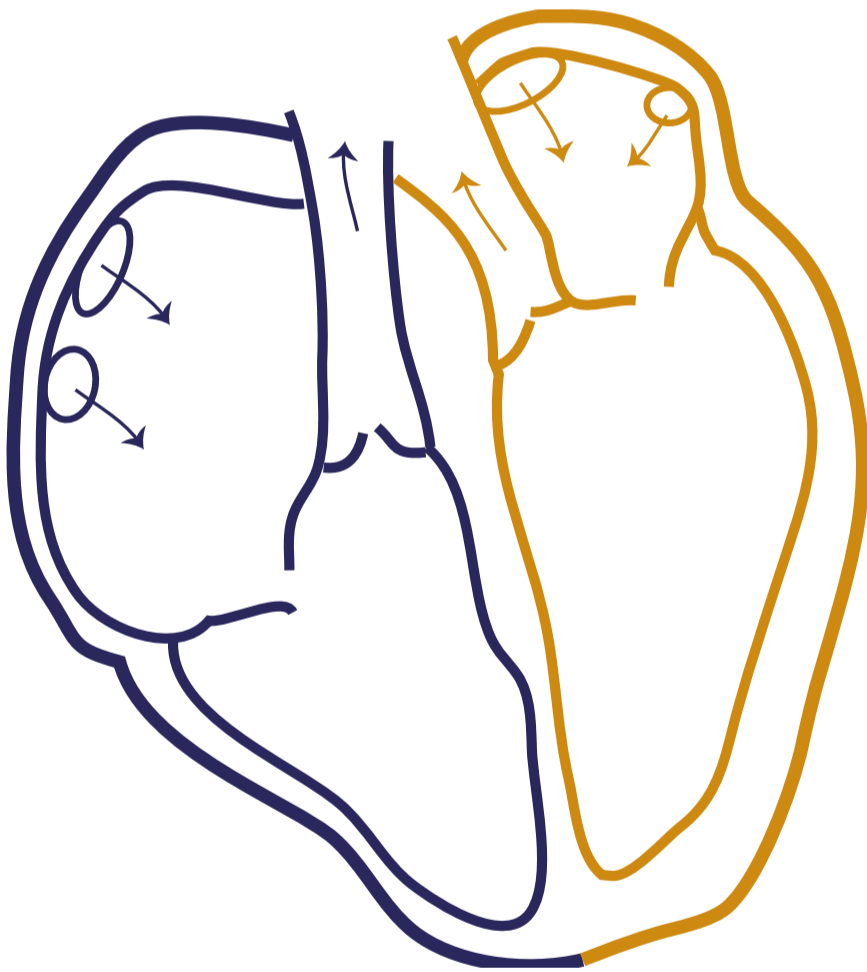
Presenters:
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Jakub Tomaszewski
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Mohammadsadegh Vaziri
Maximilian Greiner
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'Sex Specific Association of Cardiovascular Risk Factors with Incident Cancer'

Merel Maronier
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Introduction

Several cardiovascular (CV) risk factors are known to be associated with cancer. Whether CV risk factors associate differently with incident cancer in men and women is unclear. This study investigated the sex-specific associations of multiple risk factors with incident cancer. Risk factors include age, smoking, height, hypertension, type-2 diabetes, abdominal obesity, 24-h urinary creatinine excretion (UCE; reflecting muscle mass), 24-h urinary albumin excretion (UAE; reflecting endothelial dysfunction) and C-reactive protein (CRP; reflecting inflammation).

Material & Methods

This study used data from PREVEND (Prevention of Renal and Vascular End-Stage Disease), an observational, community-based prospective cohort study (1997-1998) from the Netherlands. The baseline cohort exists of n=8592, after exclusion of prevalent cancer the final sample resulted in n=8312. Age-adjusted Poisson regression was used to calculate the incidence rate ratio (IRR) reflecting cancer risk. STATA version 14.2 was used (StataCorp).

Results

During the mean follow-up period of 17.6 (Q1-Q3: 17.3-17.9) years, 682 (16.5%) and 551 (13.2%) cancer events occurred in men and women, respectively. Mean age of cancer diagnosis was lower in women than in men (59.8 vs. 53.1 years; Pdiff = <0.001). Age ≥ 65 years was strongly associated with cancer in both sexes, but was more pronounced in men: IRRmen = 3.13 [95%CI: 2.68-3.65] vs. IRRwomen = 1.66 [95%CI: 1.34-2.05]; Pdiff = <0.001). Smoking was associated with cancer in both sexes [IRRmen = 1.36[1.17-1.59] IRRwomen= 1.50[1.27-1.78]. Height and UCE was associated with cancer only in women [Height: IRR= 1.29[1.05-1.58]; Pmen= 0.351 vs. Pwomen= 0.014], [UCE: IRR= 1.47[1.22-1.76]; Pmen = 0.509 vs. Pwomen=<0.001]. In contrast, a high CRP level was associated with cancer only in men: IRR = 1.33[1.13-1.55]; Pmen= <0.001 vs. Pwomen= 0.895. No significant association was found for diabetes and hypertension.

Conclusion

Age and smoking status were strongly associated with cancer development in both sexes. Height and 24-h creatinine excretion were significant associated with cancer in women. In men, C-reactive protein, was associated with cancer. Diabetes and hypertension were not significantly associated in both sexes. This suggest that CV risk factors affect men and women differently in association of future cancer. Further examining these differences is essential for improving sex-specific cardiovascular and oncological clinical aspects.

The effect of post-infarction heart failure and high-fat diet on iNOS expression and IRE1α- XBP1 pathway activity

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Poland

Introduction

The consumption of fat-rich products is continuously growing worldwide. Dietary fat overload promotes cardiac remodeling leading to unfavorable outcomes after myocardial infarction (MI). Recent studies unveiled the critical role of nitrosative stress (NS) in the development of heart failure (HF). It consists of two important elements: the overexpression of inducible nitric oxide synthase (iNOS) and the inefficient unfolded protein response (UPR) pathway – particularly the XBP1s- IRE1α branch. We examined the impact of high fat diet (HFD) on the myocardial NS after MI-HF.

Material & Methods

We performed the study on 29 male adult Sprague Dawley rats. We assigned them to groups and fed them for 8 weeks with normal diet (NFD) and HFD. Then, on the 12th week of age, we performed surgical procedures: evoking of MI (HF-NFD, HF-HFD) and sham operation (SO-NFD, SO-HFD). 4 weeks past the procedures, we sacrificed the animals, collected heart tissue and blood for further analysis. NT-proBNP concentration in blood was measured to confirm the HF development. We performed Western blot to evaluate the levels of the following proteins in the heart tissue: IRE1α, phosphorylated IRE1α (pIRE1α), iNOS, and β-actin as a control.

Results

Both HF-HFD and HF-NFD groups developed post-MI HF according to higher plasma NT-proBNP concentration compared to SO groups. The expression of iNOS in the heart tissue corresponds to NS. The HF-HFD group presented the highest expression of all the groups, significantly higher when compared to the control (SO-NFD). Our data imply that isolated HFD or MI is insufficient to cause persistent NS. The ratio of pIRE1α to IRE1α represents the activity of the UPR pathway. The IRE1α activity was downregulated in HF-HFD, but not in the HF-NFD. The data suggest that HFD significantly downregulates the UPR pathway after MI-HF.

Conclusion

Our findings suggest that MI increases NS and downregulates the UPR pathway in HFD rats, but not NFD. Therefore, it can be implied that patients after MI should be highly restricted from high-fat products to prevent inducing NS and impairing UPR. This is a new perspective in future studies – the NS and UPR pathway as a therapeutical target in HF development.

AngioScore: an artificial intelligence tool to assess coronary artery lesions

Ewelina Błażejowska
Poland

Introduction

Background: The SYNTAX Score is a coronary angiography-based scale used to determine the complexity of coronary artery disease and the risk associated with its invasive treatment. Currently, the SYNTAX Score is assessed with an online calculator available at www.syntaxscore.com. However, the evaluation process is subjective, depends on the experience of the physician, and requires manual input of all assessed parameters. Objectives: We aimed to create an artificial intelligence-based tool that helps assess lesions objectively by determining the SYNTAX Score value. In partnership with the programmers from the Gdansk University of Technology, a prototype of an online application AngioScore was developed and trained to independently assess nine parameters of the SYNTAX Score (diseased segment, total occlusion, bifurcation, trifurcation, aorto-ostial lesion, severe tortuosity, length >20mm, heavy calcification, thrombus).

Material & Methods

Using AngioScore, two medical students independently evaluated 100 randomly selected coronary artery lesions. Once a student has marked the lesion on an angiogram derived from the 1st Chair and Department of Cardiology, Medical University of Warsaw, AngioScore determined an initial SYNTAX Score value. Next, a student identified parameters requiring manual correction and recorded their number. Statistical analysis was performed in a Microsoft Excel spreadsheet.

Results

19% of the coronary artery lesions were assessed fully correctly. Of the remaining 81%, 42% required correction of 1 of 9 parameters, 38.3% - 2 parameters, 17.3% - 3 parameters, and 2.4% - 4 or more parameters. A median number of required corrections was 1 with a standard deviation of 1.04. Incorrectly assessed lesions were in the left anterior descending artery, right coronary artery, and circumflex branch of the left coronary artery (39.51% vs. 30.86% vs. 29.63%, respectively). Parameters that most often required corrections were: diseased segment (55%), bifurcation (33%), and severe tortuosity (23%). In 25 cases of bifurcations and 5 cases of severe tortuosity, the system assessed that the lesion did not exist when it did. In 6 cases of bifurcation and 2 cases of severe tortuosity, the system assessed that a lesion existed in case of no presence of the lesion.

Conclusion

The prototype of AngioScore showed promising results regarding the accuracy of determination of the SYNTAX Score value. Thus, further development of our tool may lead to a faster and more objective way to assess coronary artery lesions.

Magnesium Supplementation May Reduce Coronary Artery Disease Complication through Downregulation of IL-18 and TNF-alpha

Mohammadsadegh Vaziri
Iran

Introduction
It is demonstrated that inflammation is involved in the pathogenesis of coronary artery disease. This study was performed to evaluate the effect of oral magnesium sulfate (MgSO4) administration on the gene expression and serum levels of inflammatory cytokines including TNF-alpha, IL-18, IL-1β, IL-6 and IFN-gamma in patients with moderate coronary artery disease (CAD).

Material & Methods
This study was a randomized, double-blind, placebo-controlled trial among 60 patients with moderate CAD (55-69% stenosis) who were selected based on angiography findings. Participants were randomly divided into two groups that received 300 mg/day magnesium sulfate (n = 30) or placebo (n = 30) for 3 months. Gene expression and serum levels of inflammatory cytokines were assessed at the baseline and the end of treatment using real-time RT-PCR and ELISA assay.

Results
After 3 months of intervention, the results showed that gene expression and serum levels of IL-18 and TNF-alpha in the magnesium sulfate group were significantly less than the placebo group ($P<0.05$). However, no significant difference in gene expression and serum levels of IL-1β, IL-6 and IFN-gamma was observed between magnesium sulfate and placebo groups ($P> 0.05$).

Conclusion
Based on the results of this study, the major anti-inflammatory effect of magnesium in patients with CAD is probably through reduced expression level of IL-18 and TNF-α. This finding indicates that the magnesium supplementation may be beneficial in alleviating CAD complications by modulating inflammatory cytokines.

Reconstruction of a full diagnostical 12-lead electrocardiogram from a 3-lead orthogonal electrocardiogram by using Novel Neural Networks

Maximilian Greiner
Germany

Introduction

The electrocardiogram (ECG) as a central sensor for monitoring patients is ubiquitous in the clinic. Up to now, a distinction has been made between a diagnostic ECG and an ECG for monitoring critically ill patients. Up to 17 electrodes are used for diagnostic purposes. For monitoring, this is too laborious and error-prone, and five electrodes are used. Using three orthogonal leads any other lead can be reconstructed by transformation-algorithms. In this work, the previous linear algorithms are compared with modern nonlinear approaches from deep learning.

Material & Methods

The PTB diagnostic ECG database was used to evaluate the accuracy of 12-lead ECG reconstruction using a multilayer perceptron (MLP) and long short-term memory (LSTM) implemented in PyTorch, compared to a multiple linear regression (MLR) approach. The evaluation was performed using Root Mean Square Error (RMSE) and Mean Absolute Percent Difference (MAPD) on 10% of the dataset, which consists of 12-lead and 3-lead orthogonal ECGs from 245 patients.

Results

The MAPD achieved by the MLP model ($p=0.03$) and for the LSTM model ($p=0.01$) is significant better in comparison to the value the MLR. A significant difference is shown in the RMSE value for the MLP ($p=0.03$) and LSTM ($p=0.01$) as well. Additionally, the LSTM model demonstrated superior performance in terms of reconstruction results, as it was able to decrease the overall error (as measured by RMSE) by 8% in comparison to the MLR.

Conclusion

The usage of neural networks for the reconstruction of a 12-lead ECG shows significant improvement for the MLP and the LSTM in comparison to multiple linear regression by overcoming the linear approach. The performance of the LSTM shows the best results due to its capability to learn long-term dependencies. In future studies, the reconstructed ECG should be evaluated beyond the metric evaluation in terms of diagnostic relevance by cardiologists.

Anti-thrombotics in transcatheter aortic valve implant. A network Meta-analysis

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Egypt

Introduction
Transcatheter aortic valve implantation (TAVI) shown its efficacy to be mainstay treatment for aortic valve diseases over surgical options, yet postoperative antiplatelet regimen after TAVI is still debatable. Thus, the aim of our network is to further investigate the safety and efficacy of direct oral anti-coagulants (DOAC) vs single- antiplatelet therapies (SAPTs) vs dual-antiplatelet therapies (DAPT) vs Vitamin K in patients undergoing transcatheter aortic valve implantation.

Material & Methods
PubMed, Web of Science, Scopus, and Embase, were systematically searched from inception to December 2022. A frequinest network meta-analysis has been conducted using random-effects method model calculating the risk ratio (OR) with a 95% confidence interval (CI).

Results
9,087 patients from 11 studies were included. Regarding short-term outcomes, compared to DOAC, DAPT, SAPT, and vit K all were associated with a significantly lower odds for all-cause mortality with OR [0.66; 95% CI 0.46-0.86], [0.44; 95% CI 0.29-0.60], [0.64; 95% CI 0.31, 0.94], respectively (Fig 1A). Although, non-of the interventions has statistically significant difference over DOAC in terms of cardiovascular death (Fig 1B), DAPT was associated with statistically significant more than 2 folds high odds for major vascular bleeding with OR [2.66; 95% CI 1.46-3.86]. Furthermore, regarding long term outcomes, both DAPT and SAPT was associated with a significantly higher bleeding rates with OR [1.78; 95% CI, 1.15-2.41] and [2.32; 95% CI, 1.29-3.35], respectively yet vitamin K was associated lower bleeding rates with OR [0.61; 95% CI, 0.24-0.98]. No intervention showed significance difference over DOAC in terms of all-cause mortality, cardiovascular mortality, and stroke (Fig 1C) except for DAPT which showed higher odds of long-term all-cause mortality OR [1.83; 95% CI, 1.29-2.37].

Conclusion
Although having long term high rates of major vascular bleeding, SAPT proven its efficacy in having lower both short term and long-term all-cause mortality compared to DAPT which have both short and long term major vascular bleeding and higher long-term all-cause mortality. Vitamin K has lower rates of both short-term all-cause death and long term major vascular bleeding yet without significance in other outcomes.

General Medicine

Presenters:
Yufi Aulia Azmi
Taha Nagib
Zhen Lin
Semih Ceylan
Elahe Salarieh

Comparison of Different Scoring Systems for Predicting In-Hospital Mortality for Patients with Fournier Gangrene in Indonesia

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Indonesia

Introduction

Fournier's gangrene (FG) is a polymicrobial infection caused by necrotizing fasciitis involving the perineal and genital areas with high mortality rates. Several different scoring systems have been proposed to predict in-hospital mortality in FG; however, no study comparing different scoring systems has been done in Indonesia. In this study, we aim to compare different scoring systems for predicting In-Hospital Mortality for FG in Indonesia.

Material & Methods

This study was done in one of the largest tertiary referral hospitals in Indonesia. All FG patients hospitalized between 2012 and 2022 were included. Six different scoring systems, i.e., Fournier's Gangrene Severity Index (FGSI), Uludag FGSI (UFGSI), Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC), quick Sequential Organ Failure Assessment (qSOFA), Charlson Comorbidity Index (CCI), and surgical Apgar score (SAS) were used. Receiver operating characteristic (ROC) analysis was done to evaluate the diagnostic performance of each scoring system. The Youden index was used to determine the optimal cut-off score. Data was presented as frequency (%) and median [interquartile (IQR)]. $P<0.05$ was considered statistically significant.

Results

There were 164 FG patients (92% male, median age 52 [42-61] years old) included in the analyses. During hospitalization, 43 (26.4%) patients died. The median score of FGSI, UFGSI, LRINEC, CCI, qSOFA, and SAS upon admission was 8 [5-12], 8 [6-12], 5 [3-7], 1 [1-2], 2 [1-2], and 8 [7-8], respectively. Area under the curve (AUC) obtained from the ROC analyses was 0.96 (95% confidence interval (CI): 0.93-0.99, $p<0.001$) for FGSI, 0.87 (95%CI 0.81-0.94, $p<0.001$) for UFGSI, 0.68 (95%CI 0.58-0.77, $p=0.002$) for LRINEC, 0.67 (95%CI 0.58-0.77, $p<0.001$) for CCI, 0.84 (95%CI 0.77-0.91, $p<0.001$) for qSOFA, and 0.78 (0.70-0.85, $p<0.001$) for SAS, indicating that FGSI had the best diagnostic performance to predict in-hospital mortality. Based on the Youden index, the optimal cut-off score for FGSI was 10 (≤10 vs > 10). Using this cut-off, the sensitivity, specificity, positive predictive value, and negative prediction value was 0.93, 0.92, 0.80, and 0.97, respectively.

Conclusion

Our study demonstrated that FGSI is the most reliable scoring system to predict in-hospital mortality for FG in Indonesia, using a score of 10 as the cut-off.

Impact of emotional intelligence on psychological components among Surgeons

Taha Nagib
Libya

Introduction
Healthcare providers, particularly surgeons, are exposed to multiple stressors that could impact their performance, as well as their psychological and physical health. This study aims to assess levels of stress, anxiety and depression among surgeons in the Libyan healthcare settings, and to examine the correlation between emotional intelligence and these three psychological conditions.

Material & Methods
A cross-sectional study was conducted in January, 2023 among surgeons in 10 tertiary hospitals located in three major western Libyan cities. A self-reported questionnaire was used for data collection. The questionnaire includes sociodemographic and work-related items, the 10-item Perceived Stress Scale (PSS) to measure stress, the four-item Patient Health Questionnaire (PHQ- 4) to measure depression and anxiety, and the 33-item Schutte Self-Report Emotional Intelligence Test (SSEIT) to measure emotional intelligence. Spearman's rank correlation was used to assess the relationship between the psychological variables of interest and emotional intelligence. A one-way ANOVA was run to determine if the emotional intelligence score is different between surgeons in different surgical specialities.

Results
Out of the sample size that was distributed (250), 171 (68.4%) was included. The median age for the participants was 35 (IQR=31-43) years, and the majority of them were males (65.5%). The prevalence of stress among surgeons was as follows: mild stress = 19 (11.1%), moderate stress = 136 (79.5%), high stress = 16 (9.4%); whereas, depression and anxiety were: 59 (43.5%), 41 (24%) respectively. The median emotional intelligence score was 117 (106-125). A significant negative weak correlation was found between emotional intelligence and stress ($r = -0.254$, $p = 0.001$), and between anxiety and emotional intelligence ($r= -0.273$, $p < 0.001$). No significant difference in emotional intelligence scores of surgeons working in different surgical specialties, ($p= 0.9$).

Conclusion
Our results show that emotional intelligence negatively correlates with stress and anxiety levels. Therefore, it is recommended to integrate emotional intelligence training into undergraduate medical education to improve future doctors emotional intelligence. Further research is recommended to identify other factors that would contribute to stress, anxiety and depression among surgeons other than emotional intelligence.

Identification and prognostic effect of extramural venous invasion in locally advanced esophageal squamous cell carcinoma

Zhen Lin
The Netherlands

Introduction

The role of extramural venous invasion (EMVI) in esophageal cancer is still unclear. This study aimed to identify EMVI and to assess its impact on survival and recurrences in esophageal squamous cell carcinoma (ESCC).

Material & Methods

Retrospectively, we reviewed resection specimens of 147 locally advanced ESCC (pT3-T4aN0-3M0) patients who had a curative intended surgery alone at the Cancer Hospital of Shantou University from March 2009 to December 2013. After confirming pT≥3 in hematoxylin-eosin tumor slides, EMVI was evaluated by Verhoeff and Caldesmon staining. The impact of EMVI with other clinicopathological characteristics and survival were analyzed using the Chi-square test, Cox regression and Kaplan-Meier method.

Results

EMVI was present in 30.6% (45/147) of the p≥T3 ESCC's and associated with lymph-vascular invasion and poor differentiation grade ($p < 0.05$). Disease-free (DFS) and overall survival (OS) in patients with EMVI-absent tumors were about 2.0 times longer than in those with EMVI-present tumors. In pN0 patients, EMVI-presence was associated with poor OS (HR 4.829, 95% CI 1.434-16.26, $p = 0.003$) and DFS (HR 4.026, 95% CI 0.685-23.32, $p = 0.018$). In pN1-3 patients, EMVI had no additional effect on survival.

Conclusion

EMVI has an independent adverse prognostic effect on survival in ESCC patients after surgery alone. EMVI should be included in pathology reports as it might contribute to identify high risk patients for potential additional treatment.

Comparison of corneal epithelial and stromal thickness and its distribution in keratoconus, ectasia susceptibility and healthy controls.

Semih Ceylan
Turkey

Introduction

Optical coherence tomography (OCT) is a noncontact imaging modality which shows the corneal epithelial thickness (CET) pattern with high accuracy thanks to its high axial resolution. In the early diagnosis of ectatic disorders, measurement of CET and its distribution across the corneal surface is clinically important. In early ectasia, epithelial thinning on the cone apex may mask the topographical changes in the anterior corneal surface. We aimed to evaluate the variation in corneal epithelial and stromal thickness along with its distribution in eyes with keratoconus (KC), ectasia susceptibility (ES) and healthy controls.

Material & Methods

Subjects were recruited from extended sample of a population-based keratoconus (KC) prevalence study conducted at the Eskişehir Osmangazi University Hospital. Subjects were classified as KC, ES and normal based on Pentacam (Oculus). Minimum and maximum epithelial (Min-ET and Max- ET) and stromal thickness (Min-ST and Max-ST) values along with their coordinate-wise locations were obtained from anterior segment OCT (Optovue Inc.) scans. Linear mixed model analysis with Bonferroni correction was used for across group comparisons. $p < 0.05$ was considered statistically significant.

Results

A total of 896 subjects were included in the study, out of which 17 were KC, 16 were ES, and 863 were healthy. The mean age was 21.6 ± 2.4 years, and 65.8% (n=590) were female. Although minimum and maximum epithelial thicknesses were similar between healthy controls and ES, KC eyes showed significantly greater Max-ET and thinner Min-ET values (approximately 3 – 4µm, all $p < 0.05$). Likewise, minimum and maximum stromal thicknesses significantly deviated in eyes with KC from their counterparts in normal and ES groups (approximately 50 – 70µm, all $p < 0.05$). A 1 mm inferior and inferotemporal deviation in the thinnest stromal thickness location (reference: corneal apex) seemed to have increased the likelihood of KC presence by an odds ratio of 14.4 (p=0.01) and 57.3 folds (p=0.005), respectively.

Conclusion

In our study, epithelial and stromal thickness variability was greater in eyes with KC, however no significant differences were observed between ES and healthy controls. These results support epithelial and stromal remodeling in KC. An inferotemporal deviation in minimum stromal thickness location significantly increased the risk of KC presence.

Health-Related Quality of Life in Patients with Melasma Compared to Healthy Controls inSari, the years of 2018-2019

Elahe Salarieh
Iran

Introduction
Melasma is an acquired hypermelanosis that occurs in the form of macules and irregular patches of light to dark brown and in the form of scaly in the areas exposed to sunlight. The importance of examining the quality of life of these patients is that it can help us understand the severity of the disease, provide better medical services to these people, and plan to improve their quality of life in terms of activity, work efficiency, mental health and Provide preventive recommendations to help them. Therefore, the purpose of this study is to investigate the quality of life in melasma patients and compare it with the healthy control group.

Material & Methods
The present study is a case-control study and is conducted between two groups, the first group includes 50 people who are suffering from melasma and the second group includes 50 healthy people who are companions of the patient and do not have exclusion criteria, and in terms of age, sex, and the group of patients are the same Demographic information of people was recorded. WHOQOL questionnaire was filled by healthy people. MASI Score was calculated for people with melasma. DLQI and MELASQOL questionnaires were also completed for the patient group. After collecting the data, data analysis was done with SPSS version 16 software and the significance level was considered less than 0.05.

Results
The average age of the patients was 38.84 ± 6.14 years with a minimum age 28 and a maximum of 54 years, and the average age of the control group was 39.22 ± 5.77 years with a minimum age of 28 and a maximum age of 52 years. The average mental health scale was significantly lower in the patient group (P-value=0.017). There is no significant difference between treatment history and marital status groups (P-value > 0.05). In our study, it was shown that MASI score has a direct relationship with DLQI results (P-value=0.007). This means that as the severity of the disease increases, the DLQI score also increases (or the quality of life decreases). According to the value of Pearson's coefficient, this relationship is weak.

Conclusion
The results of the present study showed that in the WHOQOL scale scores, only the mean of the mental health scale was significantly lower in the patient group. Also, with the increase in the severity of the disease, the DLQI score also increased (or the quality of life decreased).

Haematology and Endocrinology
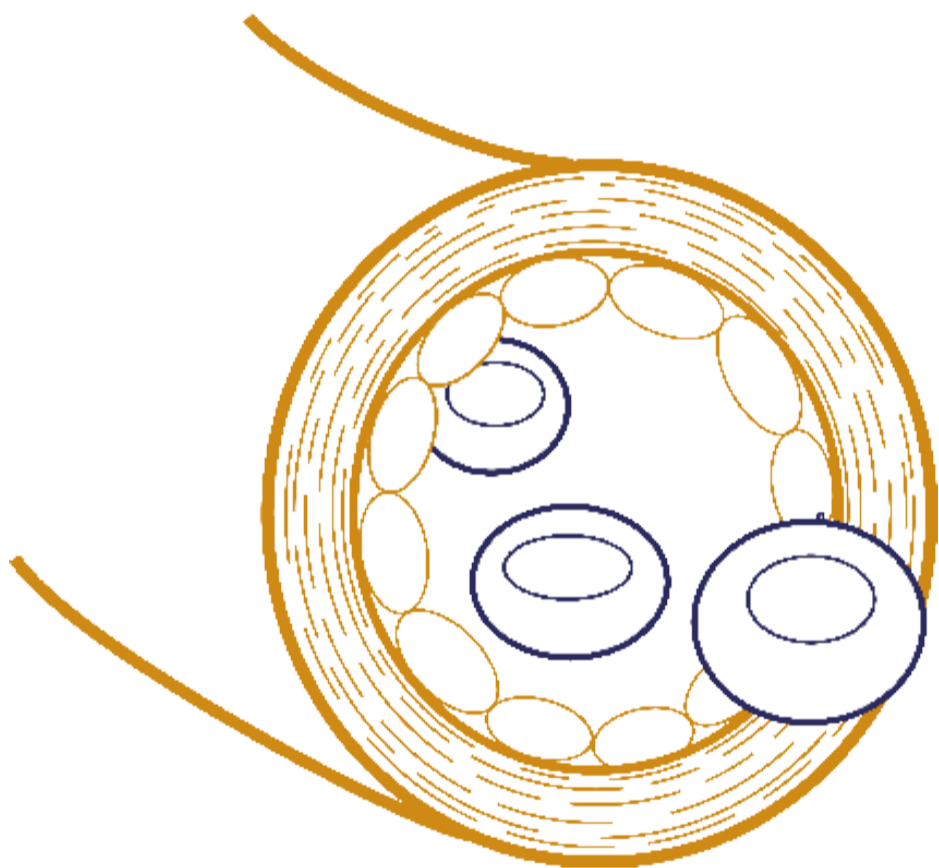
Presenters:
María Moena
Fynn Elvers
Catalina Codreanu
Kahan Mehta
Miłosz Majka

30-Second Sit-to-Stand Power Test is Better Tool to Assess the Motor Impairment than Isometric Voluntary Contraction in People with Haemophilia.

María Moena
Chile

Introduction

Joint health in people with hemophilia (PWH) must be evaluated periodically due to the risks of hemarthrosis and the potential deterioration of motor function. Usually, maximal voluntary isometric contraction (MVIC) is used to assess motor impairment in PWH. However, skeletal muscle power may be a stronger predictor of functional limitations than isometric strength. Therefore, the application of the 30-second sit-to-stand test (STS30s) can be an easy and quick functional test to evaluate motor impairment in PWH. This study aimed to compare the number of repetitions of STS30s, STS30s power (STSpower), and MVIC between PWH and the control group (CG).

Material & Methods

This cross-sectional study collects information from PWH and a sedentary CG according to the international physical activity questionnaire. The MVIC of knee extensors was assessed using a force cell attached to the dominant leg. The number of repetitions of the STS30s was used to calculate the STSpower based on the formula proposed by Alcázar et al. (2020). An independent t- test was used to compare the number of repetitions of STS30s, the absolute power of STS30s, STSpower normalized by body weight (power relative) and height (power allometric), and MVIC normalized by weight between groups MVIC. PWH received the usual prophylaxis to prevent bleeding events before the assessments. A local ethics committee approved this study.

Results

The data from the PWH (n=13) and GC (n=7) were analyzed. The mean age of the groups was (34.7 ± 11.1) and (35.8 ± 16.8), respectively. A significant difference was observed in the absolute power (p=0.018, effect size=1.21, large) and allometric (p=0.009, effect size=1.40, large) between groups . No differences were observed in the number of repetitions of STS30s (p=0.073, effect size= 0.856, large), power relative (p=0.081, effect size=0.82, large), and MVIC (p=0.068, effect size=0.86, large) between groups.

Conclusion

In conclusion, this study provides evidence that STSpower is more effective for assessing motor impairment in PWH than MVIC. These findings suggest that healthcare professionals should consider incorporating the STS30s test into their routine evaluations of PWH.

In vivo generation of thrombin in patients with liver disease without activation of the intrinsic or extrinsic pathway of coagulation

Fynn Elvers
The Netherlands

Introduction
Patients with liver diseases are in a hypercoagulable state as evidenced by enhanced in vitro thrombin generating capacity and elevated plasma levels of markers of in vivo thrombin generation. This hypercoagulable state may contribute to thrombotic risk in liver disease, as patients with liver disease are at increased risk for development of venous thromboembolism (VTE). However, it is currently unknown by which mechanism in vivo activation of coagulation occurs. We aimed to clarify mechanisms underlying enhanced in vivo thrombin generation to provide a rationale for targeted anticoagulant therapy.

Material & Methods
191 patients diagnosed with stable (SC) or acutely decompensated cirrhosis (AD), acute liver failure (ALF) or injury (ALI), acute-on-chronic liver failure (ACLF), or sepsis without underlying chronic liver disease were recruited from King's College Hospital, London from 2017-2021 and compared to reference values of 41 healthy controls. We measured levels of markers of in vivo activation of coagulation, markers of activation of the intrinsic and extrinsic pathway, their respective zymogens and natural anticoagulants.

Results
Thrombin-antithrombin complexes (TAT), prothrombin fragment 1+2 (F1+2) and D-dimer levels were increased in acute and chronic liver disease, proportional to disease severity. Plasma levels of free activated factor XII (FXIIa), C1-esterase-inhibitor (C1inh)-FXIIa, C1inh-Factor XI (FXI), C1inh-plasma kallikrein (PKa), Factor-VIIa-Antithrombin-complexes (FVIIa-AT) and activated FVII (FVIIa) were reduced in acute and chronic liver disease, even after adjusting for zymogen levels, that were also substantially reduced. Natural anticoagulants antithrombin (AT) and protein C (PC) were profoundly reduced in liver patients.

Conclusion
This study provides evidence of enhanced thrombin generation in liver disease without detectable activation of the intrinsic or extrinsic pathway. We propose that low-grade activation of coagulation is highly amplified due to improper regulation of coagulation by deficiencies in natural anticoagulants AT and PC. Future studies should further explore whether activation of the intrinsic or extrinsic pathway is responsible for the generation of thrombin. Adequately targeted anticoagulants may then be used to prevent or treat thrombotic complications of liver diseases

Thrombosis incidence in newly diagnosed multiple myeloma patients treated with immunomodulatory drugs at a university medical center

Catalina Codreanu
The Netherlands

Introduction

Newly diagnosed multiple myeloma (NDMM) patients have a high venous thromboembolism (VTE) risk, reaching 15% in some studies. Despite current thromboprophylaxis guidelines, a high VTE incidence persists. It is yet unclear whether NDMM patients have a higher arterial thrombosis (AT) risk than the general population, with incidences ranging from 1.2% to 2.7%.

Material & Methods

This retrospective cohort study seeks to calculate the VTE and AT cumulative incidence with death as competing risk (95% confidence interval (CI)) for NDMM patients receiving IMIDs at the University Medical Centre Groningen (UMCG) within 1-year. Follow-up started at diagnosis and ended at death, VTE, or at 1 year. The local committee waived ethical approval (METc 2022/285). The local guideline recommends aspirin for NDMM patients receiving IMIDs without, and "nadroparin 5700 EH once daily" for patients with VTE risk factors. VTE incidence was additionally calculated stratified per whether patients received thromboprophylaxis as advised or more and insufficient or no thromboprophylaxis. Analyses were performed in R v4.1.3.

Results

72 patients were included, 29 (40.3%) of which received aspirin, 25 (34.7%) prophylactic low molecular weight heparin (pLMWH), 5 (6.9%) no thromboprophylaxis and 13 (18.1%) other. 1 (1.4%) patient died and 1 (1.4%) was lost to follow-up. 7 (9.7%) experienced VTE (incidence 9.8 (95% CI, 4.3, 18.1)) and 1 (1.4%) experienced AT (incidence 1.4 (95% CI, 0.1, 6.8)). For the stratified thromboprophylaxis analysis, 4 patients with missing data for VTE risks were excluded. 27 (39.7%) patients had none and 41 (60.3%) had 1 or more risks. 47 (69.1%) patients received thromboprophylaxis as advised or more and had a 8.6 (95% CI, 2.7, 18.9) VTE incidence, whereas the 21 (30.9%) patients that received insufficient or no thromboprophylaxis had a 14.3 (95% CI, 3.4, 32.6) incidence.

Conclusion

VTE incidence remains unacceptably high despite thromboprophylaxis. AT incidence was within the previously reported ranges, although a larger cohort is needed to compare to the general population. Patients that received adequate or more thromboprophylaxis appear to have a lower VTE risk. New RCTs are needed investigating novel strategies such as DOACs.
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Identification of rare single-nucleotide variants associated with extreme phenotypes of type 2 diabetes.

Sara Fernanda Arechavala Lopez
Mexico

Introduction

Introduction: Type 2 diabetes (T2D) comprises a group of common metabolic disorders characterized by hyperglycemia. In Mexico, it is the leading cause of permanent premature disability and the second-most cause of mortality. Recently, efforts have been made to characterize the genetic basis of T2D in the Mexican population, revealing the existence of alleles typical of this population. We aimed to identify rare single nucleotide variants associated with extreme phenotypes of T2D and thus be able to distinguish monogenic forms of T2D from polygenic ones.

Material & Methods

Materials & Methods: In a sample of 996 exomes from patients with T2D, individuals with fasting blood glucose ≥ 250 mg/dL and carried pathogenic SNVs according to Annovar annotation were identified, the presence of MODY diabetes was ruled out. Finally, the clinical and biochemical characteristics between pathogenic SNV carriers vs non-carriers were analyzed.

Results

Results: We identified 50 unrelated individuals who presented extreme T2D phenotypes and who carried pathogenic SNVs according to the in-silico prediction. The mean age diagnosis was 50 years ($p < 0.05$, 95% CI), correspondingly, there was a significant increase in the values of glucose, total body fat, visceral fat, HbA1c, and triglycerides ($p < 0.05$, 95% CI); as well as a decrease in insulin values in carriers compared to non-carriers ($p < 0.05$, 95% CI). These SNVs were found in 529 genes, mainly expressed in endocrine tissues, liver, adipocytes, and skeletal muscle.Endocrine gland-related genes in carrier patients showed elevated levels of cholesterol, HbA1c, insulin, and triglycerides ($p < 0.05$, 95% CI), while genes related to ATP-binding sites showed high values of total body fat, visceral fat, BMI, and waist circumference ($p < 0.05$, 95% CI), genes from both pathways showed elevated glucose levels compared to non-carriers ($p < 0.05$, 95% CI).

Conclusion

Conclusions: Patients carrying genetic variants presented characteristics of the extreme T2D phenotype. With more studies, these variants could help to differentiate the monogenic forms of T2D from the polygenic allowing identifying susceptible genetic relatives, providing genetic advice, and contributing to the development of precision medicine.

Efficacy and Tolerability of Intravenous versus oral Iron for IDA in IBD Patients: An Updated Systematic Review and Meta- Analysis

Kahan Mehta
India

Introduction

Anemia is proven to be Inflammatory bowel diseases' most common extra-intestinal complication, and it has been associated with worse IBD prognosis, increased hospitalization rates, and reduced quality of life. Therefore, IBD patients must be regularly screened for IDA and adequately treated. Supplementary iron can be administered orally or intravenously (IV), but it is largely debated and many physicians still need to decide which iron should be supplemented orally or intravenously. Our goal was to compare the effectiveness and tolerability of oral and intravenous (IV) iron supplementation for treating anemia in adult IBD patients.

Material & Methods

We conducted a systematic review and meta-analysis of randomized controlled trials that included adults with IBD and compared IV to oral iron for treating iron deficiency anemia. Through December 2022, the databases PubMed, Web of Science, Scopus, and Cochrane Central Register of Controlled Trials were searched. Two reviewers independently extracted research results and data. According to the Cochrane risk of bias assessment tool (RoB2), another two reviewers graded each trial's risk of bias independently. A fixed-effect model was used to obtain pooled odds ratio (OR) estimates and their 95% confidence intervals (CI).

Results

Five trials that included 910 IBD patients were eligible. The newly published RCT, by Howaldt et al., contributed to 27% of the population in this meta-analysis. IV iron was shown to be more effective than oral iron for raising hemoglobin levels to ≥ 2.0 g/dL (OR: 1.44, 95% CI: 1.09 - 1.91, P = 0.01). The IV iron group had decreased rates of treatment withdrawal prompted by adverse effects or intolerance (OR: 0.23, 95% CI: 0.12 - 0.44, P < 0.0001). Across all studies, we detected no proof of heterogeneity, but the risk of bias was significantly high.

Conclusion

IV iron seems more efficient and well-tolerated than oral iron for treating anemia associated with IBD.

High-fat diet-induced metabolic syndrome inhibits the cardioprotective effect of ischemic preconditioning - the potential role of adipokines.

Miłosz Majka
Polska

Introduction

Metabolic syndrome is a crucial risk factor for developing cardiovascular diseases, particularly atherosclerosis and coronary heart disease. It aggravates myocardial infarction by promoting ischemia-reperfusion injury and worsens the prognosis of patients with myocardial infarction. The intervention that reduces the size of the infarction is ischemic preconditioning (IPC). However, its effect is lower in obese and diabetic patients. One of the factors that may intensify myocardial damage in myocardial infarction and limit the conditioning effect is the change in the profile of adipokines secreted by adipose tissue.

Material & Methods

Male Sprague Dawley rats were fed with high-fat (HFD) or standard (ND) diet to induce the metabolic syndrome. Next, the myocardial infarction was induced by occlusion of a branch of the coronary followed by reperfusion. In two groups (HFD and ND), myocardial infarction was preceded by IPC, consisting of two brief arterial occlusions and reperfusions. We determined the concentrations of adiponectin and leptin in blood and adipose tissue by ELISA tests, and mRNA expression of adiponectin and leptin receptors in the heart by RT-PCR.

Results

The HFD group developed the metabolic syndrome, including a two-fold increase in visceral fat and an increase in glycemia and insulin resistance. We observed an increase in leptin concentrations in plasma and adipose tissue of HFD subjects, but no differences in adiponectin concentrations. The expression of receptors for these adipokines in the heart did not differ between the groups. The ischemia-reperfusion injury was significantly ameliorated in ND subjects subjected to ischemic preconditioning, which was ineffective in HFD subjects.

Conclusion

These data show that the metabolic syndrome induced by a high-fat diet can diminish the ischemic preconditioning leading to greater myocardial damage. This effect may be related to a change in the adipokine profile, but the exact mechanism requires further study.

Neurology
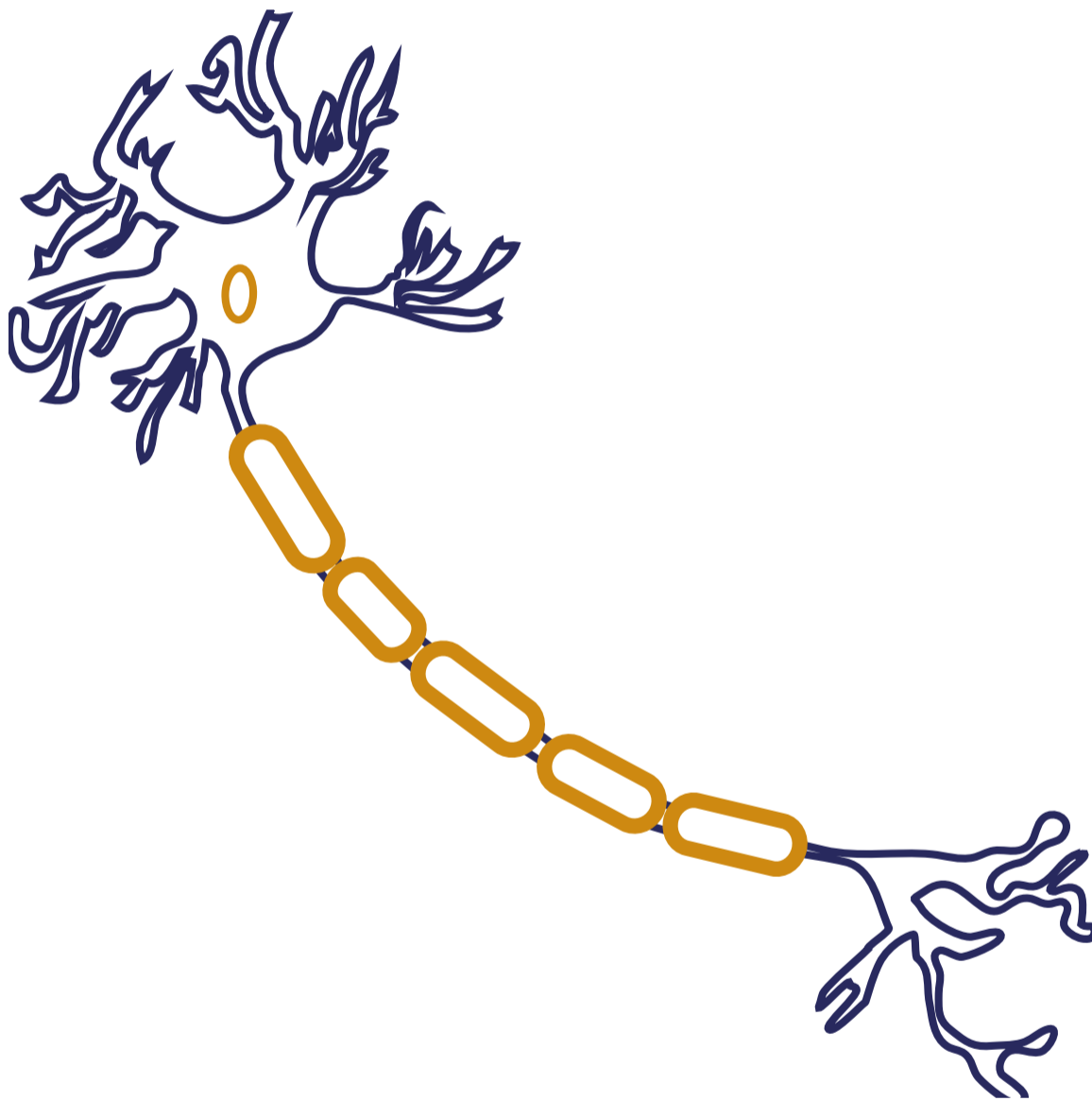
Presenters:
Blanka Buszta
Péter Kozák
Mohammad Abuawwad
Shreyans Singhvi
Ali Alishavandi
German Ramos Passarello

Ventriculoperitoneal shunts in patients with myelomeningocele – surgical approach, complications, birth weight: a preliminary study

Blanka Buszta
Poland

Introduction

Hydrocephalus is one of the most common complications after myelomeningocele (MMC) repair, leading to shunting dependence in many patients. Limited data is available on the birth weight of hydrocephalic MMC patients, and the surgical approach used during ventriculoperitoneal (VP) shunting. Infection rates and complications related to the timing of the shunt placement in MMC infants vary between studies. The aim of our research was to investigate above mentioned aspects in infants with MMC and to compare selected variables to the non-MMC hydrocephalic patients.

Material & Methods

125 patients with hydrocephalus were retrospectively reviewed. Data on surgical approach and complications (defined as infection, a need for rehospitalization, or catheter replacement) was collected. Z-test was utilized for statistical analysis. The subgroup of MMC patients included 21 infants. Additional data gathered for the analysis of MMC patients included birth weight and the interval between the MMC repair and ventriculoperitoneal shunting.

Results

Among the 21 patients with MMC, 13 (62%) developed complications after VP shunt placement, and 5 (24%) were due to infection. In the non-MMC group, complications were present in 50% of patients, with an infection rate of 12,5%. The differences in complication rate ($p=0.32$) and infection rate ($p=0.18$) were statistically insignificant. Parieto-occipital approach was preferred during VP shunting in MMC patients (used in 71% of the patients). In the non-MMC group, the frontal approach was more frequent (62%). Infants who had the shunt inserted within 14 days of the MMC repair presented with a 71% complication rate and those who underwent shunting after the 14th day had a 57% complication rate. 3 out of 5 children with a birth weight below 2500g developed complications after the VP shunting. The percentage of complications in those weighing more than 2500g at birth was equal to 56% (9 out of 16 patients).

Conclusion

The prevalence of complications after VP shunting did not significantly differ between MMC and non-MMC patients but a different surgical approach was preferred in those groups. Early or delayed shunt insertion and birth weight did not significantly influence the rate of complications, but our sample size was small which might have affected the results.

Spreading depolarization disrupts neurovascular coupling after ischemic stroke in the mouse cerebral cortex

Péter Kozák
Hungary

Introduction
Neurovascular coupling (NVC) is the mechanism to drive local perfusion increase in response to neuronal activation in the brain. NVC is impaired upon acute ischemic stroke (AIS). The pathophysiology behind NVC dysfunction is suggested to be the occurrence of spreading depolarization (SD), that causes vasoconstriction and fosters lesion maturation in AIS. Here, we demonstrate that SD evolution impairs functional hyperemia mediated by NVC despite successful reperfusion after AIS.

Material & Methods
Male C57BL/6 mice (n=11) were anesthetized with isoflurane (0.6-1.2%). Cerebral blood flow (CBF) changes were acquired using laser speckle contrast analysis (LASCA) imaging. A baseline of 10 min was followed by a transient (45 min) bilateral common carotid artery occlusion (2VO) and a subsequent 60 min reperfusion. After 60 min of reperfusion, NVC function was evaluated under isoflurane (0.1%)-medetomidine (0.1 mg/kg) anesthesia by contralateral whisker pad stimulation (~2Hz). SHAM operated animals served as control.

Results
Low CBF (<20%) early after the induction of ischemia favored spontaneous SD evolution (CBF <20% vs. >30%, SD vs. no SD; 16 SDs in 9 mice). SDs occurred in both hemispheres (bilateral) in 7, and in one hemisphere (unilateral) in 2 mice. In concert, functional hyperemia was diminished in 7, and was unilaterally intact in 2 mice (hyperemia amplitude: 8.73±3.01 vs. 17.16±6.21 %; SD vs. no SD). The amplitude of functional hyperemia after the absence of SD was comparable to the hyperemia measured in SHAM mice (17.16±6.21 vs. 16.71 %, unilateral vs. SHAM).

Conclusion
Our data confirms that SD evolution impairs NVC after AIS. SD is known to trigger a progressive, tonic vasoconstriction, called spreading oligemia that might permanently diminish NVC function. We suggest the pharmacological attenuation of vasoconstrictive prostaglandin signaling to improve CBF during spreading oligemia and to prevent NVC dysfunction after AIS.
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Guillain-Barré Syndrome After COVID-19 Vaccination: A Systematic Review and Analysis of Case Reports

Mohammad Abuawwad
Egypt

I Introduction

Cases of Guillain-Barré Syndrome (GBS) have been believed to be in association with the novel COVID-19 infection, and also with the following vaccines developed against the infection. Our work aims to investigate the incidence of GBS after COVID-19 vaccination, and to describe its clinical characteristics and potential confounders.

Material & Methods

An electronic search was conducted through four databases: PubMed, Scopus, medRxiv, and Google Scholar for all case reports and case series describing GBS manifestation in relation to COVID-19 vaccine administration. All published articles from inception until November 1st, 2022 were included. Differences between groups were assessed using Pearson chi-square test. Modified Erasmus GBS Outcome Score (mEGOS) for the ability to walk after GBS was calculated for all cases with sufficient clinical data, and Kaplan-Meier survival analysis were performed to study the effect of vaccine type on the relationship between vaccination time and complication of GBS.

Results

About 103 studies describing 175 cases of GBS following COVID-19 vaccination were included. The Acute Inflammatory Demyelinating Polyradiculoneuropathy subtype was the most reported subtype with 74 cases (42.29%), followed by Acute Motor Sensory Axonal Neuropathy and Acute motor axonal neuropathy 17 (9.71%) and 14 (8%), respectively. The affected age group averaged around 53.59 ±18.83 years, with AMSAN occurring in a rather older group (63.88 ±20.87 years, $p=0.049$). The AstraZeneca vaccine was associated with AIDP (n=38, 21.71%) more than other vaccines, followed by the Pfizer vaccine (n=23, 13.14%), $p=0.02$. The bilateral facial palsy subtype was mostly linked to adenoviral vector vaccinations, accounting for an average of 72% of the total BFP cases. Dysesthesias was the most reported sensory complication (60%, $p=0.349$). Most GBS patients survived (96%, $p=0.036$), however, despite the higher survival rate, most patients had low mEGOS scores (4 ±3.57, $p<0.01$). On average, patients developed GBS at 13.43 ±11.45 days from vaccination ($p=0.73$), and survival analysis for complication of GBS into mechanical ventilation or walking impairment yielded a severely increased probability of complication after 25 days ($p<0.01$). Intravenous immunoglobulins ($p=0.03$) along with rehabilitation ($p=0.19$). were the most commonly used treatment.

Conclusion

Although rare, GBS of all subtypes can manifest after COVID-19 vaccination. Most cases occurred after receiving the AstraZeneca vaccine, and despite low mortality rates, ambulation was compromised in most patients. A higher risk of GBS complication is associated with an onset later than 12-13 days, particularly with Pfizer, AstraZeneca, and Moderna vaccines.

A Cohort Study Comparing Melatonin-users with non-users in the treatment of Migraine Headaches.

Shreyans Singhvi
India

Introduction
Melatonin improves sleep quality and the severity of headaches when compared to baseline studies. It's a safe drug with minimal side effects and is well tolerated. This research will further highlight the potential of Melatonin for the treatment of migraine headaches.

Material & Methods
A cross-sectional study was performed on 120 participants in a hospital setting where the users and non-users of Melatonin were divided into groups of 60 each. A MIDAS (Migraine Disability Assessment Scale) questionnaire was used to assess the symptoms. To establish a correlation between different factors, the chi-square test and p-value were used. A null hypothesis was formulated with no association taken into account, and the chi-square and p-values were computed to find a possible association between the considered factors. The confidence interval for the p- value was taken at 95% with a 0.05 level of significance.

Results
It was found that there was a reduction in the intensity of pain and improvement in the quality of sleep in the Melatonin user against the non-user cohort with an average age of 30, as evident from the results of chi-square and p-value of 7.5481 and 0.006007 respectively for the number of night time awakenings (relative risk reduction= 0.539, number needed to treat= 4.291) and chi-square value of 36 and p-value of 0.00001 for the intensity of pain reduction (relative risk reduction= 0.473, number needed to treat=1.897). The values for mean frequency headache reduction went down from 3.23±0.26 in the non-user cohort to 2.1±0.67 in the user cohort.

Conclusion
Migraine is a chronic, debilitating condition causing recurring headaches with severity ranging from mild to moderate in intensity. Melatonin has drawn attention for its anti-migraine action, owing to its structural similarity to Indomethacin and free-radical neutralizing property. Therefore, Melatonin can be a promising agent for the treatment of migraine headaches.

I

Neurorescue effects of liposomal quercetin on the GABAergic and dopaminergic neurons via microglia polarization in Huntington's disease model in rats

Ali Alishavandi
Iran

Introduction
Huntington's disease (HD) is an autosomal-dominant and neurodegenerative disorder characterized by psychiatric disturbances, dementia, and motor dysfunctions. Destruction of GABAergic neurons was proved in previous studies. In addition, Microglia polarization via neuroinflammation seems to play a pivotal role in HD pathogenesis. This study aimed to investigate the polarization of microglia to the anti-inflammatory phase for protecting neurons in the striatum of a rat brain.

Material & Methods
A total of 18 male Sprague-Dawley rats were randomly divided into 3 equal groups: 1- Sham 2- HD model 3- HD model+liposomal quercetin (30mg/kg). For inducing the HD model, the rats were anesthetized, and a combination of 1ml quinolinic acid and saline (200nmol QA/2µl saline, unilateral) was microinjected into the striatum through stereotaxic apparatus. Liposomal quercetin (30mg/kg intraperitoneally) was administered once-daily treatment for two months. Behavioral and locomotor functions were assessed by open field tests. After deep anesthesia, the animals were sacrificed and their striatum were kept in formalin for exerting RT-qPCR gene expression, Cresyl violet, and immunofluorescence (IF) staining.

Results
Administration of liposomal quercetin significantly increased CD206 gene as an anti-inflammatory marker (MD=0.035; 95%CI: 0.003 to 0.069; $p<0.05$) in the treatment group compared to the HD model group. Moreover, IF staining of GABA receptor alpha2 demonstrated upregulation in the treatment group compared to the HD model group (MD= 27.29; 95%CI: 17.71 to 36.87; $p<0.001$). Also, the behavioral and locomotor activities of HD rats were decreased, which was very highly significantly improved by Liposomal quercetin (MD= 339.5; 95%CI: 298.2 to 380.8; $p<0.001$). Although the population of dopaminergic neurons in the treatment group had an incrementing trend compared to the HD model, this relationship was not statistically significant (MD= 7.68; 95%CI:
-1.20 to 16.50; $p>0.05$).

Conclusion
In the present study, treatment of HD model rats with liposomal quercetin improved the immune microenvironment of the striatum and rescued GABAergic neurons by upregulating anti- inflammatory microglia (CD206: a representative marker for M2 phenotype). Further, the effect on behavioral and locomotor functions was favorable. These findings suggest liposomal quercetin as a modulator of microglia polarization as well as a potential treatment for reducing symptoms in patients with HD.

Integration and maturation of human induced GABAergic interneurons in the mouse brain

German Ramos Passarello
Sweden

Introduction

A functional cerebral cortex depends on the coordination of two main types of neurons: glutamatergic excitatory pyramidal neurons and GABAergic inhibitory interneurons. This coordination is directed via the control of pyramidal neurons output and synchrony, which is primarily performed by a particular GABAergic subtype called parvalbumin (PV) interneurons. Loss or dysfunction of these cells leads to cognitive impairments and diverse neuropsychiatric disorders. Therefore, it is imperative to develop new strategies to replace them. A promising approach is the cell transplantation of reprogrammed interneurons, which allows for patient-specific targeted cell replacements. This approach has not been analysed in detail regarding transdifferentiated GABAergic interneurons; thus this study abords it focusing on their maturation and integration once transplanted into the mouse brain.

Material & Methods

Human GABAergic induced neurons (hGiNs) were generated from human oligodendrocyte progenitor cells. Once mature, hGiNs were transplanted in immunodeficient mice's lateral ventricle and cortex, as large and mini spheroids (Sph), respectively. After 30- and 90-days post transplantation, cells were analyzed regarding to morphology, distribution, and expression of specific interneural markers. For this purpose, the mice brains were fixed, extracted, and cut to later perform immunohistochemistry stainings. A computational analysis was performed with ImageJ to estimate the colocalization coefficient between hGiNs and specific interneural markers.

Results

Reprogrammed hGiNs implanted in the lateral ventricle as large spheroids successfully survived after 90 days post transplantation and showed the ability to infiltrate in the mouse brain. Of these cells, a small percentage remained as mature interneurons. hGiNs minispheroids implanted in the mice's cerebral cortex, successfully survived after 30 days post transplantation. These cells exhibited long processes and great ability to migrate in the mouse brain. However, they did not appear to have remain as mature interneurons.

Conclusion

In conclusion, the hGiNs implantation onto the mouse brain appears to show a trend of greater survival, distribution and morphology when implanted in the cortex as minispheroids; but greater capacity to differentiate into mature interneurons when implanted in the lateral ventricle as big spheroids. Despite further analysis are needed, these findings provide a step forward towards the development of alternative cell replacement therapies for neurological disorders.

Pharmacology
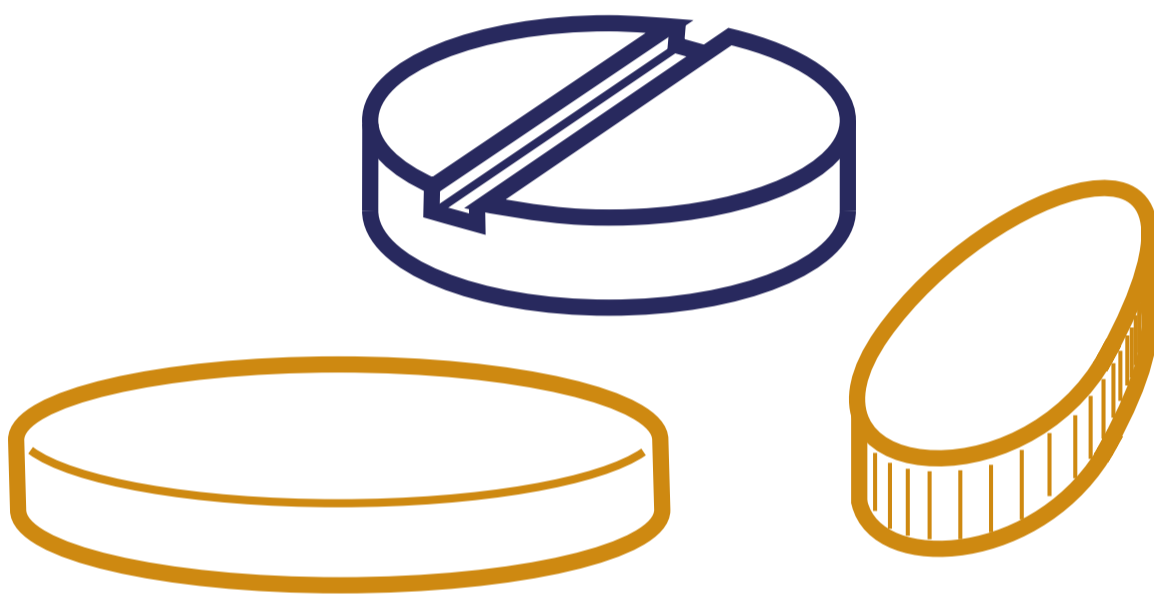
Presenters:
Mandana Farokhpayam
Mohamed Ibrahim Gbreel
Farid Masoud
Karol Sadowski
Farida Agayarli
Niloufar Hazrati

Effect of capsaicin cream on the chronic low back pain in patients with inter-vertebral disc herniation

Mandana Farokhpayam
iran

Introduction

: low back pain is one of the most common debilitating disorders worldwide, and the third cause of visit a doctor . One of the most common causes of the low back pain is spinal disc herniation. No general agreement exists on the most effective treatment for it, yet. This study aimed to determine the effect of Capsaicin cream on the low back pain in patients with inter-vertebral disc herniation in Ahvaz

Material & Methods

The present study is a double blind clinical trial in which 43 patients with chronic low back pain, according to the characteristics of the subjects were randomly divided into two groups of treatment (n=23) and control (n=20) groupsl. Data collection instrument included demographic specifications and Visual Analogue Scale (VAS) questionnaire that were completed on arrival and at the first, second and third weeks after intervention. The treatment and placebo group used the ointment for three weeks and three times a day as a thin layer on the painful position. After collecting, the data were entered into SPSS (version 18) and analyzed using the analytical – descriptive statistics.

Results

The findings showed a significant difference in the average pain intensity between the groups of the study pre-and post-intervention (p=0.0001) and the rate of using analgesics in the treatment group has been significantly decreased (p=0.008). Also in studying patients' satisfaction was significant difference existed between the two groups using the ointment (p=0.0001).

Conclusion

The results showed that Capsaicin cream has beneficial effects on pain relieving and reducing of analgesic use in patients with inter-vertebral disc herniation. Therefore to use the ointment in treatment of low back pain caused by inter-vertebral disc herniation can be recommended

The Efficacy of Saffron/Crocin in Patients with Type 2 Diabetes or Metabolic Syndrome: Systematic Review and Meta-Analysis.

Mohamed Ibrahim Gbreel
Egypt

Introduction
Nearly 6% of the world's adult population are suffering from type 2 Diabetes (T2DM). Saffron (C. sativus) modulates inflammation, insulin resistance of T2DM, oxidative stress, and hypertension. We hypothesize that it could be helpful for managing T2DM and metabolic syndrome (MS); however, there is a lack of documentation on the beneficial impacts of C. sativus supplementation on those patients. Therefore, we aimed to determine the effects of C. sativus supplementation on T2DM and MS patients.

Material & Methods
We searched four databases including the Cochrane Library, PubMed, Scopus, and Web of Science for eligible studies until February 2022. The quality of the pooled analyses was assessed by Cochrane risk of bias tool. The overall effect sizes of mean differences (MDs) and 95% Confidence Intervals (CI) were calculated using Review Manager 5.4. I2 statistics were used to assess the studies' heterogeneity.

Results
Our meta-analysis revealed significant cholesterol (MD=- 14.59, P=0.004) and LDL level reduction (MD= -9.52, P= 0.02) in MS patients compared to controls. On the other hand, MS patients showed a significant increase in BMI compared to controls (MD= 0.67, P<0.0001). Regarding T2DM patients, saffron/crocin showed significant results in most of the outcomes including systolic blood pressure (SBP), fasting blood glucose (FBG), Hemoglobin A1c, AST enzyme, and TNFα reduction (MD=-5.82, P=0.0006), (MD=-11.16, P=0.003), (MD=-0.37, P<0.00001), (MD=-1.09, P=0.005), (MD=-0.94, P=0.001) respectively. In monotherapy, Crocin alone significantly decreased SBP, HDL, FBG, and HbA1c, while saffron significantly reduced SBP, Cholesterol, Triglyceride (TG), LDL, HbA1c, and AST levels.

Conclusion
Saffron & Crocin are associated with better control of outcomes and complications in patients with T2DM and/or MS. Also, saffron had better results regarding Lipid profile.

Combination Therapy of Dexamethasone and Citicoline Prevents Cisplatin-induced Neuropathy in Mice

Farid Masoud
The Netherlands

Introduction

As the number of cases of Cisplatin-induced peripheral neuropathy (CisIPN) continues to increase, there is a need for research on ways to alleviate its adverse effects. The development of oxidative stress and free radicals are essential factors in the development of CisIPN. It has been revealed that dexamethasone and citicoline have anti-inflammatory and antioxidant properties that may decrease the occurrence and intensity of CisIPN. The current study aimed to evaluate the potential effects of dexamethasone and citicoline as novel interventions for CisIPN.

Material & Methods

In this study, 72 male mice were randomly divided into nine groups, each containing eight mice. On the first three days and one day before administering cisplatin (2 mg/kg, i.p.), the mice were injected with different doses of dexamethasone (7.5, 15, 30 mg/kg, i.p.), citicoline (10, 20, 40 mg/kg, i.p.), and a combination of both (dexamethasone 7.5 mg/kg + citicoline 10 mg/kg, i.p.).

Nociception was evaluated using the tail flick method. Additionally, levels of malondialdehyde (MDA), interleukin-1beta (IL-1β), tumor necrosis factor-α (TNF-α), total antioxidant capacity (TAC), and differences in mice weight (ΔW) were measured. Results were considered statistically significant if the p-value was below 0.05.

Results

Various doses of dexamethasone and citicoline were able to increase the latency time ($p<0.05$). Additionally, 15 mg/kg of dexamethasone decreased the level of MDA and increased TAC ($p<0.05$), and at 30 mg/kg, there was a further reduction in MDA ($p<0.05$). Similarly, 20 and 40 mg/kg of citicoline lowered MDA and raised TAC ($p<0.05$), while 10 mg/kg only lowered MDA ($p<0.05$). The levels of IL-1β and TNF-α were decreased by all doses of dexamethasone, and only at 40 mg/kg did citicoline affect these levels ($p<0.05$). Notably, the decrease in ΔW was more significant in the groups treated with dexamethasone and citicoline compared to the Cisplatin group ($p<0.05$).

Conclusion

The combination of Dexamethasone and Citicoline has been found to effectively combat Cisplatin-induced Peripheral Neuropathy by promoting anti-inflammatory responses, boosting antioxidant capabilities, and preventing lipid damage. This powerful duo has the potential to significantly alleviate the symptoms of CisIPN, making it a promising treatment option for those suffering from this condition.

I

In search of new podophyllotoxin derivatives as potential anticancer drugs - evaluation of new KL-3 effectiveness

Karol Sadowski
Poland

Introduction

Podophyllotoxin (PPT) is a plant-derived cell proliferation inhibitor used to treat anogenital warts during HPV infection. PPT stabilizes microtubules and stops the replication of cellular DNA. Therefore, in search of safer drugs, we synthesized the derivative KL-3. So far, we have shown that it is more effective against cancer cells in vitro and less toxic to healthy cells than PPT. This research further assesses the safety, effectiveness and mechanisms of KL-3 and PPT.

Material & Methods

We performed our research on the human keratinocyte line (HaCaT). We tested them with PPT (Sigma Aldrich) and KL-3 synthesized in cooperation with the University of Warsaw. We assessed the cell viability (PrestoBlue Assay) in 6 different concentrations: 0,25; 0,5; 1; 2,5; 5 and 25µM. Similarly, we analyzed the cells under electron microscopy (features of the processes, endoplasmic reticulum, mitochondria and Golgi apparatus) after 24 and 48h. We also observed the process of entering each compound with attached fluorescein into the cell in confocal microscopy after: 5; 10; 30; 60; 90; 120; 180; 240; 360min and 24h. To compare the toxicity, number of organelles and number of vesicles, we used a One-way ANOVA test in PRISM and ImageJ.

Results

KL-3 was less toxic than PPT in 0,25; 0,5 and 1 µM concentrations, at higher, there were no differences. Electron microscopy analysis revealed that after 24h treatment with 1 µM KL-3 induced transient ER stress, mitochondrial swelling and elongation of cytoplasmic processes. After 48h most of those changes were reversed with simultaneous induction of autophagy and cells remain alive. In contrast, we observed irreversible vacuolization of the cytoplasm in PPT-incubated cells and the loss of cell membrane. Confocal microscopy images proved that both compounds enter the cell as endocytic vesicles before the fifth minute. The number of endocytic vesicles after 5 min and 24h were not statistically different in both groups.

Conclusion

We proved that KL-3 is less toxic than PPT for HaCaT cells. Additionally, most KL-3 changes are reversible in contrast to PPT. Finally, we confirmed that both compounds enter the cell equally effectively. Therefore, the present study may suggest that KL-3 is a potential alternative to PPT.

Effects of piracetam on sex hormones in the blood of female white rats against the background of chronic ethanol determination

Farida Agayarli
Azerbaijan

Introduction
According to WHO, 82.1% of women living in the countries of the European Union drink alcohol. There is a wealth of information in the literature about how alcohol addiction negatively affects the nervous system, immune system, liver, and genetic information. While it affects the reproductive system, it is not completely known, and in some cases the results obtained are contradictory. Given the above, we studied the effects of piracetam on changes in the amount of sex hormones in experimental female white rats treated with chronic alcohol.

Material & Methods
During the studies, 30 female white rats were injected with piracetam 200 mg/kg intraperitoneally, and 25% ethanol was administered orally at a dose of 12 ml/kg. Control animals were injected intraperitoneally with 0.2 ml of saline per 100 g of body weight. The concentration of sex hormones was determined by the colorimetric method in the blood taken from the tail vein. We used Wilcoxon-Mann-Whitney's Student's t-test, non-parametric U-test to quantify the experimental data.

Results
The results of our study showed that the concentration of luteinizing hormone (LH) in the blood of female rats chronically treated with ethanol decreased by 37% ($p<0.001$) compared with the control group. Against the background of chronic administration of piracetam at a dose of 200 mg/kg, the concentration of LH in the blood of female rats that received ethanol for a long time was restored by 73.6% compared to the control group. The concentration of the hormone total testosterone (To) in the blood of the test females on the background of chronic ethanol consumption was reduced by about 50% compared with the control group ($p<0.001$). Against the background of long-term use of piracetam + ethanol, the concentration of the corresponding hormone was restored by 62.6%, compared with the control group. The concentration of estradiol in the studied females decreased by approximately 21% compared with the control group ($p<0.001$) against the background of chronic ethanol intake, against the background of piracetam intake, it recovered to 17%.

Conclusion
Piracetam partially restores the decrease in the amount of sex hormones in the blood of female white rats on the background of chronic ethanol intake.

Neuroprotection antigenotoxic activities of S.anacardium hydroalchoholic extract against H2O2induced oxydative damage

Niloufar Hazrati
Iran

Introduction

Introduction Neurodegeneration is a feature of many debilitating, incurable diseases, such as Parkinson's disease (PD), Alzheimer's disease (AD), amyotrophic lateral sclerosis (ALS), and Huntington disease (HD). Reactive oxygen species (ROS) are usually formed during normal metabolism. however, ROS overproduction influences cells by increasing lipid peroxidation, causing DNA damage and regulation of apoptosis proteins and could cause many neurodegenerative diseases. In order to solve this problem, natural antioxidants are excellent choices; Semecarpus Anacardium Linn is a medicinal herb which has antigenotoxic/antioxidant effects. In this study, we evaluate the neuroprotective and antigenotoxicity effect of S. anacardium against the damage induced by H_2O_2 on the PC12 cells by using the MTT test and comet assay.

Material & Methods

Method Cotyledons and nut shell of S.anacardium fruit were extracted in water:ethanol (70:30) Dried roots of S.anacardium fruit (250 g) were extracted and homogenized with dichloromethane using maceration for 72 h. The MTT assay was used to assess the H_2O_2 cytotoxicity, and the comet assay was utilized for evaluating genotoxicity as a standard method. These assays helped us in finding a method to calculate rate of DNA damage and viability of PC12 cells after combination with S.anacardium for 24 hours.

Results

Result The findings showed that 24 hour treatment with the extract exhibited protective effects at concentrations of 100 and 200 microgram/ml. The group that was treated by extract for 48 hours exhibited protective activities at concentrations higher than 25microgram/ml Interestingly, 72hour treatment with the extract at all of studied concentrations protected the cells against H_2O_2 induced cytotoxicity. According to The comet assay data, antigenotoxic effect of S. anacardium at examined concentrations (10, 25, 50, 100 and 200 uM) didn't show any genotoxicity, as compared to phosphate-buffered saline. Treatment with S. anacardium led to a significant protection of cells against DNA damage induced by H_2O_2 ($p < 0.001$) at all concentrations.

Conclusion

Conclusion S. anacardium hydroalcoholic extract increased PC12 cell viability and had a significant antigenotoxicity effect against DNA damage induced by H_2O_2. we suggest that S. anacardium might be a potential protective agent for the prevention and treatment of oxidative stress resulting diseases. In conclusion, our results demonstrated that S. anacardium hydroalcoholic extract exhibited protective effects against H2O2_induced cytotoxicity & genotoxicity however further studies are required in order to determine the exact mechanism behind such effects.

Public Health and Epidemiology

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Michael Shimelash

Uses and impact of endocrine and targeted therapy for breast cancer in Bulgaria

Kapilraj Ravendran
UK

Introduction

NCCN guidelines recommend the use of targeted therapy for human epidermal growth factor receptor 2 (HER2+) breast cancer patients (BC) and endocrine therapy for hormonal receptor (HR) positive breast cancer patients. The aim of our study was to compare the uses and impact of hormonal and targeted therapy on the 5-year overall survival (OS) of BC patients in Bulgaria.

Material & Methods

This is a retrospective population wide observational study of 3091 cases registered with BC in the Bulgarian National Cancer Registry (BNCR) in 2013. The mean age of invasive ductal carcinoma (IDC), invasive lobular carcinoma (ILC), and other types were calculated. Patients were divided into 4 groups according to the receptor: HR+HER2-, HR+HER2+, HR-HER2+ and HR-HER2-. Impact of hormonal therapy on the 5-year OS for patients registered with stage 1 or 2, HR+/HER2- was investigated along with the effects of targeted therapy on the 5-Year OS for patients registered with stage 1 or 2, HR-/HER2+ IDC. Kaplan-Meier curve with log rank and ANOVA tests were used to estimate the statistical significance.

Results

Patients diagnosed with IDC were significantly younger compared to other types such as ILC and mucinous carcinoma (MC) (60.3,62.4,68.9 respectively, p-value <0.001). 73.5% with IDC, 70.5% with ILC and 82.8% with MC were diagnosed in stage I or II. Overall, the 5-Year OS was better for patients with IDC than ILC (68.3% vs 63.1%, p-value=0.029). The most common receptor status subtype for all types was HR+/HER2-, 39.2%,46.1%, and 48.4% for IDC, ILC and MC respectively. Patients receiving hormonal therapy for stage 1 or 2 for IDC, HR+/HER2- had a better 5-year OS of 88.3% compared to 88% for patients who did not receive hormonal therapy, p-value = 0.601. Patients receiving targeted therapy for stage 1 or 2 for IDC, HR-/HER2+, had a better 5-Year OS of 83.9% compared to patients that did not receive targeted therapy (81.6%), p-value=0.712.

Conclusion

The 5-Year OS rate of BC is lower in Bulgaria compared to other nations in Europe. There are studies that suggests, encouraging the use of hormonal and targeted therapy. Our study suggests uses of these therapies can improve the 5-Year OS.

Air pollution and thyroid abnormalities: Systematic review and meta-analysis

Niloufar Jafari
Iran

Introduction
Air pollution exposure can trigger a wide range of thyroid disfunction in different groups of the population. This systematic review and meta-analysis aimed to find the association between air pollution and thyroid dysfunction in the general population and neonate, pregnant and cancerous people.

Material & Methods
Electronic databases, including Web of Science, PubMed, Scopus, and Embase, were searched for all published articles from 27 October 2021. Newcastle Ottawa Scale checklist was used to assess the quality of individual studies. Relevant demographic data and the intended results of the selected studies were extracted, and their adjusted odds ratios were pooled using random and fixed effect analysis based on the heterogenicity index.

Results
After applying the search strategies, twenty-six articles were included in our study. Overall, the association between air pollution and thyroid cancer, neonatal hypothyroidism, maternal thyroid function, and thyroid function in the general population was discussed in four, eight, ten, and four studies, respectively. There was a significant association between PM2.5 exposure and maternal hypothyroxinemia with pooled OR of 1.241 (95%CI, 1.089–1.415), p-value<0.001. There was no positive relationship between NO2 exposure and maternal hypothyroxinemia with pooled OR of
1.007 (95%CI, 0.840–1.207), p-value=0.941. The investigation of the relationship between PM2.5 exposure and congenital hypothyroxinemia showed a significant association between them, with pooled OR of 1.017 (95%CI, 1.002–1.032), p-value = 0.024.

Conclusion
Air pollution could influence thyroid function, especially in pregnant women and newborn infants. This study and other similar investigations provide evidence on air pollution toxicity for healthcare systems.
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Unravelling the epigenetic mechanisms underlying the occupational carcinogenesis of hexavalent chromium

Jelle Verdonck
Belgium

Introduction

The occupational exposure of workers to hexavalent chromium (Cr(VI)) occurs in various industries, such as the chrome plating industry, welding industry and the industry comprising surface treatment with chromates. Inhalation exposure to Cr(VI) is associated with increased risk of lung cancer. The mode of action for Cr(VI)-induced lung cancers is well described, however the exact mechanisms underlying the carcinogenesis of Cr(VI) are not well elucidated. At the mechanistic level, both genomic instability and epigenetic modifications induced by exposure to Cr(VI) have been proposed.

Material & Methods

The HBM4EU chromates study investigated, among other things, the effect of Cr(VI) exposure on oxidative stress, global DNA methylation and global DNA hydroxymethylation in blood. The study population consists of Cr-platers (n = 57), surface treatment workers (n = 46), welders (n = 110) and controls (n = 99). Post-shift urine samples and blood samples were collected at the end of the working week. Metal concentrations were measured with ICP-MS. Analysis of methylation, hydroxymethylation and oxidative stress levels were done using LC-MS/MS.

Results

The highest Cr(VI) exposure levels were observed for Cr-platers. The mean (± SD) urinary total chromium levels in post-shift urine samples per exposure activity were 2.5 (± 2.8) µg/g creatinine for chrome plating workers, 1.3 (± 1.2) µg/g creatinine for welders, 1.7 (± 1.8) µg/g creatinine for surface treatment workers and 0.35 (± 0.33) µg/g creatinine for controls. Furthermore, these platers were exposed to elevated levels of PFAS. Significant differences between workers with chromium exposure and controls were found for the perfluoroalkyl sulfonic acids, particularly for perfluorooctylsulfonic acid (PFOS). The partly high PFOS exposure in chromium platers can be explained by the former application of PFOS as fume suppressants in electroplating baths. Regarding epigenetic alterations, global DNA hypomethylation was observed. Furthermore, increased levels of oxidative stress was observed.

Conclusion

These results suggest that DNA methylation may be influenced by oxidative stress and more efforts are needed to better protect these workers.

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Epigenetic clock-derived age acceleration is associated with lung function in the population-based Lifelines cohort study

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Netherlands

Introduction

Lung function is an important marker of general health and naturally declines with aging. Next to age and environmental exposures such as smoking, genetic variants and gene regulation mechanisms like DNA methylation(DNAm) explain variations in lung function. DNAm has been postulated as a marker of biological aging that can be estimated using epigenetic clocks. The difference between this estimated biological age and the chronological age is a measure of age acceleration. Our study aimed to assess the association between age acceleration and lung function.

Material & Methods

We included 1618 study participants with DNA methylation data from the Lifelines cohort study. Lung function was measured with spirometry, and Forced Expiratory Volume in one second (FEV1) was used as the outcome. Biological age, pace of aging, and telomere length were estimated using the SkinHorvath, PhenoAge, DunedinPACE, and telomer length epigenetic clocks. Age acceleration was derived from the residuals of the regression of biological age on chronological age (except for the DunedinPACE-clock for which the estimated pace of aging was used). To assess the association between age acceleration and lung function, linear regression adjusted for chronological age, sex, height, smoking, and socio-economic factors (education and income) was performed.

Results

Of 1618 participants, 927 (55%) were males with a mean age of 47 years. Age acceleration based on the PhenoAge and DunedinPACE epigenetic clocks was significantly associated with FEV1. FEV1 was 7.7ml lower (95% CI:-12.3,-3.19) for a one year higher PhenoAge age acceleration and 488.6 ml lower (95% CI:-728.83,248.39) for a one year faster Dunedin pace of aging. Telomere length and skin Horvath age acceleration were not associated with FEV1.

Conclusion

This study shows that age acceleration measured by the PhenoAge and DunedinPACE epigenetic clock is significantly associated with lower lung function. This suggests that faster biological aging also accelerates the natural lung function decline.

Machine learning predicts cardiovascular events in patients with diabetes

Krzysztof Irlik
Poland

Introduction

Cardiovascular disease (CVD) is a leading cause of morbidity and mortality in patients with diabetes mellitus. The burden of CVD is even higher among inpatients with diabetes. Accurate prediction of cardiovascular (CV) events in this population could aid in personalized CVD prevention. In this study, we aimed to develop a machine learning (ML) model for predicting CV events among inpatients with diabetes.

Material & Methods

This was a prospective, observational study, where clinical data of patients with diabetes admitted to the Department of Diabetology in a tertiary hospital in Poland between 2015 and 2020 were analyzed using ML. The occurrence of new CV events following discharge was collected for up to 5 years and 9 months. An end-to-end ML technique, which exploits the neighborhood component analysis for elaborating discriminative predictors, followed by a hybrid sampling/boosting classification algorithm, multiple logistic regression, or unsupervised hierarchical clustering was proposed.

Results

Out of 1735 previously hospitalized patients with diabetes (53% female), 150 (8.65%) experienced a new CV event during the follow-up period. The 12 most discriminative parameters included coronary artery disease, heart failure, peripheral artery disease, stroke, diabetic foot disease, chronic kidney disease, serum potassium level, eosinophil count, and being treated with clopidogrel, heparin, proton pump inhibitor, and loop diuretic. Using these variables resulted in the area under the receiver operating characteristic curve (AUC) ranging from 0.62 (95% Confidence Interval [CI] 0.56–0.68, $p<0.01$) to 0.72 (95%CI 0.66–0.77, $p<0.01$) across five non-overlapping test folds, whereas multiple logistic regression correctly determined 111/150 (74.00%) high-risk patients, and 989/1585 (62.40%) low-risk patients, resulting in 1100/1735 (63.40%) correctly classified patients (AUC: 0.72, 95%CI 0.66-0.77).

Conclusion

ML algorithms can identify patients with diabetes at a high risk of new CV events based on a small number of interpretable and easily obtainable patient parameters.

Is change in metabolic status linked to skin cancer? (a cohort study in the northern part of the Netherlands, Lifelines

Michael Shimelash
Netherlands

Introduction
Skin cancer is the most common cancer in Caucasian populations and its incidence is on the rise. Recent studies have devoted special attention to the roles of glucose and cholesterol metabolism in the development of cancer. Similarly, other metabolism related conditions such as obesity have been linked with carcinogenesis as well. Previous research studied the link between metabolic factors, anthropometric values, and skin cancer using single cross-sectional measurement of metabolic markers, and/or anthropometric values. However, the relationship between change in metabolic and anthropometric factors and skin cancer has not been studied. This research aimed to examine possible associations between change in metabolic and anthropometric values and the risk of skin cancer in the large national cohort: Lifelines and the national pathology database: PALGA.

Material & Methods
Methods: We included 98,147 participants. Cancer cases were identified through linkage with national cancer registries. Hazard ratios (HRs) of cancer with 95% confidence intervals were be derived from time-dependent Cox-regression models. We adjusted for potential confounders such as age, sex, education level, occupation, SES, Smoking and Alcohol.

Results
Compared to participants with no change, an increase in BMI was associated with lower chances of having skin cancer (HR: 0.859 (0.742, 0.995)). On the other hand, a decrease in Waist to hip ratio was associated with higher skin cancer rates (HR: 1.319 (1.086, 1.603)). In addition, an increase in Hba1c in those aged below 45 was significantly associated with increased incidence of skin cancer (HR: 1.500 (1.026, 2.192)); While an increase in total cholesterol in those below the age of 45 was associated with less risk of skin cancer (HR: 0.713 (0.537, 0.947)). However, HDL, LDL and Triglyceride were found to have no association with incidence of skin cancer.

Conclusion
Weight changes and Total cholesterol appear to be inversely associated with the development of skin cancers. Weight change is most likely a surrogate marker for lack of chronic sun exposure, which is a risk factor for skin cancers. In younger population an Hba1c had direct relationship with skin cancer. These findings highlight the importance of lifestyle factors in the development of skin cancer and the need for further research to better understand these associations.

Surgery
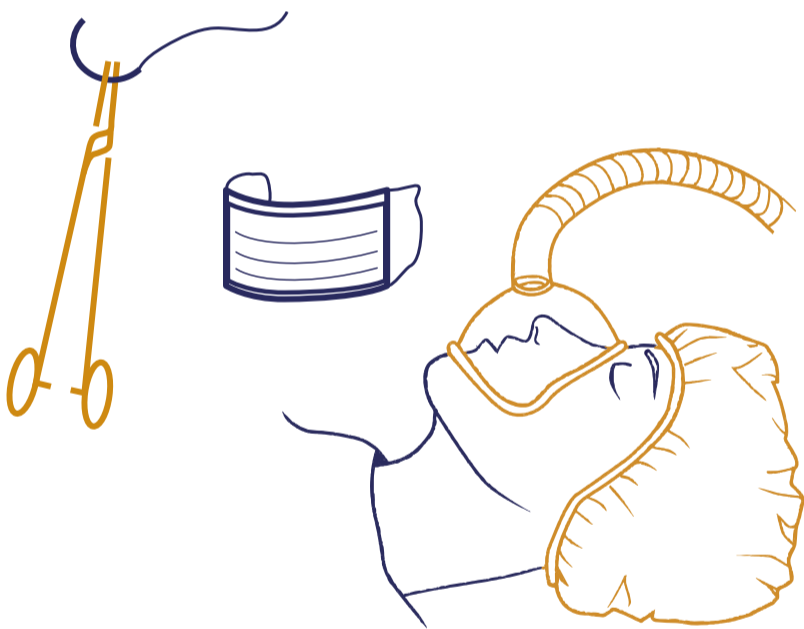
Presenters:
Harriet Louise Lancaster
Sheyda Rimaz
Beatriz Kill
Quirine Cordia
Elaine van Ee
Aydin Ayremlou

AI negative predictive performance exceeds that of radiologists in volumetric based risk stratification of baseline screen-detected lung nodules

Harriet Louise Lancaster
The Netherlands

Introduction
Lung cancer is deadlier than any other cancer due to the late stage at which it is diagnosed. When detected at stage 4, 5-year survival is <5%. If lung cancer can be detected at stage 1, survival can be increased dramatically to >75%. Early detection can be achieved through LDCT lung cancer screening in a high-risk population. Despite being proven effective, widespread implementation remains a challenge for multiple reasons. One of which, the ever-increasing workloads which radiologists face. AI could be the key to overcoming this challenge.

Material & Methods
Performance of different versions of an AI-prototype (AVIEW LCS; v1.0.34, v1.1.39.14, and v1.1.42.55) were analysed in 283 ultra-LDCT baseline scans. Results of the volumetric nodule measurements from the independent reads of the AI-prototypes were compared to the results of five experienced thoracic radiologists. An independent consensus reference read was performed which was considered the gold standard. Discrepancies between individual reads and consensus were classified as follows; positive misclassifications were nodules classified by the reader/AI as
≥100mm3, which at the reference consensus read were <100mm3, and negative misclassifications were nodules classified as a <100mm3 by the reader/AI, which at consensus read were ≥ 100 mm3.

Results
Using AVIEW LCS v1.0.34, 1149 nodules were detected of which 878 were classified as solid non- calcified. For v1.1.39.14 and v1.1.42.55, 1502 nodules were detected of which 1019 were solid non-calcified. Overall, v1.0.34 had 61 discrepancies (53 positive and 8 negative misclassifications), and v1.1.39.14 and v1.1.42.55 both had 32 discrepancies (28 positive and 4 negative). The improved AI versions (v1.1.39.14 and v1.1.42.55) had a better negative predictive value than 4 radiologists and equivalent negative predictive value to the 5th radiologist.

Conclusion
Results show that AI can exceed the negative predictive performance of experienced thoracic radiologists, meaning it could provide a solution to reducing radiologists' workload associated with lung cancer screening. These results should be validated in an external lung cancer screening dataset where the true outcome of lung nodules is known.

The Study of Using Medical Honey Dressing Compared to Stapler for Skin Graft Fixation in Burn Wounds

Sheyda Rimaz
Iran

Introduction

Skin grafts can be used effectively to cover burn injuries. A critical element of this treatment is the adherence of the graft to the wound bed. Honey has been shown to increase the adherence of skin grafts to wound beds and have antibacterial and anti-inflammatory effects thereby promote healing rate of wounds.This study aimed to determine the effect of using medical honey compared to staplers in attaching skin grafts to burn wounds.

Material & Methods

In this clinical trial study, after receiving the approval code of ethics and clinical trial numbers (IR.GUMS.REC.1400.304 & IRCT20210524051384N2),80 patients with deep 2nd &3rd-degree burns with TBSA< 40% underwent skin graft surgery. Patients were divided into two groups: using honey or stapler for graft fixation. Demographic information and the percentage of burns were extracted from patients' files. All patients in two groups were evaluated for graft rejection, number of hospitalization days, transplanted skin displacement, graft contraction, Pain(VAS Score), edema, hematoma, itching (5D Score), and infection rate. Data was collected and analyzed statistically using SPSS 20 (SPSS Inc.,Chicago, Illinois). The level of significance was set at 0.05.

Results

In this study, 80 patients were randomly divided into two groups of 40 people. There were 34 men (42.5%) and 46 women (57.5%). The average age of the patients was 39.29 ± 15.42 years.No significant difference were observed according to age,TBSA,mecanism of burn and sex. The mean hospital stay was shorter ($P = 0.034$) and infection rate, hematoma, edema, pain and itching severity ($P = 0.000$), which were less in the honey group. The graft contraction rate was lower in the stapler group ($P = 0.031$).Graft rejection was not observed in any group.

Conclusion

The results show that the use of natural honey is easy in application,and cheap for skin graft fixation in burn wounds compared to staplers that has reduced negative factors of skin graft such asduration of hospital stay days and adverse effects such as pain and itching severity, edema, hematoma, and infection rate. As a result, it has been shown that natural honey is also a very effective agent for split thickness skin graft fixations.

Effect of the Hyperbaric Oxygen Chamber Associated with the Use of Stem Cells Derived from Adipose Tissue in Degloving Injuries

Beatriz Kill
Brazil

Introduction

Degloving Injury (DI) is an acute injury caused by high-impact trauma with avulsion of the skin over the fascia and muscles, which may be associated with bone fractures, adjacent intracavitary injuries. In most cases, DI occurs in the lowerextremities. The standard treatment is aggressive debridement of necrotic tissues, with thinning of the resected part which served as an autologous skingraft. However, DI can culminate in partial tissue necrosis, infection and sepsis. Thus, it is necessary to evaluate other therapeutic alternatives, such as Hyperbaric Oxygen Therapy (HOT), which promotes increased oxygen perfusion in the tissue, allowing greater microbicidal activity and healing. Another strategy is the use of stem cells derived from adipose tissue, by paracrine effect.

Material & Methods

Thirty-two male Wistar rats, weighing between 200-250g, were analyzed. These animals were submitted under intraperitoneal anesthesia to a surgical procedure that mimicked the DI (avulsion flap, 2X8cm) in the dorsal region, all the animals had this DI sutured in the bed with separate stitches (polyamide, 40-0-) into four groups: Control group (no treatment); adipocyte-derived stem cells group; Hyperbaric Oxygen Therapy group; and Hyperbaric Therapy and stem cells (ASC) group. These stem cells were obtained from the adipose tissue of the inguinal region of rats. The animals allocated to the HOT group and the association of HOT and ASC underwent five sessions (2 ATM, 2h of exposure). The animals allocated to the ASC group and the association underwent subcutaneous injection along the DI (1X106). Genetic Analysis (qRT-PCR)

Results

This study demonstrated an increase in the viability of the DI in the LT+ASC groups (100%), the ASC group (89%) and the LT group (83%). With regard to flowmetry, there was a 2.5x increase in the distal flow in the LT group. HOT+ASC and 4x flow increase in the ASC group, both compared to the control group. In the histological analysis, there was an increase in vascular density by 4x (HOT+ASC group), 1.8x (ASC), compared to the control group. Regarding inflammatory cells, there was a 50% decrease in counts in the HOT+ASC group, 5% (ASC group) and 40% (THO) when compared to the control group. Gene expression analysis showed differences in all analyzed genes (CD-68, Il-10 Mmp9 and Tnf). By analyzing the groups, this study demonstrated a 50% decrease in CD-68 gene expression in the LT group compared to the control group. Also in relation to the TRO group, there was a 20% decrease in IL-10 gene expression versus the control group. When analyzing the gene expression of MMP-9, a 50% decrease was demonstrated in the TRO+ASC group when compared to the control group.

Conclusion

This study suggested that the use of ASC associated with HOT increases DI regeneration. Randomized clinical trials should be performed to confirm this hypothesis.

The fluorescent tracer Bevacizumab- IRDye800CW targeting VEGFα as a new intraoperative marker of meningiomas: a phase I/II clinical trial

Quirine Cordia
The Netherlands

Introduction

Meningiomas are the most commonly diagnosed intracranial tumors in adults and previous studies have demonstrated that recurrence can occur up to 21.6% of all meningioma patients. The prevention of recurrence is mainly dependent on extent of resection (EoR). Fluorescence guidance could improve the intraoperative distinction between tumor and normal tissue and hereby improve the EoR and thus reduce the number of recurrences. In meningiomas, Vascular Endothelial Growth Factor α (VEGFα) is upregulated and can be targeted with the fluorescent tracer Bevacizumab- IRDye800CW. The main aim of this project was to determine the correlation between fluorescence uptake of Bevacizumab-IRDye-800CW and histopathology.

Material & Methods

In this descriptive study, 17 patients with a convexity meningioma were intravenously administered an increasing dose of Bevacizumab-IRDye800CW (4.5, 10 and 25 mg with three patients in each dosage group). Five patients without Bevacizumab-IRdye800CW administration served as negative control. Post-operatively, tumor fluorescence uptake was measured using the Pearl fluorescence imaging device. According to standard of care, specimens were processed in 4 μm formalin fixed paraffin embedded (FFPE) blocks and consequently stained with hematoxylin and eosin (H&E), anti-VEGFα and 4',6-diamid-ino-2-phenylindole (DAPI). Tumor, dura and dural tail in each slice were determined and correlated to VEGFα expression and fluorescence signal.

Results

Bevacizumab-IRDye800CW localized subcellularly to the cytoplasm of predominantly tumor cells. Dura mater showed no fluorescence. VEGFα expression was localized to the cytoplasm of tumor tissue, but not in dura mater. Higher fluorescence intensity was found in patients with a histopathological confirmed dural tail, correlating with the presence of tumor cells. The same was applicable to bone invasion.

Conclusion

The results of the present study suggest that Bevacizumab-IRDye800CW has the potential to be a valuable tool in fluorescence guided meningioma resection. Further research is needed to show the clinical added benefit of Bevacizumab-IRDye800CW administration compared with standard of care, for example with regards to long-term recurrence free survival.

In-hospital outcomes after Thoracic Endovascular Aortic Repair for Blunt Thoracic Aortic Injury in the Pediatric Population

Elaine van Ee
the Netherlands

Introduction
Although blunt thoracic aortic injury (BTAI) in the pediatric population is rare, it is mainly managed with open repair, whereas the standard of treatment in adult patients is thoracic endovascular aortic repair (TEVAR). Studies regarding the utilization of TEVAR for BTAI have mainly been performed in the adult population and data regarding outcomes in the pediatric population remain scarce. Thus, this study aims to examine the outcomes of the pediatric population undergoing TEVAR for BTAI.

Material & Methods
A retrospective cohort study was performed, including all pediatric (≤21 y/o) and adult (>21 y/o) patients who underwent TEVAR for BTAI in the Trauma Quality Improvement Program (TQIP) database between 2010-2019. Pediatric patients were divided into three age categories: children (0-11 y/o), adolescent (12-17 y/o), and mature (18-21 y/o). Multivariable logistic regression was used to examine the in-hospital mortality and in-hospital complications after TEVAR for BTAI compared to adult populations.

Results
We identified 3,154 patients treated with TEVAR for BTAI of whom 12% were pediatric patients (children[N=1], adolescent[N=93], and mature[N=284]). Compared with the adult patients, the pediatric patients have less often diabetes (2.2% vs. 8.5%;p=.029, 0.0% vs. 8.5%;p<.001).
Furthermore, compared with adult patients, adolescent patients more often had higher aortic injury severity (G1 18% vs. 34%; G2 16% vs. 24%; G3 59% vs. 41%; G4 7.8% vs. 1.2%;p<.001). After multivariable logistic regression, compared with adult patients, adolescent patients had lower odds of in-hospital mortality (Odds Ratio (OR) 0.12 [95% Confidence Interval (CI) 0.02-0.93];p=.042). Moreover, there were no significant differences in in-hospital complications between the pediatric and adult populations.

Conclusion
Our data demonstrated no difference in in-hospital mortality between the mature and adult populations. Furthermore, these data demonstrated that the adolescent population was associated with lower risk of in-hospital mortality compared with the adult population, potentially suggesting that TEVAR might be safe in pediatric patients. Future studies should evaluate more anatomical and procedure-specific data and assess long-term outcomes following TEVAR for BTAI in the pediatric population.

Comparison of Canal transportation and centering ability of 3 rotary file systems: a CBCT evaluation

Aydin Ayremlou
iran

Introduction

Background: Proper cleaning and shaping of root canals play an important role in success of endodontic treatments. The most important advantage of NiTi files are their flexibility and ability to stay in the original path of canals. Among the NiTi files, SP1, Denco and RaCe are widely used by dentists in Iran. So far, no study has examined the performance of SP1, Denco and RaCe rotary file systems in terms of canal transportation and centering ability. Purpose: This study aimed to compare the transportation and centering ability of SP1, Denco and RaCe rotary file systems by using CBCT images.

Material & Methods

This in-vitro study was performed on 45 extracted first maxillary molars with 15-30 degrees curve (14 in each three groups of SP1, Denco and RaCe, and 3 in control). Prior to cleaning, all teeth were imaged by CBCT. Then the canals were prepared using three rotary files of Denco (Denco Gold), SP1 (SP1 AF Rotary) and RaCe. The distance from the inner wall of the canal to the outer surface of the root in the mesiodistal and baccolingual dimensions was measured in all CBCT images before and after canal preparation and were used to calculate the amounts of transportation and centering ability. Finally, the transportation and centering ability between the three rotary file systems were compared by Kruskal-Wallis test.

Results

The results showed that in all three Denco, SP1 and RaCe rotary file systems, a, b, c and d at all intervals of 2, 3 and 4 mm after canal preparation were significantly lower than their pre-prepared values (all cases P <0.05). However, at all intervals of 2, 3, and 4 mm, the amount of mesiodistal transport, baccolingual transport, and the ratio of centering ability were not significantly different between Denco, SP1 and RaCe groups (all cases P≥0.05).

Conclusion

All three Denco, SP1 and RaCe files can be used to maintain the original geometry of the canals during endodontic treatments on the maxillary first molars with a curve of 15-30 degrees.

Oral Sessions II
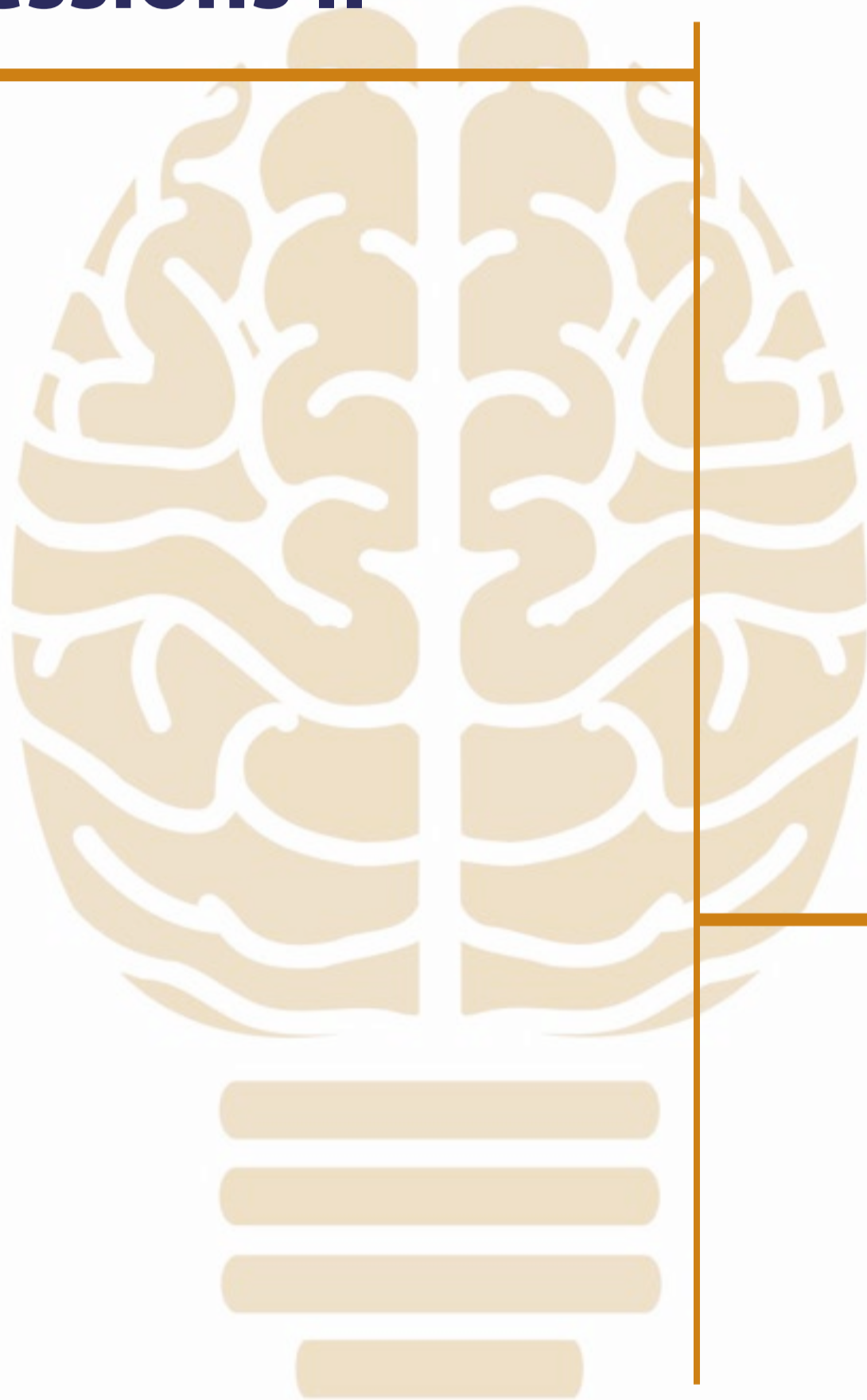
Cell Biology

Presenters:

Helena Wang
 Gabriela Jesus
Chimwemwe Mhango
Nadja Jahn

Saúl Rueda

The effect of neoadjuvant chemoradiotherapy and patient- and tumor characteristics on the microsatellite instability in esophageal carcinoma patients

Helena Wang
The Netherlands

Introduction

Neoadjuvant chemoradiotherapy (nCRT) followed by surgery (CROSS) is standard curative treatment for esophageal cancer (EC) patients. As the majority do not benefit from CROSS, it is essential to develop more personalized therapies. Defects in DNA Mismatch repair (MMR) proteins, also known as microsatellite instability (MSI), lead to an accumulation of mutation load stimulating anti-tumor response. Microsatellite instable (MSI) gastrointestinal tumors have shown to respond good to immunotherapy. Studies on MSI in gastroesophageal cancer are scarce and the effect of nCRT on MSI in EC patients is still unknown. Therefore, we aimed to assess the proportion of EC patients with MSI before and after nCRT and to find a correlation between MSI and patient- and tumor-specific characteristics.

Material & Methods

Formalin Fixed Paraffine Embedded samples of esophageal adenocarcinoma (EAC) or squamous cell carcinoma (ESCC) were collected from 139 EC patients aged >18 years and treated in the UMCG between 2000-2014. Patients with a Mandard tumor regression grade 3-5 were eligible for inclusion. Of these patients 65 were treated according to CROSS and 74 with surgery alone. Immunohistochemistry (IHC) were performed to detect the MMR proteins: MLH1, PMS2, MSH2 and MSH6. Correlations between MMR expressions were assessed using Pearson's correlation test or Spearman's rank correlation test. Differences in MMR expressions between patient- and tumor-specific characteristics were assessed using Chi-square tests or t-tests.

Results

So far, we only analysed 34 samples treated with surgery alone. From the 34 samples, 2 samples showed loss of one or more of the MMR proteins. Both MLH1 and PMS2 were lost in a 72-year-old man with pT3N0 ESCC. Moreover, we observed partial loss of MSH6 and MSH2 in a sample of a 78-year-old man with pT3N0 EAC. Results are aimed to be finalized by June 2023.

Conclusion

Based on these results, we may expect a heterogenous loss of MMR proteins in EC patients in both pre- and post-nCRT. Mapping patient- and tumor-specific characteristics that are associated with MSI in EC might give us new insights in prognosis and future selection of eligible patients for immunotherapy.

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

Gabriela Jesus
Brazil

Introduction
Diabetes mellitus affects around 1 in 10 people aged 20-79 of the world's population. Approximately 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 the recovery of damaged renal tissues. We aimed to verify whether MSC-based cell therapy or empagliflozin modulate the c-Kit+ cell population in the kidney of diabetic and obese BTBR ob/ob mice.

Material & 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 MSC treatment. At 10, 14, and 20 weeks, animals from each group were euthanized for tissue sample collection. We performed immunohistochemical (IHC) analysis and quantification using CellSens (Olympus) software. Quantitative PCR is ongoing. We used two-way ANOVA, considering the variables of time and treatment. $P<0.05$ was considered significant.

Results
Preliminary results indicate an increase in the detection of c-Kit+ cells in distinct compartments after MSC and empagliflozin therapies, including Henle´s loop, distal tubules, and collecting ducts, but not in proximal tubules. Strikingly, c-kit cells were found within the glomeruli. Mixed effects statistical analysis presently revealed a significant p-value for the treatment variable, but not for the time variable in the cortex (p-value=0.0008). Medulla and glomeruli data are still being obtained.

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

Comparative whole genome analysis reveals re-emergence of human Wa-like and DS-1-like G3 rotaviruses after Rotarix vaccine introduction in Malawi

Chimwemwe Mhango
Malawi

Introduction
G3 rotaviruses rank among the most common rotavirus strains worldwide in humans and animals. However, despite a robust long-term rotavirus surveillance system from 1997 at Queen Elizabeth Central Hospital (QECH) in Blantyre, Malawi, these strains were only detected from 1997 to 1999 and then disappeared and re-emerged in 2017, five years after the introduction of the Rotarix rotavirus vaccine.

Material & Methods
Here we analysed representative 27 whole genome sequences (G3P[4]; n=20, G3P[6]; n=1, and G3P[8], n=6) randomly selected each month between November 2017 and August 2019 to understand how G3 strains re-emerged in Malawi.

Results
We found four genotype constellations that were associated with the G3 strains that re-emerged and co-circulated in Malawi post-Rotarix vaccine introduction: G3P[4] and G3P[6] strains with the DS-1-like genetic backbone genes (G3-P[4]-I2-R2-C2-M2-A2-N2-T2-E2-H2), G3P[6] and G3-P[6]- I2-R2-C2-M2-A2-N2-T2-E2-H2), G3P[8] strains with the Wa-like genetic backbone genes (G3-P[8]- I1-R1-C1-M1-A1-N1-T1-E1-H1), and reassortant G3P[4] strains consisting of the DS-1-like genetic backbone genes and a Wa-like NSP2 (N1) gene (G3-P[4]-I2-R2-C2-M2-A2-N1-T2-E2-H2). Time- resolved phylogenetic trees demonstrated that the most recent common ancestor for each RNA segment of the re-emerged G3 strains was between 1996 and 2012, possibly through introductions from outside the country due to the limited genetic similarity with G3 strains which circulated before their disappearance in the late 1990s. Further genomic analysis revealed that the reassortant DS- 1-like G3P[4] strains acquired a Wa-like NSP2 genome segment (N1 genotype) through intergenogroup reassortment; an artiodactyl-like VP3 through intergenogroup interspecies reassortment; and VP6, NSP1 and NSP4 segments through intragenogroup reassortment likely before importation into Malawi. Additionally, the re-emerged G3 strains contain amino acid substitutions within the antigenic regions of the VP4 proteins which could potentially impact the binding of rotavirus vaccine-induced antibodies.

Conclusion
Altogether, our findings show that multiple strains with either a Wa-like or DS-1-like genotype constellation have driven the re-emergence of G3 strains. The findings also highlight the role of human mobility and genome reassortment events in the cross-border dissemination and evolution of rotavirus strains in Malawi necessitating the need for long-term genomic surveillance of rotavirus in high disease burden settings to inform disease prevention and control.

The influence of transforming growth factor-β (TGF-β) on human breast carcinoma cells

Nadja Jahn
Germany

Introduction

According to WHO, breast cancer is the most common cancer worldwide, resulting in 685,000 deaths in 2020. The most important cause of death is metastasis. The changes that enable cells to metastasize are known as epithelial-mesenchymal transition (EMT). At the molecular level, EMT is accompanied by loss of E-cadherin expression. In several murine tumor models, transforming growth factor-β (TGF-β) has been identified as an important EMT regulator. Our group demonstrated that TGF-β induces vascular endothelial cell-specific VE-cadherin in murine breast carcinoma cells and that this induction promotes the migratory, invasive, and angiogenic potential of cancer cells via activation of the TGF-β signaling pathway. In addition, VE-cadherin has also been shown to be expressed in human breast carcinoma cells, promoting their adhesion to endothelial cells and thus likely promoting invasion ability. Our aim is to investigate the importance of the TGF-β pathway for human breast carcinoma cells and, in particular, its possible interaction with VE-cadherin.

Material & Methods

Four human breast carcinoma cell lines (VE-cadherin positive: BT-20, SUM-149, MCF-7; VE- cadherin negative: MDA-MB-231) are treated with recombinant TGF-β for 3 weeks. Cells are examined with respect to proliferation (Ki-67), expression of cadherins (mRNA by RT-PCR and protein by Western Blot), as well as their localization via immunofluorescence. Furthermore, the expression of EMT markers, morphological changes and the crosstalk between TGF-β and VE- cadherin are investigated.

Results

Our preliminary results suggest that treatment with TGF-β decreases proliferation of treated versus control cells. On the other hand, TGF-β seems to promote a mesenchymal phenotype and the expression of certain EMT markers indicating mesenchymal transition. For example, we found so far for SUM-149 an increased expression of N-cadherin, Snail, Slug and Vimentin at the mRNA and protein level. Further results will be presented at the congress.

Conclusion

Our preliminary results show that VE-cadherin positive human breast carcinoma cells behave differently under treatment with TGF-β than murine ones. We can detect TGF-β dependent changes in the cells, with regard to proliferation and both EMT-markers and adhesion proteins, the tumor biological significance of which we are currently investigating.

Impact of palmitic acid exposure on SIRT1 and Class I HDACs function and its association with BDNF expression.

[1]Saúl Rueda
México

Introduction

Palmitic acid (PA) is the most common saturated fatty acid (SFA) in the human body and plays a key role in energy storage and membrane fluidity among many other physiological processes. PA is the major component of high-fat diets and it´s found in higher concentrations in people diagnosed with diabetes and obesity compared with healthy people. Recent studies have shown that neurons metabolize SFA and that in presence of a high concentration of PA, there is a dysregulation in histone deacetylases (HDACs), such as Sirtuin1 (SIRT1), which are involved in epigenetic mechanisms. The aim of this research is to evaluate in vitro time-dependent changes in the expression of HDACs, H3K9ac and Brain-derived neurotrophic factor (BDNF) after treatment with a high concentration of PA.

Material & Methods

Human neuroblastoma cells were differentiated into mature neurons employing the protocol used by Sánchez-Alegría (2021). Mature neurons were treated with PA at 300 µM for 3, 6, 12 and 24 hours. The protein levels were measured by Western blot. Immunofluorescence and confocal microscopy were used to evaluate changes in the density and distribution of H3K9ac. BDNF gene expression was measured by RT-PCR.

Results

Preliminary results: Class I HDACs, HDAC3 and HDAC2 showed an elevated expression after 3 and 24 hours of treatment, respectively. SIRT1 exhibited a lower expression at 24 hours of treatment compared with 3, 6 and 12 hours. H3K9ac showed decreased expression after 24 hours and a higher expression at 6 hours after PA treatment. No differences in H3K9ac density have been found; however, H3K9ac distribution appears to change and is closer to the cell periphery rather than the nucleus.

Conclusion

Mature neurons showed a dysregulation in the levels of HDACs after short (3 hours) and long (24 hours) exposure times to PA 300 µM. This might be due to lipid-response elements in their promoter or a disbalance in the Acetylases and acetyl-CoA metabolism. The overexpression of HDAC3 and HDAC2 may correlate with the alterations in the distribution of H3K9ac. Altogether could induce a change in chromatin that modify neuronal gene expression.
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Development of Functional Pancreatic Beta- Cells for Diabetes Mellitus Treatment using mRNA-Based Genetic Reprogramming of Human Mesenchymal Stem Cell

Ayesha Fauzi
Malaysia i

Introduction

The direct reprogramming of stem cells into pancreatic β-cell is a promising strategy for treating Diabetes Mellitus, however, its clinical implementation is limited by the potential risks associated with the use of viral vectors. An alternative approach using synthetic mRNA to differentiate pluripotent stem cells into pancreatic β-cell is proposed. The maturation of cells into specific lineage is regulated by transcription factors, which play a crucial role in the determining the fate of cells. By targeting specific transcription factors PDX1, NGN3, MAFA, PAX4 and GLIS3 it is possible to control the phenotype and specialization of human mesenchymal stem cell (huMSC) into β-cell.

This study investigates the use of synthetic mRNA transcription factors to differentiate human mesenchymal stem cells into functional pancreatic β-cell as a potential treatment for Diabetes

Material & Methods

The methodology involves several steps to assess the efficacy of using synthetic mRNA transcription factors to differentiate huMSC into pancreatic β-cell. The first step involves the synthesis of PDX1, NGN3, MAFA, GLIS3 and PAX4 mRNA through transcription, capping and tailing. Next, huMSC are transfected with different combination of these mRNA transcription factor. Cell viability is then determined using MTT assay post-transfection. Apoptosis assay using Annexin V-FITC is conducted to assess the non-toxicity nature of mRNA. Gene expression analysis via RT- PCR is also performed. Immunostaining is performed to detect the expression of β-cell markers, c- peptide and insulin, and compared between different combination groups.

Results

Results showed that terminally differentiated cells exhibit higher cell viability (>80%) compared to control groups (72.71%), indicating the non-toxicity of the mRNA-mediated differentiation approach. RT-PCR analysis showed insulin mRNA expression was highest in PNMPG differentiated beta cells when compared to control group (P<0.05). This suggest that the differentiation protocol we used effectively induced insulin expression in the cells, indicating successful differentiation into functional beta cells.

Conclusion

In summary, study demonstrates the use of synthetic mRNA transcription factors to differentiate huMSC into pancreatic β-cell resulted in higher cell viability and expression of β-cell markers compared to control groups. These findings suggest that this method may be a promising alternative treatment for Diabetes Mellitus.

Nephrology
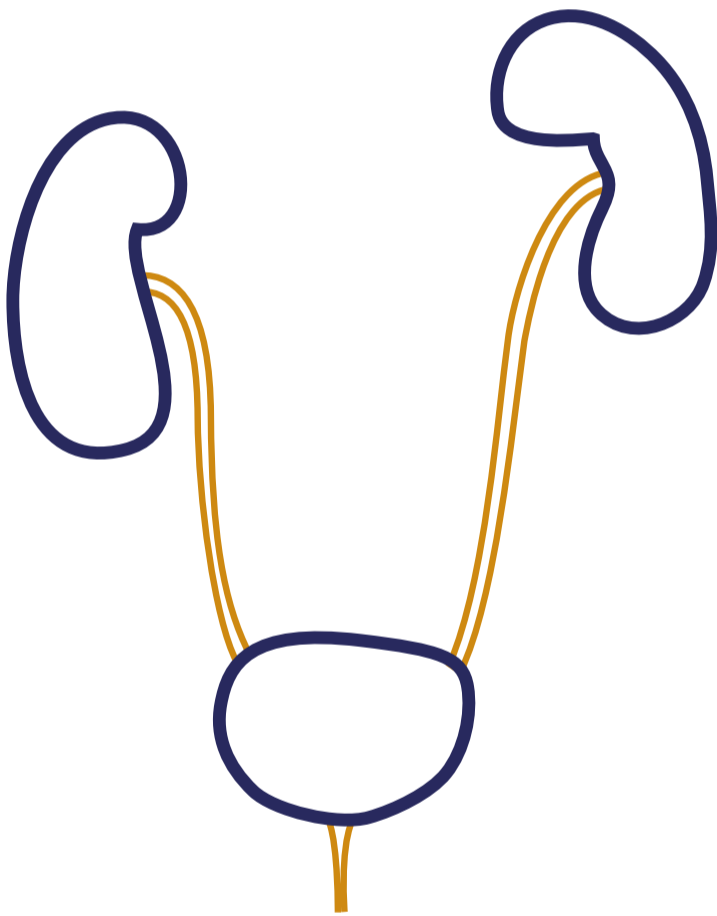
Presenters:
Eduardo Villa
Sheyda Rimaz
Yuanxin Xu
Laura Benito Zarza
Nam Nguyen-Hoang
Cassimy Neerven

The effect of hydration schemes on the incidence of cisplatin dose-limiting toxicities in head and neck squamous cell carcinoma patients

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Netherlands

Introduction

Cisplatin dose-limiting toxicity (CDLT), often caused by cisplatin-induced nephrotoxicity, is common during cisplatin-based chemoradiotherapy (CRT) in patients with head and neck squamous cell carcinoma (HNSCC). Currently, different strategies consisting of hydration using different saline infusions and varying timeframes are used to combat cisplatin-induced nephrotoxicity. The aim of this study was to assess whether a short hydration (SH) scheme in comparison with a long hydration (LH) scheme leads to less CDLT, specifically caused by nephrotoxicity, in HNSCC patients.

Material & Methods

In this Dutch multicenter retrospective cohort study, HNSCC patients from the Antoni van Leeuwenhoek (AvL) and Amsterdam University Medical Center, location Vrije Universiteit Medical Center (Amsterdam UMC), who were treated with 40 mg/m2 (Cis40) or 100 mg/m2 (Cis100) cisplatin-based CRT, were included. The AvL administered a LH scheme, whereas the Amsterdam UMC administered a SH scheme. The primary outcome was the incidence of CDLT due to nephrotoxicity. CDLT was defined as any toxicity resulting in dose-reduction of ≥50%, treatment delay of at least four days, or treatment cessation of cisplatin. Data was collected from patients from January 1st 2020 until July 1st 2022. Chi-square and Fishers' exact tests were performed to assess differences in incidence.

Results

In total, 112 patients (AvL 68 patients versus Amsterdam UMC 44 patients) receiving Cis40 and 100 patients (AvL 23 patients versus Amsterdam UMC 77 patients) receiving Cis100 were included. For patients receiving Cis100 with a LH scheme, more CDLT due to nephrotoxicity (n = 9 (39%) versus n = 13 (17%), p = 0.024), more treatment changes (n = 14 (61%) versus n = 29 (38%), p = 0.049), and a lower cumulative cisplatin dose (229.6 ± 54.5 versus 258.8 ± 62.0, p = 0.008) were observed as compared to the SH scheme. In patients receiving Cis40, no significant differences in CDLT were observed.

Conclusion

The current study demonstrates that in Cis100 the SH scheme is associated with less treatment changes due to toxicity, particularly nephrotoxicity, compared to the LH scheme. This resulted in a difference in the cumulative cisplatin dose. Therefore, for HNSCC patients receiving Cis100, the SH scheme is preferable

Fibroblast Growth Factor 23 increases the risk of COVID-19 in end-stage renal disease patients: results from a prospective cohort

Eduardo Villa
Chile

Introduction

End-stage renal disease (ESRD) patients have an increased rate of COVID-19 and mortality. These patients present a reduced humoral response to SARS-CoV-2 immunization, associated with immune dysfunction. ESRD patients also present high levels of Fibroblast Growth Factor 23 (FGF23), a bone-derived hormone that reduces immune response in vivo and in vitro. Increased FGF23 is associated with increased infectious-related hospitalizations and adverse infectious outcomes. Thus, we evaluated whether ESRD patients with high plasma FGF23 levels have an increased rate of SARS-CoV-2 infection.

Material & Methods

We performed a prospective cohort of ESRD patients in hemodialysis who had measurements of plasma intact FGF23 during 2018-2019. We determined COVID-19 infections, hospitalizations, and mortality between January 2020 and December 2021.

Results

We evaluated 119 patients. Age: 61.0 ± 10.9 years. Female: 97 (39.9%), median hemodialysis vintage: 23 months [range: 3-120 months]. During follow-up, 45 patients developed COVID-19 (18.5%), 35 patients were hospitalized, and 10 patients died (mortality: 22.2%). We found that patients with higher FGF23 levels (defined as equal or above median) had an increased rate of COVID-19 compared with those with lower levels (26.7% versus 10.1%; Hazard ratio: 2.87 [1.24-6.62], p=0.021). Multivariate analysis showed that increased plasma FGF23 was independently associated with COVID-19.

Conclusion

Our results suggest high plasma FGF23 levels are a risk factor for developing COVID-19 in ESRD patients. These data support the potential immunosuppressive effects of high circulating FGF23 as a factor implicated in the association with worse clinical outcomes. Further data is needed to confirm this hypothesis.

Developing and validating a clinical prediction model for acute kidney injury in critically ill patients

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Netherlands

Introduction
Acute kidney injury (AKI) is a global concern with a high incidence and a poor prognosis among critically ill patients. Diagnosis of AKI is frequently only detected well after its onset, at which stage the injury may be irreversible. Thus, early risk stratification is crucial in AKI management. We aimed to evaluate the predictive values of different types of readily available predictors in daily practice and develop a clinical prediction model for severe AKI within seven days after ICU admission.

Material & Methods
We used data from the Simple Intensive Care Studies II (SICS-II), a prospective cohort study including 1010 critically ill adults conducted at the University Medical Center Groningen, the Netherlands. The prognostic outcome was the development of severe AKI, defined as KDIGO stage 2 or 3, within the first seven days after ICU admission. We categorized candidate predictors (recorded within the first 24 hours of ICU stay) into four different types of variables, i.e., demographics (baseline predictors), acute physiological values, comorbidities, and pre-admission medication use, and evaluated their contribution to the prediction of severe AKI. The least absolute shrinkage and selection operator (LASSO) methodology was used for model estimation. The established model was internally validated using 10-fold cross-validation. The area under the receiver operating characteristic curve (AUROC) was assessed to evaluate model performance.

Results
Of the SICS-II cohort, 937 patients were eligible for our analyses. Severe AKI developed in 351 (37%) patients. Acute physiological values emerged as the most important predictors, increasing the AUROC of the baseline model from 0.58 to 0.77 in the cross-validation. Pre-admission medications did not contribute to predicting severe AKI. Eventually, we derived a six-variable model selected by LASSO, including BMI, renal component of the Sequential Organ Failure Assessment [SOFA] score, plasma urea concentration, arterial pH, 24-hour urine output, and presence of acute respiratory failure. The final model had an apparent AUROC of 0.79 and performed relatively well in the 10-fold cross-validation, with an AUROC of 0.77.

Conclusion
Pre-admission medication contributed no relevant information for predicting the occurrence of severe AKI within seven days after ICU admission compared to acute physiological values. Using readily available predictors in the ICU setting, we could derive a clinical prediction model with good performance.

Evaluation of Factors Related to Acute Kidney Injury in Patients with Severe Burns admitted to Burn Intensive Care Unit.

Sheyda Rimaz
Iran

Introduction
Acute kidney injury (AKI) is one of the most common complications of severe burns and affects the prognosis of patients.The incidence and predictors of AKI are limited, especially in developing countries. In this study, we aimed to investigate the incidence of early AKI and factors associated with early AKI in patients with severe burns.

Material & Methods
This present study was performed on burn patients with TBSA ≥ 20% who were admitted to Velayat burn hospital between March 2016 and November 2020 after receiving of ethics number IR.GUMS.REC.1399.414. Patients with a history of ESRD,admission after >72 h from the time of the burn incident, and those who died within the first 24 hours of hospitalization were excluded from the study. KDIGO criteria were used to define early AKI in the first 5 days of hospitalization. Multivariable logistic regression was used to model association between baseline risk factors and risk of AKI.The collected data was entered into SPSS software version 22 with a significance level of 0.05.

Results
Of the 194 patients included the mean age of the subjects was 42.99±17.58. 138 patients (71.1) were male. The mean TBSA% was 49.18±24.71. According to KDIGO criteria, 43 patients (22.2) developed early AKI during the first 5 days of hospitalization as follows: Stage I(12.4) 24 patients, Stage II (7.2) 14 patients,Stage III(2.6) 5 patients. 85 patients (43.8) died. Mortality in patients with early AKI (76.7) was significantly higher than patients without early AKI (34.4). Patients who developed AKI had more age,days of mechanical ventilation,ICU stay days,sepsis, Baux score, and modified Baux score when compared to those patients who did not develop AKI($P=0.001$). Multivariable logistic regression demonstrated association between AKI and the following variables: gender (OR = 2.872, P = 0.032), age (OR = 1.047, P = 0.000), TBSA %> 60 (OR = 6.134, P = 0.001) are independent risk factors for developing early AKI. Our study also showed that TBSA% significantly increases the severity of AKI.

Conclusion
The results of this study showed that AKI is common in patients with a major burn injury. Age, gender and TBSA% are the strongest independent predictors of early AKI.

Engineering the Renal Proximal Tubule with Micro-Patterned, Fibrous Melt-Electro-Written Membranes

Laura Benito Zarza
The Netherlands

Introduction
Current in vitro models fail to faithfully reproduce the complexity of the kidney microenvironment and its associated diseases. The relevance of the extracellular matrix (ECM) in cells' behavior and performance has been pin-pointed when developing better biomimetic models. The aim of this study is to engineer an in vivo-like membrane that recapitulates two key topographical cues from native kidney ECM: porosity and curvature. To do so, cutting-edge 3D printing technologies and microfabrication techniques were employed, and proximal tubule cell behavior and phenotype were analyzed.

Material & Methods
A melt-electrowriting (MEW) 3D printer was utilized to fabricate the membranes. Briefly, molten polymer (poly-e-caprolactone) is extruded while being subjected to an electric potential (8.2 kV), depositing very thin filaments (~8.46 µm) in a layer-by-layer fashion. To imprint curvature, aluminum substrates with half-pipe patterns were employed to guide the filament in the printing process. The relationship between physical features (porosity, pore area, winding angle, filament diameter and membrane thickness) and fabrication parameters (printing speed and number of layers) was studied. These parameters were optimized to obtain robust membranes that supported cell culture and maximized topographical guidance. Membranes with three different groove diameters (400, 600 and 800 µm) were tested and flat membranes were used as controls. Conditionally immortalized proximal tubule epithelial cells (ciPTECs) were seeded on the membranes and immunofluorescence stainings were performed to assess polarization marker expression (NaK-ATPase, α-tubulin), cytoskeleton alignment (phalloidin) and ECM deposition (collagen IV).

Results
Printing speed and number of layers were found to affect porosity and winding angle. Printing speed was optimized to 7.5 mm/s and the number of layers was set to 10, rendering membranes with a porosity of 50% and pore areas between 100 – 200 µm2. ciPTECs expressed polarization markers regardless of the groove diameter, aligned differently depending on the groove diameter and produced more collagen IV with smaller pore areas.

Conclusion
Cells were observed to adopt a more in vivo-like behavior and phenotype when seeded on curved membranes instead of flat ones. MEW 3D printing has the potential to fabricate intricate patterned porous membranes, enabling the generation of more reliable and representative models for different tissues.

Triglyceride–glucose index and incident hypertension in the general population

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Netherlands

Introduction
Hypertension poses a significant worldwide public health challenge as risk factor for cardiovascular and chronic kidney disease among others. The triglyceride and glucose (TyG) index was proposed as a surrogate for insulin resistance, but its prospective association with hypertension in White populations is unknown. This study investigated the association between the TyG index and incident hypertension in the Prevention of Renal and Vascular End-stage Disease (PREVEND) cohort.

Material & Methods
A total of 2332 adults free of hypertension at baseline were studied. Hypertension was defined as systolic blood pressure (SBP) ≥ D 140 mmHg or diastolic blood pressure (DBP) ≥ 85 mm Hg or the initiation of antihypertensive medication use. The association between baseline TyG index and incident hypertension was determined using Kaplan-Meier analysis and Cox regression models.

Results
During a median [IQR] follow-up of 11.2 [7.85–11.8] years, 637 out of the 2332 (27.3%) participants developed hypertension. In the lowest tertile of the TyG index, incident hypertension was 19.0%, compared to 25.6% in the second and 36.2% in the highest tertile. In Kaplan-Meier analysis, sex- stratified tertiles of the TyG index were prospectively associated with de novo hypertension development (log-rank test p < 0.001). Cox regression analysis confirmed a significant prospective association between a higher TyG index and incident hypertension in a fully adjusted model (aHR [95% CI], 1.90 [1.67, 2.17], p<0.001). In receiver operating characteristic (ROC) curve analyses the area under the curve of the TyG index was 0.704, virtually identical to the value for Homeostatic Model Assessment for Insulin Resistance of 0.705.

Conclusion
This study establishes the TyG index as a strong prospective predictor of incident hypertension in a European White population. From a clinical perspective, the TyG index could serve as a convenient and cost-efficient indicator for the risk of hypertension.

Infectious Disease

Presenters

Sophie Shyfrin
Samuel Lawrent Mpinganjira
Temilade Bello
Sofia Chala
Ivan Szergyuk
Taye Owoputi

Postoperative pulmonary complications and mortality rates after lung-protective ventilation (LPV) versus conventional ventilation (CV): A Meta-analysis

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Egypt

Introduction

Over 310 million major procedures are performed under general anaesthesia annually. General anaesthesia can cause a variety of respiratory complications from infection up to respiratory failure. To reduce postoperative pulmonary complications, several ventilation strategies have been proposed. However, other factors affecting ventilation, such as intraoperative ventilation duration and postoperative care, were not previously addressed. In this study, we aim to evaluate the efficacy of lung-protective ventilation (LPV) versus conventional ventilation (CV) in lowering postoperative pulmonary complications and mortality, taking factors not previously included in the literature into consideration.

Material & Methods

We searched PubMed, Web of Science, Cochrane Library, and Scopus databases up to August 2022. Data was pooled as risk ratio (RR) and 95% Confidence Interval (CI) or mean difference (MD) and 95% CI according to the type of each outcome measure. Analysis was conducted using Review Manager software 5.4.

Results

17 randomized controlled trials (RCTs) were included in our study. We found that LPV significantly reduced events of atelectasis compared to CV (RR = 0.41; 95% CI: [0.27, 0.63], P < 0.0001), and pneumonia (RR 0.39; 95% CI:[0.19, 0.79], P=0.009). Meanwhile, CV showed a significant reduction in PiO2/FiO2 ratio and PaCO2 levels at the end of surgery (MD 69.87; 95% CI:[38.55, 101.18], P<0.0001), (MD 2.61; 95% CI:[0.78, 4.44], P=0.005) respectively. According to our study, no significant differences were found between the two interventions regarding pleural effusion and acute respiratory distress syndrome outcomes. However, Lung protective ventilation was favored over conventional ventilation which significantly reduced events of atelectasis and pneumonia according to pooled analysis. Our study considered the amount of tidal volume delivered and the peak pressure. Patients in lung-protective ventilation groups had lower delivered tidal volume than those in conventional ventilation groups, according to a pooled analysis. Meanwhile, there were no variations in Peak Pressure results between LPV and CV following anesthesia induction or at the end of surgery.

Conclusion

LPV resulted in better outcomes regarding pulmonary postoperative complications like atelectasis and pneumonia. On the other hand, CV showed a significant reduction inPiO2/FiO2 ratio and PaCO2. Both interventions showed no different significant results in terms of other complications like ARDS and pleural effusion.

PACAP contributes to the maintenance of endotoxin fever through the regulation of pyrogenic cytokines and cyclooxygenase-2

Jason Sparks
Magyarország[1]

Introduction

Pituitary adenylate cyclase-activating polipeptide (PACAP) signaling is involved in various inflammatory processes. A common manifestation of systemic inflammation is fever, which is usually induced in animal models with the administration of bacterial lipopolysaccharide (LPS). A role for PACAP signaling was suggested in LPS-induced fever, but the underlying mechanisms of how PACAP contributes to febrile response have remained unclarified.

Material & Methods

We administered LPS (120 μg/kg, intraperitoneally) to mice with the Pacap gene, i.e., the gene encoding the PACAP protein, either present (Pacap+/+) (n=15) or absent (Pacap−/−) (n=14) and measured their thermoregulatory responses, serum cytokine levels, and tissue cyclooxygenase-2 (COX-2) expression.

Results

We found that the LPS-induced febrile response was attenuated in Pacap−/− mice compared to their Pacap+/+ littermates starting from ~120 min postinfusion. Administration of LPS resulted in amplification of COX-2 mRNA expression in the lungs, liver, and brain of the mice in both genotypes at 210 min postinfusion. Serum concentration of the pyrogenic cytokines interleukin (IL)-1α and β were significantly increased in Pacap+/+ mice in response to LPS compared with saline, whereas the change was not significant between the treatment groups in Pacap−/− mice. In case of IL-1α and β, the intergenotype difference between the LPS-treated groups was also significant. The serum concentrations of IL-6, IL-10, and TNFα were higher in LPS-treated than in saline-treated mice of both genotypes, however, the rise in IL-10 was significantly attenuated in Pacap−/− mice compared to Pacap+/+ mice.

Conclusion

PACAP signaling is necessary for normal fever maintenance. Our results suggest that PACAP contributes to the later phases of LPS-induced fever by modulation of COX-2 protein expression in the periphery and the brain, as well as by augmentation of pyrogenic cytokine levels in the circulation. These findings advance the understanding of the crosstalk between PACAP signaling and the "cytokine-COX-2" axis in systemic inflammation, thereby open up the possibilities for new therapeutic approaches.

The Relationship Between Dietary Habits And Controlled Status of Hypertension : A Cross Sectional Study

Nadia Alfi Syarifah
Indonesia

Introduction
Hypertension is a health problem that has a high prevalence rate in the world and is the most common case of non-communicable diseases in Indonesia. Batu City is ranked first for hypertension cases in East Java-Indonesia at 2019 with an incidence of 10,010 cases. Dietary intervention components consisting of caloric intake, food habits, and emotional eating are the factors that can increase the success of blood pressure control in hypertensive patients. This study aims to determine the relationship between calorie intake, food habits, and emotional eating with blood pressure control in hypertensive patients at the Junrejo Health Center and Batu Health Center.

Material & Methods
This study used a cross sectional method and a purposive sampling technique with a total of 265 respondents. 24 Hours Food Recall Questionnaire, Adolescent Food Habits Checklist (AFHC), Emotional Eating Scale (EES), and medical record data were used to assess caloric intake, food habits, emotional eating , and blood pressure control. The data were presented descriptively and analyzed using the Spearman Rank correlation test.

Results
The hypertension status of respondents showed 72,8% had uncontrolled hypertension. The dietary habits profile of respondents is dominated by less calorie intake category (95.5%), most of the respondents had food habbit that were classified as neutral (62.4%), and low emotional eating (93.2 %). Calories intake [$p=0.487$, $rs= 0.043$, $CI= 95\%$] and emotional eating [$p=0.719$, $rs= -0.022$, $CI= 95\%$] showed no significant relationship with controlled status of hypertension, meanwhile the results of the correlation test showed that food habits [$p=0.020$, $rs= -0.143$, $CI= 95\%$] had a significant relationship with blood pressure control.

Conclusion
Food habits which are component of dietary habits had a significant relationship with controlled status of hypertension, meanwhile calories intake and emotional eating found had no relationship with controlled status of hypertension in this study. Dietary habits might contribute to the blood pressure control in hypertensive patients.
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Studying the association between blood pressure and parameters related to sleep disorders in Tabari Cohort population

[1] *Amirhossein Hessami*
Iran

Introduction
In this highly stressed world, sleep disorders have become a prevalent problem in the society. As sleep involves in various physiological mechanisms of healthy body, insomnia and other sleep disorders can potentially lead to an increase in blood pressure, thereby resulting in premature death. Regarding this, the present study was conducted to investigate the relationship between hypertension and parameters related to sleep disorders in Tabari cohort population.

Material & Methods
In this cross-sectional study, the data from the enrollment phase of the Tabari cohort study were adopted. Tabari cohort is a part of the PERSIAN (Prospective Epidemiological Research Studies in Iran) cohort study. Hypertension was defined as systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg or a history of having high blood pressure or being treated with anti-hypertensive drugs. Data analysis was performed using descriptive and inferential statistics.

Results
A number of 10,255 patients enrolled in the Tabari cohort in which 2,281 patients (22.2%) had hypertension. Hypertension was more prevalent in sleep duration of < 6 and > 10 h than the non- hypertensive cases (12.9% vs. 11% and 6.9% vs. 5.9%, respectively; P = 0.005). The odds ratio of hypertension in patients with insomnia and hypersomnia is 1.22 (95% [CI], 1.06–1.40) and 1.22 (95% CI, 1.01–1.47) folds higher than normal sleep. After adjusting the effect of sex, age, body mass index, waist circumference, area residence, high-density lipoprotein cholesterol, triglyceride, and total cholesterol variables with multivariable logistic regression, there was no significant association. Frequency of routine hypnotic medication usage (14.6% vs. 5.7%, P < 0.001), involuntary napping (25.3% vs. 19%, P < 0.001), and leg restlessness during sleep (14.8% vs. 11.7%, P < 0.001) was higher in hypertensive individuals than in non-hypertensive cases.

Conclusion
According to results of this study sleep disorders are more prevalent in hypertensive patients. The routine use of hypnotics, involuntary napping and leg restlessness syndrome was significantly higher in patients with hypertension compared to that in the non-hypertensive patients.

Protective effect of Metformin on oxidative stress induced by Lipopolysaccharide in the cardiovascular system of rats.

[1] *Seyedeh Naghmeh Layegh Khavidaki*
Iran

Introduction

Cardiovascular disease (CVD) is considered the leading cause of morbidity and mortality in communities. Oxidative stress and inflammation play an essential role in the pathogenesis of CVD. Metformin has been shown to reduce oxidative damage and the level of inflammatory cytokines and reactive oxygen species in cells. Thus, the present study aims to manifest the potential effect of Metformin against oxidative stress and damage induced by lipopolysaccharide (LPS) in the cardiovascular system in rats.

Material & Methods

Forty male Wistar rats weighing 250 ± 10 g were preserved in a standard environment and randomly divided into five groups, including control, LPS, LPS-Met50, LPS-Met100, and LPS-Met200. The control group received 1mL/kg saline intraperitoneal (i.p.) and 1mL/kg saline (i.p.). The LPS group was injected with 1mL/kg saline (i.p.) and 1mg/kg LPS (i.p.). The other three groups were injected with 1mg/kg LPS after injection of 50mg/kg, 100mg/kg, and 200mg/kg Metformin, respectively. We evaluate the malondialdehyde (MDA), thiol, catalase (CAT) and superoxide dismutase (SOD) in serum as well as heart and aorta tissues following the sacrifice of the rats.

Results

Administration of LPS induced inflammation due to increasing MDA levels and decreasing thiol, CAT and SOD levels in serum, heart and aorta tissues compared to the control group. In contrast, treatment with all three dosages of Metformin significantly decreased MDA levels and increased thiol, CAT and SOD levels in heart and aorta specimens. Additionally, inflammation markers reduction following the increase in metformin dosage was observed. Metformin's effect on inflammatory markers in serum specimens differs relevant on the dosage. Compared with the LPS group, all three dosages of Metformin decreased MDA level and increased SOD level; nevertheless, only LPS-Met200 increased the thiol content significantly. An increase in CAT level in serum was also observed in LPS-Met100 and LPS-Met200, unlike LPS-Met50.

Conclusion

This study demonstrated that Metformin has a protective effect against oxidative stress induced by LPS in the heart, aorta, and serum of rat cardiovascular disease model. These findings suggest that Metformin could prevent or reduce the morbidity and mortality of cardiovascular disease due to its antioxidant and anti-inflammatory effects on the cardiovascular system of rats.

Hepatitis B Infection: Knowledge and Vaccination Status of Healthcare Students in Nigeria

[1] *Taye Owoputi*
Nigeria

Introduction

Hepatitis B virus (HBV) infection is a global health problem, with approximately 30% of the world's population showing evidence of past and new infection. Healthcare workers and students, due to occupational exposure to infected blood and blood product, are among the most vulnerable group of the population with a higher risk of acquiring HBV. Although a safe and effective vaccine has been developed against HBV infection, only a few of the healthcare students have completed the recommended three-dose vaccination, and even far less number knows their post-vaccination immunization status. We aimed to assess the level of knowledge of HBV infection, vaccination history of students, and factors associated with vaccine uptake among healthcare students.

Material & Methods

We conducted a cross-sectional web-based survey among 422 undergraduate Medical, Dental, Nursing and Physiotherapy students at the University of Ibadan, Nigeria, using a structured self- administered questionnaire. To cater for missing data, questions were made required as appropriate for submission to be possible. Data were analyzed using IBM SPSS version 23. The Chi-squared test was used to test for association between variables. The level of significance was set at $p < 0.05$.

Results

Out of the 422 responses, 410(97%) claimed they were aware of Hepatitis infectio. Of these 410 respondents, 94% had good knowledge score for hepatitis B infection. Age(0.0041), Department(0.0020) and Level of study(0.0177) were all significantly associated with knowledge of Hepatitis B virus infection. Also, of those that are aware, only 273(67%) have had hepatitis B screening, majority of which have had hepatitis B vaccination 248(91%). However, only 120(48%) of those vaccinated have completed the three recommended doses and unfortunately, 7(6%) claimed they went back for post vaccination serology titre. Common reasons for poor vaccination uptake include; lack of time, financial difficulties and lack of proximity to vaccination centres.

Conclusion

Our study has shown a huge gap in the hepatitis b vaccination profile of healthcare students in Nigeria who are ironically a high-risk group of the country's population both in terms of exposure to the disease and its spread. There is a need for programs to ensure vaccination uptake and post vaccination serology titre.

Nephrology
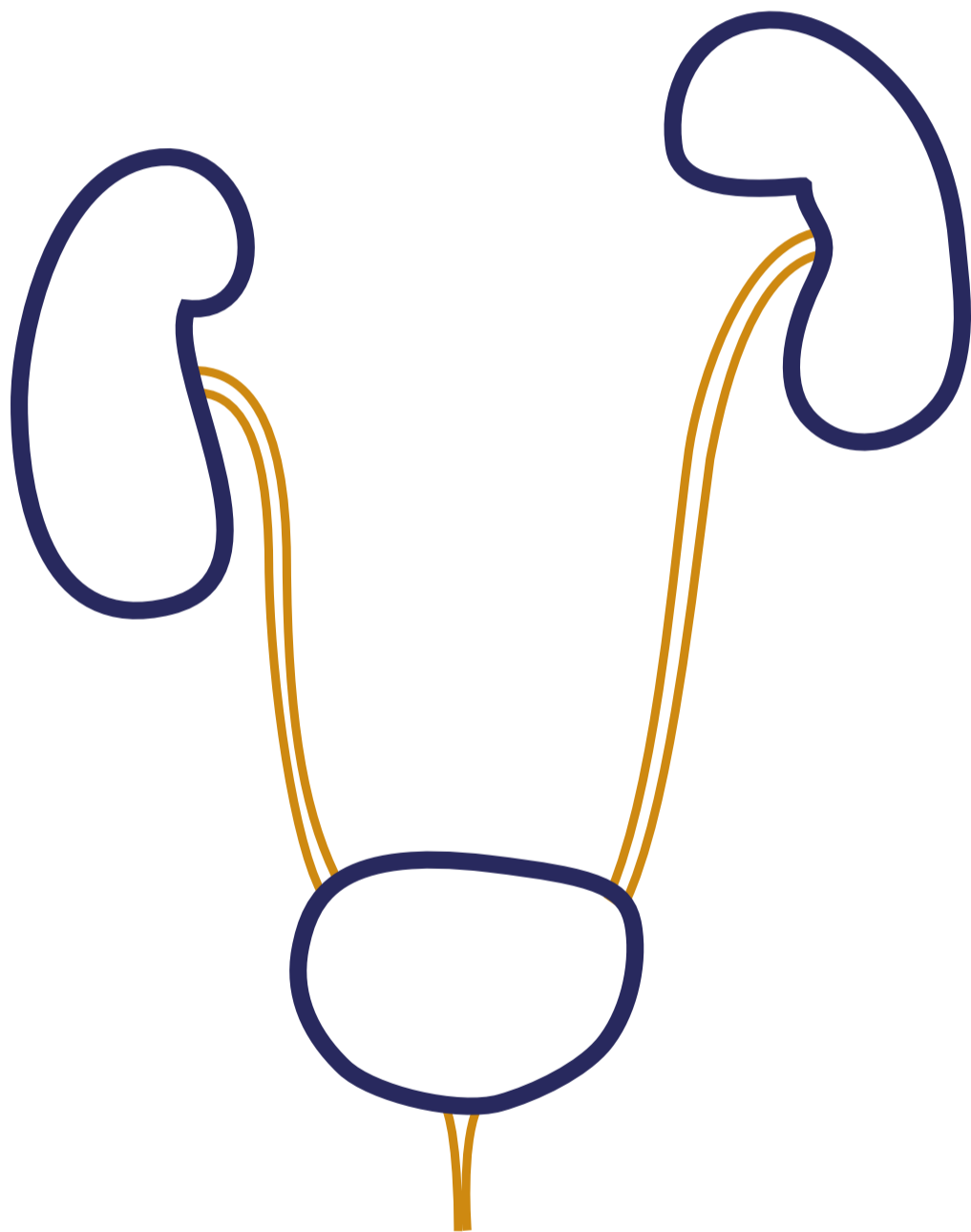
Presenters:
Laura Benito Zarza
Cassimy Neerven
Sheyda Rimaz
Eduardo Villa
Yuanxin Xu
Nam Nguyen-Hoang

Prevalence and Determinants of Self-reported Sexually Transmitted Infection among HIV infected Individuals attending PHC Facilities in Tembisa, Ekurhuleni North Sub-district.

[1] *Malebo Mahlalela*
South Africa

Introduction

Sexually transmitted infections (STIs) remain a significant global public health concern and a threat to realizing the goal of controlling the HIV epidemic, particularly in South Africa, where there is a high burden of HIV. We investigated factors associated with self-reported STIs and prevalence among HIV-infected adults on ART attending Primary Health Care (PHC) facilities in Tembisa, Ekurhuleni North Sub-district, Gauteng Province, South Africa.

Material & Methods

Between 15 September 2020 and 31 March 2021, we recruited and enrolled 217 HIV-infected adults on ART to conduct a cross-sectional study. Using a semi-structured questionnaire, we collected information on socio-demographic characteristics, STI symptoms, previous STI diagnosis, condoms, illicit drugs and alcohol abuse, and sexual risk behaviour and practices. We performed a descriptive statistical analysis to summarize data on STI prevalence and a binomial logistic regression model to assess factors associated with self-reported STIs.

Results

Of the 217 HIV-infected adults on ART, two-thirds (66%) were women, and the mean (SD) age was 36±8.4. We observed the prevalence of self-report STIs to be 27.65% (95% CI: 21.8-34.1). Vaginal discharge (34/93, 36.5%), genital warts or sore (30/93, 32.2%), and penile discharge (23/93, 24.7%) were the most reported symptoms of STIs. Seventy-four percent of adults reported using PHC facilities for their general healthcare needs. Those who were cohabiting (aOR 3.66; 95% CI, 1.01-13.18; p=0.047), practicing condomless sex (OR 2.88; 95% CI, 1.37-6.03; p=0.005), and not consistently taking ARV (aOR 4.01; 95% CI, 1.02-15.64; p=0.045) were more likely to self-report symptoms of STIs. Among individuals aged 40 years and above, the risk of self-reporting STIs was found to be low (aOR 0.32; 95% CI, 0.11-0.95; p=0.040).

Conclusion

A relatively high prevalence of self-reported STIs was observed among HIV-infected adults on ART. Condomless sexual practices, cohabiting, and not consistently taking ARVs were found to be contributing factors to the high STI prevalence. Continued efforts to improve existing health education interventions and strengthen risk-reduction counseling at healthcare facilities could address these contributing factors and reduce the risk of STI/HIV transmission among people living with HIV

Community-based interventions against violence: Access, barriers and enablers among married women living with HIV in Southwestern Uganda.

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Uganda

Introduction

Multi-sectoral community-based interventions against violence (CoBIAV) have the potential of preventing and mitigating gender-based violence including intimate partner violence (GBV) against women living with HIV in rural sub-saharan African settings where there are high cases of GBV. This paper will determine the level of access and use of the CoBIAV and examines the barriers and enablers to access and use of the CoBIAV amongst ever-married women living with HIV in rural sub-saharan African setting Uganda.

Material & Methods

We conducted a quantitative cross-sectional study among 424 consecutively sampled HIV-positive ever- married women attending Antiretroviral Therapy (ART) clinic in rural southwestern Uganda in April 2021. We adapted a questionnaire from a previous study to collect data through one-on-one interviews. We collected data on the participant's socio-demographic characteristics that included age, current marital status, and income, access to CoBIAV and potential access, barriers and enablers. We analyzed the data using Statistical Package for Social Sciences (SPSS) version 20.0. Associations were determined using Chi-square statistics and Logistics regression at p<0.05 significance level and 95% confidence interval.

Results

The participants had a mean age of 39.5 ± 10.2 years. Although not really implying their unavailability, the CoBIAV that were never mentioned by the participants included risk screening, emergency department intervention, safe women shelters, batterer treatment program and social protection services. The proportion of the women who reported to have ever accessed the available CoBIAV services was 53.3% by 2021. Women aged 36-49 years were most likely to have accessed COBIAV services. The top five accessed interventions were police services, local government official's services, health practitioner's service, counseling practitioner's services and civil society or non-governmental organization facilitated advocacy services. The enabling factor significantly associated with access to CoBIAV services was being a woman in the middle age bracket of 36-49 years. The barriers significantly associated with access to CoBIAV services among the HIV-positive ever-women identified included: having a separated/divorced marital status (aOR: 0.13, 95% CI: 0.04-0.4), being married and living with the partner (aOR: 0.1, 95% CI: 0.04-0.29) and being aware of the providers of the available CoBIAV (aOR: 0.008, 95% CI: 0.001-0.065).

Conclusion

The proportion of women living with HIV in rural southwestern Uganda who have ever had access to CoBIAV following their HIV diagnosis and disclosure was found to be just above 50% by 2021. Access to the interventions was associated with the women's marital status and awareness about the available interventions. There is still a need for stakeholders to increase access to CoBIAV through engagement of couples as well as including the batterers and increasing advocacy and public awareness about the available interventions.

T1Drink: patterns of alcohol consumption in young adults with type 1 diabetes – a CGM- supported international collaborative study

Julia Wykrota
Poland

Introduction
Type 1 diabetes (T1D) is a chronic autoimmune disease, that causes pancreatic islets B-cells to cease their insulin production. Therefore, its treatment requires intensive insulin therapy. With increasing world prevalence and its typical onset before adulthood, T1D influences almost every aspect of a person's life – including alcohol consumption. Although advised to reduce or completely abstain from alcohol use, people with type 1 diabetes present a similar rate of alcohol consumption to the population without the disease. Studies have also shown a higher incidence of binge drinking in young adults with T1D. T1Drink aims at filling the information gap in this field.

Material & Methods
Data is gathered via a dedicated website, using online questionnaires and a CGM uploading platform. Each respondent (aged 16-35) answers questions probing various areas regarding alcohol consumption in T1D. An ID-generator enables for anonymous participation. The collected patients` characteristics (Part 1) include age, diabetes duration, method of treatment and self- reported glycemic control. Part 2 focuses on diabetes-related education and beliefs about safe management of drinking. Part 3 handles lifetime experience, consumption habits, actions taken to manage diabetes and detects alcohol use disorders. Part 4 comprises recent alcohol consumption and its effect on glucose variability. Part 5 allows participants to share data from continuous glucose monitoring devices (CGM) covering days when alcohol was consumed and standard reference days.

Results
Study is conducted at an international level, currently available in 12 languages and is being spread to people with T1D through collaborators in multiple countries. The primary questionnaire was prepared in English and subsequently translated into other languages. It was launched at the end of 2022 and is open until March 2023. So far 177 responses have been submitted. During the ISCOMS conference general characteristics of the sample as well as answers to study's primary questions will be presented. Survey design and all study-related information are available at https://t1drink.umed.pl/en

Conclusion
Gathered real-life global data concerning the influence of various alcoholic beverages consumption, that differ in sugar and alcohol content on glucose variability and safety of people with type 1 diabetes, can support development of patient-centered recommendations regarding studied issue.

Prevalence of post-traumatic stress disorder signs among medical students during the war in Ukraine: a cross-sectional study.D³

Khalil Azrak
Ukraine f

Introduction
The war in Ukraine had a devastating effect on the population's mental health, including medical students. Many of them had to experience multiple traumatic events that may increase the risk of Post-Traumatic Stress Disorder (PTSD) signs. However, these students are still trying to cope and follow their highly demanding educational activities despite their possibly undiagnosed mental illnesses. That can lead to the deterioration of their quality of life and social functioning. We aimed thus to estimate PTSD symptoms prevalence among medical students and investigate the associated factors.

Material & Methods
A cross-sectional study was conducted among medical students at Bogomolets National Medical University in Kyiv, Ukraine. Data were collected between June 1 and June 30, 2022. Participants were asked to fill out a questionnaire consisting of 2 parts. The first was about Socio-demographic information. The second was Post-Traumatic Stress Disorder Checklist (PCL-5), a tool based on Diagnostic Statistical Manual 5 (DSM 5) for provisionally diagnosing PTSD. The Chi-square test was used to compare the prevalence of PTSD between categorical groups.

Results
Overall, 376 students participated. 47.1% had a PCL-5 score of ≥ 33 and were thus considered to have a high risk of PTSD. The mean age was 21.45 ± 2.66 years and the majority were females 77.7%. Negative alterations in mood and cognition were regarded as the most common cluster symptom of PTSD. Being a female, having a close person physically affected in the war, and inability to have psychotherapy were significantly associated with having PTSD signs ($p<0.05$). Regarding factors that may influence a PTSD diagnosis: 62% of participants have been internally displaced, 30.6% had a close person/relative who has been physically affected, 7.2% were directly physically affected by the war, and 63.6% reported inability to have psychotherapy now.

Conclusion
Our study revealed significantly high levels of PTSD signs prevalence among medical students. It also highlighted possible risk factors associated with developing PTSD symptoms. The results provided insight into the mental health crisis in Ukraine, which is leaving many undiagnosed and untreated. Therefore, there is an urgent need to implement screening programs for PTSD and improve access to psychotherapy to control the rising mental health issues.

Positive Attitudes Despite Moderate Knowledge: The Future of Precision Medicine in Jordan.

Lana Sbitan
Jordan

Introduction
As precision medicine gains momentum, the traditional - One Size Fits All - approach to disease prevention and treatment is becoming less reliable. Medical education must prioritize equipping physicians with the knowledge and understanding necessary to implement precision medicine effectively and keep pace with the latest developments in this field. Our study aimed to investigate the knowledge, attitudes, and perceived barriers to precision medicine among medical students, interns, and physicians in Jordan.

Material & Methods
We conducted an analytical cross-sectional study, collecting data from 607 eligible participants via a validated questionnaire from October to December 2022. Using IBM SPSS 26, we evaluated and compared precision medicine knowledge, attitudes, and perceptions among medical students and physicians. Significant associations were determined using chi-squared test for independence and fisher's exact test.

Results
In our study of 607 participants, we detected a moderate level of knowledge. The results also showed a moderate association between the participants' age, primary practice setting, and knowledge score (P<0.001, φc=0.27 and 0.29, respectively), as well as a weak association with their seniority level (P=<0.001, φc = 0.18). Most respondents (79.1%) would consider using genome-guided prescribing tools developed by researchers. Only (15.8%) thought that these tools were not clinically useful. Our findings indicate a favorable attitude toward precision medicine, with students having better perceptions than physicians (p=<0.001). Generally, physicians had greater confidence in their ability to implement precision medicine than students (P=<0.0001). Most participants (87.1%) considered expanding their knowledge in precision medicine, with students particularly eager to pursue further education in the field (P=0.019). Physicians cited limited accessibility as the main barrier to the national adoption of precision medicine (92.9%). While students believed the main challenge was the high cost of precision medicine tools (80.2%).

Conclusion
Medical students and physicians in Jordan have a positive attitude toward precision medicine and an inclination to expand their knowledge in the field. To fully achieve the potential of precision medicine, it is crucial to address the barriers impeding its successful implementation. Integrating precision medicine and genome-based technologies into medical education and training is essential to meet the need for competent physicians in the precision medicine era.

Knowledge attitude and practice toward female genital mutilation among health care providers in Khartoum state, Sudan,2022

ABEER ELABID
Sudan

Introduction
FGM/C (female genital mutilation and cutting) is a dangerous traditional practice that has detrimental effects on girls' and women's health and wellbeing. Therefore, in order to ensure that persons impacted by the practice are protected, health care providers (HCPs) are expected to be knowledgeable about how to recognize and treat these effects. get high-quality medical care.Additionally, they are able to play a significant role in the prevention of the practice thanks to their integration and validity within the communities. However, the HCPs' perspectives on FGM/C have not been studied in African contexts. By assessing the knowledge, attitudes, and practices of FGM/C among HCPs working in Khartoum and Khartoum Locality, this study aims to further this field of knowledge.

Material & Methods
This was a cross-sectional health facility-based study at four hospitals in two localities in Khartoum state in the period from October 2022 to December 2022. A multistage cluster sampling was applied, and a four-part questionnaire was prepared. Data was collected from targeted populations (house officers, registrars, and consultants in obstetrics and gynecology, pediatrics, and anesthesia, as well as medical officers and health workers), which was analyzed using SPSS version 26 .

Results
The study included 148 health care providers . There is a significant relationship between age, years of experience and knowledge, and gender and attitude. They had a moderate level of knowledge (65%); the most common type is type 1 (Sunnah); 35%; the most common causes is deeply cultural and to reduce sexual desire; and the most common complication is the need for an episiotomy during labor. The attitude was good (86%), and the practice was very low (5%). Knowledge about the concept of medicalization is 54%, 30% agree with it, and 18% believe it makes the practice safer.

Conclusion
Despite the positive attitude and low practice, the percentage of knowledge is relatively low. Because we live in a country where this practice is prevalent, approximately half of HCPs agree with medicalization and see it as making the practice safer, which is seriously very bad. So we urgently need to train our HCPs to deal perfectly with FGM and its complications.

Pharmacology, Biology, and Biochemistry

Presenters:
Sofía Cecilia García Soto
Vimalan Rengganaten
Laura Thessa Antonia Otten
HAPPY BANDA
Hoang Nam Nguyen
Mehdi Kordjazy

Molecular characterization of intrinsic resistance mechanisms to tyrosine kinase inhibitors targeting EGFR in Non-Small Cell Lung Cancer.

Sofía Cecilia García Soto
España

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[2] *Karolinska Institutet, Division of Immunology and Allergy, Department of Medicine, Solna, Sweden*

Introduction

Lung cancer is the leading cause of cancer-related mortality worldwide. The development of targeted therapies, such as tyrosine kinase inhibitors (TKIs) that target the epidermal growth factor receptor (EGFR), have significantly improved the treatment of a subgroup patients with non-small cell lung cancer (NSCLC) and activating mutations in this protein. However, patients inevitably develop acquired resistance to therapy, and even a small proportion shows intrinsic resistance.
Little is known about the mechanisms involved in this primary resistance. Therefore, this work aims to characterize molecular aberrations in clones with intrinsic resistance to EGFR-TKIs generated from NSCLC cell lines.

Material & Methods

To achieve our aim, clones with intrinsic resistance to Erlotinib or Osimertinib were generated. Transcriptomic data from selected clones were obtained through RNA-seq, and later deeply analyzed using a NOIseq package. Some of the genes that had potential interesting differential expression between resistant and non-resistant clones were analyzed through qPCR and Western blot to ascertain the data obtained through the omics analysis. Later gene silencing through shRNA and pharmacological targeting was carried out to elucidate if this could revert the resistance to TKIs and therefore evince the participation of these molecular alterations in the intrinsic resistance of the NSCLC clones.

Results

The analysis of the transcriptomic data allowed us to identify more than 400 DEs genes between the resistant clones and their parental cell line, which reflects the profound transcriptomic remodeling and tumor heterogeneity associated to resistance. As expected most altered genes were implicated in proliferation, survival and EMT. Among them DDR2, FGFR1, HER3, VIM, AXL and AKT3 had a very noticeable differential expression which has been additionally corroborated through Western blot and qPCR.

Conclusion

This molecular alterations of DDR2, FGFR1, HER3, VIM, AXL and AKT3 could be considered as new mechanisms of intrinsic resistance to TKIs in NSCLC. Further research is needed to ascertain these results, both through further in vitro functional assays and patient cohort validation. The characterization of new mechanisms of intrinsic resistance in NSCLC is key to improving targeted therapy and to establish combined therapies, which could ultimately have a great impact on patient´s clinical outcomes.

Circular RNA circZNF800 regulates oncogenic stemness properties in colorectal cancer

[1]Vimalan Rengganaten
Malaysia

Introduction

Colorectal cancer (CRC) is the second most common cause of cancer-related deaths. Despite advancements in curative chemotherapy, the existence of colorectal cancer stem cells (CrCSC) poses a significant limitation in designing treatment for CRC. Understanding the regulatory mechanisms of CrCSC maintenance could lead to targeted treatment for CRC. A novel group of non-coding RNA, known as circular RNA (circRNA), has been implicated in the regulation of various biological processes. However, the involvement of circRNAs in relation to CrCSC population remains unknown.

Material & Methods

CircRNA sequencing of CRC spheroidal cells was performed on the Illumina platform. CircRNA candidates were narrowed down using public tools for bioinformatics analysis. CRC clinical tissues were obtained with consent from Taipei Veterans Hospital. Tissue analysis was performed using qRT-PCR and RNA FISH assay. Overexpression of circZNF800 was achieved using cell-free in vitro transcription of permutated td phage that could self-circularize on RNA transcription. The CRISPR Cas13d system was optimized to selectively knockdown circZNF800 without affecting the linear RNA transcript.

Results

Based on whole RNA sequencing and bioinformatics analysis, the differentially expressed circRNAs were implicated in pluripotency regulating pathways. CircZNF800 (hsa_circ_0082096) was predicted to be a key regulator of stemness in the CRC population. CircZNF800 was shown to be significantly up-regulated in CRC tumour tissues and resides in a high proliferative population in the cancer region. Furthermore, in normal tissue, circZNF800 was found in a population expressing high levels of intestinal stem cell markers. CircZNF800 overexpression promoted CSC phenotypes including proliferation, expression of CSC and intestinal stem cell markers, all of which were reversed by CRISPR Cas13d-mediated circZNF800 knockdown. CircZNF800 was shown to sponge miR-140-3p, miR-382, and miR-579, which in turn increased the levels of ALK7, FZD3, and WNT5A, which are involved in the regulation of CSC properties. Modulating the expression of circZNF800 changes the tumorigenicity of CRC cells in mouse models.

Conclusion

In conclusion, this study highlights the potential of circZNF800 as a novel therapeutic target for CRC. Our findings demonstrate that circZNF800 plays a crucial role in maintaining CrCSC properties and its upregulation in tumour tissues suggests it could be a promising target for targeted therapy.

Mitochondrial DNA methylation in platelets using LC-MS/MS

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Laura Thessa Antonia Otten
The Netherlands

Introduction

Mitochondrial myopathies (MM) are usually caused by mutations in either mitochondrial DNA (mtDNA) or nuclear DNA (nDNA) that encodes for mitochondrial proteins. However, there remain patients suffering from MM in whom no mutations can be found, as such, treatment is difficult. Instead of mutations, epigenetic changes such as mtDNA methylation could be responsible for the malfunctioning of the mitochondria. Isolation of mtDNA is hampered by contamination of nDNA which leads to increased methylation. This study aims to set up an efficient method without contamination of nDNA to reveal the mtDNA methylation levels in blood. If this method proves effective, it might open the way to diagnose patients suffering from unidentified MM.

Material & Methods

Fresh, 1-day-old and 2-day-old EDTA whole-blood samples were used to isolate platelets. Cell counts were done to determine the platelet, leukocyte, and erythrocyte yield. mtDNA was isolated with three different methods (Abcam-kit, Promega-kit, and TRIzol) from platelets and the mtDNA concentration was measured with Nanodrop. Then, mtDNA methylation levels were determined with Liquid-chromatography/Tandem Mass-spectrometry (LC-MS/MS). Statistical analyses (pairwise t-tests corrected for multiple-testing with the Benjamini-Hochberg (BH) procedure) were done in R/RStudio.

Results

The platelet yield of fresh (mean 99.996%±0.002%) and 1-day-old samples (mean 99.982% ±0.038%) was significantly higher (p=1.8e-08 and p=1.2e-07, respectively) compared to 2-day-old samples (mean 99.892%±0.080). Consequentially, the mean leukocyte yield in 2-day-old samples was higher. The mean mtDNA yield for the DNA-isolation methods was 19.204±18.552 (Abcam) and 12.827±11.233 (Promega). The TRIzol method obtained a significantly higher yield with 1669.405±556.284 ng/10^9 platelets in comparison (p= 1.3e-06 (Abcam) and p=1.3e-09 (Promega)). No significant differences in the mean accuracy were found between the calibration lines measuring methylation levels with LC-MS/MS.

Conclusion

Platelets isolated from fresh blood yields the highest amount of platelets and the lowest amount of leukocytes. Furthermore, the most effective mtDNA isolation method seems to be TRIzol, as this method has the highest yield of mtDNA. Lastly, methylation levels can be detected in platelets; however, it remains unclear whether these levels are affected by leukocyte nDNA. If these results can be reproduced with a confirmed absence of nDNA, this method could prove to be an effective diagnostic for unidentified MM

Analysis of an IncHI2 plasmid conferring an Extensively Drug-Resistant phenotype to Salmonella Isangi from a nosocomial outbreak in Blantyre, Malawi

HAPPY BANDA
Malawi

Introduction

At Queen Elizabeth Central Hospital (QECH) in Malawi, there was a nosocomial outbreak of extensively drug-resistant (XDR) Salmonella spp. causing invasive infections from 2019 to 2021. We identified it as belonging to serogroup 6,7, but no further identification was possible. The responsible isolates were resistant to ampicillin, cefpodoxime, chloramphenicol, ciprofloxacin and co-trimoxazole, leaving few treatment options in our setting. This study aimed to identify the serotype of and antimicrobial resistance genes carried by the causative isolate using whole- genome sequencing.

Material & Methods

One isolate was sequenced at MLW using MinION sequencer. We used Flye for genome assembly, Racon and Medaka for genome polishing. We used AMRFinder to find the resistance genes, and annotation was performed using Bakta. BLAST was used to compare the Isangi plasmid with previously reported plasmids. Further analysis included pairwise comparison of the Isangi plasmid and pSTm-A54650 using Mauve aligner. Salmonella serotype was inferred with SISTR.

Results

SISTR analysis of the completed genome revealed that it was Salmonella enterica subspecies enterica serovar Isangi. We identified a 203,670 bp IncHI2 plasmid that encoded 15 AMR genes in four clusters flanked by mobile genetic elements. The genes included bla-ctx-m15 and qnrB1. The plasmid has 100% identity over 76% of the sequence to a Salmonella Typhimurium plasmid pSTm- A54650 isolated at QECH in 2014.

Conclusion

We have identified a novel plasmid similar to a plasmid identified from an S. Typhimurium isolated at QECH in 2014. The plasmid has four mobilisable AMR gene clusters similar to those found in both Salmonella and non-Salmonella genomes. It is concerning to see invasive Salmonella encoding both extended-spectrum beta-lactamases and acquired fluoroquinolone resistance genes at QECH, as ceftriaxone and ciprofloxacin constitute the current treatment regimen. Our findings call for robust stewardship practices to monitor these mobile genetic elements within the hospital settings to counter potential subsequent outbreaks.

Physician's adherence to prescribing guidelines for anti-diabetic agents is independently associated with better HbA1c control

Hoang Nam Nguyen
Vietnam

Introduction

Despite its great importance in enhancing quality of patient care and improving health outcomes, data on drug utilization among those who received treatment for diabetes has been scarce in Vietnam. We aimed to assess the pattern of prescriptions and physician's adherence to clinical practice guidelines for antihyperglycemic agents and examine factors related to better diabetes control in patients with type 2 diabetes (T2DM) in the country.

Material & Methods

We designed a cross-sectional study on 400 randomly selected adult outpatients with T2DM in 2020 at Thu Duc Regional General Hospital, Ho Chi Minh City, Vietnam. Patients aged 18 or older who had received antidiabetic treatment for at least three months were eligible for the study. Patient medical records were retrospectively examined for data collection, including demographic characteristics, comorbidities, laboratory results, and pharmacotherapy. Physicians' adherence to prescribing guidelines for antidiabetic agents was assessed according to the 2017 national guidelines of the Vietnam Ministry of Health. A prescription was considered "adherence" if the antihyperglycemic agents were aligned with the guidelines in terms of (contra)indications, therapy adjustments, and dosage. Patients were evaluated if they achieved individualized HbA1c targets based on their clinical characteristics. Multivariable logistic regression was applied to investigate independent factors related to the achievement of the HbA1c target.

Results

The average age of the study sample was 59.4 years (standard deviation 11.8 years). Females accounted for 56% of included patients. Metformin, sulfonylureas, and insulin represented the most commonly prescribed antidiabetic agents, which were ordered in 95%, 61%, and 19% of included patients, respectively. Statin, ACEIs/ARBs, and beta-blockers were the most common concomitant medications among those patients (84%, 52%, and 52%, respectively). Half of all patients achieved their individual HbA1c goal of treatment (51%, n = 202). The overall rate of physicians' adherence to prescribing guidelines for antihyperglycemic agents was 77%. The multivariable analyses revealed that physicians' adherence to clinical practice guidelines was independently related to the achievement of HbA1c control (OR = 3.25, 95% confidence interval 1.66 – 6.39, p = 0.001).

Conclusion

Over three-quarters of antihyperglycemic prescriptions in outpatients with T2DM adhered to clinical practice guidelines, representing an independent factor associated with HbA1c target achievement. The study findings suggest the need for measures to enhance physicians' adherence to prescribing guidelines (e.g. pharmacist-led intervention) to optimize patients' diabetes control.

Evidence for the involvement of nitric oxide in cholestasis-induced itch associated response in mice

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Iran

Introduction

Cholestasis is a major systemic disorder that is associated with distressing pruritus. The pathogenesis of cholestasis-induced itch is not clear. Nitric oxide (NO) is a signaling molecule which is assumed to be involved in pruritus generation. The NO synthase (NOS) enzyme family consists of three isoforms, iNOS (inducible), eNOS (endothelial) and nNOS (neuronal). Regarding the NO overproduction in cholestatic liver disease, we aimed to investigate the involvement of NO and effectiveness of NOS enzyme inhibitors in pruritus-associated behaviors due to cholestasis in mice.

Material & Methods

male mice were used during this study. The itch-associated response due to cholestasis was evaluated on days 0, 5, and 7 of the operation procedure, in order for the assessment of the utmost pruritus-induction effect of cholestasis. For bile duct ligation (BDL) the bile duct was identified and ligated in two places and sectioned between the ligatures. Sham operation consisted of laparotomy and bile-duct identification and manipulation without ligation. Scratching behavior was evaluated by measuring the number of bouts during 60 minutes after the procedures or injections. To determine the NO levels in serum, we measured nitrite levels as the NO end product in another group of animals by a colorimetric assay based on the Griess reaction.

Results

Bile duct ligation in mice elicited significant scratching on the fifth and seventh day after the procedure ($P<0.05$ and $P<0.001$), but not on the day of surgery ($P>0.05$). This cholestasis-induced scratching was inhibited by intraperitoneal treatment of mice with non-selective NOS inhibitor L- NAME (3 mg/kg) ($P<0.001$) and iNOS inhibitor aminoguanidine (100 mg/kg) ($P<0.01$). The inhibitory effect of L-NAME and aminoguanidine was reversed by pretreatment with L-arginine (100 mg/kg) ($P<0.01$). Alone injection of L-NAME, aminoguanidine, and L-arginine in BDL and sham- ligated mice did not produce scratching behaviors. On 7th day, serum NOx level in BDL group was significantly higher than control and sham animals both in serum ($P<0.001$) and skin ($P<0.01$). L- NAME and AG significantly reversed the serum and cutaneous nitrite level elevation that had been occurred after BDL ($P<0.01$ and $P<0.05$).

Conclusion

We have, for the first time, shown that BDL, as a model of acute cholestasis in rodents, by activating the NOS enzymes, especially iNOS, induces NO over-production which practically mediates itch sensation. Finally, we introduce NO and NOS as possible targets for antipruritic agents for cholestasis-induced itch. Further studies on the role of NO and other mediators in cholestasis in experimental and clinical settings are valuable.

Public Health

Presenters:
Davis Akampumuza
Malebo Mahlalela
ABEER ELABID
Khalil Azrak

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

Naghibzadeh Gonabadi, N.N.G (Niloofar)[1]

[1] *Mashhad university of medical science, Medical Physiology, Mashhad, Iran*

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.

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.

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 (5%), 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 ($\times 10^{-9}$L) 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 $6{,}1 \pm 2{,}4$ years, mean BMI $15{,}4 \pm 1{,}8$ 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$\pm$SD glycemia for regular diet was $4{,}84 \pm 0{,}20$ mmol/l, for the carbohydrates/fat ratio of 1:1 it was $4{,}03 \pm 0{,}16$, for the ratio of 1:2 it was $3{,}57 \pm 0{,}10$, for the ratio 1:3 it was $3{,}39 \pm 0{,}13$ and for the final ratio of 1:3,5 it was $2{,}79 \pm 0{,}06$ mmol/l ($p < 0{,}001$). The portions of time spent in glycemia $\leq 3{,}5$ mmol/l ($\leq 2{,}5$ 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.

Rheumatology and Immunology

Presenters:
Astalitha Lorel Tania
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Susana Castaño

H2S is involved in the regulation of intracellular pH in human umbilical vein endothelial cells

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Introduction

Intracellular pH (pHi) in human umbilical vein endothelial cells (HUVECs) from healthy pregnancies is regulated by sodium proton exchanger 1 (NHE1). NHE1 activity is inhibited by hydrogen sulfide (H2S) in rat cardiomyocytes. H2S is synthetized by cystathionine gamma-lyase (CSE) and H2S increases nitric oxide (NO) synthesis in the endothelium. We evaluated whether endogenous- or exogenous-H2S regulates the sodium proton exchangers (NHEs) activity, modulating the pHi in HUVECs from heathy pregnancies.

Material & Methods

HUVECs isolated from healthy pregnancies (n=6) (conformed to Declaration of Helsinki) at University Medical Center Groningen (Netherlands) were cultured in M199 plus 20% sera and exposed to 0-3000 µmol/L sodium hydrosulfide (NaHS, 30 min, H2S donor), aminooxyacetic acid (AOAA, 24 h, CBS inhibitor) or propargylglycine (PAG, 24 h, CSE inhibitor). The acid pulse protocol (NH4Cl) was used for pHi measurement in cells preloaded with the pH-sensitive probe BCECF-AM (12 µmol/L, 10 min) in the absence or presence of 5 µmol/L 5-N,N-hexamethylene-amiloride (HMA, NHEs inhibitor). Basal and pHi recovery rate (dpHi/dt) were calculated. Proteins (20 µg) were separated by polyacrylamide gel (10%) electrophoresis and transferred onto Immobilon-P polyvinylidene difluoride membranes. The proteins were probed against NHE1, CBS (1:500 dilution, 12 h, 4°C) and CSE (1:1000 dilution, 12 h, 4°C). Total RNA was extracted from cultured HUVECs using TRIzol Reagent. Aliquotes of 1 ug RNA was converted to cDNA using SuperScript II reverse transcriptase and random hexamere primers. CSE (assay Hs00542284_m1) and CBS (assay Hs00163925_m1) mRNA expression was measured with a Taqman Gene expression assay.

Results

Basal pHi was reduced with NaHS (pHi 7.4±0.1 vs 7.1±0.1, respectively) but unaltered by PAG (7.4±0.1) or AOAA (7.4±0.1) (mean±SEM, P<0.05, two way-ANOVA). The dpHi/dt was reduced by 56±15 % from 0.1 µmol/L NaHS but unaltered by PAG or AOAA. The dpHi/dt in the presence of HMA (i.e. NHEs-mediated) recovery was inhibited by NaHS (from 0.1 µmol/L). The NHE1 protein abundance was unaltered by inhibition of CSE; However, CSE protein abundance was lower (31±6%) compared to CBS. CBS mRNA relative expression was lower (92±38% than CBS mRNA expression in HUVECs.

Conclusion

The pHi is regulated by exogenous H2S in an NHE-dependent manner, whereas CSE- or CBS-synthesized endogenous H2S did not affect pHi likely due to its low expression in endothelial cells.

Hamster organotypic kidney culture model of early-stage SARS-CoV-2 infection highlights a two-step renal susceptibility

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France

Introduction
SARS-CoV-2, the causative agent of COVID-19, is primarily a respiratory pathogen. However, it can cause severe dysfunction in a wide range of organs outside the respiratory tract. Kidney pathology is frequently reported in patients hospitalised with COVID-19, and autopsy samples have provided valuable insights into the renal consequences of severe COVID-19 infection. However, the causes of renal damage and the events occurring in the kidney during the earliest stages of infection remain unknown. Studying the initial stages of kidney infection by SARS-CoV-2 and other pathogens is hampered by the lack of representative and ethical models.

Material & Methods
To study early-stage kidney infection, we used hamster organotypic kidney cultures (OKCs). 350-500 µm thick slices of suckling Golden Syrian hamster (*Mesocricetus auratus*) kidneys were prepared and cultured on an air-liquid interface. Their mitochondrial respiration rate was measured on a Seahorse XF Analyzer using the MitoStress Test. RT-qPCR was used to measure the viral RNA load and perform transcriptomic analysis. Viral infection and tropism were studied via immunofluorescence performed on OKC cryosections.

Results
OKCs maintained key renal structures in their native three-dimensional arrangement. They remained viable and metabolically active for at least 4 days of culture. SARS-CoV-2 productively replicated in hamster OKCs. Infection initiated in CD34+ endothelial cells and later disseminated to proximal tubules, which are commonly found to be viral antigen-positive post-mortem. We observed a delayed interferon response, markers of pro-inflammatory cell death associated with infection, and an early repression of pro-inflammatory cytokine transcription followed by their strong later upregulation.

Conclusion
While it remains an open question whether an active replication of SARS-CoV-2 takes place in the kidneys of COVID-19 patients with AKI, our model provides new insights into the kinetics of early SARS-CoV-2 kidney infection and the organ's innate immune response to the virus. In the future, it can serve as a powerful tool for studying kidney infection by other pathogens and testing the renal toxicity of drugs.

Influence of Urinary Schistosomiasis on Nutritional Status of Elementary School Children in selected Communities of Osun State, South Western Nigeria

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Nigeria

Introduction
Although, undernutrition has been reported as the major cause of children poor growth and development, the role of infection such as schistosomiasis and that of hookworms on such outcome cannot be underrated. This study therefore seeks to determine the influence of urinary schistosomiasis on nutritional status of elementary school children hoping that results obtained will help inform decision on the choice of intervention particularly in schistosomiasis endemic communities.

Material & Methods
A cross sectional study recruiting 504 elementary pupils age 5 to 16 years following a convenience sampling was adopted. Following standard procedures, urine microscopy was carried out to determine ova in urine and intensity of infection. Anthropometric measurements of height, weight and age were carried out to compute heigh for age z score and BMI for age z score using WHO reference chart. Logistic regression model was used to determine odd ratio (OR) and 95% confidence interval (CI) for the risk factors of stunting and malnutrition after adjusting for essential confounding variables at $p<0.05$.

Results
Results Sex and fathers' occupation were significantly associated with stunting ($P< 0.05$) while only father's occupation was significantly associated with malnutrition ($P< 0.05$). More of respondents whose fathers engaged in high-risk occupation were found to be malnourished (51.7%, $P< 0.05$) as compared to their counterparts from low-risk occupation fathers ((25.8%, $P=0.00$). Drinking water, domestic water source and toilet facility were significantly related to stunting and malnutrition ($P<0.05$) while schistosomiasis status and intensity of infection were also found to show statistical association with stunting and malnutrition status ($p< 0.05$). Logistic regression model showed that use of public latrine (aOR 6.3, 95% CI 2.864-13.694) was implicated with stunting. Children whose fathers engage in high-risk occupations (aOR 1.9, 95% CI 1.195-3.280) and those who drink river water (aOR 4.1, 95% CI 1.153-14.30) were also more likely to be malnourished than their counterpart. Being positive for schistosomiasis was implicated with both stunting (aOR 6.734, 95% CI 1.685-26.914) and malnutrition (aOR 8.261, 95% CI 2.504-29.684).

Conclusion
Being infected with Schistosoma haematobium poses a great risk to the health of children as the infection status increases the vulnerability of children to nutritional deficiency.

Assessment of mortality risks among COVID- 19 patients with combined vitamin D deficiency or insufficiency and lymphocytopenia

[1] Sofia Chala
Ukraine

Introduction

Currently, the conclusions regarding the effect of vitamin D on COVID-19 disease are somewhat contradictory. Some studies indicate that vitamin D levels adjusted for sex and age were not significant for COVID-19 susceptibility. But other studies indicate that low serum vitamin D levels are associated with increased risk of COVID-19, its severity and mortality. In this context, we consider it appropriate to analyze the impact of the combination of vitamin D deficiency or insufficiency and lymphocytopenia on COVID-19 outcomes.

Material & Methods

In this retrospective cohort study, we analyzed the medical records of 118 hospitalized patients with COVID-19. All the patients were tested for initial vitamin D – 25(OH)D3 level and absolute lymphocyte count on the time of admission. The method of Fisher's angular transformation was applied for CI evaluation and the absolute risks of a fatal outcome, their reduction and ratio were calculated.

Results

The frequency of detection of vitamin D deficiency or insufficiency and lymphocytopenia on the first day of hospitalization for 30 patients who later died and for those 88 patients who survived were compared. 20 out of 30 deceased patients (66.7%) had vitamin D deficiency or insufficiency and lymphocytopenia simultaneously. Of these 20 deceased individuals, there were 11 females with a mean age 67.7 years (95% CI 56.7-78.8) and 9 males with a mean age of 72.4 (95% CI 64.2-80.7). It was found that frequency of fatal outcomes in patients (without taking into account gender) with detected combined deficiency or insufficiency of vitamin D and lymphocytopenia (n=56) was 35.7% (95% CI 23.5-48.9). In contrast, in patients without combined vitamin D deficiency or insufficiency and lymphocytopenia (n=62), the mortality rate was 16.1% (95% CI 8.0-26.5).

Conclusion

If, at the time of admission, the patient did not have a combined deficiency or insufficiency of vitamin D and lymphocytopenia, the absolute risk of a fatal outcome is reduced by 19.6% (95% CI 3.8-34.5) in comparison with patients in whom this combination was detected. The risk ratio of fatal outcome in patients with combined deficiency or insufficiency of vitamin D and lymphocytopenia and in patients without combination of these factors is 2.21 (95% CI 1.14-4.32).

Electrolyte Disturbances are Associated with Mortality in Intensive Care COVID-19 Patients: a Longitudinal Analysis

[1] *Ivan Szergyuk*
Poland

Introduction

According to a substantial body of research, electrolyte abnormalities are a common manifestation in coronavirus disease 2019 (COVID-19) patients. Given their many important physiologic roles, such as immune function, cardiac function, and protection against oxidative stress, disturbances in electrolyte balance may worsen outcome of COVID-19 illness. This study aimed to investigate electrolyte imbalances in COVID-19 patients and assess their relation to mortality.

Material & Methods

Adult COVID-19 patients hospitalized in the Security Forces Hospital in Saudi Arabia from June 8th till August 18th, 2020 were enrolled in this retrospective observational study. We examined baseline characteristics, comorbidities, acute organ injuries, medications, and electrolyte levels including sodium, potassium, chloride, calcium, bicarbonate, phosphate, and magnesium on ICU admission, as well as every following day of ICU stay, until death or discharge. Patients were stratified according to survival, and differences in variables between groups were compared using Mann-Whitney's U test or Fisher's exact test. Longitudinal electrolyte profiles were modeled using random intercept linear regression models.

Results

A total of 60 COVID-19 patients were enrolled. Compared to survivors, non-survivors had significantly higher sodium and phosphate on admission and death, higher potassium and magnesium at death, and significantly lower calcium at death. Abnormalities in admission levels of chloride and bicarbonate were also more frequently observed in non-survivors. Furthermore, in the deceased group, we observed a daily increase in potassium and phosphate levels, and a daily decrease in sodium and chloride. Finally, calcium increased in non-survivors over time, however, not as significantly as in the survivor group. The exact mechanisms of electrolyte imbalance are uncertain, however, among the comorbid conditions and medications analyzed, only acute cardiac injury, heart failure, and antiplatelet use during hospitalization might explain some of the observed differences as these were more prevalent in non-survivors.

Conclusion

Admission levels of electrolytes as well as subsequent daily changes over the course of ICU stay appear to be associated with mortality in COVID-19 patients. Our findings regarding disruption of electrolyte homeostasis in COVID-19 and associated survival outcomes offer not only insight into the pathophysiology of SARS-CoV-2 infection, but also suggest potential therapeutic options for minimizing disease severity.

Rates and Predictors of COVID-19 Transmission to Household Contacts of a COVID-19 Laboratory Confirmed Case in Blantyre Malawi

Samuel Lawrent Mpinganjira
Malawi

Introduction

Projections of COVID-19 transmission have been based on estimates developed countries which are different from low-income countries in multiple aspects including disease burden, age distribution, social interaction, household sizes, and socio-economic status. We aimed to determine rate of transmission of COVID-19 amongst household contacts of a laboratory confirmed case and predictors of COVID-19 transmission amongst the household contacts.

Material & Methods

We conducted a prospective cohort observational household-based study between December 2020 to October 2021. We enrolled individuals from Blantyre urban and rural who tested positive for COVID-19 and their household contacts and followed them up for 28 days. We took samples COVID-19 PCR test and blood for HIV, malaria and serology tests. Proportions were used to determine the secondary spread i.e. households with at least one contact testing positive. Chi Square was used to test for significance. Cox regression models were fitted to assess the risk factors for infection.

Results

171 index cases and 410 household contacts were enrolled. In comparison with the index cases, the contacts were generally younger [(median age and range) 31 (7-86) vs 41 (7-79)]; unmarried [58% vs 26%]; and unemployed [40% vs 18%]. Out the 120 households that tested positive on enrolment, 84 (70%) had at least one contact who tested positive during the 28 day follow up. No difference in transmission between urban and rural settings (P value: 0.834, 95%CI). Third wave was more transmissible than second wave (P=<0.05, 95%CI). Except for reported availability of tap water; age, sex, education, HIV status, location, size of the house, size of household and BMI did not predict risk of transmission to household contacts.

Conclusion

There is high rate of transmission of COVID-19 in household across both rural and urban settings regardless of age, sex, employment, marital status, BMI, and size of the household. Lack of tap water within a household is a predictor of COVID-19 transmission to household contacts. Majority of contacts test positive by day 28 of follow up. Delta was highly transmissible in comparison with Beta.

Thorax Medicine

Presenters:
Mohamed Ibrahim Gbreel
Nadia Alfi Syarifah
Amirhossein Hessami
Seyedeh Naghmeh Layegh
Khavidaki
Jason Sparks
Gonzalo Fuentes

Post-partum depression and its correlates among women attending post-natal care clinics in Blantyre, Malawi

Omega Mbewe
Malawi

Introduction

Postpartum depression is one of the most underrated public health concerns affecting both the mother's health and child's development. We assessed the prevalence of postpartum depression and correlates in women who attended postnatal care services in selected health centers in Blantyre district, Malawi.

Material & Methods

This was a descriptive cross-sectional study. Simple random sampling method was used to recruit mothers who were interviewed. The PHQ9 was used to assess depression. Data was analyzed using Stata 12. A cut-off point of five was used to Bivariate and multivariable logistic regression analysis examined the demographics variables in relation to postpartum depression.

Results

A total of 184 were interviewed. Half (50%) of the mothers were depressed. Lack of partner support (P = 0.011; 95% CI, 0.64-0.48, OR=4.53), complications during pregnancy (P = 0.016; 95% CI, 0.401-0.042, OR=2.90), and mother's poor health since delivery (P = 0.042; 95% CI, 0.45-0.008, OR=3.66) were factors linked with postpartum depression.

Conclusion

This study depicts high prevalence of postpartum depression among women in Blantyre. Lack of partner support, complications during pregnancy and mother's poor health since delivery are linked with postpartum depression. Routine screening of women for postpartum depression should be encouraged for early detection and intervention.

The role of estrogen and inflammatory markers in the pathogenesis of pelvic venous disorders (PeVD) – a preliminary study.

[1] *Marcin Czeczelewski*
Poland

Introduction

Pelvic venous disorders (PeVD) are defined as the presence of pelvic varicose veins accompanied by chronic pelvic pain lasting more than 6 months. PeVD accounts for 16% to 31% of chronic pelvic pain cases. The etiology of PeVD is multifactorial and includes both mechanical and humoral factors that contribute to venous vasodilatation and insufficiency. The purpose of this study is to compare the concentration of estrogen and inflammatory cytokines in the blood drawn from pelvic varicose veins and the systemic circulation of women with PeVD.

Material & Methods

The samples were collected from 14 patients (mean age 34.8). The phlebography procedure was performed under local anesthesia from the right femoral vein using the Seldinger technique. Blood samples for the study were collected during the selective catheterization of the ovarian vein before the embolization procedure. Blood aspiration was performed using a 5-French pigtail catheter.
Control blood samples were drawn from the patient's antecubital veins at the beginning of the procedure. Wilcoxon Signed Rank Tests and Pearson correlation were used in the statistical evaluation.

Results

The median of erythrocytes, leukocytes, platelets, and hemoglobin concentrations were statistically significantly greater in the blood from varicose veins ($p>0.05$). A statistically significantly higher concentration of IL-6 (55.24 vs. 49.78 pg/mL; $p=0.046$) was observed in pelvic veins compared to antecubital veins. There were no statistically significant differences in CRP, fibrinogen, vWF, and fibrinogen concentrations ($p>0.05$). Estradiol levels were multiple times higher in the pelvic varicose veins in 12 patients. The concentrations of inflammatory parameters were not statistically significantly correlated with the severity of pain symptoms.

Conclusion

Endovascular embolization is a safe and effective procedure, remaining the best therapeutic option for patients with PeVD, which, in addition to relieving pain, significantly improves patients' quality of life. IL-6 levels and estradiol levels are increased in pelvic varicose vein blood in comparison with systemic blood. Stasis and hormonal factors may induce chronic local inflammation of the vein wall. Further studies on a larger group of female patients are necessary to provide a better understanding of the pathophysiology of PeVD.

PREDICTORS OF THE RISK OF DEVELOPMENT OF POLYCYSTIC OVARY SYNDROME IN ADOLESCENTS

[1] *Iryna Sokolnyk*
Ukraine

Introduction

The development of a woman's reproductive function largely depends on how well the puberty period proceeds and ends favourably. However, polycystic ovary syndrome (PCOS) is increasingly being registered among pubescent girls, the course of which determines further childbearing, fertility, metabolic and other functions. Aim of the study was to determine the factors contributing to the development of PCOS in puberty.

Material & Methods

By conducting an open randomised "case-control" study, sociometric (questionnaire), genealogical (presence of pathology in the family tree) and mathematical-statistical (multifactorial analysis to evaluate the impact of adverse factors; to check the significance of the overall measure of communication - non-parametric Pearson test (χ2) and the odds ratio (OR); the reliability of connection at χ2 ≥ 3.84, $p<0.05$, OR > 1.2 [95% CI]) methods were used in 32 girls with PCOS aged 11-18 years (14.2 ± 2.1) and 30 healthy individuals of the corresponding age (14.1 ± 2.2) to analyse socio-biological and genealogical factors of the probability of PCOS development.

Results

It was established that the most determining risk factors for the development of PCOS are genetic burden (OR = 3.22 [1.03-9.47], $p<0.05$), previous inflammatory and infectious diseases of the genitourinary system (OR = 4.15 [1.11-12.43], $p<0.05$), thyroid pathology (OR = 2.34 [1.01-6.33], $p<0.05$), adrenal diseases (OR = 4.59 [2.01-13.44], $p<0.05$), hormonal ovarian dysfunction (OR = 4.21 [2.11-8.71], $p<0.05$), hyperproduction of insulin (OR = 4.66 [2.11-11.74], $p<0.05$), obesity (OR = 4.26 [2.15-16.29], $p<0.05$), autoimmune diseases (OR = 2.22 [1.08-6.15], $p<0.05$), stress (OR = 3.63 [2.18-14.03], $p<0.05$), surgical interventions on ovaries (OR = 4.23 [2.12- 14.56], $p<0.05$), bad habits (OR = 3.11 [1.13-9.48], $p<0.05$), unfavourable social history (OR = 2.16 [1.31-9.41], $p<0.05$), unfavourable biological history (OR = 2.39 [1.12-9.93], $p<0.05$), menarche age up to 11 years (OR = 2.41 [1.07-7.43], $p<0.05$).

Conclusion

The established anamnestic risk factors for the development of PCOS in adolescents will help to develop a set of individual preventive measures.

ORAL STIMULATION FOR PRETERM INFANTS TO IMPROVE FEEDING PERFORMANCE: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Indonesia

Introduction

Indonesia is ranked fifth with the highest number of preterm infants in the world. Studies have indicated 40-70% preterm infants have oral feeding difficulties. These problems impact more than infants nutrition, but also increases the length of stay and hospitalization cost, limits the emotional mother-child bonding, and it's independently linked to neurodevelopmental issues. It requires an ongoing intervention that can immediately start to decrease the potential long-term challenges.

These studies aim to investigate the effect of oral stimulation for feeding performance improvement in preterm infants.

Material & Methods

In this systematic review and meta-analysis, PubMed, ScienceDirect, and Cochrane databases were searched from inception to July 2022 using PRISMA guidelines. Randomized Controlled Trials (RCTs) studies were included. The CONSORT criteria were used to assess the risk of bias. The effect sizes were estimated as log risk ratios and standard mean differences (SMDs) with 95% confidence intervals (CIs), using the Review Manager ver. 5.4

Results

Of the 98 screened studies, 12 RCTs met the eligibility criteria for qualitative analysis; 9 were included in the meta-analysis, with a total of 756 participants, born above 25 weeks from Europe, America, Asia, and Africa. Our meta-analysis found that oral stimulation reduced the transition time to oral feeding [MD = -2.07 (-3.02, -1.11); p<0.00001], as well as increasing the infants intrinsic nutritive sucking skills [MD = 1.13 (0.49, 1.77); p=0.03], overall intake [MD = 2.09 (1.00, 3.17); p<0,00001], and the rate of milk transfer [MD = 0.74 (0.22, 1.26); p=0.15] in preterm infants.

Conclusion

In conclusion our study shows that a simple way to implement oral stimulation in the experimental group has a clinically positive and statistically significant effect for feeding difficulties in preterm infants shown by several feeding performance parameters.

Effects of therapeutic play on adherence to non-invasive positive pressure therapy in preschoolers: a randomized clinical trial

Beatriz Negrão
Brazil

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/

Human papillomavirus vaccines protect against the most common genotypes found in patients that underwent cervical conization procedure

Sanja Toshevska
North Macedonia

Introduction

Striving for early detection and prevention of cervical cancer, algorithms are increasingly focused on Human papillomavirus (HPV)-based screening. Simultaneously, cervical conization procedure is the method of choice for diagnosing and treating patients with precancerous or early cervical cancer. This activity focuses on HPV types found in patients that underwent conization of the cervix with the cold knife cone procedure or large loop excision of the transformation zone (LLETZ).

Purpose: To determine the most common HPV types in these patients according to age ≤ 30 and >30 years and whether the quadrivalent (6, 11, 18, 16) or 9-valent (6, 11, 18, 16, 31, 33, 45, 52, 58) recombinant vaccines target studied genotypes.

Material & Methods

In this retrospective study we reviewed 151 cases of cold knife conization and LLETZ performed between January and December, 2022, at the University Clinic of Gynaecology and Obstetrics in North Macedonia. HPV typization was performed before surgery, conventional cervical smears were analysed as well as histological grade of cervical intraepithelial neoplasia (CIN).

Results

Patients aged ≤ 30 years accounted for 23 (15.2%) of the 151 study patients. The most common HPV types in these patients were type 16 presented in 16 (69.6%) patients, type 53 presented in 6 (26.1%) patients and type 52 presented in 3 (13%) patients. However, 128 (84.8%) were aged above 30 years. In this group the most common HPV types were type 16 presented in 32 (25%) patients, type 31 presented in 12 (9.4%) patients, type 45 presented in 9 (7%) patients.

Conclusion

HPV type 16 had the highest persistence rate in both groups. Accordingly, the quadrivalent recombinant vaccine targets type 16, the most common HPV type, but lacks coverage for the other common types. Contrarily, the 9-valent recombinant vaccine targets all HPV genotypes except one, type 53, found in these patients. HPV vaccines remain one of the most fundamental and important primary prevention methods against cervical cancer.

Poster Sessions I
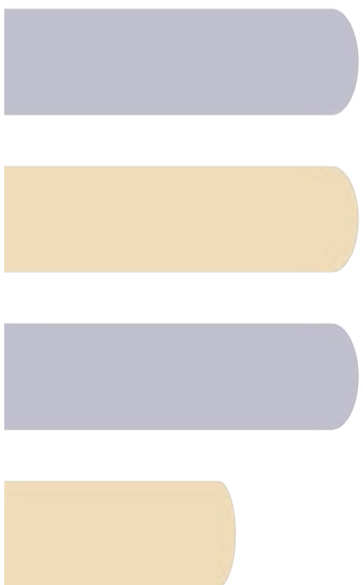
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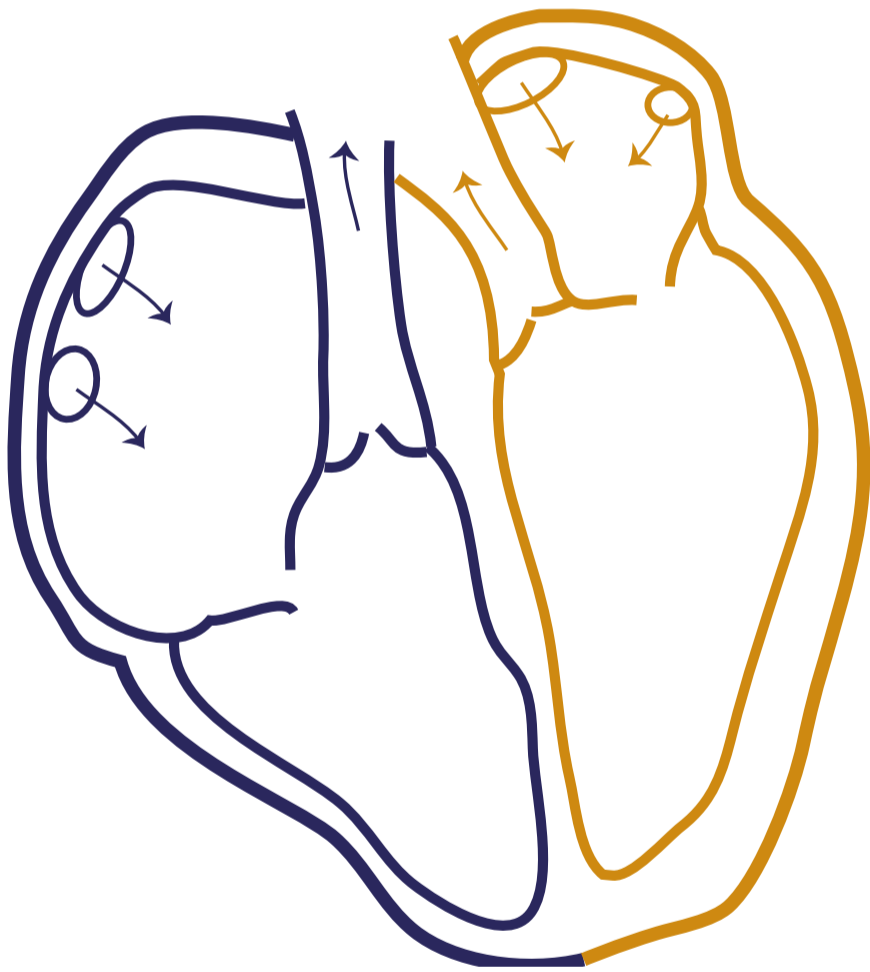
Presenters:
Katarina Obradović
Pegah Nekooeizadeh
Agata Suleja
Joske van der Zande
Yasaman Pourasadi
Krishin Yerabolu
Nikola Serge

The relation between C-reactive protein and serum amyloid A in patients with autoinflammatory diseases

[1]Carien Dermer
The Netherlands

Introduction

Autoinflammatory diseases are rare disorders of the innate immune system characterized by fever and other signs of inflammation. A feared complication of autoinflammatory diseases is the development of AA amyloidosis. AA amyloidosis is caused by the extracellular deposition of the soluble serum amyloid A (SAA) protein as insoluble amyloid fibrils leading to organ damage. Prolonged high levels of SAA are a prerequisite to develop AA amyloidosis. Since measurement of SAA is relatively expensive and sometimes unavailable C-reactive protein (CRP) is often used as a surrogacy marker to test for inflammation. The aim of this research is to evaluate the relation between CRP and SAA.

Material & Methods

A retrospective cohort of patients with an autoinflammatory disease (n=99) where SAA and CRP blood testing was performed in the period between 2015 and 2021 in the University Medical Centre in Groningen was used to investigate the correlation between CRP and SAA.

Results

CRP and SAA have a high correlation (rho=0.755, $p<0.001$). A CRP value of below 0.45 mg/L results in a 100% sensitivity level for SAA below 4 mg/L. CRP below 5 mg/L is a good predictor of SAA below 4 mg/L with a sensitivity of 85.4% and a specificity of 83.6%. Only prednisone and erythrocyte sedimentation rate (ESR) significantly influence the relation between CRP and $\log_{10}$ SAA.

Conclusion

There is a significant correlation between CRP and SAA. CRP levels below 5 mg/L proved to be highly predictive of SAA levels below 4 mg/L. However, clinicians should .

Enhanced oxidative stress response in systemic sclerosis patients – assessment using coumarin boronic acid assay

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Poland

Introduction

Systemic sclerosis (SSc) is a rare autoimmune disease characterized by tissue fibrosis, microcirculatory dysfunction, and complex etiology, including genetic and environmental factors. Interestingly, emerging evidence suggests that SSc is related to increased oxidative stress, which contributes to further tissue and vascular damage. The present study aimed to measure systemic protein hydroperoxide (HP) generation in the peripheral blood of SSc patients using a straightforward real-time coumarin boronic acid (CBA) assay.

Material & Methods

Oxidative stress response in the peripheral blood was assessed in 55 patients with SSc and 44 well-matched controls using real-time monitoring of HP formation by the CBA assay. We also analyzed the relationship between HP generation and SSc clinics, systemic inflammation, and cellular fibronectin, an emerging biomarker of endothelial damage.

Results

SSc was characterized by a significantly faster (2-fold) fluorescent product generation in the CBA assay and higher cumulative HP formation (3-fold) compared to controls ($p<0.001$, both). The dynamics of HP generation were not associated with the form of the disease (diffuse vs. limited SSc) or autoantibody profile. However, it was increased in patients with more severe illness and certain clinical manifestations (i.e., pulmonary hypertension, digital ulcers, and cyclophosphamide treatment) and in smokers (current or past). Higher serum CRP, blood eosinophil count, and cellular fibronectin with lower hemoglobin levels were independent determinants of increased HP formation.

Conclusion

This study indicates a pro-oxidant imbalance in SSc, likely related to systemic inflammation and endothelial injury. However, extensive observational and experimental studies are needed to verify the impact of oxidative stress on unfavorable clinical outcomes.

Role of phase separation in the pathogenesis of type 1 – interferonopathies due to mutations in SAMHD1

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Germany

Introduction
Aicardi-Goutières syndrome (AGS) is an early-onset encephalopathy caused by mutations in nine genes (e.g. SAMHD1) mainly involved in nucleic acid metabolism and sensing. Patients show significant global developmental delay and manifestations in several organs such as chilblain lesions of the skin. We have previously demonstrated that formation of membraneless organelles is impaired in cells lacking SAMHD1. Membraneless compartments such as stress granules form by phase separation. The aim of this project is to understand the role of SAMHD1 deficiency on the formation and kinetics of membraneless compartments at DNA damage sites.

Material & Methods
To determine the kinetics of FUS-GFP recruitment to DNA damage sites, a distinct region of the nucleus of HeLa cells with or without shRNA-mediated knockdown of SAMHD1 was micro- irradiated using a 405 nm laser followed by live cell imaging. To analyze the effects of genotoxic stress in SAMHD1 deficiency, HeLa cells and primary patient-derived fibroblasts were monitored at different time intervals after 2 Gy or 6 Gy X-ray exposure using Western blot analysis and immunofluorescence microscopy.

Results
Using micro-irradiation in HeLa cells, we here show that recruitment of the DNA damage response component FUS is faster, but significantly shorter in SAMHD1-depleted cells compared to shRNA controls. We describe an increased amount of double-stranded RNA (dsRNA) in SAMHD1-deficient cells, which seems to interfere with the proper recruitment of FUS to DNA damage sites by binding of FUS to dsRNA in the cytosol. Western blot analyses confirm a chronic DNA damage in
SAMHD1-deficient patient fibroblasts and indicate an altered kinetic of DNA damage marker proteins after ionizing radiation compared to wild type controls.

Conclusion
In agreement with previous experiments, SAMHD1 deficiency appears to alter phase separation of FUS at DNA double strand breaks after micro-irradiation, probably due to the binding of FUS to unprocessed dsRNA in the cytosol. Further experiments are envisioned to investigate the consequences of an altered phase separation in SAMHD1-deficient cells with regard to DNA damage repair and their role in AGS pathogenesis.

Humoral Response Of Anti-sars-cov-2 Vaccination After Kidney Transplant Compared To Patients On Dialysis

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Brasil

Introduction

There is some concern that using immunosuppressive drugs on kidney transplants might reduce the effectiveness of SARS-CoV-2 immunization. We aimed to evaluate the impact of immunosuppression after kidney transplantation on anti-SARS-COV-2 antibody titers compared to patients on dialysis during 1-year follow-up.

Material & Methods

This is a prospective study that enrolled chronic kidney disease (CKD) patients who were submitted to transplant recipients (D0) or were waitinglisted and stayed on dialysis (D0 in a paired time). All patients had never had COVID-19 and had been fully anti-SARS-CoV-2 vaccinated according to the Brazilian scheme before inclusion. No additional doses were shot after the study enrollment. The antibody titers were measured at D0, 30, and 90 days after transplantation (and in a paired time for patients who stayed on dialysis).

Results

116 patients were included: 48.3% remained on dialysis (n=56) and 51.7% (n=60) received a kidney transplant. They were 48.6 years old, 61.2% were men, and 60.3% were Caucasian (n=70). CKD etiology was undetermined in 37.9%, chronic glomerulonephritis in 21.6%, and diabetes in 16.5%. All KTR received a single-dose (3mg/kg) of r-ATG followed by oral prednisone and tacrolimus as maintenance drugs and sodium mycophenolate (60%) or azathioprine (36.7%) or everolimus/sirolimus (3.3%). KTRs were older (44.9 vs. 52.5 years, p=0.002) and had remained for a longer period on dialysis (2.0 vs. 7.0 years, p<0.001). Sex, race, and CKD etiology were similar between the groups. Considering all patients, the antibody titers at D0, 30, and 90 days were 11,038UI/ml (IQR 2,099-30,115), 6.930UI/ml, and 3,467UI/ml (IQR 827-10,967), respectively. Until 90 days, no patients in both groups presented anti-SARS-CoV-2 seroreversion. In the repeated measures, antibody titers were similar between dialysis patients and KTRs at D0 (12,102 vs. 9,956UI/ml), day 30 (6,904 vs. 7,307UI/ml), and day 90 (3,525 vs. 3,423UI/ml), p>0.05.

Conclusion

Humoral response was similar between KTRs and dialysis patients. Immunosuppressive drugs had no significant impact on anti-SARS-CoV-2 antibody titters during a 90-day follow-up.

Impact of hypoxia on epithelial function upon exposure to Clostridioides difficile toxins

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Introduction

Physiological hypoxia in immunological niches such as the bone marrow, intestinal mucosa and lymphoid tissue, regulates innate and adaptive immune responses by modulating cellular proliferation, differentiation and effector function. This is mainly mediated via transcriptional changes driven by hypoxia inducible factors (HIFs). However, in diseased tissue such as in tumors, infected or inflamed tissues, hypoxia facilitate tissue damage and increase disease severity. The aim of our project is to understand how C. difficile toxins A (TcdA) and B (TcdB) interact with hypoxic factors (HIF-1/2/3 α) and how this affects the course of inflammation in C. difficile infection.

Material & Methods

The C2BBe1 colonic epithelial cell line was used to study the effects of C. difficile TcdA and TcdB on mucosal epithelium under hypoxic compared to normoxic conditions. Hypoxia was induced by atmospheric oxygen reduction (1% O2) or chemically with CoCl2 treatment. Following exposure to toxins, we assessed production of proinflammatory cytokines and epithelial barrier permeability.

Results

Notably, C2BBe1 cells could be stimulated to produce IL-8 in response to challenge with TcdA and TcdB but the production of TNF, IL-6 and IL-1ß was not triggered. IL-8 production was increased after 24h with TcdB but not TcdA. With dual TcdA and TcdB exposure, TcdA interfered with IL-8 production induced by TcdB, thus reducing IL-8 release. Furthermore, we found that 1% O2 but not CoCl2-induced chemical hypoxia reduced the amount of IL-8 secreted by C2BBe1 cells exposed to TcdB. Moreover, in comparison to normoxia and CoCl2 conditions, we observed an increase in epithelial permeability (as a sign of tissue damage) under 1% O2 with TcdA alone or combined TcdA and TcdB, indicating that IL-8 levels do not necessarily reflect the degree of tissue damage.

Conclusion

The results show that TcdA and TcdB effects on the cytokine response and epithelial barrier function are, indeed, modulated by hypoxia. Notably, the effects observed with chemically induced hypoxia induced by CoCl2 differed from those obtained at 1% O2. Future work will be aimed at understanding the underlying molecular mechanisms to provide a deeper insight into the role of hypoxia in toxin-mediated epithelial cell damage.

Evaluating Serum Levels of IL-33, IL-36, IL-37 and Gene Expression of IL-37 in Patients with Psoriasis Vulgaris

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Introduction

Serum levels of interleukin (IL)-33, IL-36 and IL-37 have been reported to be up-regulated in various T helper (Th)1/Th17 mediated autoimmune/inflammatory diseases. Although IL-33 and IL-36 expression are increased in skin lesions of patients with psoriasis, their serum levels in such patients have not yet been adequately studied. We aimed to evaluate serum level of IL-33, IL-36 and IL-37 cytokines and IL-37 gene expression in patients with autoimmune/inflammatory disease of psoriasis and to explore their correlation with disease severity. Such evaluation further clarifies disease pathogenesis and may be utilized in clinical practice

Material & Methods

47 patients with psoriasis vulgaris and 47 healthy individuals were included. Serum IL-33, IL-36 and IL-37 levels were measured by Elisa and gene expression of IL-37 measured by real time PCR in all participants. The disease activity was assessed by the psoriasis area and severity index (PASI). Linear Correlation between interleukin measures and PASI score was calculated. Also sensitivity and specificity of such measurements were determined.

Results

Serum IL-36 and 37 levels in patients with psoriasis vulgaris were significantly higher than those in healthy controls($P=0.007$ and $P=0.027$) and positively correlated with disease activity (PASI score). Serum IL-33 levels in patients were equal to those in healthy controls($P=0.1$) but positively correlated with disease activity. Serum IL-36 levels were significantly higher than serum IL-33 levels($P<0.05$). Gene expression of IL-37 levels in patients were higher than healthy controls($P<0.001$) but was not correlated with disease activity.

Conclusion

Serum IL-36 and IL-37 levels are generally increased in psoriasis vulgaris and correlated with disease severity. Therefore, serum IL-36 and IL-37 levels may be markers of treatment and diagnosis of psoriasis.

Evaluation of the immunogenicity of human papillomavirus 16/18 L1 virus-like particle vaccine with glucomannan in comparison with CERVARIX® in mice

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Iran

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 used in Cervarix® is a combination of aluminum hydroxide and monophosphoryl lipid A which is called AS04. In this study, we evaluate the changes in the Immunogenicity and efficacy of the HPV vaccine when we add glucomannan as a proven adjuvant.

Material & Methods
Seventy C57BL/6 mice were divided into five experimental groups, one positive control group (Cervarix®) and one negative control group (PBS). Experimental groups were vaccinated with a mixture of adjuvants, HPV types 16 and 18 L1 virus-like particles (L1VLP) alone, L1VLP in combination with AS04, glucomannan, and also a 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-Y, TNF- a) 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.

Gynaecology and Obstetrics
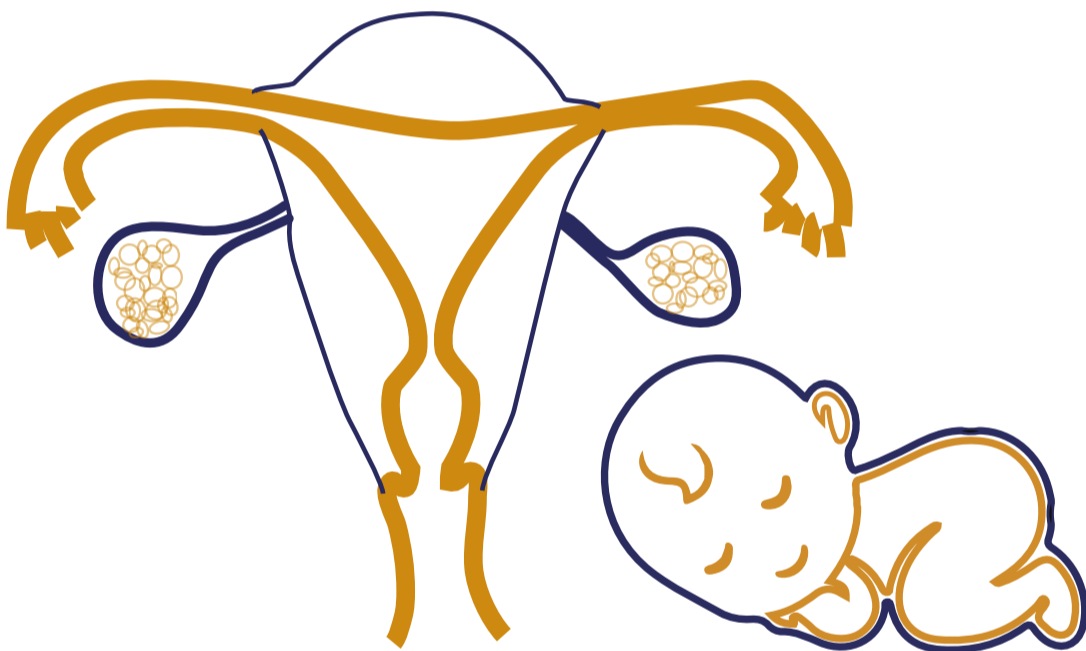
Presenters:
Vindhya Methalayil
Fales Kalaundi
Glory Kaunda
Namuun Batsaikhan
Catalina Rosario Guerra-Silva
Humphrey Beja
Elham Ahmadi
Paola Valero

Lack of Awareness on Menstrual Hygiene among Adolescent Girls : A Cross-sectional study in an Urban town in South India

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India

Introduction

Learning about Menstrual hygiene is a vital aspect of health education for adolescent girls. The topic of menstruation is still considered a taboo in India, which leads to lack of proper information among the adolescents. Increased knowledge about menstruation right from childhood may escalate safe practices and help in mitigating the suffering of millions of girls. Though many reproductive health classes have been claimed to be taken for students, their effectiveness remains unchecked. This study aims to assess the level of awareness regarding Menstrual Hygiene, among school going adolescent girls, and to check the practices followed by them during menstruation.

Material & Methods

A cross-sectional study was carried out on 3378 adolescent girls between the ages 10 to 19, using an online questionnaire over a period of 1 month (December 2022). Details on demography, knowledge about menstruation, menstrual practices and hygiene followed were collected. The data obtained were tabulated and analysed using SPSS Version 27.0. 11 schools were visited with the aim to provide adequate classes on menstrual hygiene.

Results

Most of the respondents attained menarche at the age of 12. However, 39% were unaware of menstruation prior to menarche. A majority (89%) used sanitary pads as the absorbent. 11% used cloth and period panties, out of which only 41% sundried them properly before the next use. 39% of the girls did not change their pad every 6 hours, and 43% did not bathe twice during the cycle. An average of 57% participants faced menstrual issues like dysmenorrhea and bleeding for more than 7 days. Alarmingly, 38% students have had urinary tract infections (UTI) after menarche. 44% of the students deemed that their school lacked adequate washrooms and disposal systems.

Conclusion

This study proves that there is still a wide scope for educating adolescents. Unsanitary practices like prolonged use of absorbents, improper disposal and diseases like UTI indicate the lack of awareness among the girls. Thus, targeted education classes must be provided, enabling a healthier lifestyle.

KNOWLEDGE, PRACTICE AND UTILIZATION OF PARTOGRAPH AMONG HEALTH CARE WORKERS IN SOUTHWEST HEALTH ZONE, MALAWI

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 Malawi

Introduction
Maternal mortality remains a global concern and Malawi is not exempted. Global estimates of half a million deaths were reported among women in 2015. About 99% were from low and middle income countries, with Sub-Saharan Africa accounting for the majority (66%). In the year 2015-2016 Malawi recorded 439 maternal deaths. Most of these deaths are preventable as many are attributed to inappropriately timed referral to the obstetric unit and poor management within obstetric units. Monitoring of women in labor to detect deviation from normal and carrying out timely decisions using a partograph is a global obstetric practice to reduce these maternal deaths due to some of the direct obstetric causes. However, lack of knowledge about the tool among the obstetric care givers has been a major challenge

Material & Methods
A cross-sectional quantitative study was conducted to examine knowledge, practice, and utilization of partograph among obstetric care givers in Southwest health zone of Malawi. 107 health workers were purposively sampled and interviewed using a questionnaire and 289 (10%) partographs were randomly selected from 2,890 partographs in the previous month of July 2021 prior to the study for review. Data was analyzed using IBM-SPSS version 20 and descriptive, bivariate analysis and binary logistic regression were performed on the data

Results
Partograph use among health workers in southwest health zone was 100%. Knowledge on definition of partograph was 51.4%. The practice of the partograph was high in the southwest zone (70.6 %). Managerial policy to use partograph ($< .005$) was found to influence partograph utilization among health workers. The odds of utilization of partograph among health workers which was found to be slightly lower among female health workers (OR 326: CI .111-.958). One of the major challenges experienced by 39.3% health workers was unavailability of partographs in health facilities.

Conclusion
Partograph use among health workers in southwest zone- Malawi was found to be high, however the effective use was poor evidenced by incomplete filling. The practice of the partograph to detect deviations was poorly done despite high utilization which may have contributed to poor maternal outcome.

Prevalence of Sexually Transmitted Infections among Pregnant women in peri-urban health centers in Blantyre, Malawi

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Malawi

Introduction

Sexually transmitted infections still remain a problem of public health importance. Pregnant women are at an increased risk of contracting STIs, which have the potential to cause undesirable effects and significant maternal and neonatal morbidity. STIs are associated with adverse pregnant outcomes including spontaneous abortions, stillbirths, prematurity, low birth-weight, postpartum endometritis and various sequelae in the surviving neonates. We aimed to determine STIs prevalence among pregnant women who visited antenatal care clinic in peri-urban health centers in Blantyre, Malawi and to ascertain factors contributing to the determined prevalence. Estimating the prevalence would alarm and cause provision of timely interventions and management before the STIs cause the complications in many women. Although a good number of studies have been done regarding the impact or prevalence of STIs in context of pregnant women, there is still limited statistical data to clearly demonstrate the prevalence of STIs among pregnant women in our local setting, hence we were determined to carry out this research to fill the existing gap.

Material & Methods

Quantitative and qualitative research was carried out in three peri-urban health centers of Blantyre, Malawi. Pregnant women of age range 14-43 years in all trimesters were target population.

Quantitative method was used to collect secondary data of number of women (total of 5700 visited ANC from January-June 2022) diagnosed with STIs during antenatal clinic (ANC) visit. Qualitative primary data was obtained from pregnant women(N=91) using convenience non-probability sampling. Questionnaires were used to collect primary data and Microsoft excel for data analysis.

Results

Overall STI prevalence was found to be 33.4%. The prevalence from the three health centers were 43.8%, 27.5% and 26.01%. Young maternal, multi-parity, unemployment, and immunosuppression were factors found to contribute to high prevalence. Infections were highest in second trimester (41%) compared to third (36%) and first (23%) trimesters.

Conclusion

The study has shown a high prevalence (33.4%) of sexually transmitted infections among pregnant women implying that if left unattended as required, significant increase in maternal and neonatal morbidity and poor pregnancy outcomes may occur. Public health intervention programs e.g., sexual and reproductive education should be strengthened to promote the sexual and reproductive health of pregnant women.

Prevalence and risk factors associated with pre-existing comorbidity among pregnant women in Ulaanbaatar

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Mongolia

Introduction

Pre-existing comorbidity during pregnancy is one of risk factors developing pregnancy complications such as ectopic pregnancy, preterm birth, neonatal respiratory distress syndrome and placental abruption. As stated in a previous study including 64299 postpartum women, prevalence of preterm birth in Ulaanbaatar was 15.4% (n=9866) which is higher prevalence compared with international mean value. This study aims to estimate the prevalence of pre-existing comorbidity and risk factors including age, education and habitancy.

Material & Methods

We carried out the study using retrospective study design. We analyzed 64229 patient histories of pregnant women who delivered at tertiary referral hospitals consisting of Amgalan Maternity hospital, Urguu maternity hospital and Khuree maternity hospital during 2017 to 2022. We used a randomized sample method for estimating study sample size. Analysis was performed using SPSS 29 version.

Results

We involved a total of 69229 pregnant women who delivered at the hospitals in Ulaanbaatar, from 2017 to 2022. The prevalence of pre-existing multimorbidity in pregnant women was 62.4% (n=40079). The percentages of pregnant women with comorbidity were 26.4% (n=29719) with caries, 9.8% (n=11182) diagnosed with tonsillitis, 6.3% (n=7299) with syphilis, 3.3% (n=3808) with hepatitis B and 3% (n=3513) with kidney disease. There were no statistical significance differences between the prevalence of pre-existing comorbidity and study participants' socioeconomic status such as age, education and habitancy.

Conclusion

According to the data published in Mongolian Health Development Center in 2012, 21.6% of total postpartum women had pre-existing comorbidity, which illustrates that prevalence of pre-existing comorbidity among pregnant women have been increasing during recent years. We found that there was no statistically significant association between prevalence of pre-existing comorbidity during pregnancy and age, education and habitancy. Therefore, there is a necessity to study risk factors leading to pregnancy complications. To investigate risk factors and causes of pre-existing disease during pregnancy is crucial to decreasing the prevalence and preventing pregnancy complications such as ectopic pregnancy and preterm birth.

Maternal obesity and gestational diabetes mellitus cause human umbilical vein endothelial cell dysfunction increasing the intracellular pH

[1] *Catalina Rosario Guerra-Silva*
Chile

Introduction

Maternal obesity in pregnancy and gestational diabetes mellitus (GDM) associate with foetoplacental endothelial dysfunction. The intracellular pH (pHi) is involved in the endothelium-dependent vasocontractile and vasodilatory response. We evaluated the role of hydrogen sulfide (H_2S), synthesized mainly by cystathionine gamma-lyase (CSE), and the blockage of Na+/H+ exchanger 1 (NHE1) in the pHi of human umbilical vein endothelial cells (HUVECs).

Material & Methods

HUVECs were isolated from full-term pregnancies (n = 8) with or without GDM of mothers with pre- pregnancy normal weight (NW) or obesity (OB) (Clinical Hospital CHRISTUS-UC, with patients consent). HUVECs were cultured in medium 199 plus sera up to passage 2 and incubated (12 h) with 100 µmol/L sodium hydrosulfide (NaHS, H_2S donor) or 100 µmol/L propargylglycine (PAG, CSE inhibitor). The pHi was measured in BCECF-AM preloaded cells (12 µmol/L, 10 min) by acid pulse assay. Basal pHi and pHi recovery rate (dpHi/dt) were determined in the absence or presence of 5 µmol/L 5-N,N-hexamethylene-amiloride (HMA, NHEs inhibitor).

Results

Cells from GDM show higher basal pHi (7.44 ± 0.15) than normal pregnancies (7.20 ± 0.04). In normal pregnancies, NaHS increased the pHi in NW (7.95 ± 0.36) but had no effect in OB. PAG increased the pHi (7.43 ± 0.62) in NW cells but lowered it in OB (6.86 ± 0.4). NaHS decreased the pHi in GDM cells (6.99 ± 0.78) and increased pHi in normal pregnancies cells (7.92 ± 0.46). The same pattern was seen with PAG (6.74 ± 0.23 vs 7.52 ± 0.53 for GDM and normal pregnancy, respectively). The dpH/dt was higher in OB (0.007 ± 0.027 pH units/10s) compared with NW (0.001
± 0.01 pH units/10s). It was increased by NaHS and PAG in NW (0.008 ± 0.013 and 0.008 ± 0.012, respectively), and by NaHS in OB (0.017 ± 0.019) but unaltered by PAG..

Conclusion

Higher pHi in maternal obesity and GDM may result from lower H_2S generation in HUVECs. This phenomenon is dependent on NHEs activity cells from women with pre-pregnancy obesity.

Primary dysmenorrhea among University students in Northern Uganda: associated symptoms, and management

Humphrey Beja
Uganda

Introduction
Primary dysmenorrhea (PD) is menstrual pain not associated with any pelvic pathology. PD is one of the most common gynecologic complaints in young women. In Uganda, there is scarcity of literature on the PD associated symptoms and management strategies used by women of reproductive age. This study aimed to describe primary dysmenorrhea associated symptoms and management strategies used by undergraduate students in northern Uganda.

Material & Methods
This was a descriptive cross-sectional study conducted among female undergraduate students of Lira University in northern Uganda. Systematic sampling was used to select study participants who met the inclusion criteria and 232 study participants were recruited. The data was collected using a self-administered questionnaire. Data analysis was aided by Statistical Package for Social Sciences (SPSS) (version 23), descriptive statistics were used.

Results
The prevalence of primary dysmenorrhea was 211/232(90.9%). The most commonly experienced dysmenorrhea associated symptoms were; change in appetite 79/211(36.0%), breast engorgement 84/211(39.8%), and depressed mood 107/211(51.4%). Pain relievers were the most commonly used management strategy 160/211(77%), Paracetamol was the most commonly used pain reliever 62/211 (29.8%). The most commonly used non-pharmacological management strategies used were; exercise 100/211(47.6%), resting 94/211(44.5 %) and relaxation 93/211(44.1%).

Conclusion
A broad range of primary dysmenorrhea associated symptoms are experienced by undergraduate university females but they do not use the appropriate management strategies. All University authorities should prioritize menstrual health and design programs to educate the female students on the management of dysmenorrhea associated symptoms using both pharmacological and non-pharmacological strategies and make the drugs accessible.

The Regenerative Role of Adipose-Derived Mesenchymal Stem cells in Uterine Injury: Histopathological Evaluation

[1] Elham Ahmadi
Iran

Introduction
Uterine injury results from trauma to the endometrium and healing process is orchestrated by complex actions within different cells in which specific molecular pathways have emerged. It is accompanied by the formation of fibrotic tissue and adhesion bands. The atrophic endometrium is generally a symptom of uterine injury, which results from the obliteration of the uterine lining leading to infertility.

Material & Methods
In the current study, we established a mouse model of uterine injury and demonstrated that systemic injection of adipose-derived mesenchymal stem cells (AD-MSCs) efficiently will target fibrosis pathway in the uterus through different aspects, as shown by reduced matrix content that mainly produced by myofibroblast through the deposition of alpha smooth muscle actin (αSMA) and Collagen.

Results
Atrophic endometrial epithelial cells rapidly regenerated and formed a normal uterine epithelial layer, indicating a robust epithelial-regenerating capacity of treatment. Fibrosis and adhesion are associated with chronic inflammation and there is widespread enthusiasm for using of AD-MSCs due to the immunomodulatory role of AD-MSCs especially because of noninvasive procedure of harvesting from the same individual.

Conclusion
Clinical application of stem cell therapy could extensively alleviate patients suffering from impairment of the endometrium and infertility through uterine regeneration. Ultimately with removing extracellular components, have the ability to regrow and repair the uterine lining and to improve functionality to the point of implantation and pregnancy.

Intracellular pH is differentially modulated by insulin in HUVECs from mothers with gestational diabetes mellitus according to their pre-pregnancy BMI

Paola Valero
Chile

Introduction
Human umbilical vein endothelial cells (HUVECs) from gestational diabetes mellitus (GDM) show alkaline intracellular pH (pHi). It is unknown if insulin causes differential pHi modulation in HUVECs from women with different pre-pregnancy body mass index (BMI). Objective: To determine whether insulin modulates the pHi in HUVECs from GDM depending on the pre-pregnancy maternal BMI.

Material & Methods
HUVECs were isolated from full-term pregnancies (Clinical Hospital CHRISTUS-UC, with patients consent) from normal pregnancies with normal pre-pregnancy weight (Nnw, n = 9), overweight (Now, n = 4), or obese (Nob, n = 3), or GDM (GDMnw, n = 4; GDMow, n = 3; GDMob, n = 4). The pHi was measured in BCECF-AM preloaded cells (12 µmol/L, 10 min) by acid pulse assay. Basal pHi and pHi recovery rate (dpHi/dt) were determined in the absence or presence of insulin (1 nmol/L, 8 h), hexamethylene amiloride (HMA, 5 µmol/L, NHEs inhibitor), and zoniporide (Zn, 0.1 µmol/L, NHE1 inhibitor). NHE1 protein abundance was determined by Western blot.

Results
Basal pHi was higher in Nob (7.82 ± 0.21) (mean ± SEM, ANOVA one tail, $P<0.05$), GDMnw (8.23 ± 0.10), GDMow (7.95 ± 0.31), and GDMob (7.54 ± 0.14) vs. Nnw (7.06 ± 0.06) or Now (7.03± 0.06). Insulin reduced the GDMob-increased basal pHi. NHE1 contribution was higher in Nnw compared with Now (45 ± 7 vs 1 ± 3%, respectively) and Nob (1 ± 6%). NHE1 contribution to the basal pHi was higher in GDMow vs. GDMnw (99 ± 30 vs 1 ± 7%, respectively), Nnw vs. GDMnw (45 ±7 vs 1 ±7%, respectively), GDMow vs. Now (99 ± 29 vs 1 ± 3%, respectively), and GDMob vs. Nob (24 ± 6 vs 1 ± 6%). Insulin decreased NHE1 contribution in Nnw but not in Now and Nob. Insulin increased NHE1 contribution only in GDMnw reaching similar values as in Nnw. Insulin reduced the NHE1 protein abundance in cells from GDMob.

Conclusion
NHE1 involvement in the pHi recovery and insulin effect depends on the pre-pregnancy BMI in women that develop GDM (Support: Fondecyt 1190316, VRI+DIDEMUC PUC, ANID 21221870. UTalca (Chile) and UMCG (NL) PhD fellowships).

Rheumatology and Immunolgy

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The relation between C-reactive protein and serum amyloid A in patients with autoinflammatory diseases

[1]Carien Dermer
The Netherlands

Introduction

Autoinflammatory diseases are rare disorders of the innate immune system characterized by fever and other signs of inflammation. A feared complication of autoinflammatory diseases is the development of AA amyloidosis. AA amyloidosis is caused by the extracellular deposition of the soluble serum amyloid A (SAA) protein as insoluble amyloid fibrils leading to organ damage.

Prolonged high levels of SAA are a prerequisite to develop AA amyloidosis. Since measurement of SAA is relatively expensive and sometimes unavailable C-reactive protein (CRP) is often used as a surrogacy marker to test for inflammation. The aim of this research is to evaluate the relation between CRP and SAA.

Material & Methods

A retrospective cohort of patients with an autoinflammatory disease (n=99) where SAA and CRP blood testing was performed in the period between 2015 and 2021 in the University Medical Centre in Groningen was used to investigate the correlation between CRP and SAA.

Results

CRP and SAA have a high correlation (rho=0.755, $p < 0.001$). A CRP value of below 0.45 mg/L results in a 100% sensitivity level for SAA below 4 mg/L. CRP below 5 mg/L is a good predictor of SAA below 4 mg/L with a sensitivity of 85.4% and a specificity of 83.6%. Only prednisone and erythrocyte sedimentation rate (ESR) significantly influence the relation between CRP and $\log_{10}$ SAA.

Conclusion

There is a significant correlation between CRP and SAA. CRP levels below 5 mg/L proved to be highly predictive of SAA levels below 4 mg/L. However, clinicians should .

Prevalence and Risk Factors Associated with the Cognitive Impairment Among Type -2 Diabetes Mellitus Patients

Tarun Kumar Suvvari
India

Introduction

Globally, diabetes mellitus is one of the major causes of increased morbidity. Diabetic nephropathy, retinopathy, and neuropathy are routinely screened among diabetic patients, whereas the cognitive decline associated with diabetes mellitus is not given much attention. Cognitive impairment can further develop into neurocognitive disorders. Along with raising diabetes prevelence, cognitive impairment would also increase. So, routine screening for cognitive decline should be done among diabetes mellitus patients. we aimed to find out the prevalence of the cognitive impairment and its associated risk factors among type -2 diabetes mellitus patients and to evaluate the association between HbA1c levels and cognitive impairment.

Material & Methods

An observational cross-sectional study was conducted at department of Medicine, tertiary care hospital for 2 months. Montreal Cognitive Assessment (MoCA) test that consists 30 questions was used to assess the cognitive function. Indepth history, Clinical which includes BMI, HbA1c levels, duration of diabetes, Blood sugar (fasting and postprandial) were also collected. Descriptive statistics was used, and the Chi-square test was used to determine the statistical significance. Pearson correlation coefficient was used to find out the relation between MoCA score and glycemic parameters.

Results

A total of 96 patients were included in the study. Mean HbA1c is 9.08 + 1.73 and Mean MoCA Score is 25.14 + 1.63. Mild Cognitive impairment (MCI) was noted in 56 % of patients. Attention was the most common cognitive domain defect found in all MCI patients - 100%. Delayed Recall and Memory was 2nd most cognitive domain defect found - 92.5%. Higher HbA1c, High FBS, Higher PPBS was found to be statistically associated with MCI (P<0.05). A negative correlation was found between HbA1c, FBS, and PPBS levels and MoCA scores.

Conclusion

More than half our study participants reported mild cognitive impairment. It highlights the need for implementation of routine cognitive testing for diabetes patients. There is a strong negative correlation between MoCA scores and parameters of glycemic control - higher levels of HbA1c, FBS, & PPBS is seen in people with less MoCA score indicating mild cognitive impairment. Further studies were need to evaluate whether improving the glucose levels helps in improving cognition or not

Western-type diet aggravates chronic inflammation which may lead to brain damage in a mouse model of obesity

Zsófia Ruppert
Hungary

Introduction
Unhealthy diet may induce chronic, systemic inflammation, which has negative effects on many different organs. Therefore obesity is an important risk factor for several chronic diseases, not only diabetes or fatty liver, but also neurodegeneration. In this study, we aimed to compare the effects of a high-fat, high-fructose Western-type diet (WTD) and a simple high-fat diet (HFD) on inflammation and metabolic disturbances in different organs.

Material & Methods
3 months-old, male C57BL6/J mice were divided into 3 groups (n=15): a normal chow-fed, control group; a HFD-fed group; and a WTD group. Body weight was measured monthly, while the oral glucose tolerance test was performed after 5 months of diet. Pathological changes in the liver were investigated on hematoxylin-eosin-stained sections. Gene expression was studied by qPCR in visceral adipose tissue and brain samples. To explore neurogenesis, we used doublecortin immunostaining on brain sections. For statistical analysis, one-way ANOVA was performed; the level of statistical significance was set at $p < 0.05$.

Results
We found, that fructose substantially worsened the effects of HFD, as the levels of obesity, glucose intolerance and hepatic steatosis were significantly higher in the WTD group compared to not only the control group but also the HFD group. These changes were accompanied by a significant increase in the expression of pro-inflammatory genes in the visceral white adipose tissue, suggesting a higher level of systemic inflammation in response to WTD compared to HFD alone.

Indeed, a slight but statistically significant elevation in the expression of microglia and macrophage markers was also seen in the brains of the WTD-fed mice. Interestingly, in certain WTD-fed animals, we found a higher number of doublecortin immunopositive neurons. We suppose that WTD induced more severe brain damage in these animals, which may be compensated by the activation of the neurogenesis.

Conclusion
Our results show, that the WTD leads to more severe obesity and inflammation than the HFD alone, and negatively affects the function of several organs, including the brain. Our research may help to understand the harmful effects of our lifestyles, and promotes the development of therapies for obesity-related disorders. This work was supported by funding from NKFIH FK138390.

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.

Infectious Disease
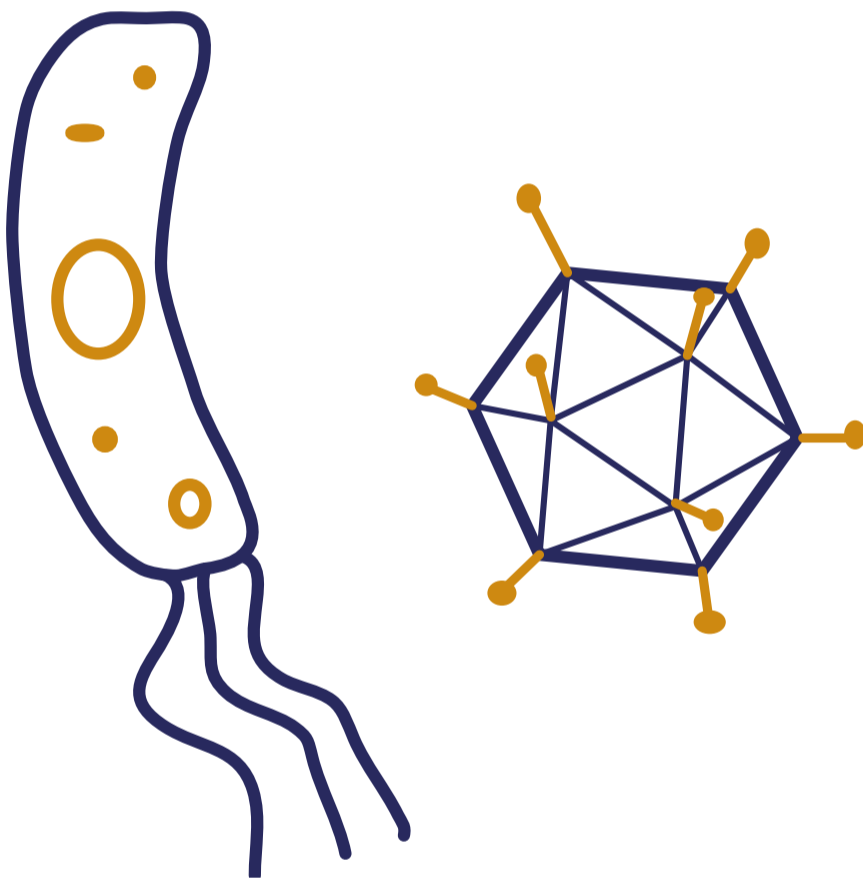
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Characteristics and clinical outcomes of patients tracheostomized by COVID-19

[1]Felix Vidal
Chile

Introduction

The disease caused by SARS-CoV-2 results in a clinical presentation of atypical pneumonia, with different levels of severity. About 5% of patients present Acute Respiratory Distress Syndrome (ARDS) requiring admission to the intensive care unit (ICU). Hospitalized patients with positive PCR for COVID-19, 28.4% underwent orotracheal intubation and required invasive mechanical ventilation (IMV). During the COVID-19 pandemic, ARDS was the most common indication for tracheostomy (60%). The aim of this study was to describe the clinical characteristics, and outcomes as hospital stay, days on invasive mechanical ventilation, in-hospital complications and in-hospital mortality of people affected by severe COVID-19 pneumonia who underwent tracheostomy.

Material & Methods

Data were retrospectively collected from hospital records of tracheostomized patients at the Clinical Hospital of the University of Chile, from January to December 2021.

Results

Of 44 patients tracheostomized by COVID-19 the mean± SD age was 60±15.35 years; as for sex, 59.1% were men; median BMI was 32 kg/m2 (IQR 27.1 - 36.4). The comorbidities with the highest prevalence were hypertension (72.7%), obesity (50%) and diabetes (43.2%). The main reason for hospital admission was COVID-19 pneumonia (50%). A total of 88.6% had a medical indication for TQT for prolonged mechanical ventilation. Regarding the type of TQT, most of them were percutaneous (88.1%). In addition, 84.1% presented health care-associated infections (HAI) during hospitalization. Regarding the outcomes during hospitalization, the median number of days of IMV of those who were extubated was 45 (IQR 38 - 55.5) while the mean ± SD of the days of IMV in deceased patients was 58.7 ± 25.84. 29.5% of the total number of patients tracheostomized by COVID-19 died during hospitalization.

Conclusion

People tracheostomized by COVID-19 are characterized by being mostly men (59.1%) with a mean age of 60 years and presenting comorbidities. The prolonged mechanical ventilation was the most frequent indication for the performance a tracheostomy (88.6%). Of the study population, 84.1% presented a health care-associated infection. COVID-19 Tracheostomized patients had a high in- hospital mortality.

Evaluation of Practice, Attitude and Knowledge about Irrational Use of Antibiotics for Common Cold Infection in Sudan

[1] *Zainab Alghali Elsaid Muhammed*
Sudan

Introduction
Background: As majority of upper respiratory tract infection have a viral origin, antibiotic prescription for common cold has become a common practice in medicine. The prescription of an inappropriate and unnecessary antibiotics is the main cause of the development and increase of antibiotics resistance. Objective: The main objective of this study is to evaluate the awareness of the community about the wrong concept of using antibiotics for the common cold infection

Material & Methods
This cross-sectional study was conducted in Shendi state from May 2019 to January 2020, comprised random population of different ages 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 comprises the majority 44%. All had 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 said 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 common cold.

Conclusion
Low level of knowledge about the nature of common cold infection and high levels of arbitrarily use of antibiotic for common cold in this study make it necessary to provide educational programs to raise the awareness about common cold and antibiotic resistance
.

A revolution in scientific research – development of 3D cell culture models

[1] *Melina Hardt*
Austria

Introduction
3D ex vivo models which might better represent and come closer to the human in vivo system as 2D in vitro cell culture systems have become increasingly important for scientific researchers in recent years. These 3D models are useful for studying virus-host interactions, developing new therapeutics and investigating migration or invasion of different types of cancer.

Material & Methods
Air-Liquid-Interface cultures were cultured using human cell lines Calu-3 from lung carcinoma or A549 from adenocarcinoma, cultured for 10 days and infected with different respiratory viruses such as SARS-CoV-2 and influenza B. The replication rate was determined via RT-qPCR and the infection was visualized after fixation and embedding via immunohistochemistry with a specific antibody against the viruses. Another 3D model was developed using a bioprinter from TissueLabsR to spot an alveolar-mimicking lung-specific matrix. Microscopic channels made out of PluronicsR were created within the matrix and removed by cooling, leaving empty channels within the hydrogel matrix for treatment with interleukin. Cultured A549 cells were layered on top of the matrix, and migration into the matrix was studied using different time points.

Results
No differences of the replication rate of these variants could be observed by RT-qPCR determination of the supernatant. However, the amount of infected cells stained during immunohistochemistry differed. Furthermore, A549 cells differentiated in 3D models and could be infected by SARS-CoV-2 as opposed to cells cultured in 2D models. A549 spotted on top of the 3D printed matrix formed cell clusters with leader and follower cells. After several days of cultivation, they started to invade the matrix in cell complexes. Examination via immunohistochemistry staining of vimentin showed that the A549 cells retained their epithelial differentiation.

Conclusion
3D models will play a major key role in studying infectious diseases or cancer research. The created 3D culture systems enable to simulate the in vivo conditions and the use of ALI cultures helps scientific researchers to study virus-virus and virus-host interactions. Besides this, the implementation of bioprinted matrix supports scientific researchers to study the behaviour of cancers e.g. the invasion and migration of cancer cells.

Quantitative spatial mapping of complex host response dynamics to SARS-CoV-2 infection

Esther Föderl-Höbenreich
Austria

Introduction
With the emergence of new SARS-CoV-2 variants of concern (VOCs), it has become increasingly important to understand the differences in host-pathogen interactions in response to the viral infection and their potential epidemiological implications. These newly arising VOCs present increasingly sophisticated immune escape strategies, as exemplified by the raging B.1.529 variant, which differs massively from its predecessor VOCs. Portraying transcriptional host cell responses appears to be a promising strategy to understand the disparate infectivity rates and discordant inflammatory signaling observed in patients infected with different VOCs

Material & Methods
We infected a lung adenocarcinoma cell line (Calu-3) with different VOCs including the original strain wuhan-Hu-1, delta and omicron variant. To examine differences in the transcriptional profile, we resorted to Molecular Cartography (MC), a novel multiplex smFISH technology that allows spatial monitoring of 84 target genes.

Results
We identified a substantial number of differntially regulated genes (DRG) in infected cells, which all VOCs had in common, while DRG in bystander cells varied markedly between VOCs. Noteworthy, NFKBIA, which is associated with interferon signalling, was massivly upregulated in wuhan-Hu-1 and delta infected cells, whereas NFKBIA levels in omicron infected cultures were comparable to mock infected cells. Further, antiviral genes were correlatively expressed in infected cells.
Interestingly, only bystander cells of cells infected with omicron accomplished correlative expression of antiviral genes, suggesting an increased cellular capability to fend off approaching omicron virions and might explain the reported decreased pathogenicity in the lower respiratory tract.

Conclusion
The rapid evolution of SARS-CoV-2 lead to several virus variants with modified genomic features resulting in altered pathogenicity, transmission rates and antigenicity. By using a set of only 84 genes, we identified molecular signatures unique to individual VOCs. Portraying the transcriptional host cell responses appears a promising strategy to rapidly estimate the biological behaviour of newly occurring variants and therefor may provide early information in order to enable proper risk assessment.

Immunomodulatory effect of Thymosin- alpha1 on innate inflammatory response induced by SARS-CoV-2 infection: evidence in a PBMC-based in vitro model

[1] *Daniela Ricci*
Italy

Introduction

The property of Thymosin alpha 1 (TD1) to act as regulator of immune homeostasis has been defined in physiological and pathological contexts ranging from cancer to infection. Interestingly, papers demonstrated its mitigating effect on the "cytokine storm" as well as on the regulation of T- cell exhaustion/activation in SARS-CoV-2 infected individuals. Despite the increasing knowledge on TD1-induced effects on T cell response confirming the distinctive features of this multi-faceted thymic peptide, little is known on its effects on innate immunity to SARS-CoV-2 infection. Here, we interrogated an in vitro experimental setting based on human peripheral blood mononuclear cell (PBMC) cultures stimulated with SARS-CoV-2 to disclose TD1 property on the main cell players of early inflammatory response to infection, namely monocytes and myeloid dendritic cells (mDC).

Material & Methods

PBMC were collected from asymptomatic and hospitalized patients with SARS-CoV-2 infection or matched healthy donors to evaluate phenotype and activation status of different innate immune cell populations by cytofluorimetric analysis. Furthermore, PBMC obtained from healthy donors were stimulated for 24 hours with SARS-CoV-2 alone or in combination with synthetic Tα1. After stimulation, flow cytometric analysis was conducted to evaluate phenotype of different innate immune cell populations. Cytokine release was evaluated in culture supernatants by cytometric bead array.

Results

Moving from ex vivo data showing an increase in the frequency of inflammatory monocytes and activated mDC in COVID-19 patients, a PBMC-based experimental model recapitulated in vitro a similar phenotypic profile. SARS-CoV-2-stimulated PBMC showed an increased percentage of CD16+ inflammatory monocytes and mDC expressing enhanced surface levels of CD86 and HLA-DR activation markers in response to SARS-CoV-2 stimulation. Interestingly, the addition of TD1 to SARS-CoV- 2-stimulated PBMC cultures dampened the activation status of monocytes and mDC by regulating their immune-phenotype and by reducing the release of pro-inflammatory mediators, while promoting the production of the anti-inflammatory cytokine IL-10.

Conclusion

This study confirms the immunoregulatory properties of Tα1 in acting as homeostatic molecule also in the context of the innate immune response stimulated during SARS-CoV-2 infection. Moreover, this evidence shed light on inflammatory pathways and cell types involved in SARS-CoV-2 infection that are likely targetable by newly immune-regulating therapeutic approaches.

Atorvastatin therapy in COVID-19 adult inpatients: A double-blind, randomized controlled trial

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Iran

Introduction

Efficacious therapies are urgently required to tackle the coronavirus disease 2019 (COVID-19). This trial aims to evaluate the effects of atorvastatin in comparison with standard care for adults hospitalized with COVID-19.

Material & Methods

We conducted a randomized controlled clinical trial on adults hospitalized with COVID-19. Patients were randomized into a treatment group receiving atorvastatin + lopinavir/ritonavir or a control group receiving lopinavir/ritonavir alone. The primary outcome of the trial was the duration of hospitalization. The secondary outcomes were the need for interferon or immunoglobulin, receipt of invasive mechanical ventilation, and O2 saturation (O2sat), and level of C-reactive protein (CRP) which were assessed at the onset of admission and on the 6th day of treatment.

Results

Forty patients were allocated and enrolled in the study with a 1 to 1 ratio in atorvastatin + lopinavir/ritonavir and lopinavir/ritonavir groups. Clinical and demographic characteristics were similar between the two groups. CRP level was significantly decreased in the lopinavir/ritonavir + atorvastatin group ($P < 0.0001$, Cohen's d = 0.865) so that there was a significant difference in CRP level on the 6th day between the two groups ($P = 0.01$). Nevertheless, there was no significant difference in O2sat on day 6. Although the duration of hospitalization in the lopinavir/ritonavir + atorvastatin group was significantly reduced compared to the control group ($P = 0.012$), there was no significant difference in the invasive mechanical ventilation reception and the need for interferon and immunoglobulin.

Conclusion

Atorvastatin + lopinavir/ritonavir may be more effective than lopinavir/ritonavir in treating COVID-19 adult hospitalized patients.

Development of a semi-automatic, isolating and portable health-station for swab collection and patient data entry.

Prosper Magare
Zimbabwe

Introduction

There has been a recent increase in the occurrence of pandemics. The 2019 novel coronavirus (SARS-CoV-2), officially referred to as COVID-19 by the WHO, as an example, spread to more than 180 countries. The existing healthcare infrastructure in Low to Middle Income Countries (LMIC) such as Zimbabwe has shown to be inadequate to allow for effective isolation between the patients and the health care workers especially in remote areas. New efficient methods of collecting patient data, storing and migrating it are therefore necessary. Sedentary lifestyles and obesity are exacerbating both national and global epidemics. This warranted increased attention by physicians and other health care professionals. Hence, collection of data such as the body-mass index from patients is necessary. Clinicians feel overwhelmed by these challenges and point to an absence of practice tools and lack of time to process all the patients.

Material & Methods

This research involved development of a semi- automatic, isolating and portable health station for swab collection. An android application for patient data entry was also developed. Semi-automatic measurement of temperature using, mlx90614 infrared temperature sensor, height using an ultrasonic sensor and weight using load cells for health records enhanced non-contact assistance to patients. Backup power supply was achieved using a solar system through a changeover switch.

Results

The health station developed isolated the patient from the healthcare worker. Communication and vision were made possible by the use of acrylic glass which is transparent. Temperature measurement by the designed device was compared to the standard clinical temperature measurement using an oral thermometer and had an error margin of 1.5%. Height measurement using the device was consistent with measurement from a standard tape measure. Weight measurement using the device presented an error of 2%.

Conclusion

This work minimizes the chance of infection to the health care professionals by providing them isolation from a potential source of highly contagious disease. The model developed was tested for safety and efficacy so that it can be acceptable to be used for healthcare provision. There is however need to improve the accuracy of the sensors in measuring height, weight and temperature but using more accurate sensors.

Happy hypoxia in Covid -19 and its Predictive factors: A retrospective study.

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India

Introduction

Happy or silent hypoxia is a condition found in COVID-19 patients, it is characterized by the presence of hypoxia without dyspnea. Since the outbreak of the pandemic physicians caring for patients with hypoxia and free of dyspnea are operating in the dark, the lack of scientific evidence and non linear chaotic nature of pandemic make challenge to predicting the condition like happy hypoxia, however the epidemiological studies will help in analyzing the trend and risk factor associated with it. Our study suggested the hypothesis that hypoxia is one the strongest predictor of mortality in COVID-19 patients.

Material & Methods

It was a retrospective study based on past hospital medical records, Clinical, laboratory, and treatment data were collected and analyzed at the Covid-19 Tertiary care center in Kerala, India. The study duration was from 1st April 2021 to 30th Sep 2021. The study population comprised patients aged> 18 years age and with blood oxygen saturation < 94%.. statistical analysis for the data was performed using Microsoft excel and analysis was performed with SPSS version 21 software, a value of $p < 0.05$ was considered the threshold of significance

Results

A total of 1655 Covid-19 patients included in the study. There were among 998 (60.3%) patients were present with hypoxia, 628 (62.9%) patients had hypoxia with dyspnea and 370(37.07%) patient had silent or Happy hypoxia. A total of 127 death under hypoxia with or with out dyspnea was confirmed during the study period, among them 80 (62.99%) with dyspneic hypoxia and 47 (37%) to happy hypoxia, the result confirmed that mortality to covid 19 by happy hypoxia was 2.83%. In co-morbidities Hypertension lead in dyspneic hypoxic group with 62.7% and 37.26% (P= 0.833) in happy hypoxic group, Diabetes mellitus is the major co-morbidity in happy hypoxic with 45.9% and in dyspneic hypoxia it was 54.3% (P = 0.863).

Conclusion

This study finds co-morbidities including diabetes and hypertension lead to mortality among the hypoxic group. Finally, the use of a pulse oxy-meter is paramount important in the general public to monitor respiratory status, this helps to reduce delays in early medical care

Medical Biochemistry

Presenters:
Parmanreet Kaur Bhatti
Daria Adasheva
Tsaniya Indrayani
Davit Marjanidze
Razie Hadavi
Javad Razaviyan
Szymon Lipiec

AN INSILICO APPROACH FOR ANEURYSM GROWTH

Faısal Ahmed Mohammed Garbou
Turkiye

Introduction

Cardiovascular diseases have the highest mortality and morbidity rates. Each year, cardiovascular disease (CVD) is estimated to be the cause of 32% of all deaths worldwide[1]. During blood flow in the circulatory system, the vessel wall is constantly exposed to mechanical forces and can play a role in the development of pathologies if the arterial endothelium morphology is abnormal. In an aortic artery with an aneurysm, these changes may result in a rupture of the endothelium. An accurate pre and post-operative risk of an abdominal aortic aneurysm rupture is an important guide for planning aortic aneurysm repair surgery. Clinical studies have determined the risk with maximum aneurysmatic diameter based on medical imaging technologies. [2] However, it is known that the risk is not necessarily reflected by the maximum diameter alone [3]. Therefore, additional information is required for accurate risk assessment of an aneurysm before and after surgical repair. This study was designed to numerically evaluate the remodeling in aortic aneurysm morphologies and underlying mechanical factors. This study compared the relationship between the changes in aneurysm morphology and hemodynamic parameters in patients who were scanned at regular intervals. In flow visualizations based on virtual aortic models obtained from computed tomography datasets of three different scans, it was determined that the endothelial segments with distinctive changes in wall shear stress (WSS) distribution showed high consistency with the morphological change segments seen in the next periodic scans of the same patients.

Material & Methods

Five patients diagnosed with thoracic aortic aneurysms and aged between 70-75 were included in the study. Virtual aorta models were created from the CT images of the patients taken at three-month intervals. Three-dimensional (3D) models were created with VTK algorithms and a model mesh for finite element analysis was created with Simmetrix libraries. Blood flow was simulated by computational fluid dynamics analysis and visualized in Ceetron Analyzer Cloud [4]–[6]. In this study, we focused on WSS visualization, a parameter that cannot be measured in the clinical setting but can be calculated by multi-physics algorithms. Blood was considered Newtonian fluid and boundary conditions were established from case-specific data obtained from the clinic [7]. The initial velocity gradient was obtained from the Doppler ultrasound reports of the patients.

Results

Numerical simulation results were visualized as WSS distribution on the arterial wall. The WSS in the proximal ascending aorta was reported to be up to 1800 ± 100 Pa for patients with aortic aneurysms, while it was reported to be up to 700 for healthy people in the literature. Studies have shown that WSS can alter the material properties of thoracic aortic aneurysms through arterial wall remodeling, making the aortic wall more prone to swelling as shown in the figure which represents the growth segments of the following scan.

Conclusion

After this preliminary study, it has been observed that the most obvious effect of WSS on the change of endothelium morphology starts from the segments where dramatic decreases in WSS distribution are seen. The numerical analysis results were obtained in line with our hypothesis that shape change rates that may be encountered in the next scan could be predicted. This work was able to present significant findings on the evaluation of studies on aneurysm growth with insilico methods and it is possible to strengthen it with more scan datasets.

Validation study of a questionnaire to evaluate the expectations of patients candidates for obesity surgery.

Sandra Silva
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Introduction

Considered an endemic, multifactorial, progressive, and recurrent disease, obesity is a major risk factor for other severe clinical conditions and has become a global healthcare problem. Bariatric surgery is a safe and effective treatment for severe obesity, leading to significant and sustained weight loss. However, recent literature has shown dissatisfaction with weight loss and body Imaging. A growing incidence of weight recurrence has led to psychosocial problems and follow-up loss. In clinical practice, goals for postoperative weight loss from the patient perspective are commonly discrepant from the multidisciplinary team. High or even unrealistic expectations in the long-term lead to dissatisfaction with body image and can be associated with recovery weight gain, became knowledge about expectations essential. This study aimed to translate, adapt, and validate to Brazilian Portuguese the European Obesity Academy Questionnaire: Expectations about Surgical Treatment - EOAQ-EST, created by Fischer and researchers in 2014.

Material & Methods

Methodological study for translation and cross-cultural adaptation to Brazilian Portuguese of the EOAQ-EST on patients with severe obesity candidates for bariatric surgery at a referral academic hospital from January 2021 to February 2022. Inclusion criteria were severe obesity with Body Mass Index (BMI) $\geq 40kg/m^2$ or $\geq 35kg/m^2$ with associated medical conditions, older than 18 years, and preserved cognitive ability to understand the questionnaire. The study was approved by the local Ethics Research Committee. The methodological steps were translation, back-translation, revision of a panel of experts; pilot study with 30 bariatric surgery candidates and retest; statistical analysis; application for validation.

Results

161 participants, mean age of 46 years (sd = 10 years), 85.1% (n=137) were female. In part 3 of the questionnaire it was analyzed internal consistency and the confirmatory factor analysis, as well as the other analyses, indicated bifactor model composed of a general factor and three specific factors (social, personal, and healthcare) achieved the construct validity.

Conclusion

This study was carried out translated from the original English version into Portuguese, and adapted for the Brazilian culture of EOAQ-EST it can contribute to multidisciplinary teams in the preparation of candidates for bariatric surgery. New longitudinal multicenter studies are suggested for new validity tests.

Evaluation of patients' satisfaction after two types of short scar facelift techniques using the FACE-Q Aesthetics

Lotte Hijkoop
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Introduction

Nowadays, facelift surgeons have a tendency to use less invasive short scar facelift techniques; These techniques are claimed to be associated with higher patient safety, reduced postoperative downtime, having equal results and patient satisfaction. At the same time, studies assessing patients' satisfaction following short scar facelifts with valid outcome tools are lacking.

Material & Methods

This study is aiming to evaluate long-term patients' satisfaction in two short scar facelifting techniques used in our clinic: the P urse-String R einforced S MAS- ectomy (PRS) facelift and the En-bloc facelift. Patients who received the PRS facelift (by BvdL) or the En-bloc facelift (by HS) between January 2014 and December 2019 in Bey by Bergman Clinics were asked to participate and were sent four FACE-Q Aesthetics scales.

Results

A total of 49 out of a consecutive series of 175 patients who had facelift surgery completed the questionnaires. The results showed postoperative mean ± SD scores of 68.9 ± 19.2 on social function, 53.7 ± 19.7 on satisfaction with facial appearance, 49.8 ± 26.0 on the outcome, and 54.6 ±
28.7 on their decision. No differences were found between the techniques for none of the determinants (social function p=0.93 , facial appearance p=0.40 , outcome p=0.76 , nor decision p=0.55). All complications were minor. Ancillary procedures were performed frequently.

Conclusion

Both the PRS facelift and the En-bloc facelift result in long-term overall patients' satisfaction with no significant difference between the two techniques. Future prospective studies with even longer follow-up definitely are warranted.

Lipoaspirate Decantation Time Impact on Lipocyte Viability

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Introduction

Most common plastic surgery procedure is liposuction. For better results autologous fat grafting is common. Success of fat grafting may depend on lipocytes viability (LV). There are few factors that may have effect on LV including liposuction method - Suction assisted liposuction (SAL) or Power assisted liposuction (PAL) and decantation time.

Material & Methods

The prospective study included 20 women (matched by age and BMI) who underwent abdominoplasty with abdominal skin flap removal in the Nordclinic, Lithuania in 2021/2022. Liposuction method, LV, decantation time were measured. A total of 206 (10 ml each) fat tubes were collected. First group included removed abdominal tissue flaps, which underwent SAL (n=10), second group – PAL (n=10). Adipocytes were isolated from lipoaspirate. Enzymatic isolation and centrifugation methods were used. Then adipocytes were sampled from the central part of the adipocyte layer. The cells were stained with Hoechst nucleus-selective dye. Alamar Blue Assay was used to assess LV. Absorbance was measured with spectrophotometer (Tecan Sunrise, Switzerland). Data analysis was performed using SPSS 29.0 software package. A significance level of 0.05 was chosen to test statistical hypotheses.

Results

The median age was 37 years in both groups. At least 4 samples from each tissue flap were collected. SAL group mean (SD) viability was 0.09 (0.01) OD, PAL group mean (SD) viability was 0.09 (0.01) OD (p>0.05). The median of BMI in both groups was 29 kg/m2. Mean decantation time (SD) in SAL group was 85.5 (20.6) min, in PAL group was 98.7 (36) min (p>0.05). Statistically significant correlation was not found between LV and decantation time.

Conclusion

LV did not differ between SAL and PAL groups. Decantation time did not differ between SAL and PAL groups. No relation was found between LV and decantation time in this study. Future studies are needed to evaluate other factors which could impact LV.

Effect of BMI on fat parameters during ultrasound-assisted liposuction

Kristupas Suslavičius
Lithuania

Introduction
Complications after fat grafting (FG) surgery are becoming increasingly common nowadays, with more than 5% of patients experiencing them. Unfortunately, their causes are still unclear. It is known that one of the most crucial factors for successful FG is the viability of the lipocytes (LV). It is also important that plastic surgeons recommend that patients gain weight before the procedure, in the belief that this will help prevent complications. In the last decade, only a few studies have investigated the influence of body mass index (BMI) on LV, oil mass (OM), and adipocyte mass (AM) and found no association therefore this study aims to investigate these parameters further.

Material & Methods
The prospective study involved 92 women who underwent abdominoplasty with abdominal skin flap removal and ultrasound-assisted liposuction, a new technology in the medical field. Inclusion criteria were age between 25 and 60, no co-morbidities or harmful habits. A total of 92 fat tubes were collected. In the laboratory, adipocytes were isolated from lipoaspirate. Enzymatic isolation and centrifugation methods were used and samples were separated into fractions. Alamar Blue Assay was used to assess LV. Absorbance was measured with a spectrophotometer. Using GraphPad Prism 9 software package means ($\pm$), median values (min-max) were used and the Spearman correlation test was performed.

Results
The median age was 38 (29-54) years. A total of LV 92 samples were tested (mean 69.86$\pm$11.75). The median BMI was 27.29 (25.15-33.32). The median of AM was 73.02% (63.76%-99.17%). A negative moderate statistically significant correlation was found between the BMI and LV ($r=-0.4305$ $p=0.0001$). A positive weak statistically significant correlation was found between AM, TFW and BMI ($r=0.2769$, $r=0.3263$; $p<0.05$). We found a very weak negative statistically significant correlation between BMI and OM ($r=-0.2769$ $p=0.0075$). There was no statistically significant correlation between BMI and age ($p>0.05$).

Conclusion
Higher BMI may be associated with lower LV after liposuction. A higher BMI has a lower OM count and a higher AM count, probably because only more viable lipocytes can survive in the presence of higher OM. Based on the data, we can assume that a higher BMI may increase the likelihood of having poor adiposity during FG.

SedAI - Exploring a methodology for determining sedation depth in elective gastroenterological examinations via artificial intelligence using raw clinical data.

Felix Ende
Germany

Introduction

For sedation during elective gastroenterological procedures, propofol is currently mostly used as a well-controlled sedative for total intravenous anesthesia (TIVA). It is administered by an additional assistant using the basic bolus principle via manually controlled infusion (MCI). For sedation to optimize the procedure for both patient and investigator, it should be in a range that ensures the patient's loss of consciousness but does not lead to side effects for the patient. Accordingly, the quality of sedation depends on the experience and subjective assessment of the assistant. The SedAI study of the EKFZ for Digital Health Dresden creates a clinically annotated, multimodal biosignal database of sedation in endoscopy from raw clinical data analyzed with CNNs (convolutional neural networks). SedAI enables objectification and optimization of sedation.

Material & Methods

The study is a single-arm, multicenter, prospective, observational diagnostic study with 1272 participants. Subjects undergoing elective endoscopy under sedation and anticipated endoscopy duration of at least 20 minutes are included. The Modified Observers Assessment of Alertness/Sedition (MOAA/S) score will be used for initial uniform assessment of sedation depth. This score allows the annotation of biosignal data (EEG, ECG, RR, SPO2, accelerometry). CNNs are used to derive the MOAA/S based on the raw data.

Results

Preliminary tests linking EEG parameters to MOAA/S score have already been performed with 171 patients at the University Hospital Halle.1132 changes of state of consciousness (SOC) were documented. 43 EEG parameters were calculated. The area under curve (AUC) ranged from 0.51 - 0.82 with complex and frequency optimized parameters achieving values in the upper range.

Conclusion

Based on the pretest data, it can be concluded that complex analyses of EEG data lead to improved predictive power of sedation depth. The obtained values are not sufficient for clinical application. It can be expected that the use of CNNs and investigation of further parameters will bring a significant advantage for sedation in endoscopy.

Neurology
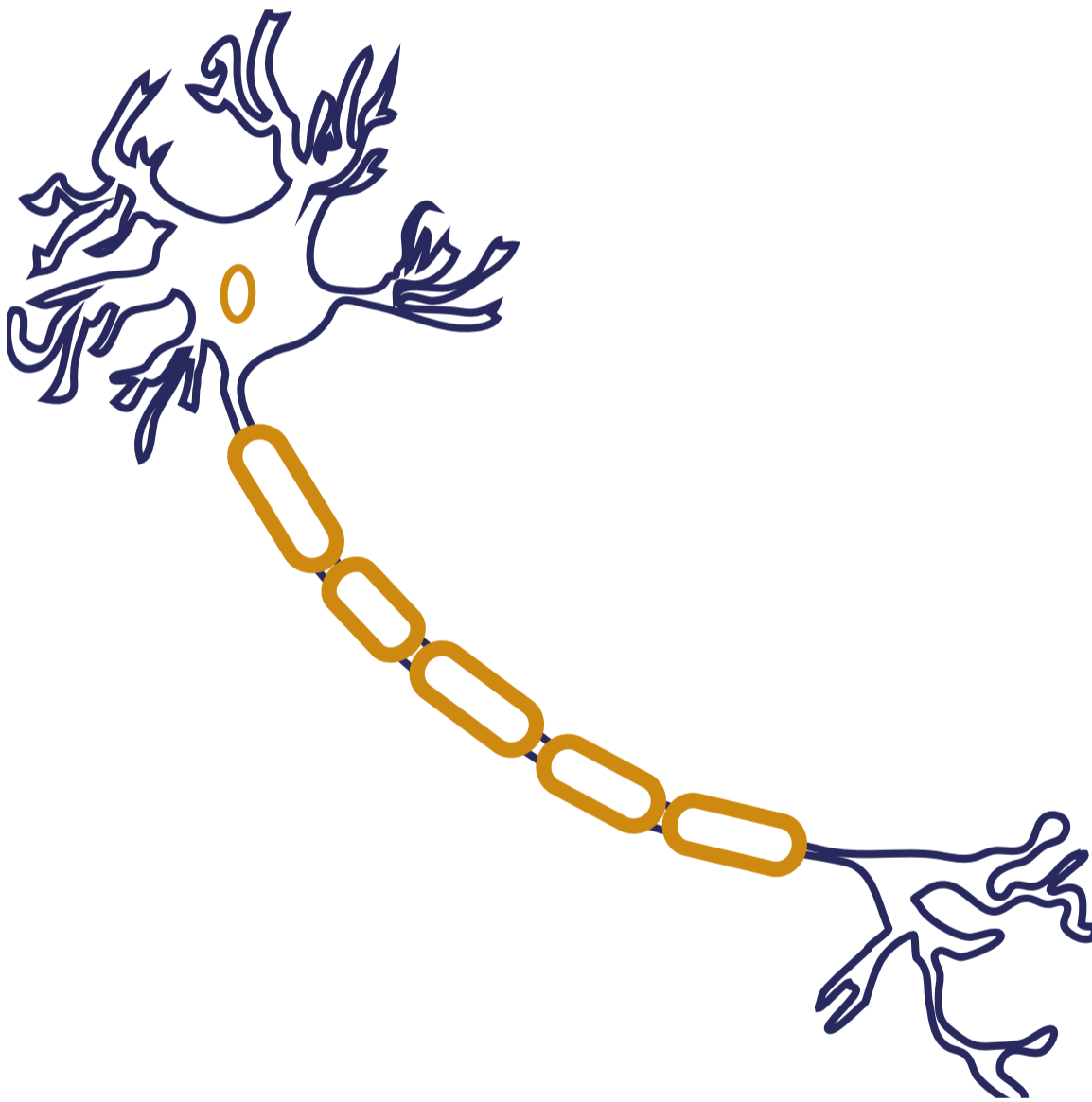
Presenters:
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Shirin Yaghoobpoor
Youssef Soliman
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Diagnostic Accuracy of Imaging Devices in Glaucoma

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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 Iba1 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.

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.

Oncology

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Differences in cognitive reserve index between examinees of different gender and age

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Introduction
Cognitive reserve is result of individual life experience, which is based on brain plasticity, respectively on increased dendritization and synaptogenesis, as the consequence of learning process. Higher values of cognitive reserve potentially indicated a greater neuroprotective protective influence. Estimate the validity of cognitive reserve index in the population of middle and old age examines and determine possible differences among male and female respondents, also between different age groups.

Material & Methods
: Our study included 124 participants aged 40-80 years. The validity of cognitive reserve index were assessed by the CRIq Nucci 2012. CRIq is a method for the quantitative measurement and comprehensive evaluation of the CR, that individuals have accumulated throughout their lifetimes. The questionnaire include 24 questions classified into 3 sections: CRI-Education, CRI-Working Actitivity, CRI-Leisure time.

Results
In examined population the average values of cognitive reserve index have been determined (109.9±18.1). Men had higher average values of the index, but the difference was not proved to be statistically significant (p>0.05). Statistically significant difference between the years of the work experience, use of motor vehicles, hobbies, housekeeping and gardening was observed between men and women (p<0.05). Statistically significant existence of age differences was established in some indicators (p>0.001). The group from 60-71 had the highest CRIq index score (115.6±16).

Conclusion
Whole study determined the moderate average of Congnitive reserve index. There are differences of cognitive reserve index in relation of gender which is higher in men, but not statistic important. There are significant statistic differences between genders for some indicator. The differences of cognitive reserve index in relation of gender were found.

Insulin-like growth factor 1 (IGF-1) and associated binding proteins in multiple sclerosis (MS): A systematic review and meta-analysis

Shirin Yaghoobpoor
Iran

Introduction
Multiple sclerosis (MS) is a chronic progressive autoimmune disorder of the central nervous system (CNS) which can cause inflammation, demyelination, and axon degeneration. Insulin-like growth factor-1 (IGF-1) is a single-chain polypeptide mainly synthesized in the liver and brain. IGF-1 causes the proliferation, survival and differentiation of neuronal and non-neuronal cells. therefore, it can be used in the treatment of neurodemyelinating diseases such as MS. The current systematic review and meta-analysis mainly aims to compare the levels of IGF-1 in MS patients and healthy controls and to investigate IGF binding proteins (IGF-BP) and growth hormone (GH) between MS patients and healthy controls.

Material & Methods
In this study, we systematically searched electronic databases such as google scholar, PubMed, Scopus, and web of science (WOS) up to November 2022. we searched the keywords of "insulin-like growth factor", "insulin-like growth factor binding protein", "growth hormone", and "multiple sclerosis". finally, we included studies that have these criteria: the observational studies with prospective, case-control or cross-sectional designs, studies that measured IGF-1, GH, IGFBP-1, IGFBP-2, and IGFBP-3, studies that reported mean values and standard deviations (SDs) of the growth factor in both patient and healthy control groups or stated required information for calculating these effect sizes. also, studies that did not have a control group and the studies which didn't assessed any of the IGF-1, GH, IGFBP-2, or IGFBP-3 and letters, comments, short communications, reviews, meta-analyses, ecological studies and animal studies were excluded.

Results
Finally, we included 11 eligible studies were conducted from 1998 to 2018. The sample size of included studies varied from 20 to 200 resulting in a total sample size of 1067 individuals, 531 MS patients and 536 healthy controls. the mean age of patients and controls was 38.96 and 39.38 respectively. The average EDSS among patients was 4.56. We found that Blood levels of IGF-1 (SMD= 0.20, 95% CI=-0.20 to 0.59, I2= 82.4 %, K= 8, n=692), CSF level of IGF-1 (SMD= 0.25, 95% CI=-0.06 to 0.56, I2= 0.0 %, K= 3 n=164) and Blood levels of GH were not significantly higher in the patient than controls (SMD= 0.08, 95% CI=-0.33 to0.49, I2= 77.0% K=3, n=421). also, The blood levels of IGFBP-1 (SMD= 0.70, 95% CI=0.01 to1.40, I2=77 %, K= 4, n=255), The blood levels of IGFBP-2 (SMD=0.43, 95% CI=-0.34 to 1.21, I2=64.2 %, K=3, n=78) and Blood levels of IGFBP-.3 were not significantly higher in the patients than controls too (SMD= 1.04, 95% CI=-0.09 to 2.17, I2= 95.6%, K=6, n=443).

Conclusion
Our study showed that there was no difference in serum levels of IGF-1, IGFBP-1 and IGFBP-2 between the MS group and healthy controls. But some studies show an increase in the serum level of IGFBP-3, and some studies show a decrease.

The Impact of RAS Inhibition on Parkinson's Disease Risk in Hypertensive Patients: A Meta-Analysis

IYoussef Soliman
Egypt

Introduction

The presence of the renin-angiotensin system (RAS) in the nigrostriatal system has been confirmed in many studies. Animal studies indicated that dopamine depletion was associated with increased NADPH-oxidase complex activity and increased expression of angiotensin I and angiotensin II receptors, which decreased when dopamine levels returned to normal. Multiple clinical studies have examined the role of RAS inhibition in delayed PD progression, but they have conflicting results. Our meta-analysis aims to find whether RAS inhibition is associated with a decreased risk of PD or not

Material & Methods

We searched Web of Science, Cochrane Central, PubMed, and Scopus for all relevant studies. Our primary outcome is PD risk measuring using hazard ratio (HR). We used a leave-one-out meta-analysis to test the robustness of our evidence. Analysis was done using Rstudio, using the meta package.

Results

Seven studies were included in our study. We found that RAS inhibition led to a statistically significant lower risk of PD development (HR 0.77, 95% CI [0.63, 0.95], $p = 0.012$). Analysis based on the type of RAS inhibitor used revealed that both angiotensin receptor antagonists (ARBs) (HR 0.70, 95% CI [0.54, 0.95], $p = 0.005$) and angiotensin-converting enzyme inhibitors (ACEIs) (HR 0.88, 95% CI [0.7, 1.00], $p = 0.05$) led to a statistically significant lower risk of PD.

Conclusion

Our study is the first meta-analysis to report that RAS inhibition might be associated with delayed PD progression. Therefore, we suggest that RAS inhibitors may be prescribed for hypertensive patients at high risk for PD as a regimen for their hypertension.

THE EFFICACY OF STEM CELL THERAPY IN PATIENTS WITH PARKINSON'S DISEASE; A SYSTEMATIC REVIEW AND MEAT-ANALYSIS

Moamen Mostafa Asla
Egypt

Introduction

Parkinson's disease (PD) is the second most prevalent chronic neurodegenerative disorder. A variety of treatment approaches are used; however, the disability persists as the disease advanced. In recent decades, attention has turned to treatment using stem cells (SCs) in many degenerative diseases, including PD. With their ability to regenerate and differentiate into other cells, they can restore the normal functions of damage tissues. We aimed to get a cumulative evidence about the efficacy and safety of SCs in PD patients.

Material & Methods

We searched Five electronic databases (PubMed, Web of science, Scopus, Ovid, Cochrane Library) for relevant articles through May, 2022. We pooled data using random effect model through OpenMeta-analyst software. We assessed the quality of the eligible articles using Methodological Index for Non-randomized studies (MINORS).

Results

A Total of 376 patients were included in 25 identified eligible articles. Most of these studies are non- controlled with a follow up duration more than 2 years. The most commonly used cells were mesenchymal stem cell, neural progenitor cells, human retinal pigment epithelium (hRPE) cells, and fetal mesencephalic cells. The effect estimated of SC therapy on UPRDS total and motor scores, showed significant improvement during "off" stage (M -17.72, 95% CI [-27.13, -8.3], $p = 0.01$, n= 102 pts), (M -8.56, 95% CI [-14.56, -2.56], $p = 0.01$, n= 108 pts) respectively. However, non-significant improvement in "on" stage in both total, and motor scores (M -8.65, 95% CI [-23,97, 6.38], $p = 0.26$, n= 74 pts), (M 1.57, 95% CI [-7.87, 11.01], $p = 0.74$, n= 46 pts) respectively.
UPRDS ADL showed non-significant findings in both "off and on" stage ($P > 0.05$). PETs showed a significant increase in Fluorodopa PET uptake in both putamen post-transplant ($P > 0.05$). No serious adverse effects were reported in the studies.

Conclusion

SCT showed improvement in patients with Parkinson's disease, both clinically and radiologically, with no serious side effects reported. We recommend conducting more controlled trials in a larger number of patients.

First seven days evaluation of serum matrix metaloproteinase 9 values in stroke patients

Sanja Toshevska
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Introduction

One of the essential characteristics of acuteischemic stroke (AIS), is the occurrence of the brain edema (BE). Matrix metalloproteinase-9 (MMP-9) belongs to the family of proteolytic enzymes connected with zinc, which in stroke, are involved in the degradation of the basal lamina and extracellular matrix components in the neurovascular unit, and increase the BE specially in first seven days of stroke. Purpose: To determine and evaluate MMP-9 values in serum in acute phase of AIS.

Material & Methods

The study was prospective and included 57 patients with AIS. Neurologic deficit of the patients was evaluated by the National Institute Health Stroke Scale (NIHSS). Serum MMP-9 level was determined by enzyme-linked immune sorbent assay (ELISA). Patients were evaluated in three phases: 1st, 3rdand 7th day since the AIS.

Results

The mean age of the patients was 64.5 ± 9.4. Within the follow-up period, there was significant rise of the NIHSS score in the first three days: 12.59 ± 4.8; 14.32 ± 4.89, and significant rise of serum MMP-9, with greatest values on the third day: 143.8 ± 37.2ng/ml (p=0.000). There was a positive, significant correlation (r=0.89, p=0.000) between the serum MMP-9 concentration and the NIHSS score.

Conclusion

The first three days of IS, serum MMP-9 values were rising as well as the neurologic deficit and the BE. Determination and evaluation of the MMP-9 in serum, is an easy, non-invasive, laboratory procedure for detecting and follow up of BE.

Efficacy and safety of stem cell transplantation for multiple sclerosis: a systematic review and meta-analysis of randomized controlled trials

Asmaa Nawar
Egypt

Introduction
Multiple sclerosis (MS) is a common autoimmune neurologic disease affecting patients' motor, sensory, and visual performance. The approved disease-modifying therapies aim at delaying the disease progression with considerable adverse events and limited efficacy for progressive MS subtypes. stem cell transplantation (SCT) shows remyelinating and immunomodulatory functions, making it a potential therapeutic option for MS. In this study, we aimed to investigate the clinical efficacy and safety of SCT in patients with MS.

Material & Methods
We searched for eligible randomized controlled trials (RCTs) in PubMed, Web of Science, Scopus, and Cochrane Library. Efficacy endpoints included the expanded disability status scale (EDSS), timed 25-foot walk (T25-FW), nine-hole peg test (9-HPT), paced auditory serial addition test (PASAT-3), and the change in MRI lesions volume and number. Safety endpoints included adverse events and mortality rates.

Results
We pooled the data of 8 RCTs in this meta-analysis, including 401 MS patients. SCT caused a statistically significant improvement of EDSS after 2, 6, and 12 months ($p=0.0005$, $p = 0.02$, and $p<0.00001$, respectively). Similar improvement after 6 months of treatment was noted in T25-FW in 290 patients (MD= -0.54, $p=0.01$). However nonsignificant effects were observed in 9-HPT and PASAT-3 scores ($p=0.24$ and $p=0.35$, respectively). Our subgroup analyses respecting the effect of stem cells doses and sources on EDSS also revealed nonsignificant results. Regarding the radiological measures, SCT improved the volume of MRI T2 lesions after 6 and 12 months ($p=0.001$, and $p=0.0003$, respectively). However, the effect on MRI T2 lesions number was nonsignificant ($p=0.99$). SCT caused no deaths during the follow-up period, and the only significant adverse event was local at the infusion site in 160 patients (RR= 2.88, 95% CI [1.14, 7.27], $p=0.03$).

Conclusion
SCT can improve the disability and walking ability of MS patients in addition to reducing brain lesions volume. The transplantation was safe and tolerated, with no mortality or significant serious adverse events.

Age Compromises Post-Traumatic Neural Stem Cell Proliferation in the Hippocampus

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Introduction

Traumatic brain injury (TBI) affects 2.5 million people in the United States each year. A wide range of neurological complications persists in TBI survivors, especially learning and memory loss due to cell death in the hippocampus. To date, there is no effective drug available that prevents cell death after a TBI. Fortunately, neural stem/progenitor cells (NSC) continuously proliferate and support neurogenesis in the hippocampus for a lifetime. Post-traumatic neurogenesis brings about a great promise of neural repair and is positively correlated to functional outcomes. However, it is observed that functional outcomes are inferior in elderly patients. We hypothesized that age compromises the brain repair of elderly patients by impairing post-traumatic neurogenesis, contributing to the inferior outcomes.

Material & Methods

To prove the hypothesis, we induced TBI by controlled cortical impact (CCI) model in mice, which mimics TBI in humans. By BrdU labeling in a nestin-enhanced green fluorescent protein (EGFP) transgenic mouse line, we evaluated NSC proliferation after TBI at different ages: 3-week-old, 2-month-old, 6-month-old, and 12-month-old mice were chosen to represent 2-year-old, 18-year-old, 30-year-old, and 45-year-old human, respectively. Cell quantification data were shown as average
± standard deviation and analyzed via One-way ANOVA followed by post hoc test using SPSS. Significance was set at $p < 0.05$.

Results

Our data showed that as age increases, the baseline of NSC proliferation gradually declined, resulting in a 95% drop of baseline in 12-month-old animals compared to 3-week-old cohorts. At each individual age group, TBI increases NSC proliferation compared to age matched sham cohorts. Up to 6-month-old in mice, NSCs were able to reach similar level of proliferation after TBI, which dramatically decreased at the age of 12-month-old.

Conclusion

Our results indicated that poor functional recovery of the aged population might result from an inadequate response of aged NSCs: as age increases, neural proliferation following TBI decreases. These results bring about the possibility that stimulation on aged NSC proliferation may serve as a therapeutic target to achieve better functional recovery in elderly TBI patients, particularly in regard to learning and memory.

Angiotensin II Receptor Blocker, Valsartan, Has Beneficial Effects on Lung Metastases Caused by Colorectal Cancer

Fereshteh Asgharzadeh
Iran

Introduction
Lung metastasis is the main cause of death in patients with colorectal carcinoma (CRC). Angiotensin II has been confirmed to facilitate cancer cell progression and metastasis. In this study, the possible anti-metastatic effects of an angiotensin II receptor type 1 (AT1R) antagonist, valsartan, have been investigated in an experimental CRC lung metastasis model.

Material & Methods
An animal CRC lung metastasis model was used, involving intravenous injection of CRC cells. The experimental groups included (1) control group; (2) 5-FU (5-fluorouracil) group (5 mg/kg/ every other day; ip); (3) valsartan group (40 mg/ kg/day; po); and (4) valsartan + 5-FU group (combination group; valsartan 40 mg/kg/day, oral gavage, and 5-FU 5 mg/kg/ every other day; ip). After 11 days, macroscopic and histological evaluations of lung tissues have been done for evaluation of lung metastatic nodules. In addition, inflammatory and angiogenic markers and oxidative stress index were measured in lung tissue.

Results
Our results showed that administration of valsartan especially in combination with 5-FU significantly reduced lung metastatic nodule and metastatic area ($p < 0.05$) in macroscopic and histological evaluations stained by hematoxylin–eosin. Measurement of inflammatory, angiogenic, and oxidative/antioxidative markers in lung tissue indicated that the level of IL-6, angiogenic markers (VEGF and VEGFR-1), and antioxidative markers significantly reduced in combination group ($p<0.05$) while the MDA as a marker of oxidative stress increased ($p < 0.05$).

Conclusion
These results suggest that valsartan in combination with standard chemotherapeutic agents can have a synergistic effect in treatment of lung metastasis of CRC.

Pathology

Presenters:
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Lenka Joksimovic
Mohammad Mobin Mirimoghaddam
Sama Soliman
Viallanta Tiulienieva
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OpenHRD - an open source platform for calculation of homologous recombination deficiency scores from OncoScan microarrays

Ariadna Lara Gutierrez
Austria

Introduction
Homologous recombination deficiency is an important biomarker for PARP inhibitor therapy in ovarian cancer. Existing open-source tools lack standardized parameters and require IT expertise. This project aims to establish a web-based bioinformatic analysis system for robust assessment of genomic instability.

Material & Methods
OncoScan-CNV data was obtained from DNA of formalin fixed embedded specimens. The analysis platform uses raw OncoScan microarray images and applies several open-source pipelines such as "Easy Copy Number", "Oncoscan_tools", "Allele-specific copy number analysis of tumors" for the segmentation analysis. HRD calculation was performed by combination of custom R-scripts and the "HRDscore" pipeline. All samples were concurrently analyzed by a commercial diagnostic HRD Test and the pipeline was optimized to reach similar GIS scores.

Results
The analysis comparison between several bioinformatics pipelines revealed that the combination of "Easy Copy Number" (EaCoN), and "Allele-specific copy number analysis of tumors" (ASCAT) provided similar results to the proprietary Chromosome Analysis Suite software (ChAS, Thermo Fisher) for raw data normalization and segmentation. The OpenHRD pipeline for homologous recombination deficiency (HRD) calculation is a compilation of EaCoN, ASCAT, our custom R-scripts and "HRDscore". It is served with Django Python and Celery Task Queue web frameworks. The application of the fully automated OpenHRD pipeline with standardized parameters on 20 samples fitted an R2 value of 0.82 with results obtained with the commercial Myriad MychoiceDX test in a training cohort of ovarian cancer. The model was further validated on a separate testing cohort of ovarian cancer samples with a R2 value of 0.69 .

Conclusion
Several studies have shown that HRD is a reliable marker for treatment decisions in PARPi therapy. In this study we provided a simple, standardized, web based system to analyze HRD, which is able to process the microarray scan raw image data and generate reliable HRD score values. Initial validation of the HRD platform has been performed in ovarian cancer, and extension to prostate and pancreatic cancer is ongoing. The OpenHRD platform is freely available upon registration at. https://dga.medunigraz.at/wp/?page_id=278.

Association between eGDR, waist circumference and interleukin 1 in patients with metabolic syndrome

Lenka Joksimovic
Serbia

Introduction

Metabolic syndrome (MS) is a complex metabolic disease that includes: visceral obesity, insulin resistance, reduced glucose tolerance, hypertension and dyslipidemia. The presence of these disorders significantly increases the risk of thrombosis in patients with MS. Often, in order to facilitate the monitoring of the patient's condition, various indicators derived from routine analyzes are developed. One such parameter is the estimated glucose disposal rate (eGDR), a parameter that tells about the dynamics of glucose transfer to peripheral tissues.

Material & Methods

64 patients with a diagnosis of MS (criteria from 2009) participated in the study. All patients were monitored and sampled within the Center for Endocrinology, Diabetes and Metabolic Diseases of the University Medical Center of Kragujevac. Waist circumference was measured by a routine procedure, while the concentration of IL-1 was determined by the ELIZA method from the patient's serum. eGDR (mg/kg/min) is calculated by the following formula: $21.158 - (0.09*WC) - (3.407*HT) - (0.551*HbA1c)$ [WC=waist circumference (cm), HT= hypertension (da= 1 /ne= 0) and hemoglobin A1c=HbA1c (%)]. According to data from the literature, we divided MS patients into two groups, the group with eGDR over 6 and under 6 mg/kg/min. The group with lower eGDR values consisted of patients with a worse metabolic status (24 patients). Using statistical methods, we examined the normality of the distribution, and then the correlation between the values of waist circumference and IL-1 and eGDR.

Results

In the group of patients with eGDR values below 6, the average eGDR value was 4.35 ± 0.89. Except in the cases of waist circumference (rs-.692; p=0.000), IL-1 (rs-.782; p=0.004), we did not find any correlation of other parameters with the level of eGDR.

Conclusion

In the group of patients with low eGDR, eGDR negatively correlates with waist circumference and IL-1 values, and further research is needed to define the exact relationships between these parameters.

HER2GAN: Overcome the scarcity of HER2 breast cancer dataset based on transfer learning and GAN model

Mohammad Mobin Mirimoghaddam
Iran

Introduction

Breast cancer is the most common and lethal cancer in women all around the world, two important parts of the management of breast cancer are targeted treatments and prognosis assignment. In both fields, human epidermal growth factor receptor 2 (HER2) positivity plays a crucial role. One of the primary issues in the IHC debate is the evaluation of breast cancer score in IHC slides while taking into consideration structural and morphological features and the scarcity of appropriate data. In order to address these issues, several recent studies have used machine learning and deep learning techniques. This paper introduces a new approach based on supervised deep learning to cover the problem.

Material & Methods

In this manuscript we made the following contributions: 1) We used a GAN model to generate high- quality HER2 images from histopathological images to make up for the scarcity of data in this field.
2) We experimented with different upstream transfer learning models and selected the best-performing ones. 3) We used the generated synthetic data to augment the dataset to be utilized in training the networks for improving patient decisions. 4) We reduced time consumption for HER2 score decision-making using deep learning networks. A GAN-based model is proposed for generating HER2 images with the greatest quality as well as identifying and classifying HER2 levels. The original and generated images have been evaluated using transfer learning methods. All of the models have been trained and tested using data that is publicly available and in private collections

Results

we achieved a high accuracy of 93% with the combined generated and original images used for training and testing.

Conclusion

This study advances the idea that using conditional generative adversarial networks as a data augmentation technique can be used to synthesize pathology images at unprecedented levels of realism, thus, giving hope that the chronic scarcity of labelled data in the pathology field can be resolved with the help of these generative models. The InceptionV3 and InceptionResNetV2 models demonstrated the outstanding quality of the details in the synthesized images.

Influence of Remote Ischemic Conditioning of a hind limb on capillary blood flow in Artificial Focal Brain Ischemia

Sama Soliman
Russia

Introduction
Ischemic stroke causes microcirculatory disorders leading to tissues damage . Remote conditioning is suggested to limit the effect of cerebral ischemia on the capillary blood flow. In our study we aim to assess changes in capillary blood flow and levels of Syndecan -1 in plasma in different ischemic periods using remote conditioning protocol

Material & Methods
artificial ischemic stroke was performed on Wistar Rats by occluding the middle cerebral artery using J.Koizumi technique for 30 minutes , followed by 48 hours of reperfusion. Remote Conditioning was performed after Artificial ischemic injury by clamping the right femoral artery 3 times for 10 minutes with 15 minutes apart Animals were divided into 4 groups : Intact group,Sham- operated group ,Animals with 30 minutes of MCA occlusion ,Animals with 30 minutes Of MCA occlusion together with remote conditioning Linear blood flow velocity was measured for all groups using Ultrasound Doppler (Minimax,St.Petersburg) .Syndecan -1 was measured in blood plasma using ELISA .

Results
Results were calculated using sign test , Whitney U test and Wilcoxon test . Differences were statistically significant at $P < 0.05$, $P < 0.01$. Linear blood flow velocity For animals group with 30 minutes of MCA occlusion didn't recover ($0,239\pm0,019$*, p<0.05) And was lower by 28% in comparison to sham - operated group ($0,336\pm0,018$) , While linear blood flow velocity of Sham-operated group in comparison with Animals with 30 minutes Of MCA occlusion together with remote conditioning ($0,302\pm0,017$) didn't differ statistically . ELISA for Syndecan-1 in blood plasma was 30 % (p <0.05) higher in animals with 30 minutes of MCA occlusion in comparison to sham- operated group (41.4* ± 1.3 ng/ml, and 31.9 ± 1.1 ng/ml respectively) And 112% (p <0,01), higher in Animals with 30 minutes of MCA occlusion together with remote conditioning. (67.8** $\pm 5,8$ ng/ml and 31.9 ± 1.1 ng/ml respectively).

Conclusion
Syndecan-1 is the molecule which lead to increase in capillary blood flow to the ischemic injuries. In 30 minutes of artificial ischemic stroke followed by remote conditioning within 48 hours after ischemia the expression of Syndecan -1 in Blood plasma has increased and the linear blood flow velocity in skin of ipsilateral hind limb was decreased

METHOD OF ASSESSMENT OF NEW VESSEL FORMATION IN THE UTERO-PLACENTAL AREA

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Ukraine

Introduction

During the entire period of pregnancy, two processes take place in the uteroplacental area (UPA) with varying intensity – angiogenesis and vasculogenesis. UPA biopsy material allows to use the immunohistochemical method for visualization of the endothelium of newly formed vessels. Willebrand factor (VWF) is a glycoprotein also as marker of young endotheliocytes. Vimentin (V) is the main protein of the cytoskeleton, which is expressed in endothelial and other mesenchymal cells.

Material & Methods

UPA and myometrium biopsies were obtained using the original method developed by us. The material was fixed in a 10% buffered neutral formalin solution for 24 hours, followed by ethanol dehydration and paraffin embedding. On serial histological sections with a thickness of 5 µm, immunohistochemical studies were performed with primary antibodies against Willebrand factor and vimentin with thermal antigen exposure and a streptavidin-biotin antibody visualization system LSAB2 according to the standard protocol of DakoCytomation (USA). The value of the optical density of immunohistochemical staining for VWF and V was measured on digital copies by computer microdensitometry. For each indicator, statistical calculations were performed in computer program PAST 4.05 (O.Hammer, 2021).

Results

On average, endothelial cells of arteries were more intensively stained with Willebrand factor, endothelial cells of vessels of the venous type and microcirculatory one were stained less intensively. Immunohistochemically staining for vimentin was detected in the endothelium of arteries, veins, capillaries, leiomyocytes and fibroblasts of UPA. Neovascular processes in the UPA were represented by VWF and V positive islets in the amount of 4-8 in 1 mm2 of the UPA section in the projection of the central part of the placenta and 9-18 in 1 mm2 of the UPA section in the projection of the peripheral part - 0.428±0.0014 of immunohistochemical staining for VWF and 0.310±0.0018 of immunohistochemical staining for V.

Conclusion

Immunohistochemical techniques for Willebrand factor and vimentin on biopsy material of UPA and myometrium methodologically allow to evaluate the processes of angiogenesis, vasculogenesis and endothelial dysfunction differentiated in the projection of different parts of the placenta. This method of identifying the endotheliocytes of the vessels of the UPA can be used to diagnose various types of pregnancy pathology, primarily the uteroplacental form of placental insufficiency

Periodontal microbes affecting the endothelial transcriptome in patients with Alzheimer's disease

Kamelija Horvatović
Croatia

Introduction

Among various familiar etiopathology of Alzheimer's disease (AD), periodontitis is one of the most recent factors suspected to be affecting the onset of this disorder. This in silico study is testing whether the transcriptomic changes in endothelial cells (EC) induced by common periodontal pathogens such as Fusobacterium nucleatum (FN) or Porphyromonas gingivalis (PG) match changes detected in the EC of AD patients.

Material & Methods

RNA-seq datasets GSE222136 and GSE125050 were acquired from the NCBI GEO database. Differentially expressed genes (DEGs) between different pathologies (FN, PG or AD) and untreated or healthy controls were identified following the DESeq2 pipeline, while the weighted gene co-expression network analysis (WGCNA) pipeline was used to identify highly correlated gene modules. Functional enrichment analysis was performed on DEGs and modules of interest.

Results

In total 15 gene modules were identified of which six modules with 89 key genes were significantly correlated with PG treatment, and four modules with 352 key genes with FN treatment, with most notable change being interferon signaling. 553 and 834 DEGs were identified in PG- and FN- treated ECs, respectively, while 1384 were significantly altered in ECs of AD patients. After comparing all the results, MIRHG1, SLC24A40, and ABHD13 were detected as shared significantly upregulated DEGs in all three pathologies indicating altered RNA interference mechanisms, affected ion channels, and cell adhesion.

Conclusion

This integrated study identified several potential gene candidates of underlying microbe-driven pathological changes in EC physiology that might be key players in AD onset and/or progression.

Longitudinal Quantification of Sub-Regional Hippocampal Amyloid-Beta Burden in Ex-Vivo slices from the AppNL-G-F Mouse Model of Alzheimer's Disease

Yuqing Chen
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Introduction

Amyloid-beta (Aβ) pathology is suggested to precede the onset of clinical Alzheimer's disease symptoms by up to two decades. The humanised AppNL-G-F knock-in model of amyloidopathy has accelerated pathogenesis and can be used to study AD progression. Here we used it to quantify the temporal and spatial characteristics of Aβ plaque accumulation as they first appear in the hippocampus, and as pathology continues to develop.

Material & Methods

AppNL-G-F knock-in mice and wild-type mice at 1, 3, 6, and 9 months of age were transcardially perfused with PBS followed by 4% paraformaldehyde (PFA), followed by preparation of coronal slices for immunohistochemistry analysis. Samples were stained with anti-Aβ antibody (6E10) together with a neuronal marker, NeuN, and DAPI. Images were taken of sub-hippocampal regions (CA1, CA3, DG), in left/right hemispheres, and ventral/dorsal segments using a confocal microscope (Leica SP8). Summation of intensity across Z-stacks in Fiji was used to quantify Aβ plaques in regions of interest.

Results

We found age to be a statistically significant factor on determining area density, with hippocampal deposition observed by 3 months. Bin analysis showed a near-exponential reduction in plaque number with increasing plaque size, increasing with age. Regionally, there was an increase in plaque density in CA3, with non-linear regression analysis indicating area density for CA3 is most strongly correlated with age. Within the CA1 region, the densest plaque formation was in the pyramidal cell layer. Further analysis at the aged 9-month time point suggested a differential pathology across the axial plane and greater left-hemispheric lateralisation.

Conclusion

This data provides further evidence for the protracted timeline to which AppNL-G-F knock-in mice recapitulate key AD neuropathologies including insoluble amyloidosis beginning before 3 months in the hippocampus. It also indicates potentially novel differential sub-regional Aβ accumulation patterns, axial variations, and hemispheric asymmetries, offering mechanistic insights for plaque localisation and differential susceptibility to Aβ. This could aid advancement of Aβ-targeting therapies.

Pharmacology
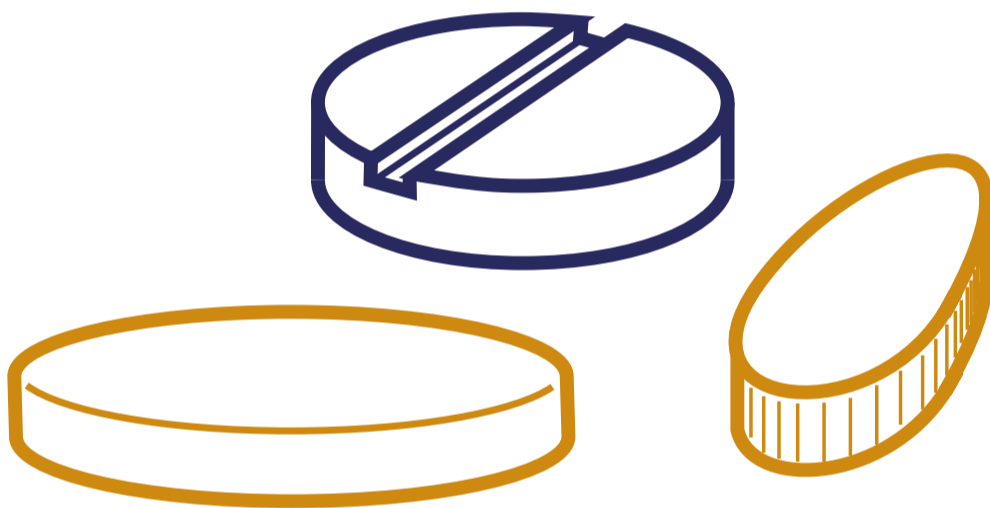
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Predicting milk/plasma ratio (M/P) of chemicals in human breast milk with their structural characteristics

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Iran

Introduction

Feeding infants with safe milk from the beginning of their life is an important issue. Consuming permeable drugs during breastfeeding period by mother, could lead to serious side effects to infant. To obtain milk to plasma (M/P) concentration ratio, analytical methods such as high performance liquid chromatography (HPLC) have been used. However, many factors including laboratory condition and lactation time affect the M/P ratio. The aim of this study is to develop mechanistic models to predict the M/P ratio of drugs during breastfeeding period based on their structural descriptors.

Material & Methods

Two hundred and nine different chemicals with their M/P ratio were used in this study. They were categorized into two groups based on Malone classification: 1: Drugs with M/P>1, considered as high risk 2: Drugs with M/P>1, considered as low risk Thirty eight chemical descriptors were calculated by ACD/labs and Data warrior software to assess the penetration of drugs during breastfeeding period. Later on, four specific models based on the number of hydrogen bond acceptors, polar surface area, total surface area and number of acidic oxygens were established for predicting. The mentioned descriptors can predict the penetration with an acceptable accuracy. For the remaining compounds of each model, logistic regression with SPSS 21 was done to give us a mechanistic model. Only structural descriptors with p-value<0.1 remained in the final model.

Results

Four different models were obtained to predict the penetration of drugs into human milk. Lipophilicity and ionization indexes such as number of hydrogen bonds and polar functional groups play vital roles in predicting the penetration of drugs during lactation period. Moreover, multiple validation methods such as test train and cross validations were used to confirm the potency of each model. The overall accuracy for the best model was 80%.

Conclusion

About 3-4% of milk consists of lipids, and the amount of lipid after parturition increases. Lipid soluble drugs diffuse alongside with fats from plasma to mammary glands. Compounds with higher ability to form hydrogen bonds and higher polar surface area are less permeable to milk because they are almost insoluble in the amount of fats of milk.

Anti-tumor effect of memantine, an N-methyl- D-aspartate receptor antagonist, against DMH-induced colon cancer in rats

Kosar Jannesar
Iran

Introduction
Glutamate levels are significantly higher in colon cancer cells than in normal cells. Increased expression of N-methyl-D-aspartate (NMDA) receptors has been observed in tumor cell lines that cause angiogenesis. Vascular endothelial growth factor (VEGF) promotes proliferation and endothelial migration through the calcium influx. As a result, NMDA receptors may be a therapeutic target of cancer, and inhibition of these receptors may reduce tumor growth. In this study, the effects of memantine, an NMDA receptor antagonist, on histology, tumor size, and number, as well as VEGF level in 1,2 dimethylhydrazine (DMH)-induced colon cancer in rats were investigated.

Material & Methods
Thirty male Wistar rats were divided into three groups: the control group, the colon cancer group (30 mg/kg of DMH solution was injected subcutaneously twice a week for 24 weeks), and the memantine group (20 mg/kg).

Results
The results showed that the injection of DMH induced colon polyps ($P<0.001$) in the colon cancer group, but memantine 20 mg/kg showed protective effects and reduced the number and size of colon polyps ($P<0.001$). The level of VEGF also increased significantly ($P<0.05$) in the colon cancer group compared to the control group. Treatment with memantine 20 mg/kg/day reduced VEGF level significantly ($P<0.01$) in comparison to that of the colon cancer group

Conclusion
The present in vivo study, for the first time, showed the anti-cancer effects of memantine in colon cancer, which can be attributed partially to a reduction in VEGF level.

Perceived barriers and facilitators for the implementation of a model-informed pregnancy formulary

Mirèse Kleuskens
The Netherlands

Introduction
In the absence of evidence-based dose recommendations taking into account the physiological changes that occur during pregnancy, pregnant women are at risk of overdosing and underdosing. Project Model Adjusted Doses for all Mothers (MADAM) uses physiologically-based pharmacokinetic (PBPK) modelling as a new source of evidence for generating dose recommendations for inclusion in a model-informed pregnancy formulary (MIPF). A better understanding of stakeholders' needs and perspectives in this regard can support a greater use of the formulary. Therefore this study aimed to explore the perceived barriers and facilitators for the implementation of a MIPF in the Netherlands through a stakeholder analysis.

Material & Methods
Online focus groups and individual interviews were conducted to gain insights into the perspectives of two groups of stakeholders in the Netherlands with regards to the barriers and facilitators for implementing a MIPF in clinical care: prescribing and non-prescribing healthcare practitioners (HCPs) providing pharmacological care to pregnant women on the one hand, and currently or recently pregnant women on the other hand. A hybrid thematic analysis was used to identify perceived barriers and facilitators according to both groups of stakeholders.

Results
Thirty-one HCPs and 11 pregnant women participated in nine focus groups and six individual interviews. Barriers and facilitators were categorized into four domains and 16 categories. The majority of HCPs and pregnant women found a MIPF to be a relevant innovation. Pregnant women indicated information on physiological changes that were built into the models and on foetal exposure as facilitators and lack of information on foetal safety as a barrier. Dose recommendations per trimester, evaluation of the model-informed doses by a clinical board and a mobile application were facilitators according to HCPs. They indicated the complexity and novelty of PBPK modelling, a lack of clinical validation of the model predictions and intra-individual variations in dose exposure and effect as important gaps to address.

Conclusion
A MIPF was seen as a promising innovation by the stakeholders. Their perspectives will be further investigated through an international online survey. Combining these methods makes it possible to anticipate on the barriers and facilitators as part of the implementation process of an user-driven MIPF.

Effects of mexidol on sex hormones in the blood of female white rats against the background of chronic ethanol determination

Sabina Hasanzade
Azerbaijan

Introduction
Since the 1980s, the growth dynamics of alcoholic beverage consumption in most countries of the world have led to a substantial increase alcohol-related diseases. İn recent years, the consumption of alcoholic drinks has been observed more among women of reproductive age. We set ourselves the goal of conducting a study of the effect of mexidol, a modern representative of antioxidant drugs, on the changes in the reproductive hormonal balance of female white rats prescribed chronic alcohol drinking.

Material & Methods
Studies were carried out on 30 visually healthy female white rats, weighing 180 ± 20 g, kept under normal conditions in the vivarium. As a corrector, mexidol (Russian Federation) 200 mg/kg intra- abdominal, and ethanol 12 ml/kg, 25% in a dose was prescribed. The animals of the control group were injected intraperitoneally with a physiological solution of 0.2 ml per 100 g of weight.

Results
The level of LH in the blood of research females against the background of chronic ethanol administration decreased by 38% ($p<0.001$) compared to the control group. Although the concentration of LH in the blood of animals receiving chronic ethanol was reduced by 17,7% ($p<0.001$) compared to the indicators of the control group, against the background of Mexidol at a dose of 200 mg/kg, it was 28% ($p<0.01$) more than the indicators of animals that received chronic ethanol separately. Although the concentration of total testosterone in the blood of animals receiving chronic mexidol+ethanol decreased by 13.1% ($p<0.001$) compared to the control group, it was 51.5% ($p<0.02$) more than the indicators of the animals that received chronic ethanol separately. The concentration of estradiol hormone was reduced by approximately 22% compared to the indicator of the control group ($p<0.001$). Due to mexidoo+ethanol effect, the level of estradiol hormone in the blood decreased by approximately 9.5% ($p<0.001$) compared to the control group, but it was 24.2% ($p<0.001$) higher than that of the animals that received chronic ethanol separately.

Conclusion
Mexidol at a dose of 200 mg-kg significantly restores the decrease in the amount of reproductive hormones caused by the chronic administration of 25% ethanol at a dose of 12 ml-kg.

Omega-3 fatty acid ameliorates aging- associated liver damage via modulation of senescence/Sirt-1 axis

Jana Sendy
Saudi arabia

Introduction
Aging is a biological process that is accompanied by decline in general cellular functions. Aging is associated with decline in liver functions as well as alteration in hepatic tissue structural features. To date, there is no effective treatment to help with aging-related liver disease. Omega-3 fatty acid has been shown to help with skin aging. The aim of this study is to investigate the anti-aging effect of omega-3 fatty acid on improving liver damage.

Material & Methods
For this purpose, naturally old rats (15 months old) were used in comparison with young rats (5-6 months old). For each group, rats were divided into two subgroups, one served as control and the other one was administered omega-3 fatty acid (270 EPA/kg + 180 DHA/kg) via oral gavage daily for 30 consecutive days.

Results
Liver function and damage status as evident by AST, ALT levels and hepatic structural pathological investigation were greatly improved in omega-3 old rats group compared with old rats control group. Moreover, oxidative stress status as evident by hepatic MDA, GSH and SOD levels was enhanced in omega-3 old rats group compared to old rats control group. Mechanistically, omega-3 supplementation has been shown to slow down biological effects of aging. As such, our results showed that omega-3 administered rats had lower expression levels of the senescent markers p16 and p21 compared to old rats control group. In addition, omega-3 supplementation significantly increased Sirt-1 levels and significantly reduced p53 levels in omega-3 treated old rats compared to old rats control group. Altogether,

Conclusion
our study suggests that omega-3 administration may ameliorate aging-induced liver damage by reducing aging-induced oxidative stress and modulating p16/p21/p53/Sirt-1 axis.

Rotenone as a oxidative stress model and the neuroprotective role of tramiprosate in cholinergic neurons: therapeutic strategy in alzheimer's disease.

Carolina Velez Quintero
colombia

Introduction

Alzheimer's disease (AD) is the most prevalent neurodegenerative disorder worldwide. Currently, there are no treatments to stop neurodegeneration and its molecular mechanisms are not fully understood. Studies in in vivo models found that rotenone (ROT) triggers multiple neuropathological mechanisms present in AD in in-vivo models such as oxidative stress and tauopathies, while the molecule tramiprosate, a taurine analogue with GABAergic activity, may intervene in pathways associated with its development. Therefore, our objective was to evaluate the effect of rotenone and tramiprosate on Tau phosphorylation, oxidative stress, activation of apoptotic pathways and response to acetylcholine in a cholinergic neuronal model (ChLN).

Material & Methods

We evaluated the effect of rotenone on the generation of pathological mechanisms present in AD in a transdifferentiated cholinergic neuronal model (ChLN) from umbilical cord Mesenchymal stem cells . We also analyzed the effect of single or combined tramiprosate therapies on these pathological mechanisms in ChLN with and without the cytotoxic drug rotenone by means of MTT assays, immunofluorescence and molecular docking.

Results

Exposure to ROT (50μM) for 6h decreased the ΔΨm, caused oxidative stress, hyperphosphorylation of Tau at its Ser202/Thr205 reciducts, activation of apoptotic pathways such as JNK and cholinergic dysfunction. Individual treatment with tramiprosate (50-250μM) for 96h, decreased the expression of the proapoptotic marker caspase3, and reduced the expression of the protein aggregation marker p-Tau.Ser202/Thr205 . combined treatment with Tramiprosate(50μM)+methylene blue (0.25μM) reduced H_2O_2 formation, and also increased the ΔψM in this neuronal model. ChLNs incubated with a combined therapy of tramiprosate+MB+curcumin (50 μM.0,25μM,1μM respectively) simultaneously with ROT (50μM) for 6h decreased Tau phosphorylation, partially restored caspase-3 expression, and restored the response to ACh in ChLNs. These results are ratified by ligand-protein studies between tramiprosate and the active sites of Tau,gsk3β,psen1,c-Jun,Caspase3, and PUMA.

Conclusion

It was concluded that ROT is a good chemical model of AD by replicating the activation of pathological pathways associated with its development in ChLN. and that tramiprosate, alone or in combination, shows promising results for the treatment of this pathology by binding to the active sites of proteins involved in pathological pathways related to neurodegeneration.

Public Health
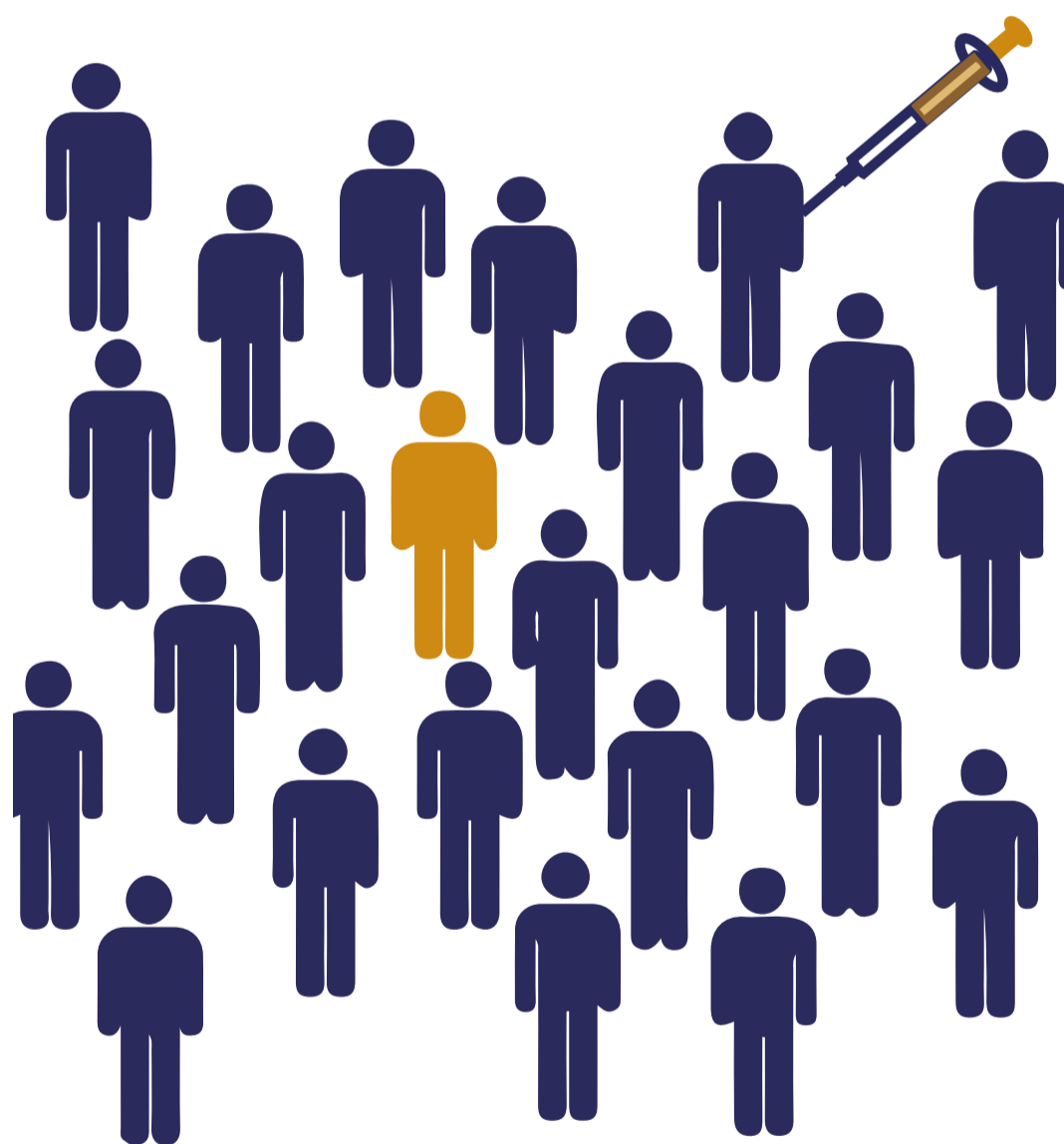
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Intern doctors' knowledge, attitudes, and practices towards artificial intelligence and the Internet of medical things used in the health field.

Ahmed alsoufi
Libya

Introduction

Artificial intelligence (AI) and the internet of medical things (IoMT) are modern technologies in medicine that are used to improve health care services and reduce human error. Our goal was to determine intern doctors' knowledge, attitudes, and practices concerning AI and IoMT and interacting with software principles relevant to medicine.

Material & Methods

In our cross-sectional study, we developed a self-administered questionnaire that included five sections: demographic characteristics, previous AI and IoMT related training and educational experience, self-assessment of their technical skills, and a subscale of knowledge, attitudes, and practices related to the interaction between medical devices, electronic medical record systems, IoMT and machine learning. The responses were rated on a Likert scale, and there were also questions could answered with "yes" or "no". Statistical analysis was performed using descriptive statistics, percentages, and correlation tests. The study focused on doctors at different stages of their internship in various training hospitals in Libya.

Results

The questionnaire was completed by 177 (76%) of 230 intern doctors (mean age 27 years ± 1.34). The majority of the participants were females (83%), 104 (58.8 %) of the total described their technical skills as intermediate, whereas only 6 (3.4%) described it as advanced. Among interns, 55 (31.1%) had received previous advanced technical education regarding computers and software outside of medical school but 72 (18%) received training related to technologies of (IoMT) inside of their medical school curriculum. Although 37.9% of intern doctors believed they were unable to interact with the advanced software of medical machines and modern technologies in hospitals, results showed that 53% of the interns got good knowledge regarding artificial intelligence use and their attitude showed statistically significant positive associations with knowledge (p value < 0.01) and with practice (p=0.01).

Conclusion

The findings show the lack of knowledge regarding basic technical information, which might create a gap in the technical skills that are needed from physicians of the future. Therefore, we highly recommend that medical education has to change to stay up to date with the faster advancement of technology in the medical field.

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.

Effect of proinflammatory cytokines on PAPP- A-specific IGFBP-4 proteolysis in human cardiomyocytes

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Russia

Introduction

Heart failure (HF) is the cardiovascular disease that results in impairment of heart blood function. HF is frequently accompanied by chronic inflammation and hypertrophic changes in myocardium. NT-IGFBP-4 and CT-IGFBP-4 fragments that are formed as a result of specific IGFBP-4 (insulin- like growth factor binding protein-4) proteolysis by PAPP-A (Pregnancy Associated Plasma Protein A), appeared to be prognostic markers of acute heart failure development. The mechanisms that lead to increased level of IGFBP-4 proteolysis in HF remain unknown. Recently in our laboratory it was shown that PAPP-A specific proteolysis of IGFBP-4 augments in hypertrophied cardiomyocytes. Thus, the aim of the study was to investigate the input of inflammatory reactions in magnification of PAPP-A specific proteolysis of IGFBP-4.

Material & Methods

Induced pluripotent stem cells derived cardiomyocytes (IPSC-CMs) cultures were differentiated according to the standard protocol. IPSC-CMs were stimulated by several concentrations of TNFD, IL-1D and IL-6. After stimulation p65 protein expression in IPSC-CMs was detected by immunoblotting with specific monoclonal antibodies. NT-IGFBP-4 concentration in conditioned medium of stimulated and control IPSC-CMs was measured using fluoroimmunoassay specific to neo-epitope formed under the proteolytic action of PAPP-A.

Results

The content of cardiomyocytes in IPSC-CMs was determined as 95% by immunocytochemistry. The level of p65 protein expression in stimulated IPSC-CMs increased 2-3 times compared to non-stimulated IPSC-CMs. The level of PAPP-A-specific IGFBP-4 proteolysis in IPSC-CMs stimulated both individually by TNFD, IL-1D and IL-6 and by their combination was 2-3 times increased compared to control cultures.

Conclusion

Thus, we have demonstrated that PAPP-A-specific degradation of IGFBP-4 in IPSC-CMs is increased when they are exposed to proinflammatory cytokines. Since chronic inflammation accompanies HF, it can be assumed that augmentation of the level of cardiospecific IGFBP-4 proteolysis under the action of PAPP-A in heart failure is associated with inflammatory processes occurring in the heart as well as its hypertrophic changes, as it was previously shown.

Investigating the credibility of HbA1c levels as a screening tool for Diabetes Mellitus in Transfusion Dependent Thalassemia Major patients.

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Introduction
HbA1c is considered to be the gold standard biochemical indicator to track glycaemic control in DM. However HbA1c estimation may be impeded by conditions which alter red cell half-life such as haemolysis, haemorrhage, red cell transfusion and presence of minor Hb species like HbA2 and HbF. Thalassemia is an inherited blood disorder that involves inadequate production of one or more globin chain of haemoglobin resulting in destruction of large number of RBC leading to brief exposure time to glucose. The estimation of HbA1c levels is based on RBC lifespan of 120 days, diminished RBC survival tends to alter its levels. In transfusion dependent thalassemia (TDT) patients, the circulating Hb is that of donors, therefore caution should be taken to carefully assess and interpret HbA1c values in these patients.

Material & Methods
In this Cross Sectional comparative study, we included 35 Transfusion dependent thalassemic patients (TDT) and 35 non-thalassemic healthy individuals matched for age ($\pm$ 1 year), gender and BMI ($\pm$ 1 kg/ m2). Fasting venous blood samples were obtained in EDTA vials on the day of the scheduled blood transfusion (pre transfusion samples) for FBS, HbA1c and CBC measurement . Similarly fasting blood samples were obtained from the control group. HbA1c was measured by high performance liquid chromatography technique (HPLC) technique. FBS values were classified according to the ADA criteria.

Results
HbA1c was statistically significantly higher in cases (6.937143% [$\pm$0.4976922 %]) than in controls (5.300000% [$\pm$0.3514675%]) (P<0.001). 85.7% TDT patients had HbA1c in the diabetic range (> 6.4%). None of the controls were diabetic . No significant difference was found in FBS levels between cases (92.97 [$\pm$9.141] mg/dL) and controls (89.20 [$\pm$7.584] mg/dL) (P=0.065). Significant differences are found in BMI, RBC COUNT, Hb ,PCV,MCV and MCHC between cases and controls (P<0.001).

Conclusion
The raised HbA1c levels in most of the TDT patients raises concern. The use of HbA1c as a screening tool for DM is inappropriate in TM. The levels could be falsely elevated, as we found out in our study. It is advised to use alternative index such as fructosamine levels, glycated albumin or continuous glucose monitoring.

Impact of Nicotine Variations in Electronic Cigarettes Exposure on Plasma Glutathione Peroxidase Levels in Rats

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Introduction

Electronic cigarettes (e-cigarette) are products that deliver a nicotine-containing aerosol to users by heating a solution. In recent years, most people assume that the use of e-cigarette is claimed to be a safer alternative compared to tobacco cigarettes even though it contains various harmful chemicals which are also found in cigarettes. However, to the best of our knowledge, exposure e- cigarette on plasma glutathione peroxidase (GPx) has not been yet carried out. Based on these reports, this study was designed to investigate the impact of e-cigarette exposure on GPx level changes in rats.

Material & Methods

In this study, 28 (8 to 12-week-old) male Wistar rats were randomly divided into 4 groups, Rats were treated for 8 weeks as follows: N group (n=7) was maintained as control without intervention; V0 group (n=7) was exposed by 0 mg/mL nicotine; V6 group (n=7) was given exposure with 6 mg/mL nicotine; V12 group (n=7) was exposed by 12 mg/mL nicotine. V0, V6, and V12 groups received 25 cycles of e-cigarette exposure (a cycle consists of 5 seconds puff duration, 30 seconds interval duration, and 30 seconds exhaust duration. GPx was assessed by spectrophotometer and expressed in U/mg units. The data were analyzed using One-Way ANOVA with LSD post-hoc.

Results

The plasma GPx levels were lower significantly in V12, V6, V0 groups compared to the normal (N) group ($p < 0.05$).

Conclusion

The present study shows that e-cigarette exposure decreases the concentration of GPx levels plasma in rats

Nanoparticles as a Viable Method for Increasing the Sensitivity of ELISA in the Detection of IgG Class Antibodies

Davit Marjanidze
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Introduction

Our study aimed to improve the detection limit of the enzyme linked immunosorbent assay (ELISA) method for determining immunoglobulin G (IgG) class antibodies against the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) nucleocapsid protein. ELISA is a widely used biochemical analytical method for detecting a target substance through an antigen-antibody reaction. Biomarkers in biological samples are frequently close to or below the ELISA detection limit. Thus, increasing the sensitivity of enzyme-linked immunosorbent assay is of great importance for medical practice. Our study intended to assess the possible application of nanoparticles for this purpose. We proposed that the use of citrate-capped silver nanoparticles (cc-AgNPs) would be a viable method for improving the detection efficiency of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) using conventional ELISA.

Material & Methods

We used 80 blood samples, collected previously by our research group for SARS-CoV-2 analysis (research purpose). A standard ELISA SARS-CoV-2 IgG method was modified by the addition of 5 μl 50 nm citrate-capped silver nanoparticles to each well for colorimetric detection. Each sample was measured with standard and nanoparticle-enhanced ELISA. The results were calculated according to the manufacturer's formula and classified as positive, equivocal, or negative.

Results

Nanoparticle enhancement increased absorbance values in 66 cases (82.5%). 19 equivocal cases were corrected as positive, 3 equivocal cases as negative, and 1 negative case as equivocal. There were 26 equivocal cases with standard ELISA and 5 with nanoparticle-enhanced ELISA in total.

Conclusion

We expected that using silver nanoparticles would improve the signal over a standard ELISA run. In this study ELISA enhanced with silver nanoparticles was able to detect lower quantities of IgG and produce fewer equivocal cases. Our findings suggest that the enhancement of ELISA kits with nanoparticles can be a practical, affordable way to increase accuracy and detection limit.

An investigation of the expression of bioinformatically candidate miRNAs targeting PI3K pathway in TNBC

Razie Hadavi
Iran

Introduction

The triple-negative breast cancer (TNBC) is an extremely aggressive form of breast cancer that has a high mortality rate. There is evidence that miRNA can target the PI3K pathway, which is often activated in TNBC patients. A primary goal of this study was to use bioinformatics to predict miRNAs targeting the crucial genes of this pathway. In addition, it was to measure the expression of the miRNAs and their targets in TNBC.

Material & Methods

The miRNAs targeting PIK3CA and AKT1 genes were predicted using bioinformatics tools. There were 18 TNBC samples, normal adjacent tissues, and cell lines, including MDA-MB231, MCF-7, and MCF-10A, whose total RNA was extracted, cDNA synthesized, and the quantitative real-time polymerase chain reaction was performed. The analysis of the receiver operating characteristic (ROC) curve was done for the evaluation of the diagnostic value of predicted miRNAs in TNBC patients.

Results

As a result of our analysis, it was indicated that miR-576-5p, miR-501-3p, and miR-3143 are predicted to be miRNAs that target PIK3CA, AKT1, and both of these mRNAs, respectively. There has been significant down-regulation of these microRNAs in clinical samples as well as in cell lines while up-regulation of the target mRNAs was observed. As a result of ROC curve analysis, it was found that miRNAs had a sensitivity of 80%, and a specificity of 85%.

Conclusion

As a result of our research, we found that there is a reverse correlation between miRNAs and their target genes, and therefore there is a possibility for these miRNAs to be proposed as new targets for the treatment of TNBC.

Expression analysis of miRNAs Targeting mTOR and S6K1 Genes, including miR-96, miR-557, and miR-3182 in Triple-Negative Breast Cancer

Javad Razaviyan
Iran

Introduction

Triple-negative breast cancer (TNBC) is one of the most aggressive types of breast cancer with a high risk of recurrence and poor prognosis. In the development of TNBC, abnormal expressions of genes in the mTOR signaling pathway and miRNAs that target them play an essential role. The aim of the current study was to determine the expression of the mTOR and S6K1 genes, as well as their targeted miRNAs, in TNBC clinical samples and MDA-MB231, MCF-7, and MCF-10A cell lines.

Material & Methods

In this study, bioinformatics algorithms were used to predict miRNAs targeting the 3 -UTR of mTOR and S6K1 mRNAs. Using quantitative real-time PCR (RT-qPCR) method, we analyzed the expression of genes and miRNAs in the samples of MDA-MB-231, MCF-7, and MCF-10A as well as 20 clinical samples of TNBC. A receiver operating characteristic (ROC) curve analysis has been conducted in order to assess the potential diagnostic potential of candidate miRNAs as biomarkers.

Results

As a result of this study, miR-96 and miR-557 targeted mTOR and S6K1 mRNAs, respectively, while miR-3182 targeted both genes at the same time. It was observed that miRNAs were down-regulated in TNBC clinical samples and cell lines, but their target mRNAs up-regulated. There was a decline in the expression of these miRNAs according to the ROC curve analysis.

Conclusion

The present study suggests that miR-96, miR-557, and miR-3182 are effective inhibitors of mTOR and S6K1 genes which may be beneficial in the TNBC-targeted therapy.

Surgery
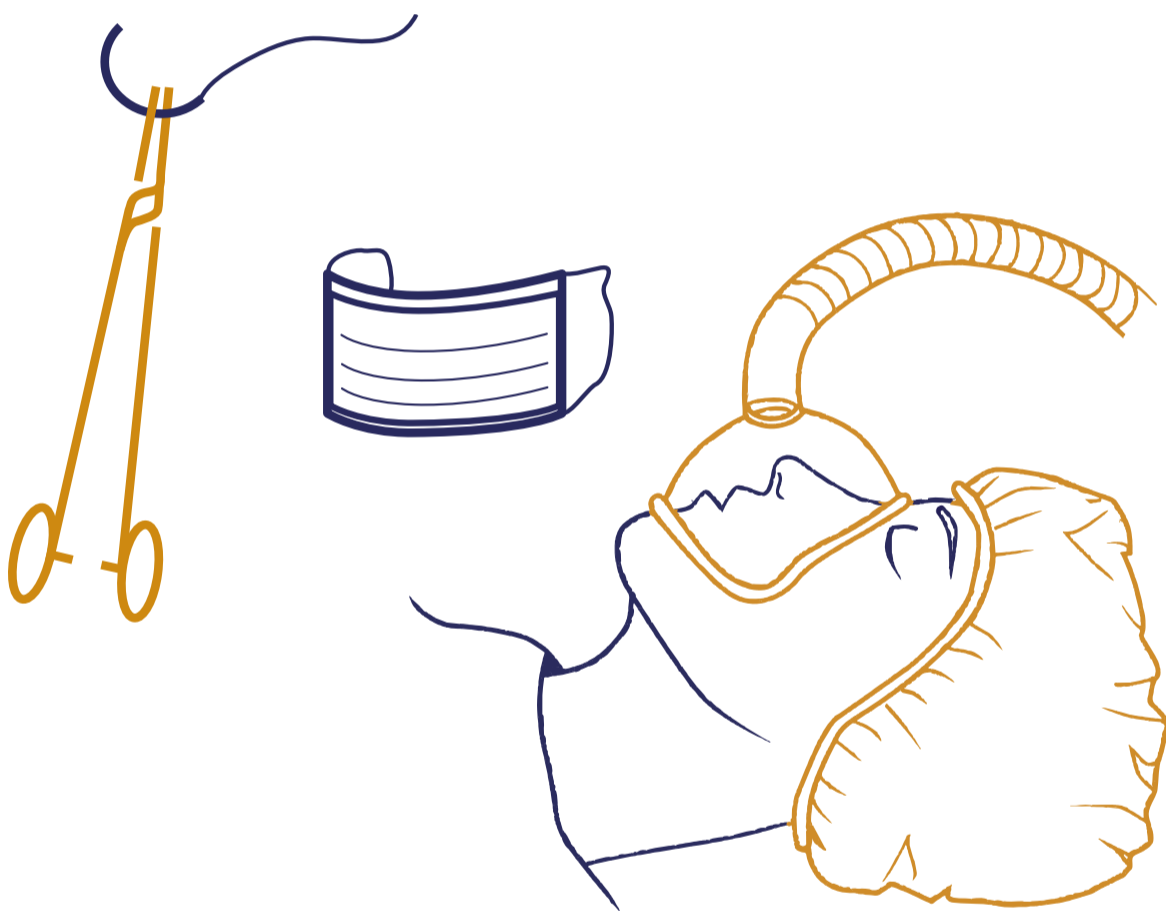
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In-silico and in-vitro identification of biotherapeutic peptides derived from bee venom and royalisin against breast cancer cells.

Sabrina Khor Xin Yi
Malaysia

Introduction
Cancer has become one of the leading causes of death in many countries around the world. Among the various types of cancer, female breast cancer is the most diagnosed cancer and the second cause of mortality among women. There is still a high number of cases reported over the years as there is a lack of selectivity of conventional cancer therapeutics targeting both normal and cancer cells and the rise of drug-resistant cancer cells. Peptide-based therapeutics is a promising and a novel approach in targeting and disrupting tumour cells with various advantages such as low molecular weight and toxicity.

Material & Methods
In this study, we aimed to design potential biotherapeutic anticancer peptides (ACPs) from bee venom (Melittin, Phospholipase A2, Tertiapin, Mast cell degranulating peptide and Apamin), and Royalisin from Apis mellifera. By utilizing advanced computational biology approaches, a set of 3 overlapping peptides spanning the entire sequence of different bee venoms was fragmentized. Each ACP contains 15-amino acid residues with one residue overlapping with the adjacent peptide. In-vitro anti-proliferative and haemolytic activities of ACPs were also determined.

Results
A total of 19 ACPs were successfully designed with a high anticancer properties prediction score and low toxicity and hemolytic activities. With this, 4 ACPs were selected for downstream analysis due to their inhibitory action targeting several anti-apoptotic proteins (Bcl-2, Bcl-xL and MCL1) in metastatic breast cancer cells. From in-vitro studies, both A_1 and R4I7I displayed strong anti-proliferative activity against MDA-MB-231 and T47D when comparing with the positive control, Cisplatin.

Conclusion
Newly designed peptides, A_1 and R4I7I, have successfully displayed anti-proliferative activity against metastatic breast cancer cells. Nevertheless, further investigations are needed to reveal the underlying mechanisms of anticancer actions.

Interferon-gamma may help to overcome TNF- related apoptosis-inducing ligand (TRAIL)- resistance in adenocarcinoma of mammary gland cells

Mateusz Gotowiec
Polska

Introduction

TNF-related apoptosis-inducing ligand (TRAIL) is a cytokine with potent anticancer activity mediated via death receptors, expressed nearly exclusively in tumorigenic tissues. However, many types of cancers are resistant to TRAIL-mediated apoptosis, due to low expression of death receptors (DR4, DR5). Interferon-gamma (IFN-γ) can be used to overcome the resistance, via activation of interferon regulator factor 1 (IRF-1) which causes overexpression of death receptors in target cells. Establishing whether combined TRAIL and IFN-γ treatment causes cancer cell apoptosis may help to formulate new therapy for chemotherapy-resistant mammary gland cancers.

Material & Methods

Rat adenocarcinoma of mammary gland cells (RBA, ATC1747) were seeded onto a 96-well plate with 10% FBS VLE Dulbecco's growth medium at cell concentrations of 15 000 cells per well. After 24 hours, TRAIL or/and IFN-γ were added to cells with a variety of concentrations ranging from 0,01 to 10 000ng/ml. Cells were incubated for 48 or 72 hours and afterwards, a tetrazolium compound and an electron coupling reagent (MTS+PES) were added. Absorbance at 490nm was measured using a microplate reader after 1-hour incubation and relative viability was determined.

Results

The viability of adenocarcinoma cells decreased significantly ($P<0.01$) when exposed to high concentrations of IFN-γ and further higher concentrations of TRAIL. The effective dose (ED50) for IFN-γ was equal to 40ng/ml and ED50 for TRAIL was equal to 250ng/ml. Combination treatment using lower concentrations of TRAIL and IFN-γ was more effective than both monotherapies.

Conclusion

The results show that TRAIL-resistance, common in many cancer types, can be overcome using IFN-γ. The mechanisms of such decreased resistance require further study. Cellular therapies based on delivering both cytokines into the tumour microenvironment may increase patient survival suffering from multi-drug resistant cancers.

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XAV939 effect in serum versus serum free media on human U87MG glioblastoma proliferation, viability formation in vitro 3D- model

Mohamed Rawash
United Kingdom

Introduction

Glioblastoma multiforme (GBM) is the most lethal grade IV brain tumour associated with the formation of spheroids and a median survival rate of 14 to 16 months. The gold standard treatment for GBM is surgical resection followed by the alkylating agent temozolomide (TMZ), however, it always shows recurrence and resistance due to the presence of cancer stem cells. XAV939 was reported to inhibit one of the key pathways in glioblastoma, Wnt/β-catenin, in small lung cancer and neuroblastoma. Additionally, 2D culture fails to mimic the tumour microenvironment, however, 3D culture was found to mimic the tumour extracellular matrix (ECM) key factors. In this study, we aim to examine the effect of XAV939 on in vitro GBM 3D model proliferation and survival.

Material & Methods

U87MG was cultured in 2D culture followed by 3D culture in alginate hydrogel beads for a two-time manner's experiments; 5 days and 12 day in serum vs serum-free media. XAV939 effect on cell proliferation was assessed by live/dead staining using fluorescent microscope, while cellular viability was examined by MTS assay. Also, spheroids formation was detected by colony forming assay and ImageJ analysis, before and after XAV939 administration.

Results

XAV939 in serum and serum-free media showed reduced cellular proliferation with a promising effect on cell viability at the concentration of 20uM. Also, it showed reduced spheroids' size compared to the control, and increased size compared to day 7 spheroids, before treatment, in serum and serum-free media. However, XAV939 concentrations of 20uM and 40uM inhibited spheroids formation, with significant effect on cell viability in serum and serum-free media.

Conclusion

In conclusion, XAV939 in serum and serum free media reduced the cell proliferation, viability and spheroids formation, however Serum free media was associated with increased cell death and increased cellular viability

GD2 as a Novel Target For CAR T Cell Therapy in Glioblastoma: A Systematic Review And Meta-Analysis in Preclinical Studies

Fandi Hendrawan
Indonesia

Introduction

Glioblastoma multiforme (GBM), the most common malignant tumor of the brain, is usually treated using the Stupp protocol. Unfortunately, median and 5-year survival rates after the standard multimodal therapy are still considered low due to immunosuppressive properties of GBM. GBM immunotherapy is broadly designed to minimize the immunosuppressive agents while increasing the number and activity of effector T cells. Disialoganglioside GD2 (GD2) is one of the most consistently expressed antigens in brain tumors among chimeric antigen receptors (CAR) T cells and it only exists in small amounts for healthy tissues. Moreover, GD2 that is in healthy tissues will not interfere with antibody binding to GD2 positive tumor cells making it a promising target in immunotherapy. GD2 CAR T cells, one of the immunotherapy for glioblastoma, ability to reduce the tumor size and increase the survival rate of the animal models are studied in this review.

Material & Methods

This systematic review and meta-analysis were conducted and reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement. PubMed and Scopus databases were used to identify abstracts using predefined search terms. Two independent reviewers reviewed the abstracts and were selected according to inclusion and exclusion criteria.

The ability of GD2 CAR T cells to reduce the tumor size was reported as the mean difference between treated and untreated animal models. The random effect size was calculated based on the obtained HRs and SEs to evaluate the survival rate of the mice. Standard chi-squared test and I2 statistics were applied to evaluate potential heterogeneity between the included studies.

Results

After excluding 620 articles, four articles were selected for analysis. GD2 CAR T cell therapy showed a significant reduction in tumor size (Mean difference = -0.17; 95% CI = -0.33, -0.01). GD2 CAR T cell therapy also significantly increases the survival probability (HR = 7.00; 95% CI = 2.39, 20.55).

Conclusion

Preclinically, GD2 CAR T cell has a potential benefit on the GBM case, reducing the GBM tumor size and prolonging the survival rate of the animal models. This showed the potential for the development of GD2 CAR T cell therapy GBM treatment.

Measuring altered tumour metabolism in metastatic melanoma with 18F-FDG PET: can this contribute to predicting immunotherapy response?

Wolter Veldman
The Netherlands

Introduction
Immune checkpoint inhibition (ICI) is the cornerstone of advanced melanoma treatment. However, not all patients respond and some experience immune-related toxicity. Biomarkers identifying patients most likely to respond are needed. Melanoma is characterised by high tumour glucose uptake, likely resulting in high lactate and low pH-levels in the tumour microenvironment due to high glycolysis rates. This altered tumour metabolism may negatively impact cytotoxic T-cell function, essential for ICI effectivity. Measuring tumour glucose uptake using whole-body 18F-FDG- PET scans, could help identify patients most likely to respond to ICIs.

Material & Methods
We obtained 18F-FDG-PET scans and clinicopathological data from a prospective patient set (POINTING, NCT04193956). ICI response was assessed by RECIST 1.1. At baseline, 18F-FDG PET parameters were obtained using semi-automated segmentation (Accurate). Peak standardised uptake value (SUVpeak) represents highest uptake in tumour lesions and total metabolic tumour volume (MTV) represents volume of metabolically active tumour tissue. Overall survival (OS) was defined as the time from starting ICI-treatment till death or last follow-up. Log-rank test was performed to determine optimal MTV cut-off value dividing patients into two groups with the most significantly deviating survival curves.

Results
47 newly diagnosed advanced melanoma patients were included. Median age was 59 years (range 30-81). All patients received ICIs: 32 patients (68%) nivolumab, 3 (6%) pembrolizumab, and 12 (26%) nivolumab/ipilimumab. Median follow-up was 15 months (range 3-45). 12 (25%) patients achieved complete response as best response, 14 (30%) achieved partial response, 6 (13%) stable disease and 15 (32%) showed progression. Tumour lesion SUVpeak varied greatly within and between patients (median 4.0, range: 0.8-28.2). Median total MTV was 31.3 mL (range 2.2– 1057.6). Total MTV of responding patients (CR, PR, SD) was lower than for progressive patients (Wilcoxon rank-sum p=0.002). Sensitivity analysis revealed total MTV cut-offs between 10.2 mL and 24.3 mL resulting in significant Log-rank test statistics for OS. The total MTV cut-off leading to the most significantly diverging OS curves was 15.8 mL. Patients with an MTV-value lower than this cut-off had better OS (log-rank p=0.07).

Conclusion
Patients responding to ICI had a lower total MTV. Low total MTV was associated with better patient survival.

INFLUENCE OF DENTAL INTERVENTION ON MICROCRYSTALIZATION OF ORAL LIQUID

Vladyslav Nedelchev
Ukraine

Introduction
Oral liquid quickly reacts to the influence of various factors on the human body in the form of a change in the physical and chemical composition of saliva, which leads to a decrease in resistance to caries. We aimed to evaluate the degree of microcrystallization in patients before and after dental treatment, depending on the type of intervention, taking into account concomitant factors.

Material & Methods
20 patients were examined. It was determined DMF-index, OHI-S, gingivitis index, and complex periodontal index. The oral liquid was taken twice – before and after a dental intervention. Microcrystallization of saliva was studied according to the method of P.A. Leus. During the study, the patient's age and gender, place of residence, concomitant (chronic/congenital) disease, and bad habits were determined.

Results
Among the examined persons - ultrasound cleaning (40%), and therapeutic treatment (60%). After treatment, we observe a change in the direction of more pronounced crystallization (II-I type). In men in (30%) cases, in women - (25%). These are mainly patients after ultrasonic teeth cleaning (%) (1 category) In contrast, changes towards a decrease in crystallization or its complete absence are present in (25%) men and (20%) women. (Category 2) Men followed this trend after therapeutic treatment (60%). An unsatisfactory state of oral hygiene was also observed in (more than 1.0). In women of this category, the opposite picture is observed - patients with the most respectable oral cavity were prone to the absence of microcrystallization. Part of the patients in this category are smokers (67%). The majority of category 1 patients spent less than an hour in the chair (64%), from 1 to 2 hours - (27%), and more than 2 hours (9%). Category 2 patients spent 1 hour or more in the chair (67%).

Conclusion
The obtained data make it possible to predict the course of regeneration of the oral cavity after therapeutic measures and prevent the development of secondary complications through preventive measures.

Evaluation of MMR proteins and HER2 expression in hepatobiliary cancers: Our experience from a tertiary care hospital in Maharashtra, India

Snehil Dhaka
India

Introduction

Biliary tract cancer is an uncommon cancer type with an overall poor prognosis and limited therapeutic options. Cancers of biliary tract include adenocarcinomas of gallbladder, ampulla of Vater, and cholangiocarcinomas. These malignancies are often diagnosed late due to their non specific symptoms and slow growth. Microsatellite instability (MSI) results from a build up in mutations at microsatellite sequences due to insufficiency of DNA mismatch repair (MMR) proteins, and is complimentary for immune modulating therapy. We aimed to retrospectively study the prevalence of DNA mismatch repair (MMR) function and Human Epidermal Growth Factor Receptor 2(HER2) by immunohistochemsitry(IHC) in cancers of biliary tract.

Material & Methods

This was a retrospective cross- sectional study carried out in the department of Pathology at a tertiary care hospital in Western Maharashtra, India. Archival formalin fixed paraffin embedded blocks of patients who were diagnosed to have hepatobiliary cancers from 01 Jan 2017 to 31 Dec 2019 were retrieved and stained for MMR proteins (MSH2, MSH6, MLH1 and PMS2) and HER2 by IHC. Slides were studied for retained nuclear signal in MMR proteins with normal cells and lymphocytes acting as internal controls. The current guidelines for MSI IHC screening and HER2 assessment in colonic and gastric cancers respectively were followed.

Results

Among a total of 26 archival .blocks studied, 8/26 patients (30.8%) had gallbladder carcinomas, 13/26 (50%) and 5/26 (19.2%) had intrahepatic and extrahepatic cholangiocarcinomas respectively. HER2 expression was score 0 in all 26 cases. Staining for MSI markers(MSH2, MSH6, MLH1 and PMS2) showed expression of all MMR proteins in 16/26(61.5%) cases. Deficient expression of at least one MMR protein was seen in 10/26(38.5%) cases. All of these 10 patients were more than 60 years of age, thus signifying more loss of MSI associated with increasing age. Deficient PMS2 expression was most frequent (7/26;26.9%), followed by MLH1 (4/26; 15.4%). MSH2 and MSH 6 were found expressed in all cases.

Conclusion

These findings support that HER2 testing may not be indicated in biliary tract cancers. Deficient MMR protein expression in 38.5% cases highlights the potential importance of immunotherapy in these patients. However, the findings in the present study need to be supported with larger studies including molecular methods.

Ophtalmology and Otorhinolaryngology
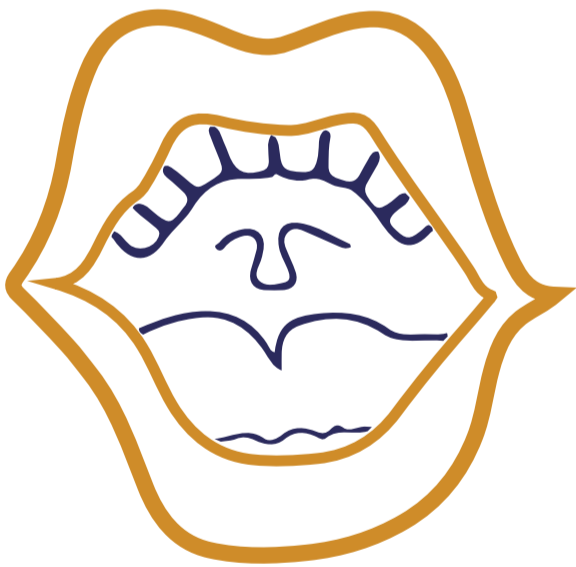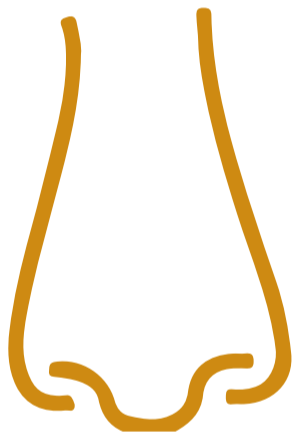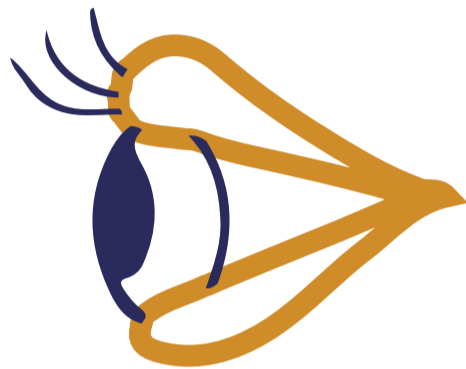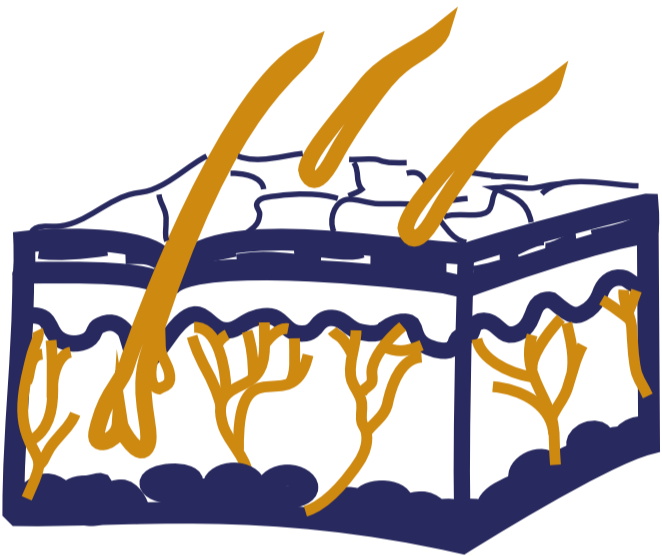
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Evaluation the relation between coronary artery calcium score in CT angiography and patients' lipid profile with possible coronary artery disease

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Iran

Introduction

Coronary heart disease is known as a life-threatening factor that makes a person susceptible to atherosclerosis and coronary heart disease. Therefore, identifying these risk factors is still a challenge.The diagnosis and identification of risk factors for coronary heart disease, including the role of impaired lipid profile, is considered in this study. The purpose of this study is to investigate the relationship between lipid profile and atherosclerosis of the coronary arteries as a risk factor and the importance of its control and treatment in Cardiovascular diseases.

Material & Methods

In this study, 120 patients with possible coronary artery disease without previous history who referred to the CT angiography center participated. For these patients, HbA1c and blood lipid profile tests, which include: triglyceride (TG),Total cholesterol, low density cholesterol (LDL) and high density cholesterol (HDL) were measured. Also, in the findings of their CT angiography , the amount of calcium in their coronary arteries was checked and measured, and the information was analyzed with statistical methods. We divided people into two groups based on the amount of calcium in their coronary arteries. And we divided people with calcium levels above zero.

Results

The level of triglyceride, total cholesterol, low-density cholesterol and hemoglobin A1C in group A is lower than group B, and the difference in triglyceride, total cholesterol and low-density cholesterol is significant ($P<0.05$).) and in hemoglobin A1C it is close to significance ($P=0.065$). On the other hand, the density with high cholesterol in group A is higher and close to significance ($P=0.055$).

Conclusion

We divided the data into two groups: the group that had zero calcium level in CT angiography and the group that had calcium level above zero. Based on the results of triglyceride level, total cholesterol and low-density cholesterol in the group with zero calcium level was lower than the other group, and high-density cholesterol in the group with zero calcium level was higher than the other group.

Circadian Rhythm Genes are associated with Survival in Ovarian Cancer

oncology 1

Andres Clarke
Ireland

Introduction

Circadian desynchrony has been shown to alter key cellular processes leading to cancer pathogenesis. Our aim was to perform an in-silico analysis to further investigate the apparent link between circadian rhythm(CR), overall(OS), and progression free(PFS) survival in ovarian cancer(OC).

Material & Methods

Kaplan-Meier (KM) Plotter was used to examine the expression of CR genes(n=17) on PFS and OS. TIMER/TIMER 2.0 databases were used to examine possible links between nine tumour resident immune cell types (B-cells, macrophages, cancer-associated fibroblasts(CAFs), T- regulatory cells, CD4+ T-cells, CD8+ T-cells, neutrophils, dendritic cells, and NK cells) and CR genes in context of OC.

Results

Low expression of PER2, CLOCK, NR1D1, SSTR2, NR2F2, and RAMP1 was associated with poor OS, and low expression of PER2 was also associated with shorter PFS. Conversely, high expression of BMAL1, RARB, and NR2C2 was associated with poor OS, and high expression of BMAL1, RARB, and OXTR was associated with shorter PFS. Of the immune cell types reviewed, CAFs significantly correlated($p \leq 0.05$) with 14/17 CR genes investigated. There was correlation seen in the other immune cells: macrophages(12/17), neutrophils(10/17), B-cells(9/17), dendritic cells(9/17), CD8+ T-cells(6/17), NK cells(6/17), CD4+ T-cells(5/17) and T-regulatory cells(4/17).

Expression of key oncogenes BRCA2 and ERBB2 correlated with($p \leq 0.05$) the majority of CR genes(15/17). Using CIBERSORT, Cox regression of age, CR genes, and M1-macrophages produced a hazard ratio(HR) less than one($p \leq 0.05$), while the same analysis using M2- macrophages produced a HR greater than one($p \leq 0.05$). In KM plots where four alternating combinations of high/low gene expression with high/low macrophage infiltration were compared, BMAL1 and CSNK1E exhibited opposing hazard ratios when comparing M1 and M2 macrophages.

Conclusion

This work further supports the hypothesis that CR genes may influence OC survival outcomes through associations with oncogenes such as BRCA2 and ERBB2. The influence of M1 and M2 macrophages on survival was contingent upon expression status of many CR genes. For the M1-subtype, high levels of macrophage infiltration yielded better survival solely in conjunction with low BMAL1 and CSNK1E expression. Conversely, the M2-subtype yielded poorer survival at high infiltration levels solely in conjunction with high BMAL1 and CSNK1E expression.

Utilization of HCM-AF Risk Score in forecasting occurrence of atrial fibrillation - 5- year observation

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Poland [4,5,6]

Introduction

Hypertrophic cardiomyopathy (HCM) is a genetic disease causing numerous life-threatening complications. Atrial fibrillation (AF) in HCM population constitutes an important step in progression of the disease. Recently developed American tool – HCM-AF Risk Calculator allows accurate prognosis of AF occurrence in HCM patients. Our aim was to assess clinical application of HCM-AF Risk Score in the prediction of 2 and 5-year clinical outcome of Polish patients with HCM.

Material & Methods

Retrospective cohort study included 92 consecutive patients with HCM (50% female, median age 53.5) and baseline sinus rhythm diagnosed at the 1st Chair and Clinic of Cardiology, Medical University of Silesia in Katowice in 2013-2018. Analysis involved clinical characteristics, laboratory tests, echocardiography, Holter monitoring, 2- and 5-year clinical outcome (total mortality, re-hospitalization, ICD implantation, heart failure) regarding the baseline HCM-AF Risk Score.

Results

According to HCM-Risk Score stratification 11 patients (11.9%) from analyzed cohort had low, 17 patients (18.5%) had intermediate, and 64 patients (69.1%) had high risk of AF. In patients from low-risk cohort mortality was 18.2% whereas AF incidence was 9.1% and 18.2% in 2- and 5-year follow-up respectively. However, in the intermediate-AF-risk cohort mortality was 11.8% and AF incidence was 17.7% and 25.5%. In high-risk group AF has been detected in 25 (43.9%) patients within 2-year-follow-up and 32 (56.1%) within 5 year-follow-up, total mortality was 43.9% and HF progression was significant.

Conclusion

HCM-AF Risk Score seems to be useful in both prediction of AF occurrence and clinical outcome in HCM patients. Polish HCM population is characterized by relatively high HCM-Risk Score coexisting with high AF occurrence thus AF screening should be obligatory in this group.

Investigating cost-related medication non- adherence in patients with coronary heart disease and possible factors related to it

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Iran

Introduction

Cardiovascular diseases, especially coronary heart disease (CHD), are the most important cause of human mortality. At the same time, these diseases are considered as one of the most preventable non-communicable diseases. Although there are many drugs available for treatment of these diseases, non-adherence to medication due to cost is an important obstacle to achieve favorable treatment outcomes in them.

Material & Methods

This study is a cross-sectional descriptive-analytical study in which CHD patients referred to the cardiology department of Masih Daneshwari Hospital who were under medical treatment with relevant drugs for at least 3 months were included in the study. An information collection form was completed for each disease. This form consists of 3 main sections: patients' socio-demographic characteristics, patients' medical and drug records, and the two-item cost-related medication non- adherence questionnaire the 2-item CRN scale (CRN-2). The data were entered into SPSS statistical software and the relationship of various factors with CRN was analyzed by using appropriate statistical tests. In all statistical tests, $p<0.05$ was considered as a significant level.

Results

200 patients suffering from CHD including 135 men and 65 Female with an average age of 60.88 ±15.33 entered the study. In response to the first and second questions of the CRN questionnaire, 115 patients (57.5%) and 60 patients (30%) confirmed the existence of cost-related non-adherence to medication respectively and in total, 133 patients (66.5%) had cost-related non-adherence to medication. In the final model of the regression analysis, the total daily drug consumption, income level and being a smoker had significant relationships for the occurrence of positive CRN (OR=0.9, p=0.006). CHD exists in many Iranian patients with cardiovascular disease. Health policies should be based on reducing drug costs and considering that as an important factor in drug compliance, so that the needs of medical services due to drug non-compliance can also be reduced. In these programs, patients with higher drug regiment costs, lower income and health literacy levels should be prioritized. Cost-related drug non-adherence exists in many Iranian patients with cardiovascular disease. Health policies should be based on reducing drug costs and considering drug cost as an important factor in drug compliance, so that the needs of medical services due to drug non- compliance can also be reduced.

Conclusion

CRN exists in many Iranian patients with cardiovascular disease. Health policies should be based on reducing drug costs and considering drug cost as an important factor in drug compliance, so that the needs of medical services due to drug non-compliance can also be reduced.

Blood Pressure Trajectories and Genetic Risk of Hypertension

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Introduction

Hypertension affects one in two US adults. Due to the strong heritability of hypertension, genetic variations may explain a large portion of the variation in blood pressure (BP). This study assessed the trajectory of BP traits based on the genetic risk of hypertension.

Material & Methods

Polygenic risk score (PRS) combines the risk contributed by common genetic variants into a single indicator. For this study, the PRS was generated using the continuous shrinkage method from the systolic BP genome-wide association study summary statistics derived from 417,001 individuals in the UK Biobank and applied to individuals genotyped under the TransOmics for Precision Medicine Program. Using the PRS, individuals were classified into low (<20th percentile), intermediate (20th- 80th percentile), and high (>80th percentile) PRS groups. Blood pressure values were corrected for antihypertensive use (systolic:+15mmHg, diastolic:+10mmHg). The Kruskal-Wallis test was used to compare BP traits across PRS categories stratified by age. Restricted cubic splines were used to depict the non-linear relationship of BP traits with age stratified by PRS categories.

Results

Among 25,251 participants (median age: 53.4 years; 55.9% women; 38.5% non-white population), the median systolic (131 vs.116 mmHg) and diastolic BP (78 vs. 71 mmHg) were higher in the high PRS group compared with the low PRS group (p:<0.001). On stratifying by age, higher systolic and diastolic BP values in the high PRS compared with the low PRS group across the age range were noted (Table). The systolic BP was consistently and incrementally higher with higher genetic risk for hypertension across the age range (likelihood ratio test $\chi 2$: 108 for systolic BP; $\chi 2$: 61 for diastolic BP; p:<0.001) (Figure).

Conclusion

The trajectory of BP traits varied with the genetic risk of hypertension. Clinical implementation of PRS may allow identification and promote primordial prevention strategies in individuals at a higher risk of developing hypertension.

Relationship between compacted versus noncompacted myocardial layers and conduction disturbances among patients at Pauls Stradins Clinical University Hospital

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Latvia

Introduction
Given that noncompaction cardiomyopathy has recently been established as a diagnosis and is not classified as a cardiomyopathy according to the WHO, it is not fully understood how common this condition is in the population and how many of the patients suffering have accompanying conduction disturbances. The aim of this study was to determine the incidence of noncompaction cardiomyopathy among patients at Pauls Stradins Clinical University Hospital and to assess the accompanying rhythm abnormalities in ECGs where such patient data was available.

Material & Methods
Retrospective single-center study included adult patients who had cardiac MRI performed at Pauls Stradins Clinical University Hospital in the timespan from January 1, 2021, to October 1, 2022. In order to assess the compacted and noncompacted layers of the myocardium, syngo.CT Cardiac Function software was used. Mathematical data processing was performed using descriptive statistics.

Results
Out of 811 cardiac MRIs that were performed in the respective period of time, noncompaction cardiomyopathy was detected in 5,5% (n=45) of the cases. 49% of the patients (n=22) were women and 51% (n=23) were men. In 71% (n=32) of the cases, ECGs were available for assessment. It was concluded that the highest compacted versus noncompacted myocardial layer ratio in patients with atrial fibrillation was in segment 12; in patients with left bundle branch block in segment 17; among patients with non-specific ST-T changes – in segments 7 and 13; in patients with SA blockade – in segment 16; in patients with ventricular extrasystoles – in segment 6.

Conclusion
More than half of the patients presented with abnormal ECG findings, indicating that there is a relationship between conduction disturbances and the presence of a prominent noncompacted myocardial layer in the left ventricle. It was concluded that most of the conduction disturbances presented in patients who had the highest noncompacted versus compacted myocardial layer ratio in segments 6, 12, and 13.

Miscelleanous I

M I
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Presenters:
Niki Pouyanfar
Samuel Olawale
Michael Winkelbauer
Tarun Kumar Suvvari
Zsófia Ruppert

Synthesis and characterization of MIL-100(Fe) for methotrexate delivery in rheumatoid arthritis

Niki Pouyanfar
Iran

Introduction

Methotrexate, as the drug of choice in treatment of rheumatoid arthritis (RA), is the reason for different adverse effects and the presence of the drug in areas of the body that are not involved in the disease, may worsen the side effects. To address this issue, novel drug delivery systems are utilized to ensure targeted delivery and minimal side effects. Metal-organic frameworks (MOFs) are one of the nanocarriers used for this purpose. These carriers have high porosity and capacity for drug loading. A kind of MOF that due to being acid-responsive, can be used in the acidic environment of the joints in RA, is MIL-100(Fe) and the goal of this research is synthesis, characterization, and in vitro evaluation of this nanoparticle, in RA drug delivery. Coating the MOF can also assist in targeted delivery of the disease.

Material & Methods

Trimesic acid and $FeCl_3.6H_2O$ were used alongside methotrexate for MOF preparation. Chitosan, EDC, and hyaluronic acid were also applied for MOF coating. Drug loading and release of the nanoparticle were evaluated with, and without coating. Also, UV-Vis and FT-IR tests for methotrexate characterization, XRD, BET, FESEM, FT-IR, and zeta potential tests for MIL-100(Fe) characterization, and FT-IR and zeta potential tests for the coated MOF evaluation and as a means to show the success of the coating process.

Results

MOF synthesized via microwave-assisted route, was initially loaded with methotrexate, then coated with chitosan, and lastly, the chitosan coating was attached to hyaluronic acid via EDC. The needle-like MOF was approximately 275.371±39.799 nm in length, and 44.758±3.276 nm in width. The coating around the nanoparticle, prevented the burst-release of methotrexate. The drug delivery system was stable in water for 7 days. For the coated MOF, EE% and LC% were around 93% and 12.6%, respectively.

Conclusion

MIL-100(Fe) nanocarrier coated with hyaluronic acid and chitosan was found efficient for targeted delivery of methotrexate in rheumatoid arthritis. Animal studies, application of photodynamic therapy, and utilization of MRI is suggested for future works.

The impact of neck and low back pain on the level of disability and depression among healthcare students in Nigeria

Samuel Olawale
Nigeria

Introduction
Neck and back pain are global health challenges, and about half of the healthcare students, experienced these pains at one point in their training. The impact of these pains could lead reduction in physical activities and personal care and aside from that, it put a toll on their mental health. Therefore, we surveyed the prevalence of neck pain and low back pain, and their impact on the presence of depression and level of disability among healthcare students at the University of Ibadan.

Material & Methods
We conducted a cross-sectional web-based survey, using a structured self-administered questionnaire among 420 undergraduate Medical, Dental and Physiotherapy students at the University of Ibadan, Nigeria, who were sampled by proportionate stratified random sampling method. Data were analysed using STATA version 16.0 and Chi-squared test was used to test for association between variables. The level of significance was set at $p < 0.05$.

Results
Of the 420 participants recruited, 338 (80.5%) responded. Among the respondents, period prevalence (pain in the last 7 days), and point prevalence of neck pain are 32% (95%CI: 26.8-37.8), and 18.4% (95%CI: 14.2-23.4) respectively while that of back pain is 39.9% (95%CI: 34.3-45.8), and 22.7% (95%CI: 18.1-28.0) respectively. Factors that are significantly associated with neck and back pain are gender (p=0.01) and department (p=0.015) respectively. Assessing the impact of these pains among those who had pain in the last 7 days, 34.8% (p=0.002) of them with neck pain have depression and 88.8% and 10.1% (p=0.01) have minimal and moderate disability respectively while 30.6% (p=0.02) of respondents with back pain have depression, and 88.3% and 10.8% (p=0.001) have minimal and moderate disability respectively.

Conclusion
Although the prevalence of neck and low back pain is low in this study, about a third of the respondents suffer from depression and a majority have some form of disability. It is therefore imperative to screen and intervene early to protect the population of the future healthcare force

Skeletal muscle dECM for contractile skeletal muscle tissue engineering

Michael Winkelbauer
Switzerland

Introduction

Despite decades of research in engineering contractile muscle tissues, current state-of-the-art techniques allow limited cell encapsulation and lack of biomimetic growth environment for the cells. As a result, most engineered muscle constructs fail to exhibit macroscopic contractility. Here, we demonstrate the isolation of dECM from porcine muscle and modification for photo-crosslinkability. To fabricate contractile muscle tissues the proprietary Biofabrication process Filamented Light (FLight) is facilitated and the manufactured constructs were cultured in static tension conditions to derive contractile muscle tissues.

Material & Methods

Porcine skeletal muscle was chemically decellularized, histologically characterized and the residual dsDNA quantified. Subsequently, the protein content was qualitatively assessed using SDS-Page and quantitatively by mass spectrometry. The dECM was solubilized by pepsin digestion and functionalized with norbornene groups (dECM-NB) to enable photo click-chemistry. Photorheological characterization and compression testing were performed for different concentrations of dECM-NB and thiolated gelatine (Gel-SH) using lithium phenyl-2,4,6-trimethylbenzoylphosphinate (LAP) as photoinitiator. Cell-laden muscle constructs were fabricated using 8 s FLight projections at 85 mW/cm2 and cultivated for 28 days. On days 1, 7, and 28 gene expression was quantified and constructs were examined immunohistochemically. The construct contractility was assessed using ImageJ analysis of brightfield video recordings. Myosin heavy chain staining and multinucleation were assessed via Immunohistochemistry.

Results

Porcine dECM was successfully decellularized (residual dsDNA 2.5 ng/mg dECM) and solubilized by pepsin digestion. This yielded a thermally cross-linkable hydrogel at a concentration of 6 mg/mL. Functionalization of dECM with norbornene groups combined with Gel-SH (0.5% dECM-NB; 2.5% Gel-SH; 0.05% LAP) resulted in a photo-cross-linkable resin and enabled rapid biofabrication of constructs in <10 seconds. Young's modulus was tailorable in the range from 0.6 – 5 kPa. First trials of C2C12 myoblast incorporation showed localized twitching of muscle cells. As a next step, optimized formulations are being tested and compared to collagen- or pure gelatine-based hydrogels.

Conclusion

dECM-based photosensitive hydrogels have a significantly more complex protein composition than collagen or gelatin-based hydrogels. This inevitably contributes to the improved reconstruction of the tissue niche and provides a superior potential to regenerate muscles in vitro. However, the impact of this complexity on macroscopic contractility is subject of ongoing research.

Skeletal muscle dECM for contractile skeletal muscle tissue engineering

Tarun Kumar Suvvari
India

Introduction

Globally, diabetes mellitus is one of the major causes of increased morbidity. Diabetic nephropathy, retinopathy, and neuropathy are routinely screened among diabetic patients, whereas the cognitive decline associated with diabetes mellitus is not given much attention. Cognitive impairment can further develop into neurocognitive disorders. Along with raising diabetes prevelence, cognitive impairment would also increase. So, routine screening for cognitive decline should be done among diabetes mellitus patients. we aimed to find out the prevalence of the cognitive impairment and its associated risk factors among type -2 diabetes mellitus patients and to evaluate the association between HbA1c levels and cognitive impairment.

Material & Methods

An observational cross-sectional study was conducted at department of Medicine, tertiary care hospital for 2 months. Montreal Cognitive Assessment (MoCA) test that consists 30 questions was used to assess the cognitive function. Indepth history, Clinical which includes BMI, HbA1c levels, duration of diabetes, Blood sugar (fasting and postprandial) were also collected. Descriptive statistics was used, and the Chi-square test was used to determine the statistical significance. Pearson correlation coefficient was used to find out the relation between MoCA score and glycemic parameters.

Results

A total of 96 patients were included in the study. Mean HbA1c is 9.08 + 1.73 and Mean MoCA Score is 25.14 + 1.63. Mild Cognitive impairment (MCI) was noted in 56 % of patients. Attention was the most common cognitive domain defect found in all MCI patients - 100%. Delayed Recall and Memory was 2nd most cognitive domain defect found - 92.5%. Higher HbA1c, High FBS, Higher PPBS was found to be statistically associated with MCI (P<0.05). A negative correlation was found between HbA1c, FBS, and PPBS levels and MoCA scores.

Conclusion

More than half our study participants reported mild cognitive impairment. It highlights the need for implementation of routine cognitive testing for diabetes patients. There is a strong negative correlation between MoCA scores and parameters of glycemic control - higher levels of HbA1c, FBS, & PPBS is seen in people with less MoCA score indicating mild cognitive impairment. Further studies were need to evaluate whether improving the glucose levels helps in improving cognition or not.

Western-type diet aggravates chronic inflammation which may lead to brain damage in a mouse model of obesity

Zsófia Ruppert
Hungary

Introduction

Unhealthy diet may induce chronic, systemic inflammation, which has negative effects on many different organs. Therefore obesity is an important risk factor for several chronic diseases, not only diabetes or fatty liver, but also neurodegeneration. In this study, we aimed to compare the effects of a high-fat, high-fructose Western-type diet (WTD) and a simple high-fat diet (HFD) on inflammation and metabolic disturbances in different organs.

Material & Methods

3 months-old, male C57BL6/J mice were divided into 3 groups (n=15): a normal chow-fed, control group; a HFD-fed group; and a WTD group. Body weight was measured monthly, while the oral glucose tolerance test was performed after 5 months of diet. Pathological changes in the liver were investigated on hematoxylin-eosin-stained sections. Gene expression was studied by qPCR in visceral adipose tissue and brain samples. To explore neurogenesis, we used doublecortin immunostaining on brain sections. For statistical analysis, one-way ANOVA was performed; the level of statistical significance was set at $p < 0.05$.

Results

We found, that fructose substantially worsened the effects of HFD, as the levels of obesity, glucose intolerance and hepatic steatosis were significantly higher in the WTD group compared to not only the control group but also the HFD group. These changes were accompanied by a significant increase in the expression of pro-inflammatory genes in the visceral white adipose tissue, suggesting a higher level of systemic inflammation in response to WTD compared to HFD alone.

Indeed, a slight but statistically significant elevation in the expression of microglia and macrophage markers was also seen in the brains of the WTD-fed mice. Interestingly, in certain WTD-fed animals, we found a higher number of doublecortin immunopositive neurons. We suppose that WTD induced more severe brain damage in these animals, which may be compensated by the activation of the neurogenesis.

Conclusion

Our results show, that the WTD leads to more severe obesity and inflammation than the HFD alone, and negatively affects the function of several organs, including the brain. Our research may help to understand the harmful effects of our lifestyles, and promotes the development of therapies for obesity-related disorders. This work was supported by funding from NKFIH FK138390.

Poster Session II

Cardiology II
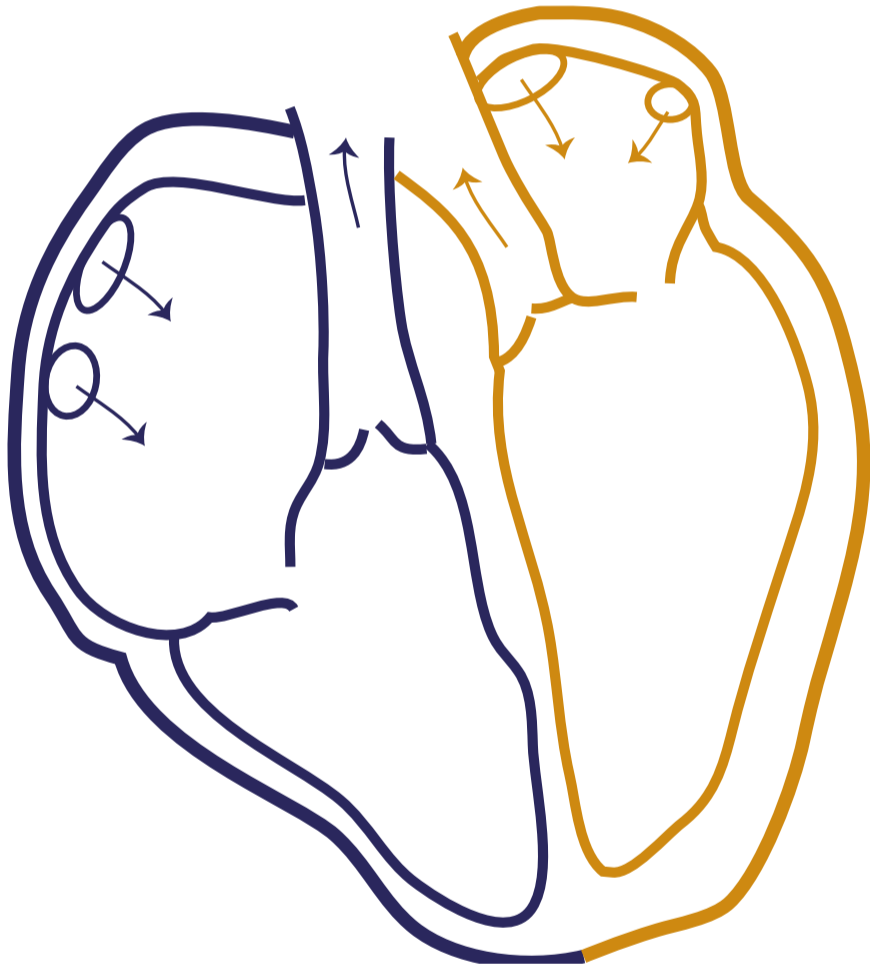
Presenters:
Katarina Obradović
Pegah Nekooeizadeh
Agata Suleja
Joske van der Zande
Yasaman Pourasadi
Krishin Yerabolu
Nikola Serge

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.

Sleep Disorders and Motor Neuron Diseases: correlations with disease progression, cognitive insights and quality of life.

Dario Bottignole
Italia

Introduction
The MNDs are a heterogeneous group of neurological conditions, defined by the progressive degeneration of motor neurons. Sleep disorders in MNDs patients may have a relevant impact on the disease progression and prognosis through different mechanisms, and their presence leads the necessity of a multi-disciplinary approach.

Material & Methods
Patients followed by the ALS Centre of the University Hospital of Parma underwent: 1) a home-based cardio-respiratory monitoring during sleep; 2) a neurological evaluation and a battery of selected sleep screening questionnaires; 3) a focused neuro-psychological assessment.

Results
Six patients were affected by a sleep disorder. The bulbar-onset phenotype presented a higher risk of sleep-related breathing disorders and day-time sleepiness. SVC decay rates showed to be directly correlated with the risk of nocturnal hypopnoic/apnoeic events, impaired cognitive performances were related to higher risk of developing sleep apnoeas. Sleep impairments were associated to worse results in mental health items of SF-36.

Conclusion
Our study proved how sleep disorders were associated to a worse clinical status and negatively affected patients' mental and emotional health, thus worsening their prognosis.

Covid-19 breakthrough infection characteristics; a case-control study during delta wave of covid-19 pandemic

alireza abbasi
Iran

Introduction
Although global Covid-19 immunization helped mitigate the SARS-coV2 pandemic, the incidence of covid-19 breakthrough infections is growing quickly. These infections tend to have milder symptoms and a better prognosis. As a novel phenomenon, clinical presentations must be evaluated to prevent misdiagnosis.

Material & Methods
in this nested case-control study, 291 vaccinated patients and 580 non-vaccinated patients were enrolled. The frequency of covid-19 infection signs and symptoms and some other clinical parameters were compared between these two groups.

Results
length of hospital stay (3.86 ± 1.24 vs 10.64 ± 2.37, $p< 0.001$), rate of ICU admissions (1% vs 44.82%, $P=0.004$), and mortality rate (0% vs 5.68%, $p< 0.001$) were significantly lower in the vaccinated group. The frequency of fatigue (25.42% vs 55.68%, $p< 0.001$) and dizziness (36.08% vs 41.55%, $p=0.004$), and underlying cardiovascular (14.43% vs 34.65%, $p=0.01$) disease was significantly higher in the unvaccinated group, while myalgia (73.88% vs 46.20%, $p=0.02$) and paresthesia (23.36% vs 17.58%, $p=0.01$) were significantly higher in patients with breakthrough infection. In binary logistic regression analysis, length of stay (coefficient=2.24, $p=0.016$), myalgia (coefficient=0.989, $p=0.019$), nausea and vomiting (coefficient=2.97, $p< 0.001$), and mortality rate (coefficient=27.25, $p=0.001$) were differentiating variables between the vaccinated and non- vaccinated groups.

Conclusion
Patients with covid-19 breakthrough infection had a better outcome, with shorter hospital stays, fewer ICU hospitalizations, and reduced death. While vaccination has reduced covid-19 symptoms such fatigue and dizziness, myalgia and paresthesia have been increased.

INFLUENCE OF THE COVID-19 PANDEMIC ON HEART RATE DISORDERS IN PATIENTS WITH PERMANENT ELECTRICAL CARDIAC DEVICES

Katarina Obradović
Serbia

Introduction
SARS-CoV-2 is an RNA virus that penetrates the cell and leads to a multiple organ dysfunction including the cardiovascular system to a significant extent. The aim of the study was to determine the influence of the COVID-19 pandemic on the frequency and the kind of heart rate disorders in patients with an cardiac implantable electronic device (CIED) as well as the significance and impact of SARS-CoV-2 positivity test rates and the resulting comorbidities.

Material & Methods
A total of 998 patients of both genders were included in the study, monitored between March 2018 and December 2021. The data (indications for implanting a CIED, comorbidities, cardiac rhythm disorders, the percentage of atrioventricular pacing) were taken from the Health Information System of the Institute for Cardiovascular Diseases of Vojvodina. SARS-CoV-2 presence was confirmed through valid tests results via the National Portal of the Ministry of Health of the Republic of Serbia.

Results
There is a statistically significant difference in the frequency of cardiac rhythm disorders in the total number of patients and COVID-19 positive patients during the pandemic (67.2%, 88.9%), with a tendency of an increase, compared to the number before (45.5%, 44%). The number of VES/NSVT was significantly higher in the course of the pandemic in comparison to the number before (238, 35), as well as the number of VT/VF (276, 146). A higher percentage of patients with comorbidities had cardiac rhythm disorders during the pandemic, but statistically significant associations were found in patients with COPD (p=0.028) and the history of CVI (p=0.037).

Conclusion
Cardiac rhythm disorders, in this patients, are statistically significantly more frequent in the era of the COVID-19 pandemic, compared to their occurrence before the pandemic, especially in patients positive on COVID-19 test. The frequency of ventricular rhythm disorders was significantly higher during the pandemic in comparison to the period before it. The presence of comorbidities, especially COPD and previous CVI has significantly contributed to the increase in the frequency of cardiac rhythm disorders. The frequent need for higher AVP was observed in confirmed SARS- CoV-2 positive patients.

Efficacy and Safety of Approved medicine for adult Spinal Muscular Atrophy: A Systematic Review and Meta-Analysis

Moamen Mostafa Asla
Egypt

Introduction

Recently, several approaches have emerged to treat patients with spinal muscular atrophy (SMA), most notably increasing SMN protein levels through antisense oligonucleotide (AS) or pre-mRNA splicing modifier. Nusinersen and risdiplam were approved by the US food and drug administration (FDA) for adult SMA patients. However, clinical evidence for its efficacy in adults is still inconclusive. We conducted this meta-analysis to establish the clinical efficacy and safety of them on the adult patients.

Material & Methods

Through February 2022, a literature search was conducted using the Web of Science Library, Scopus, PubMed, Wiley, and Cochrane. The search was then updated in December 2022. Our primary outcome measures were the drugs' effects on the patients' motor functions. Data were pooled for analysis using OpenMeta Analyst software for Windows. we used the Methodological Index for Non-Randomized Studies scale (MINORS) to assess the quality of each study.

Results

: 29 studies met the eligibility criteria, including 25 studies related to nusinersen and only 4 studies related to risdiplam. After 6 months of follow-up, nusinersen showed a statistically significant improvement of the HFMSE (M 1.49, 95% CI [0.99, 2.00], $p = 0.001$, n = 371 pts) and the 6MWT (M 12.47, 95% CI [7.03, 17.92], $p = 0.01$, n= 160 pts). However, its effect on the RULM was not statistically significant (M 1.49, 95% CI [-0.03, 3.01], $p = 0.06$, n= 328 pts). Similar results were present after 14 months of follow-up. Regarding risdiplam, the findings of RULM showed a significant improvement during a year of follow-up (M 1.5, 95% CI [0.53, 2.47], $p = 0.01$, n = 32 pts). Frequent adverse events included headache, back pain, nausea, infections, and vomiting, which were more likely related to the disease progression or the lumbar puncture procedure as in nusinersen treatment rather than the drugs themselves. No significant serious adverse effects were reported for either.

Conclusion

Nusinersen can improve motor and respiratory functions in adult patients with SMA, and its effects become more pronounced with extended follow-up periods. Risdiplam has shown promising results, but more clinical trials on adults with more sample size are needed. Both of nusinersen and risdiplam are generally tolerated and have an acceptable safety profile.

Au nanoclusters loaded with GLP-1 agonist as a potential treatment for Parkinson's Disease

Elly Robles
Mexico

Introduction

The second most prevalent neurodegenerative disease globally is Parkinson's disease (PD). Since current PD medications are solely used to treat symptoms, patients will eventually experience cumulative impairment and neuronal death. The glucagon-like peptides GLP-1 are a class of molecules that have successfully treated type 2 diabetes mellitus. In contrast with PD drugs, this type of molecules target the relief cellular respiration processes by glucose regulation and increased insulin production. Due to their similarity with diabetes' molecular interactions, and association with motor and cognitive impairment, GLP-1 agonists' therapeutic effects have started to be studied in Parkinson's Disease. Additionally, in previous studies gold nanoclusters have shown to provide neuroprotective effects and inhibit alpha-syn aggregation in mice models. In this work, to evaluate the combined effect of these therapeutic agents SH-SY5Y cells were treated with Au nanoclusters loaded with GLP-1 agonist exendin-4 on a PD cell model.

Material & Methods

Four groups were treated for 72 hours: control group, 6-OHDA, exendin-4-loaded nanoclusters, and 6-OHDA with the nanosystem. DAPI staining, Neurite length measurements, and LDH assays were performed on the cell groups. XRD, TEM, and FTIR microscopy were used for nanoparticle characterization.

Results

When analyzed with TEM and XRD techniques, the gold nanoparticles displayed a 1-3 nm size. The nanosystem exendin-nanoparticle reversed the oxidative damage in a PD SH-SY5Y cell model. Following light microscopic analyses, the stained cells with DAPI the group treated with 6- OHDA and treated with the nanosystem showed similar cell cell viability when compared to the control group. Furthermore, the treatment increased the neurite outgrowth by more than 80% compared to the 6-OHDA group.

Conclusion

We successfully synthesized a nanoparticle-drug system that significantly reversed oxidative stress and cell damage in the PD model. The use of GLP-1 agonists with nanotechnology have not been combined before in PD, we hope to open a new research perspective and that the combination of these technologies may enhance PD patients' therapeutic care leading to improved clinical outcomes.

Effect of Triiodothyronine on Remyelination Enhancement After Mesenchymal Stem Cell Intraperitoneal Injection in Cuprizone Model of Multiple Sclerosis

Yousef Terme
Iran

Introduction

Multiple sclerosis (MS) is one of the most important inflammatory diseases of the central nervous system, yet its etiology is not well defined. Cell therapy for MS has become one of the newest therapies, even in its clinical phase. We used thyroid hormone subcutaneously to enhance effects of the transplanted stem cells for remyelination in corpus callosum.

Material & Methods

First, human bone marrow mesenchymal stem cells (BM-MSCs) are cultured with α-MEM containing 10% FBS. Demyelination model was induced in mice for 6 weeks by administration of the cuprizone, and in the fourth and fifth week after the first dose of Cuprizone, the stem cells were administered intraperitoneally to the mice. From the fourth week to the end of the sixth week, the thyroid hormone was subcutaneously injected into the mouse. At the end of the sixth week, the rats were killed and subjected to tissue evaluations using the LFB staining technique for myelin pods also MBP and PDGF-α receptor immunohistochemistry. The expression of MBP, TR-β1, TR-β2 genes was investigated by realTime-PCR.

Results

In histology studies, demyelination has been induced by cuprizone, and this is clearly evident in the luxol fast blue staining and immunohistochemistry and molecular techniques. In the Luxol fast blue and Immunohistochemistry technique for MBP and PDGF-αR increased recovery in the combination group with the cell and the T3 hormone was seen compared to other groups. In the molecular studies, the combination group did significantly increase the expression of the MBP, TR- β1 and TR-β2 genes. However, TR-β2 gene played a more significant role.

Conclusion

In this project, a combination therapy strategy has been used to accelerate myelination in the mice cuprizone model. We used sequential injection of thyroid hormone simultaneously and repeated injection of the stem cells for two consecutive weeks to accelerate the process. In groups where we used combined cell and thyroid injection, we observed an increase in myelination compared to other groups that we used only from cells or hormone.

Epidemiology

Presenters:
Thuraksorn Thura
Anjali Patel
sahar sobhani
Samuel Olawale
Marwa I. Ewis
Ammar Ayman Bahbah
Asra Moradkhani

Can High Platelet Volume be used as a Predictor for Atherosclerosis and Poor Functional Status in Patients with Ischemic Stroke?

Thuraksorn Thura
Thailand

Introduction
Incidence of ischemic stroke in Thailand has constantly increased in the past decades, and that places DALYs due to the disease in the top three ranking. From previous exploratory studies, high mean platelet volume (MPV) is somewhat associated with ischemic stroke and worse activities of daily living (ADL). However, several studies have shown conflicting findings. To establish the predictive role of MPV, a confirmatory study with proper confounder adjustment is essential. To examine the relationship of MPV and the occurrence of large artery atherosclerosis (LAA) and poor functional outcome.

Material & Methods
We conducted a retrospective cohort study which included 134 patients with first acute ischemic stroke in Phrae hospital, Thailand between October 2020 to September 2022. Patients with prior disabilities(n=12) or brain abnormalities (n=22) were excluded. Data was collected from hospital database. MPV was classified into two groups: high-MPV (>9 fL) and low-MPV (≤9 fL; the reference). The primary outcome is the occurrence of LAA (yes/no), and the secondary outcome is the ADL functional status assessed by the Barthel index which was classified into two categories: improved (≥75 points) and poor (<75 points), determined by the difference in ADL scores at 3 month and 1 month after hospital discharge. Confounders such as sex, age, body mass index (BMI), and comorbidities were set at priori. Multivariable logistic regression was used to quantify the strength of association (adjusted odds ratio; ORs) and 95%CI. We assessed the interconnectedness of variables by a directed acyclic graph (DAG) before the analyses.

Results
Mean age of high-MPV and low-MPV patients were 66.0 years (SD=11.6), and 69.5 years (SD=13.0) respectively. More than 50% were female in both groups. No statistical differences in BMI and comorbidities between both groups. After confounders adjustment, the odds of having LAA in high-MPV group was decreased by 18% compared to the reference (adjusted OR=0.82; 95%CI: 0.19-3.20), and the odds ratio of poor functional status was 1.48 (95%CI: 0.48-4.55).

Conclusion
MPV is associated with physiologic changes of platelets in some phrases of ischemic stroke but has no predictive role on predicting large artery atherosclerosis and poor functional status in patients after hospitalization.

Prevalence of depression and its severity in Tuberculosis patients along with its associations with various epidemiological factors.

Anjali Patel
India

Introduction
In India, psychiatric disease is frequently overlooked among tuberculosis (TB) patients. Depression is a prevalent comorbidity among them that is often undiagnosed, mistreated and further contributes to non-adherence. Prevalence of depression and its severity among TB patients has recently garnered interest with a few studies exploring this association. However, since data in this niche is fairly limited, our study sheds further light on this public health hazard.

Material & Methods
In this cross sectional observational study, 425 adults with pulmonary and extrapulmonary TB without any pre-existing depression or psychiatric illness were enrolled at the DOTS clinics of 11 UHCs in Surat from July-November 2022. Sample size was calculated using 2 proportions- 40.83% and 23.6% (extremes of range of prevalence found in Indian population) with equal allocation and absolute error of 10%. Patients were screened for depression using the Patient Health Questionnaire (PHQ-9) and were correlated with other clinical and epidemiological variables. Groups were analyzed using the chi-square test and a p-value < 0.05 was considered statistically significant.

Results
Overall prevalence of Depression among TB patients was 23.29%, with a majority of patients classified as mildly depressed. Multivariable logistic regression indicated that patients were more likely to develop depressive symptoms belonging to groups having Marital life affected (OR=5.799 p<0.001), Interpersonal relation with family Ok (OR=3.815 p=0.002), Unemployed (OR=2.265 p=0.003), Occupation affected (OR=2.875 p<0.001), TB (Relapse) (OR=2.741 p=0.028) as compared to their counterparts.

Conclusion
The impact of TB and other chronic diseases goes beyond physical impairment. Recognising clues early and providing holistic care to patients should be the way forward.

The association between Whole body Phase angle with Alanine Aminotransferase and Aspartate Aminotransferase.

sahar sobhani
Iran

Introduction

Phase angle (PhA) is a variable obtained from bioelectrical impedance, surely related to cellular integrity and also PhA shows water distribution among intra- and extracellular space. it's a prognostic index of morbidity and mortality in various diseases and a predictor of body cell mass and also as a severity indicator for liver diseases. The aim of this study was to evaluate the applicability of phase angle (PhA) as a severity indicator of chronic liver diseases.

Material & Methods

This cross-sectional study consisted of 7216 participants from October 2017 to April 2021 of the PERSIAN Organizational Cohort Study in Mashhad. The serum levels of ALT and AST with bio impedance measures were obtained at the time of enrollment. Multiple regression analysis was performed to assess the relationship between whole body phase angle and serum levels of the aforementioned laboratory tests

Results

The serum level of AST and ALT had a negatively association with 50 kHz whole-body phase(β-Coefficient= -0.15, P=(0.001), (β-Coefficient=- 0.11, P=(0.004), respectively. AST, ALT serum levels showed significant relationship with Viseral fat area (P>0.05).

Conclusion

From the findings of this study, Whole body Phase angle consistently appeared a good predictor of elevated hepatic enzymes. Thus, it can be helpful in clinical settings to identify patients at risk of chronic liver disease.

Impact of Sofosbuvir-based National Treatment Program on the Burden of Hepatitis C Virus Disease in Egypt

Ammar Ayman Bahbah
Egypt

Introduction

Egypt is one of the most endemic countries with liver cirrhosis due to hepatitis C virus (HCV- cirrhosis). Sofosbuvir is a newly approved antiviral for HCV disease with promising efficacy and safety profile. In 2014, Egypt adopted a nationwide treatment program for HCV with expanded coverage for sofosbuvir. We aimed to determine the impact of sofosbuvir use on the burden of HCV-cirrhosis in Egypt as reflected in its prevalence and related disability.

Material & Methods

Age-standardized rates for prevalence (ASPR) and disability-adjusted life years (DALYs) of HCV-cirrhosis in Egypt were extracted from the Global Burden of Disease database. A paired t-test was used to compare the mean change in the ASPR and DALYs in two equal time periods around 2014: 2010-2014 (before sofosbuvir) and 2015-2019 (after sofosbuvir).

Results

From 2010 to 2019, HCV-cirrhosis exhibited a significant reduction in the ASPR (7322.65 per 100,000 at 2010 versus 2528.94 per 100,000 at 2019, $P<0.01$) and DALYs (399.11 per 100,000 at 2010 versus 333.1 per 100,000 at 2019, $P<0.01$) in Egypt. However, the reduction of ASPR was significantly accelerated after sofosbuvir approval and use (-7.87% versus -22.8% before and after sofosbuvir, respectively, $P<0.01$). A similar trend was observed for the DALYs where the mean rate of reduction was -5.1% from 2015 to 2019 (after sofosbuvir) compared to -2.8% from 2010-2014 ($P<0.01$).

Conclusion

By reducing the ASPR and DALYs, sofosbuvir substantially reduced the burden of HCV-cirrhosis in Egypt. Implementing similar programs across other HCV-endemic regions should be considered due to the projected social and economic benefits.

The prevalence of all types of diabetes and dysglycemia in the Eastern Mediterranean countries: a meta-analysis study

Asra Moradkhani
Iran

Introduction

Diabetes mellitus is a rapidly increasing metabolic disorder and the 4th leading cause of death from chronic non-communicable diseases and considering the lack of meta-analysis studies to cover the prevalence of different types of diabetes. The main aim of this study was to investigate the pooled prevalence of type 1 and 2 diabetes, gestational diabetes, and prediabetes in the Eastern Mediterranean region.

Material & Methods

for doing a comprehensive search strategy related to objectives in the presence of meta-analysis, all international databases like PubMed (Medline), Scopus, Embase, and Web of Sciences were searched to December 2022. The quality assessment of the final selected studies was done according to JBI Checklist for analytical Cross-Sectional studies. The subgroup analysis was done based on gender, country, area, criteria of diagnosis, and Gross Domestic Product (GDP) level.

Results

Among 5,238 relevant primary studies, 186 articles were entered into the meta-analysis. The pooled prevalence of total diabetes was 15% (95% CI: 13 – 16 %), undiagnosed diabetic 6% (95% CI: 4 – 7 %), known diabetes 8% (95% CI: 7 – 10 %), type 2 diabetes 13% (95% CI: 11 – 16 %), type 1 diabetes 1% (95% CI: 1 – 2 %), prediabetics 15% (95% CI: 13 – 18 %), impaired glucose tolerance 9% (95% CI: 7 – 11 %), impaired fasting glycemia 8% (95% CI: 6 – 11 %), and gestational diabetes mellitus was 11% (95% CI: 9 – 14 %) in the Eastern Mediterranean region.

Conclusion

The results of the present study indicate a high prevalence of all type of diabetes and pre-diabetes in the EMRO, indicating not very efficient Health cares that require making decisions on control, screening, management, and assessment of risk factors, allocating facilities, preventive and therapeutic measures in different areas, as well as formulating health policies and evidence-based decision-making should be used.

Epidemiological Trends of Liver Cirrhosis in the Middle East and North Africa from 1990 to 2019

Marwa I. Ewis
Egypt

Introduction

Liver Cirrhosis due to hepatitis B (HBV) and C (HCV) viruses is a major cause of morbidity and mortality in the Middle East and North Africa (MENA) region. Nationwide programs for HBV vaccination and HCV detection and treatment have been established to tackle this issue in the MENA region. However, the impact of such programs has not been investigated thoroughly at a regional and country level. This study aimed to explore the epidemiological trends of liver cirrhosis due to HBV and HCV in the MENA region from 1990 and 2019.

Material & Methods

Age-standardized rates per 100,000 for prevalence (ASRP) and disability-adjusted life years (DALYs) of liver cirrhosis and other chronic liver diseases due to HBV and HCV were extracted from the Global Burden of Disease database. Wilcoxon Signed Rank Test was used to compare the ASRP and DALYs in 1990 versus 2019. Mean annual change as a percentage from 1990 to 2019 was calculated for each country.

Results

In 2019, ASRP of liver cirrhosis due to HBV showed a significant reduction from 5286.84 in 1990 to 3009.1 in 2019 ($P<0.001$). Likewise, a significant decrease was observed for DALYs from 342.47 in 1990 to 141.21 in 2019 ($P<0.001$). Saudi Arabia showed the highest annual decrease in both ASRP (-2.25%) and DALYs (-2.39%). Similarly, the ASRP of liver cirrhosis due to HCV showed a significant decrease (2849.71 versus 1823.49 in 1990 and 2019, respectively, $P<0.001$). Regarding DALYs, a significant decrease was observed in 2019 compared to 1990 (338 and 256.8 in 1990 and 2019, respectively, $P<0.001$). At a country level, Tunisia had the highest annual increase in the ASRP (0.28%) and the lowest reduction in DALYs (-0.25%).

Conclusion

The burden of liver Cirrhosis due to HBV and HCV has been significantly decreasing in the MENA region, as reflected in its prevalence and related disability. A similar public health strategy should be considered in other areas with the significant burden of liver cirrhosis.

Genetics
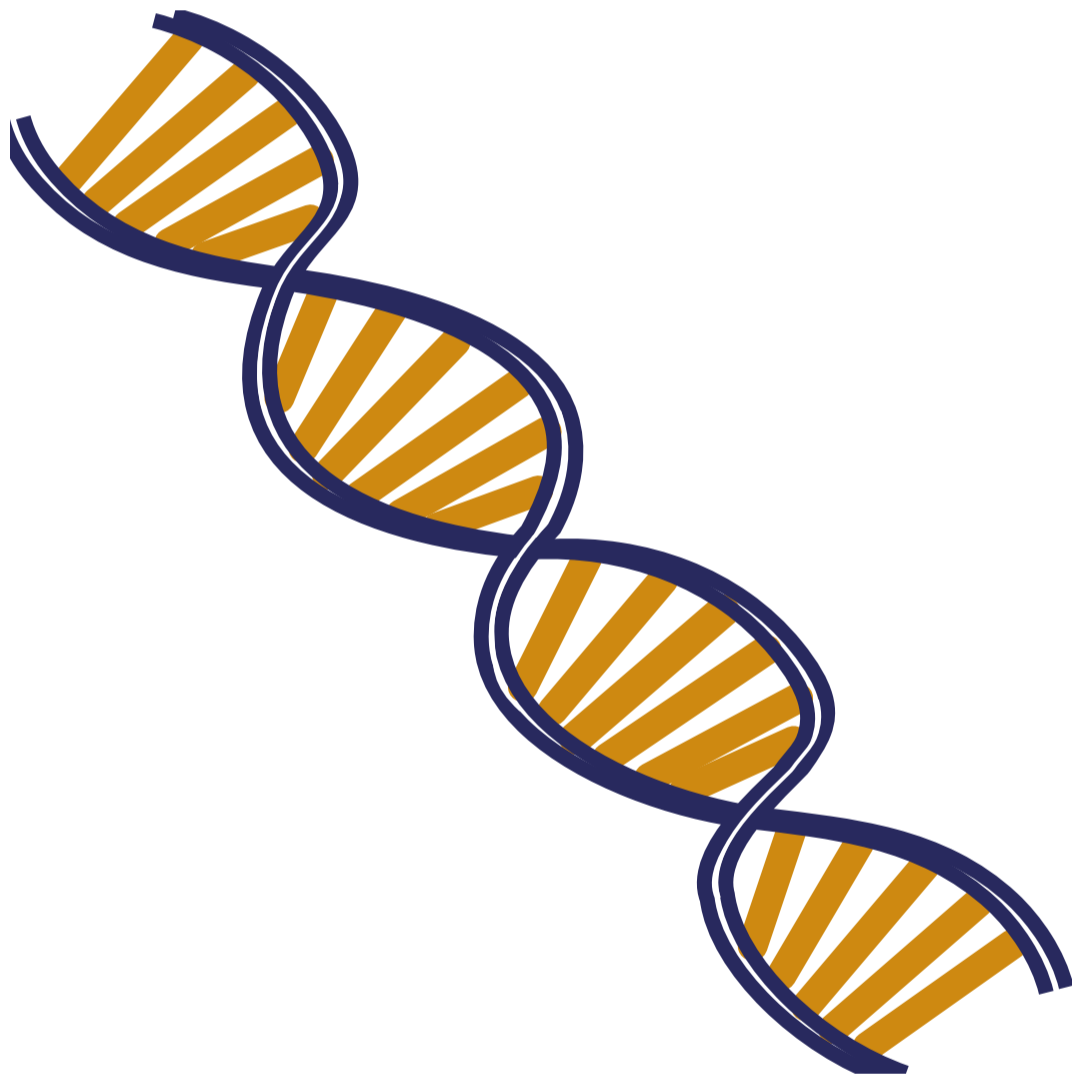
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Amrit Sandhu
Javad Razaviyan

Consequences of obese-ageing on cognition and brain function: obese vs. lean mice.

Mansi Rajput
Germany

Introduction

Obesity is an epidemic affecting around 1 billion people worldwide. It is a form of chronic systemic inflammation that accelerates ageing. Melanocortin-4 receptor (Mc4r), predominantly expressed in hypothalamus in brain, is responsible for energy homeostasis, food intake, and body weight. The deficiency/mutation of MC4R causes genetic obesity in humans. Mc4r is also expressed in hippocampus, memory hub of brain. Recent studies have shown that Mc4r deficiency in hippocampus is responsible for dementia-like disorders. In this project, we are investigating how cognition and optimal brain function changes due to obese-ageing in Mc4r-deficient mouse model. We seek to identify candidate genes causing cognitive impairment and dysfunction in brain; and eventually target those candidates therapeutically to undo the damage caused by obesity and promote healthy ageing.

Material & Methods

We have six cohorts of mice i.e., 6-month-old WT and KO; 1-year-old WT and KO. We performed a series of behavioral tests (Open field test, Novel object recognition test, and Morris Water-maze test) to examine the cognitive abilities and thereafter compute cognitive scores (CS) of KO mice compared to WT mice. We sacrificed the participating mice and isolated their brain. Pro-inflammatory markers in serum were tested with ELISA. Oil-Red O' staining and immunostaining were performed on brain cryo-sections.

Results

The KO mice in all age groups exhibited significant weight gain. Cognitive scores showed that CS of 6-month-old KO mice were as good as WT. However, a significant decline was seen in CS of 1-year old KO mice as compared to WT. Pro-inflammatory markers in serum were significantly high in 6-month-old and higher in 1-year-old KO mice. Oil-Red O' staining on brain showed increased lipid content in KO mice. Immunofluorescence-staining with microglia marker, CD11b, showed increased infiltration of microglia in the brains of 1-year-old KO mice.

Conclusion

Decline in cognition in KO mice with ageing. Systemic inflammation with obese-ageing. Neuroinflammation in brain of obese aged mice. New candidate biomarkers of obesity/ageing selected for further investigation.

Impact of Sofosbuvir-based National Treatment Program on the Burden of Hepatitis C Virus Disease in Egypt

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Egypt

Introduction

Egypt is one of the most endemic countries with liver cirrhosis due to hepatitis C virus (HCV- cirrhosis). Sofosbuvir is a newly approved antiviral for HCV disease with promising efficacy and safety profile. In 2014, Egypt adopted a nationwide treatment program for HCV with expanded coverage for sofosbuvir. We aimed to determine the impact of sofosbuvir use on the burden of HCV-cirrhosis in Egypt as reflected in its prevalence and related disability.

Material & Methods

Age-standardized rates for prevalence (ASPR) and disability-adjusted life years (DALYs) of HCV-cirrhosis in Egypt were extracted from the Global Burden of Disease database. A paired t-test was used to compare the mean change in the ASPR and DALYs in two equal time periods around 2014: 2010-2014 (before sofosbuvir) and 2015-2019 (after sofosbuvir).

Results

From 2010 to 2019, HCV-cirrhosis exhibited a significant reduction in the ASPR (7322.65 per 100,000 at 2010 versus 2528.94 per 100,000 at 2019, $P<0.01$) and DALYs (399.11 per 100,000 at 2010 versus 333.1 per 100,000 at 2019, $P<0.01$) in Egypt. However, the reduction of ASPR was significantly accelerated after sofosbuvir approval and use (-7.87% versus -22.8% before and after sofosbuvir, respectively, $P<0.01$). A similar trend was observed for the DALYs where the mean rate of reduction was -5.1% from 2015 to 2019 (after sofosbuvir) compared to -2.8% from 2010-2014 ($P<0.01$).

Conclusion

By reducing the ASPR and DALYs, sofosbuvir substantially reduced the burden of HCV-cirrhosis in Egypt. Implementing similar programs across other HCV-endemic regions should be considered due to the projected social and economic benefits.

Three-dimensional geometrical analysis of Gore Viabahn VBX bridging stentgrafts after Fenestrated Endo Vascular Aortic Repair, short term results

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Introduction
Balloon expandable covered stents (BECS) are used as bridging stents in Fenestrated endovascular aortic repair (FEVAR) for abdominal aortic aneurysm. The proximal end of the BECS is flared with for a secure connection with the fenestration. Geometric rendering of the BECS flare enables to determine the actual flare geometry and may help to detect or predict complications during follow-up. The aim of this study was to assess the flare geometry of the Gore Viabahn VBX (VBX) with dedicated software on postoperative computed tomography angiography (CTA) scans.
Material & Methods

This multicentre retrospective study included patients who underwent FEVAR between 2018 and 2022 in three vascular centres participating in the VBX Expand Registry. At least one target vessel was treated with the Gore Viabahn VBX as bridging stent. Two CTA scans, either between 0 and 6 months (FU1) and 9 and 24 months (FU2) post-FEVAR, had to be available for inclusion. The flare geometry of the VBX stentgrafts, including flare-to-fenestration distance, flare-to-fenestration diameter ratio and flare angle, was analyzed on these scans using a vascular workstation and previously validated dedicated Vascular Image Analysis (VIA) software.
Results

Of 43 patients, 90 VBX BECS were analyzed. The median follow-up time was 35 [29-51] days on FU1 and 14 [13-15] months on FU2. The mean flare-to-fenestration distance was 5.6 ± 2.0 mm on FU1 and 5.7 ± 2.0 mm on FU2 (p=0.834). The mean flare diameter was 8.5 ± 1.4 mm on FU1 and 8.5 ± 1.4 on FU2 (p=0.719), the mean diameter of the BECS at the level of the fenestration was 7.2 ± 1.1 mm on FU1 and 7.1 ± 1.1 mm on FU2 (p=0.831), resulting in a flare-to-fenestration diameter ratio of 1.19 ± 0.17 and 1.20 ± 0.19, respectively (p=0.545). The mean flare angle was 31 ± 15 degrees on FU1 and 33 ± 16 degrees on FU2 (p=0.328). One VBX stent showed an endoleak type 3c after 1 year follow-up, which was then successfully relined with a VBX. In this case the shortest flare-to-fenestration distance was 0 mm at both FU1 and FU2. Two VBX stents were occluded. A celiac trunk occlusion was reported on FU1, with a flare-to-fenestration distance of 18 mm and a flare-to-fenestration diameter ratio of 0.85. Another left renal artery occlusion was reported on FU2 with a crushed flare, which was already visible on FU1.
Conclusion

The mean flare geometry of the VBX stent did not change significantly during one-year follow-up. Three-dimensional geometric analysis of the flare may contribute to identify the mode of failure of complications with bridging stents used in FEVAR.

Inhibition of miR-155 using exosomal delivery of antagomir can up-regulate PTEN in Triple Negative Breast Cancer

Javad Razaviyan
Iran

Introduction

One of the more aggressive types of breast cancer (BC) is triple-negative breast cancer (TNBC), which makes up approximately 15% of all types and usually has a poor prognosis. Due to the fact that there is no effective treatment for TNBC, novel strategies, particularly targeted therapies, are necessary to treat this disease. The exosome is a nanoscale microvesicle that can be synthesized from a variety of cell sources and transports a wide range of intracellular cargoes, including miRNAs. The development of cancerous transformations in cells is greatly influenced by the presence of microRNA (miRNA), which is a small, non-coding RNA. There is evidence that PTEN serves as a tumor suppressor and that its deregulation can increase the risk of breast cancer and result in poor prognosis. One of the most effective inhibitors of PTEN is miR-155. This study examined the expression of PTEN in TNBC cells treated with miR-155 loaded exosomes.

Material & Methods

The MDA-MB-231 cells, as a model of TNBC, were grown under standard conditions, and exosomes were isolated from the conditioned medium (CM) using a commercial kit. Exosomes were loaded with miR-155 antagomir via electroporation. Total RNA was extracted 24 hours after treating the cells with antagomir-loaded wxosomes. In order to analyze the expression, cDNA was synthesized using specific primers and quantitative real-time PCR was performed.

Results

This study involved the analysis of RT-qPCR results from 14 TNBC clinical samples to determine the relative expression of PTEN and found a significant downregulation. An increase in the expression of PTEN was observed in MDA-MB231 cells treated with manipulated exosomes containing miR-155 antagomir. In antagomir-treated cells by exosomes, miR-155 expression declined 3.2-fold and PTEN expression increased 2.38-fold.

Conclusion

These results of the present study demonstrate that exosomes are an effective method of delivering oligonucleotides such as miRNA mimics and antagomirs in targeted therapies due to their ability to transport and encapsulate these molecules within the cells.

Prevalence of depression and its severity in Tuberculosis patients along with its associations with various epidemiological factors.

Anjali Patel
India

Introduction
In India, psychiatric disease is frequently overlooked among tuberculosis (TB) patients. Depression is a prevalent comorbidity among them that is often undiagnosed, mistreated and further contributes to non-adherence. Prevalence of depression and its severity among TB patients has recently garnered interest with a few studies exploring this association. However, since data in this niche is fairly limited, our study sheds further light on this public health hazard.

Material & Methods
In this cross sectional observational study, 425 adults with pulmonary and extrapulmonary TB without any pre-existing depression or psychiatric illness were enrolled at the DOTS clinics of 11 UHCs in Surat from July-November 2022. Sample size was calculated using 2 proportions- 40.83% and 23.6% (extremes of range of prevalence found in Indian population) with equal allocation and absolute error of 10%. Patients were screened for depression using the Patient Health Questionnaire (PHQ-9) and were correlated with other clinical and epidemiological variables. Groups were analyzed using the chi-square test and a p-value < 0.05 was considered statistically significant.

Results
Overall prevalence of Depression among TB patients was 23.29%, with a majority of patients classified as mildly depressed. Multivariable logistic regression indicated that patients were more likely to develop depressive symptoms belonging to groups having Marital life affected (OR=5.799 p<0.001), Interpersonal relation with family Ok (OR=3.815 p=0.002), Unemployed (OR=2.265 p=0.003), Occupation affected (OR=2.875 p<0.001), TB (Relapse) (OR=2.741 p=0.028) as compared to their counterparts.

Conclusion
The impact of TB and other chronic diseases goes beyond physical impairment. Recognising clues early and providing holistic care to patients should be the way forward.

The association between Whole body Phase angle with Alanine Aminotransferase and Aspartate Aminotransferase.

sahar sobhani
Iran

Introduction

Phase angle (PhA) is a variable obtained from bioelectrical impedance, surely related to cellular integrity and also PhA shows water distribution among intra- and extracellular space. it's a prognostic index of morbidity and mortality in various diseases and a predictor of body cell mass and also as a severity indicator for liver diseases. The aim of this study was to evaluate the applicability of phase angle (PhA) as a severity indicator of chronic liver diseases.

Material & Methods

This cross-sectional study consisted of 7216 participants from October 2017 to April 2021 of the PERSIAN Organizational Cohort Study in Mashhad. The serum levels of ALT and AST with bio impedance measures were obtained at the time of enrollment. Multiple regression analysis was performed to assess the relationship between whole body phase angle and serum levels of the aforementioned laboratory tests

Results

The serum level of AST and ALT had a negatively association with 50 kHz whole-body phase(β-Coefficient= -0.15, P=(0.001), (β-Coefficient=- 0.11, P=(0.004), respectively. AST, ALT serum levels showed significant relationship with Viseral fat area (P>0.05).

Conclusion

From the findings of this study, Whole body Phase angle consistently appeared a good predictor of elevated hepatic enzymes. Thus, it can be helpful in clinical settings to identify patients at risk of chronic liver disease.

Micro- and Cell Biology
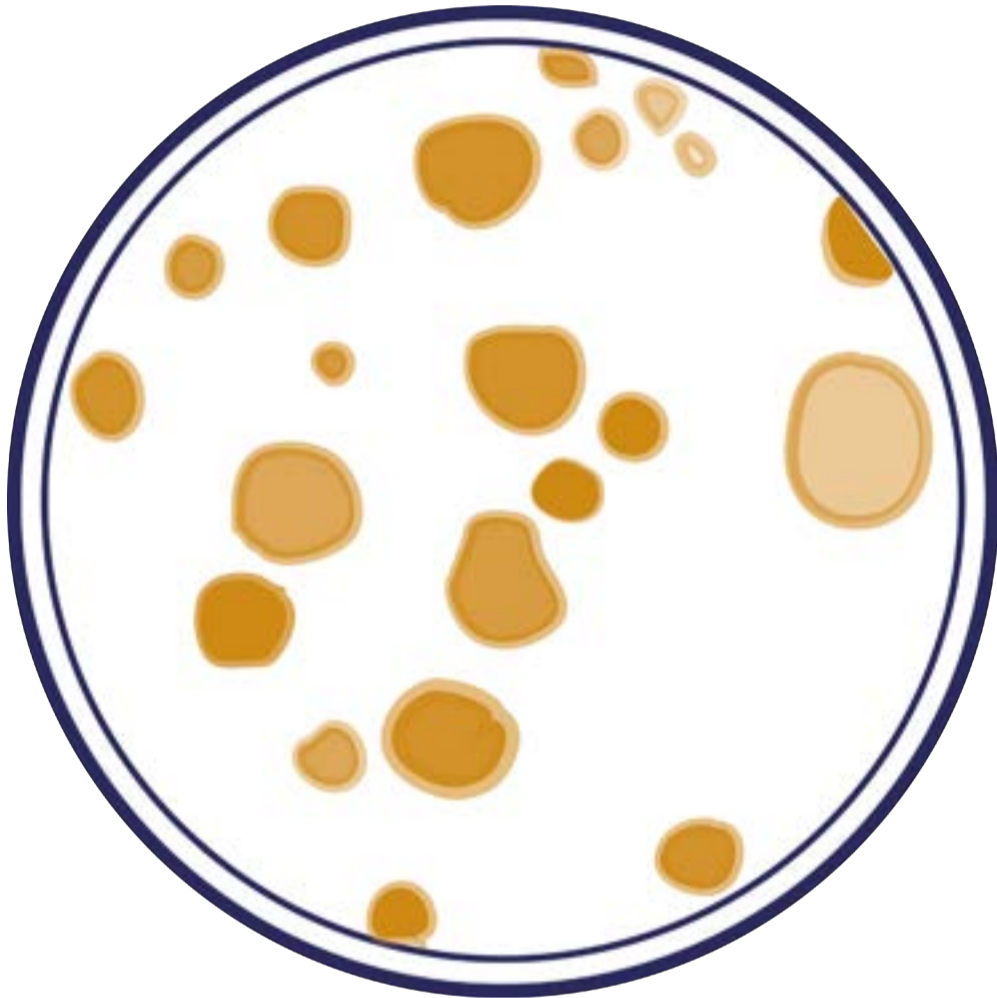
Presenters:
Elene Lipartia
Varsha Bijali
Divya Garg
Sofiia Rizatdinova
Tarun Kumar Suvvari
Sofiya Haluts
Regina Joyce Ferrer
Iván Daniel Salomón Cruz

Non-coding RNA analysis indicates MIR21 is induced upon kidney acute rejection and may attenuates T cell TNFα-related response.

Nathália Franchon Marques Tejada
Brazil

Introduction

Non-coding RNAs (ncRNAs) are pleiotropic molecules involved in transcription regulation. Although reported in cancer and renal diseases, their comprehension in kidney acute rejection (AR) is incipient, mainly focused on diagnosis prediction. In this sense, we aim to identify reproductive ncRNAs in AR, exploring in in silico repository their potential pathways related to failure, which could guide further therapeutic targets.

Material & Methods

Microarrays comparing AR to stable grafts were query on Gene Expression Omnibus employing the keyword "kidney transplant". Differentially expressed ncRNAs were stated as transcriptions presenting identical notations and $p < 0.05$. To identify which ncRNA relates to failure, GSE21374 was used for univariate logistic regression. The reproducible genes had their processes evaluated by GSEA enrichment, their targets accessed by NPInter and their protein-protein interactions (PPI) determined with STRING software. To compare results to leukocyte ncRNA expression, microarrays from effector vs. naïve T-cells (GSE93776, GSE37213) were analyzed for the same tests.

Results

From eight datasets found, four ncRNA were globally reproducible and related to failure. Among them, TUG1 and SNORD68 did not enriched common processes between studies, while MIR21 (Failure odds-ratio: 2.42, 97.5% CI 1.29-5.10) and MIR6756 (Failure odds-ratio: 3.90, 97.5% CI 1.61-11.30) upregulation were associated with GSEA TNFα signaling pathway. Accessing ncRNA targets, we only found differentially expressed targets for MIR21. These MIR21-target genes were generally upregulated, showing also a PPI with genes enriched in GSEA TNFα signaling. Since we expected miRNA downregulates gene expression, we hypothesized MIR-21 induction was secondary to inflammation. Indeed, in vitro analysis of T-cells pointed out that MIR-21 and GSEA TNFα signaling increases upon activation, which is more pronounced when MIR-21 is silenced. Either in leukocytes or AR datasets we found common PPI between targets and TNFα-related genes suggesting a possible similar pathway.

Conclusion

MIR-21 is increased in AR and effector T-cells, being related to a TNFα signaling enrichment, which is remarkable upon microRNA dampening. Since MIR-21 targets are also upregulated, our data suggest that MIR-21 is induced during leukocyte activation, aiding to attenuate TNFα pathway in AR. Further investigation inducing MIR-21 may contribute to control graft inflammation and failure.

Variability in Serum Sodium Concentration and its Prognostic Significance in Severe Burn Injuries: A Retrospective Study

Daniel Rahimi Nejat
Iran

Introduction

Sodium is the main active extracellular electrolyte in the body. A connection has been reported to exist between dysnatremia and a higher risk of death in patients with a severe condition. In burn patients, hypernatremia is related to a poor prognosis. In this study, it was hypothesized that significant plasma sodium variations can be a risk factor for higher mortality rates in severe burn patients.

Material & Methods

This present analytical cross-sectional study was performed on burn patients with ≥ 20% total body surface area (TBSA %) who were admitted to Velayat burn hospital(Rasht, Iran) between March 2018 and March 2020 after receiving the approval of the Vice-Chancellor for Research and the code of ethics number IR.GUMS.REC.1399.281.The medical history of the patients was reviewed, and data, including the discharge status, age, sex, TBSA %, serum sodium level, length of hospital and ICU stay, and need for mechanical ventilation, were extracted. Multivariable logistic regression was used to model association between baseline risk factors and risk of mortality. The collected data was entered into SPSS software version 22 with a significance level of 0.05

Results

Of the 300 patients included the mean age of the subjects was 47.48±13.46 years. 153 patients (51) were male and the mean TBSA score was 39.75±21.92%. Overall, 21.3% of the patients had hypernatremia, and 11.3% developed hyponatremia. Based on the results, 36.7% of the patients expired. Overall, the number of deaths was higher in hyponatremia/hypernatremia than the normal group (P=0.01). Multivariable logistic regression demonstrated association between mortality and the following variables: mean sodium concentration (OR =1.106, p=0.003), mechanical ventilation days(OR= 1.381, p = 0.000), age (OR= 1.093, p= 0.000), TBSA % (OR= 1.113, p = 0.000) are
independent risk factors for developing early mortality. Our study also showed that hypernatremic patients had significantly higher frequency of mechanical ventilation(P=0/000).

Conclusion

Dysnatremia, especially hypernatremia, is a frequent disorder in severe burn patients, which can be an independent predictor of mortality. Therefore, adjustment of serum sodium levels can be an enhancing factor for survival. Besides, more practical strategies are required to prevent and manage this fatal complication in burn patients.

Midterm changes in iliac limb apposition after endovascular aortic aneurysm repair

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Introduction
Literature is scarce on the course of iliac endograft limb apposition after endovascular aortic aneurysm repair (EVAR), which is why this study was conducted.

Material & Methods
A retrospective observational imaging study was performed to measure iliac apposition of endograft limbs on the first post-EVAR computed tomography angiography (CTA) scan and on the latest available follow-up CTA scan. With center lumen line reconstructions and CT-applied dedicated software, the shortest apposition length (SAL) of the endograft limbs was assessed as well as the distance between the end of the fabric and the proximal border of the internal iliac artery or the endograft-internal artery distance (EID).

Results
Ninety-two iliac endograft limbs were eligible for measurements, with a median follow-up of 3.3 years. At the first post-EVAR CTA, the mean SAL was 31.9 ± 15.6 mm, and the mean EID was 19.5 ± 11.8 mm. At the last follow-up CTA, there was a significant decrease in apposition of 10.5 ± 14.1 mm ($P < 0.001$) and a significant increase in EID of 5.3 ± 9.5 mm ($P < 0.001$). A type Ib endoleak developed in three patients due to a reduced SAL. The apposition was <10 mm in 24% of limbs at the last follow-up vs 3% at the first post-EVAR CTA.

Conclusion
This retrospective study documented a significant decrease in post-EVAR iliac apposition over time, partly due to retraction of iliac endograft limbs at mid-term CTA follow-up. Further research is mandatory to identify whether regular determination of iliac apposition may predict and prevent type IB endoleaks.

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 peculiarities of humoral and cellular immune response after SARS-CoV-2 Infection

Elene Lipartia
Georgia

Introduction

The specific immune response during and following the severe acute respiratory syndrome coronavirus 2 infection (SARS-CoV-2) is of particular interest as this could aid in the creation of an effective diagnostic strategy. Although the same sample determination of both of these immune response indicators has not yet been carried out, information defining humoral, or T-cell mediated immune responses following SARS-CoV-2 infection is available.

Material & Methods

A cross-sectional study by application of enzyme-linked immunosorbent assay (ELISA) method on blood samples from 49 patients who recovered from COVID-19 (35 females and 14 males; age range: 17-55 years) after a paucisymptomatic disease that did not require hospitalization or corticosteroid therapy has been performed. The results were analysed statistically for the aim to determine their statistical significance, $p < 0.05$.

Results

The biomarkers related to humoral and T-cell-mediated immune response after SARS-CoV-2 infection were identified. It was discovered that: a) 28 (57.1%, $p < 0.05$) participants were positive for a biomarker of the humoral immune response against SARS-CoV-2 – anti nucleocapsid protein IgG, and b) 16 cases (32.7%, $p < 0.05$) were negative or equivocal for the same biomarker of a humoral immune response against SARS-CoV-2 (5 cases; 10.2%, $p < 0.05$). In samples negative for humoral biomarker the increased median levels of Ki67 (14.95 ng/ml, range: 11.8-18.9 ng/ml) and IL-2 (1702 pg/ml, range: 1400-2002 pg/ml) were revealed in comparison for positive for anti nucleocapsid protein IgG samples specific levels of Ki67 (8.3 ng/ml, range: 5.7-10.9 ng/ml) and IL-2 (73 pg/ml, range: 52-97 pg/ml).

Conclusion

SARS-CoV-2 infection can induce both a humoral and a T-cell-mediated immune response. Patients with a negative status of humoral immune response determined through identification of immunoglobulin G (IgG) antibodies directed against SARS-CoV-2 nucleocapsid protein, exhibited an increased expression of specific biomarkers of T-cell-mediated immune response (Ki67 and IL- 2).

Smoking prevalence in the obese population in the EU countries

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Introduction

Smoking cessation is part of the holistic management of obesity but the prevalence of smoking and smoking cessation in the obese population is not well known. We aimed to determine the prevalence of smokers and ex-smokers and associated factors in the older obese population in EU countries.

Material & Methods

A sample of the European population ≥ 50 years of age (46,359, 57.36% of female, mean age 70.85±9.31, mean BMI…27.16±4.76); subpopulation with obesity: 10,624, mean age 69.49±8.56, mean…BMI 33.67±3.72) from 27 countries from a wave 8 (2019/2020) of the Survey of Health, Ageing and Retirement in Europe (SHARE) was used. Obesity was defined as BMI≥30. The data was collected from computer-assisted personal interviews using one common questionnaire, translated into national languages. Diagnosis of diabetes and smoking status were based on the self-report of participants, diagnosis of obesity was based on BMI level. X2 test and multinomial logistic regression models were used for statistical analyses.

Results

The average prevalence of smoking in the whole population was 16.61/27.20/56.28% (smoker/ex- smoker/non-smoker group). The average prevalence of smoking in the population of obese was 15.02/30.70/54.28 % (smoker/ex-smoker/non-smoker group). Obesity was associated with higher ex-smoker prevalence, whilst normal weight, overweight (p<0.001), lower education, age 50-74, living without a partner and being male were associated with higher smoking prevalence. Lower ex- smoker prevalence was associated with ≥ 80 years of age and being female. All p<0.001. Among countries´ obese populations, the highest prevalence of ex-smokers (63.04 %) was seen in the Netherlands. The highest prevalence of current smokers (25.07%) was found in Bulgaria.

Conclusion

Higher prevalence of ex-smokers in the obese group might reflect this diagnosis being an impulse for smoking cessation, nevertheless smoking prevalence remains high among the older obese population in Europe. Smoking cessation interventions should be addressed repeatedly not only in this group.

Neurology II
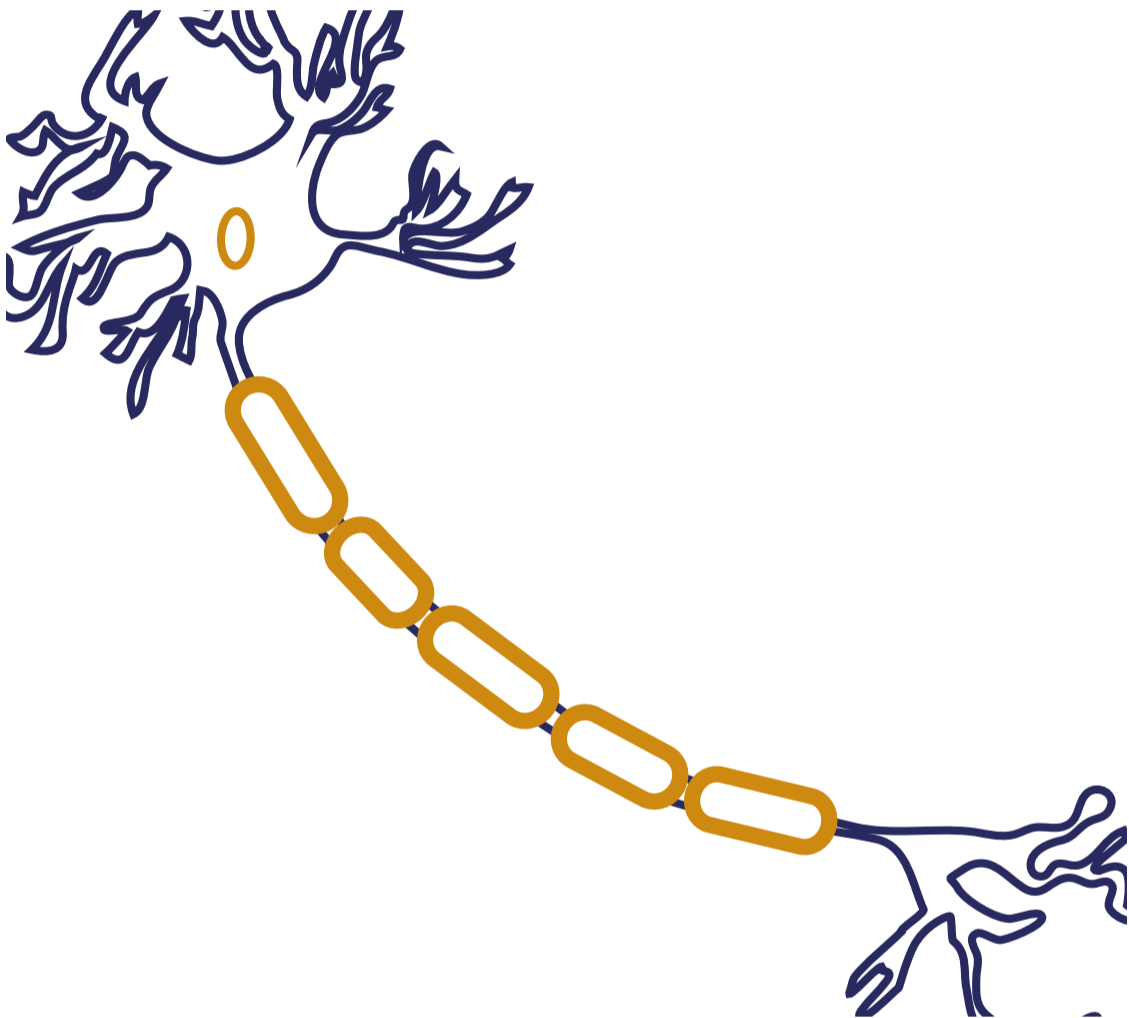
Presenters:
Dario Bottignole
alireza abbasi
Ewen Se Thoe
Moamen Mostafa Asla
Elly Robles
Yousef Terme
Nicholas Baidoo

Acceptance of COVID-19 vaccines by pregnant women and young children.

Marianne Checri
Italy

Introduction

Immunization is the best weapon against eliminating infectious diseases and alleviating their burden. According to the World Health Organization (WHO), about 3 million deaths are prevented each year by immunization. During the COVID-19 pandemic several vaccines were developed and implemented. However, COVID-19 vaccines uptake faced hesitancy due to different reasons and vaccination rates remained low especially among pregnant women and young children. The primary objective of this thesis is to define the acceptance of COVID-19 Vaccine among pregnant women and children below 11 years of age in Lebanon, to fill the data gap about the number of vaccinated individuals among this age group. The secondary objective was to define the reasons behind vaccine hesitancy and address those issues.

Material & Methods

A descriptive cross-sectional study was conducted using an online survey in the general population, the survey was conducted from August till October 2022 to meet the primary objective of this thesis. A literature review was performed to learn about the acceptance of COVID-19 vaccine in general and among pregnant women and children.

Results

113 participants filled the survey, 83% women refused to take the COVID-19 vaccines during pregnancy, while 77% mothers wouldn't provide their children aged under 11 years old with the COVID-19 vaccine. The reasons behind vaccine hesitancy or completely refusing COVID-19 vaccine were the lack of physician recommendation about vaccine intake, the ineffectiveness of COVID-19 vaccine against the new strains and the short time allocated to clinical trials.

Conclusion

The acceptance of COVID-19 vaccines in Lebanon by pregnant women, future pregnant women and mothers of young children aged below 11 years old remains low even though the vaccine is recommended for these groups. The findings of this study highlight the importance of improving awareness about the benefits of the vaccines and reduce the concerns about their safety. In addition to the importance of the physician recommendations.

Factors predisposing hospitalized COVID-19 patients to falls

Ivan Szergyuk
Poland

Introduction

Falls are a significant public health issue, given the high rate of hospitalizations and fatalities, as well as the costs to the patient and the healthcare system incurred by the falls. During the current coronavirus disease 2019 (COVID-19) pandemic, falls have been identified as a potential presenting symptom in patients infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), however, data on factors increasing fall risk in this patient population is limited. This study aimed to examine the factors that may predispose hospitalized COVID-19 patients to falls.

Material & Methods

In this retrospective observational study, hospitalized COVID-19 patients were examined for fall incidence, as well as demographics, comorbidities, clinical and laboratory data. Patients were stratified according to their fall status and their characteristics were compared using Fisher's exact test or Mann-Whitney's U test.

Results

A total of 312 hospitalized COVID-19 patients were enrolled (median age, 75 years; males, 51.3%), of whom 11 (3.5%) fell. There was a greater prevalence of falls among patients that experienced arrhythmias than those that did not (28.6% vs 1.7%; $p<0.001$). Additionally, a significantly greater proportion of those that were discharged to the internal ward and to the intensive care unit fell (10.3% and 10.0%) compared to those that were discharged home (1.6%) [$p=0.008$]. Thyroid stimulating hormone (TSH) was significantly elevated in patients that fell (5.3 vs 0.97 µIU/mL, $p=0.013$), while alanine aminotransferase (ALT) was significantly lower in fallers (17.1 vs 33.5 IU/L, $p=0.041$).

Conclusion

In conclusion, COVID-19 patients that experience arrhythmias may be at increased risk for falls and fall prevention strategies should be aimed at this vulnerable patient population to reduce fall-related injuries and the associated costs. A holistic approach involving both hospital staff training and patient education, with a focus on screening for multiple potential risk factors should be effective in helping minimize fall risk. To best of our knowledge, this study is one of the first to study falls in COVID-19 patients, and hence should be followed with studies with larger cohort size and analyzing for association to further validate our findings

nefits in overall mortality, neurological outcome, delayed cerebral ischemia, or hydrocephalus.

Prodromal phospholipid signature of cognitive dysfunction and dementia

Iván Daniel Salomón Cruz
Colombia

Introduction
Advances in genomics have made it possible to identify genetic factors associated with lipid metabolism and cell membrane damage as components that predispose to the development of Alzheimer's-type dementias. The "early" diagnostic tools are not so with respect to the detection of the aggregation of toxic proteins in the brain, when the brain deterioration is already irreversible; it also generates high costs such as PET-amyloid and PET-Tau; others are very invasive to obtain, as in the case of cerebrospinal fluid. Therefore, the main objective of this research is the Validation of a profile and composition of phospholipids predictive of cognitive dysfunction and Alzheimer's type dementia in plasma as a basis for the development of a prototype of a diagnostic tool.

Material & Methods
The profile and composition of plasma phospholipids will be analyzed in four phases of pathology progression (from 0m to 18m) in 3xTgAD mice together with previous characterization of cognitive performance and histopathological analysis. Also, changes in the profile and composition of phospholipids in the plasma of patients with familial Alzheimer's (E280A) will be verified in five phases from presymptomatic to late symptomatic (8 years to over 40 years) together with previous characterization of cognitive performance. The profiles will be analyzed by statistical tools CCA and PSL-DA. In addition to the analysis by bioinformatic tools for the identification of cellular pathways involved.

Results
Preliminarily, results of the phospholipid profiles in mice and humans will be presented, as well as proposals of the earliest cellular processes mainly involved in the alteration of the lipid signature, and a proposal of a lipid signature prediction formula as a basis for the development of a diagnostic tool.

Conclusion
Changes in phospholipid profiles in states of dementia precede the histopathological markers described, which are could register in plasma in a prodromal manner as a tool for early diagnosis of cognitive dysfunction

Efficacy and Safety of Vilazodone treatment for Major Depressive Disorder (MDD): A 3390 patients' meta-analysis of randomized controlled trials.

Mohamed Gbreel
Egypt

Introduction
Major depressive disorder (MDD) is a global health condition related to mental and physical consequences, functional impairment, and medical expenses. A wide range of antidepressant drugs could be prescribed for MDD patients. In this study, we aim to investigate the efficacy and safety of Vilazodone treatment for relieving MDD symptoms upon valid scores.

Material & Methods
Five databases were searched for literature search and seven included randomized clinical trials were finally meta-analyzed. All data were presented either as a mean difference (MD) in pooling continuous outcomes or risk ratio (RR) in pooling dichotomous outcomes with 95% confidence intervals (CIs).

Results
We included 7 randomized controlled trials (RCTs) with a total number of 3804 patients; 3390 of them were eligible to be pooled in our analysis. Patients' ages ranged from 13 to 42.4 years. vilazodone was given orally once a day with different doses throughout the included trials ranging from 10 to 40 mg for the duration of 8 to 12 weeks. The results significantly favored vilazodone over the placebo regarding the Montgomery–Åsberg Depression Rating Scale (MADRS) (MD =-4.69, 95% CI: [-6.83, -2.55], $P< 0.0001$), Clinical Global Impression (CGI) severity (MD=-0.29, 95% CI:
[-0.41, -0.17], $P< 0.00001$), and CGI improvement (MD =-0.36, 95% CI: [-0.44, -0.28], $P< 0.00001$). The pooled effect size significantly favored Vilazodone in terms of nausea, vomiting, diarrhea, somnolence, dry mouth, insomnia, and dizziness compared to controls.

Conclusion
Vilazodone treatment is an effective, well-tolerated, and safe drug for MDD patients in terms of multiple outcomes.

Oncology II

Presenters:
Mohammad Mobin Mirimoghaddam
Dionisia Mavritsakis
Ruicheng Fan
Anna Bętkowska
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Ahmed Hafez Allam

Perceived Stress and Coping Strategies among Medical Students in a Tertiary Institution in Southwest Nigeria

Samson Ojedokun
Nigeria

Introduction

Stress in medical school has become a common phenomenon and studies have shown that students tend to adopt dubious strategies to cope and survive the higher general demands during medical training. This study aimed to determine the level of perceived stress and coping strategies among medical students in Nigeria

Material & Methods

The study was a descriptive design carried out among two hundred and eight medical students of the Ladoke Akintola University of Technology. The Cohen perceived stress scale (PSS) and Brief cope scale were instruments adapted for the study. Data obtained were analyzed using SPSS version 21.0. Descriptive and analytical statistics were presented as frequencies, percentages, means, and standard deviations. The Chi-square test determined associations and significant associations at $P < 0.05$.

Results

Of the total respondents 69.6% has a low perceived stress level and 30.4% reported a high level of perceived stress. The study showed a statistically significant relationship between monthly income and perceived stress (p-value = 0.046). Religion (3.01±0.93), Positive reframing (2.89±0.81), self- distraction (2.82±0.81), acceptance (2.81±0.86) and planning (2.60±0.86) among others, were the common coping strategies observed.

Conclusion

This study demonstrated a high level of perceived stress among medical students, especially in the 2nd and 4th year of their medical training, more among female students. A significant association was found between stress and funding.

Cognition and psychophysical health deterioration of medical residents due to inadequate sleep and compensatory substance abuse - A cross-sectional study.

Dhairrya Diwan
India

Introduction

Sleep is a pillar of human health. Insufficient sleep has deleterious effects on psychophysical health. Multiple researches state that insufficient sleep is associated with poor mental and cognitive functioning. Long working hours of medical trainees is consequential to sleep deprivation and stress compounding. Previous researches have established a substantial correlation of sleep with psychophysical performance. But a focused research on overworked medical residents in Indian hospitals is called for.

Material & Methods

Study Area: The honorable ethics committee approved this study at MMIMSR, Mullana which is a tertiary care teaching hospital. Study Period: 2 months (June and July 2021) Sample Size: 105 residents from different years and specialities were given forms prior to which they were briefed about the purpose of data collection. Following categories were formed: Group 1- General medicine, Respiratory medicine, Paediatrics, Radiology Group 2- General surgery, Anaesthesia, Otorhinolaryngology, Orthopaedics Group 3- Ophthalmology, Dermatology, Psychiatry, Radiotherapy Group 4- Obstetrics and Gynaecology Group 5- Pathology, Social and preventive medicine, pharmacology Data Analysis: Data entry was done in excel sheets. Subsequently, imported to SPSS for statistical analysis. Categorical data was assessed using chi square test and T test.

Results

Analysis concluded that one-third of the residents suffered severe anxiety scores (36.2%) out of which group 4 i.e gynaecology residents (80%) had severe HADS anxiety score. Overall residents reported severe depression score (23.8%) out of which group 2 i.e general surgery and allied branches (40%) reported severe depression score. Same groups showed disturbed sleep on PSQ1
i.e 72% and 50% respectively. A significant association of sleep deprivation with anxiety and depression with $p=0.013$ and $p=0.001$ was noted respectively. The study also presented correlation between depression and tobacco consumption on chi-square (p value= 0.042) and anxiety correlated with coffee consumption (p value= 0.012).

Conclusion

Sleeping hours of medical residents is severely below WHO recommendation. Thus, constant stress and anxiety is observed with severe depressive symptoms and is aggravated by alcohol and tabaco abuse. Even caffeine, a commonly consumed wakefulness enhancing agent is associated with debilitating cognition- a worsened anxiety symptom. This study elicits the vitality of appropriate workhours of residents as they are the backbone to the medical infrastructure of an emerging nation

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.

The distribution of calretinin immunoreactive neurons in ageing human colon is region and sublayer specific.

Nicholas Baidoo
United Kingdom

Introduction

The incidence of gastrointestinal disorders such as constipation, incontinence and faecal impaction increases among the elderly. Calretinin-immunoreactive (IR) enteric neurons are crucial in the maintenance of secretomotor function in the gut. We investigated the influence of old age on the pattern of distribution of calretinin-IR enteric neurons in the myenteric(MP) and submucous(SMP) plexus of human ascending(AC) and descending(DC) colon and further examined their fibre density in the mucosa.

Material & Methods

Macroscopically normal AC and DC colon; aged 22 – 91 years were obtained from patients undergoing lower bowel cancer resection. 24 AC samples; adults (22-60 years; 6 male, 6 female) and elderly (70 – 91 year; 6 male, 6 female) and 24 of DC samples; adults (38-57 years; 6 male, 6 female) and elderly (70 – 88 year; 6 male, 6 female) were immunolabelled with calretinin antibody to identify calretinin-IR enteric structures. Stained sections were digitally scanned, systematically evaluated and new procedures were used to ensure unbiased densitometric analysis. Effect of age was determined by two-tailed independent student's test.

Results

The number of calretinin-IR cell bodies per ganglion was greater in the SMP than MP but unchanged in density in the adult (male and female) AC and DC samples. No significant change in the density of calretinin-IR enteric neurons with age at the MP of both the AC (Mean density: $1.2 \pm 0.3 \times 10\text{-}3$ vs $0.9 \pm 0.2 \times 10\text{-}3$ per mm2 of plexus) and DC (Mean density: $1.4 \pm 0.2 \times 10\text{-}3$ vs $1.3 \pm 0.3 \times 10\text{-}3$ per mm2 of plexus). With increasing age, density of calretinin-IR neurons and fibres were loss at the submucosal of AC (not DC) and mucosal level (both AC and DC) but loss was greater in the AC compared to DC. Sex related differences were not found when data combined in both the AC and DC samples.

Conclusion

These results indicate that ageing of the human colon does not result in the loss of calretinin-IR structures at the MP but changes do occur at the submucosa (AC only) and mucosa level (both AC and DC). This change may differentially affect the secretomotor function of ageing AC than the DC.

Post-Traumatic Stress Disorder and Post-Traumatic Growth in Patients with Breast Cancer: A Retrospective Cross-Sectional Study in a Developing Country

Mohammad Mobin Mirimoghaddam
Iran

Introduction

Cancer treatment is one of the most stressful events in life. Breast cancer is the most common neoplasm among menopausal women. Regarding the shortage of evidence on its psychological effects, we aimed to evaluate the status of post-traumatic growth (PTG) and post-traumatic stress disorder (PTSD) in patients with breast cancer.

Material & Methods

In this cross-sectional study, patients with breast cancer referred to the oncology radiotherapy clinic of Imam Reza and Omid Hospital were selected consecutively. We assessed PTG/PTSD scores in these patients. The independent sample t-test, Mann–Whitney U test, ANOVA test, and Pearson correlation coefficient were used to compare the findings in IBM SPSS Statistics for Windows, version 23.

Results

A total of 136 patients with a mean age of 11.3 ± 48.6 years old were studied. PTSD scores in patients who had recently been diagnosed with the disease were significantly higher than in those who had been diagnosed for a more extended period ($p = 0.001$). The mean score of PTSD was significantly different according to the treatment options ($p = 0.001$). Results showed no significant correlation between PTSD and PTG ($r = 0.006$, $p = 0.95$).

Conclusion

Our study suggested that type of treatment performed for patients and the time of diagnosis significantly affect PTSD, indicating the need for psychological therapy in these patients

Ophtalmology and Otorhinolaryngology
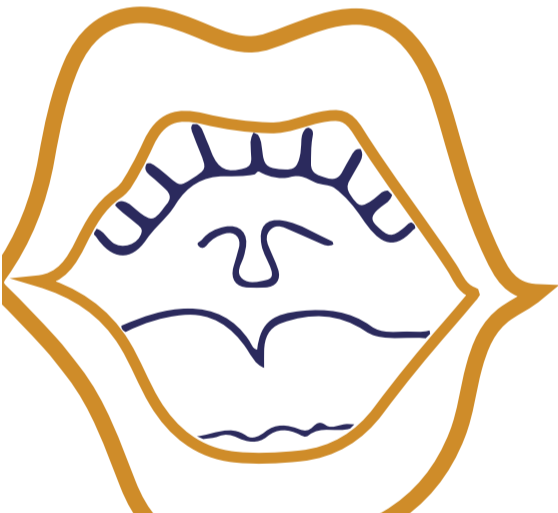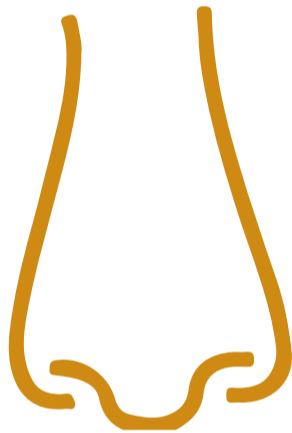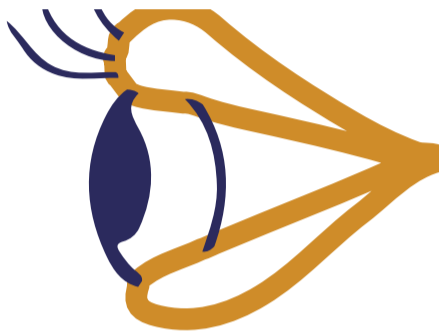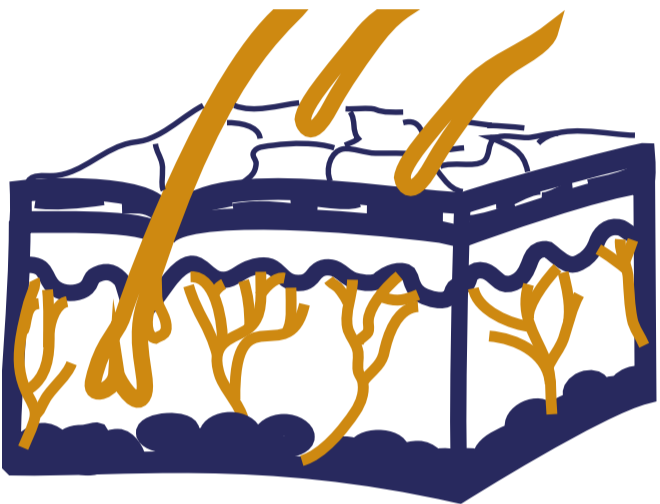
Presenters:
Dev Desai
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High prevalence of Schistosoma mansoni infection among adults with chronic non – communicable diseases in Malawi – a cross-sectional study at Mangochi district hospital

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%.

Genetics, rhythm, and cognition: effect of BDNF Val66Met polymorphism on adolescents' circadian rhythms and attentional performance

Luisa C Lopes
Brasil

Introduction

Cognitive performance is impacted by sleep habits, chronotypes and genetic characteristics. Variations in circadian mechanisms generate different individual preferences timing for sleep and activity, called chronotypes, affecting the performance of cognitive skills during the day. There is a tendency to eveningness during adolescence. The Val66Met (rs6265) polymorphism, in the human Brain-Derived Neurotrophic Factor gene, plays a significant role in the cognitive performance and circadian rhythm patterns. This study aimed to evaluate the effect of BDNF Val66Met polymorphism on adolescents' circadian patterns and cognitive performance on attention tests.

Material & Methods

Eighty-five healthy high school students were included. All students were evaluated in the morning by the Psychological Battery for Attention Assessment, which assessed the ability to concentrate, and the divided and alternate attention. Students were categorized as carriers and non-carriers of the rs6265 polymorphism by using the TaqMan rt-PCR technique. Their chronotype profiles were classified as Morningness-Eveningness according to the score of Horne and Ostberg questionnaire. A subgroup of 42 students was objectively assessed for their sleep-wake habits, wearing an actigraph for nine days.

Results

Carriers of the BDNF polymorphism performed better than the non-carriers in the alternate task (107.23±12.06 vs. 98.65±17.61; 95%CI=-0.74–15.0). No association was found between the presence of the r6269 polymorphism and the Morningness-Eveningness scale score (95%CI=-5.68-4.0). With regard to actigraphic results, the carriers of the polymorphism showed significant differences, compared to non-carriers, in the Total Sleep Time (6.48±0.69 vs. 5.97±0.65; 95%CI=0.038-0.98), Total Time in Bed (7.33±0.63 vs. 6.79±0.80; 95%CI=-0.024-1.07) and Social Jet Lag (2.43±0.95 vs. 1.68±1.04; 95%CI=0.026-1.47).

Conclusion

The presence of BDNF polymorphism demonstrated a partial and counterintuitive impact on attentional performance, affecting only alternate attention. The genetic trait studied showed an impact on activity-rest rhythms, when objectively measured by actigraphy.

Genome-wide Association Study of Non- alcoholic Fatty Liver Disease: novel insights into genetic associations in South Asia

Ho Kiu Giselle Ngan
United Kingdom

Introduction
With a global prevalence of 25%, non-alcoholic fatty liver disease (NAFLD) is one of the leading causes of end-stage liver disease and liver transplantation. Despite being paralleled by the increasing incidence of obesity, more non-obese individuals are developing NAFLD especially in India, highlighting the role of genetics in pathogenesis of NAFLD. Therefore, we performed the first GWAS to identify genetic risk factors associated with NAFLD in the South Asian population.

Material & Methods
536 cases and 397 controls were included from the Trivandrum NAFLD cohort. Genome-wide association analysis was performed using PLINK 2.0 following quality control and data imputation. Additionally, trans-ancestral meta-analysis was carried out across our cohort and datasets of individuals from European ancestry.

Results
Multiple genetic variants with suggestive evidence of association ($p < 1 \times 10^{-5}$) were identified in the Trivandrum NAFLD cohort, including rs1256113 (MTHFD1), rs2069923 (MAP3K2), rs10877190 (LRIG3) and rs10467865 (RIN3), although no associations were identified with NAFLD at genome-wide significance ($p < 5 \times 10^{-8}$). Meta-analysis confirmed associations in PNPLA3 gene (rs2294915). More importantly, a novel variant, rs2980888 in TRIB1, was discovered to be associated with NAFLD at genome-wide significance for the first time.

Conclusion
Results from our study suggest a potential divergence in genetic risk profile in the South Asian population as compared to other populations. In addition to identification of association between novel variant rs2980888 in TRIB1 and NAFLD, this novel study creates a multitude of possibilities for further research into genetic risk factors and pathogenesis of NAFLD.

Risk of chronic pancreatitis is increased in carriers of the c.180C>T CTRC variant: case- control studies and meta-analysis.

Gergo Berke
Hungary

Introduction
Chymotrypsin C (CTRC) is a digestive serine protease produced by the pancreas that regulates intrapancreatic trypsin activity and provides a defensive mechanism against chronic pancreatitis (CP). CTRC exerts its protective effect by promoting degradation of trypsinogen, the precursor totrypsin. Loss-of-function missense and microdeletion variants of CTRC are found in around 4% of CP cases and increase disease risk by approximately 3-7-fold. In addition, a commonly occurring synonymous CTRC variant c.180C>T (p.Gly60=) was reported to increase CP risk in various cohorts but a global analysis of its impact has been lacking.

Material & Methods
Here, we analyzed the frequency of variant c.180C>T in Hungarian and pan-European cohorts and estimated the effect size by calculating odds ratio. Furthermore we performed meta-analysis summarizing the new and published genetic association data of 5379 patients and 9675 controls. Finally, we performed mRNA expression analysis on cDNA samples obtained from surgically resected pancreas specimens from 10 patients heterozygous for the c.180C>T CTRC variant.

Results
When allele frequency was considered, meta-analysis revealed a significant increase in the overall frequency of patients versus controls (14.2% and 8.7% respectively; allelic odds ratio (OR) 2.18, 95% confidence interval (CI) 1.72-2.75). When genotypes were examined, c.180TT homozygosity was observed in 3.9% of CP patients and in 1.2% of controls, and c.180CT heterozygosity was present in 22.9% of CP patients and in 15.5% of controls. Relative to the c.180CC genotype, the genotypic OR values were 5.29 (95% CI 2.63-10.64), and 1.94 (95% CI 1.57-2.38), respectively, both significant however indicating stronger CP risk in homozygous carriers. We also obtained preliminary evidence that the variant is associated with reduced CTRC mRNA levels in the pancreas.

Conclusion
Taken together, the results indicate that CTRC variant c.180C>T is a clinically relevant risk factor, and should be considered when genetic etiology of CP is investigated. The preliminary functional data indicates that the c.180C>T variant is associated with lower CTRC mRNA levels in the pancreas, potentially explaining the mechanism of increased disease risk.

Analyzing the amplification of Auditory sensation in visually impaired individuals and comparison with normal individuals

Dev Desai
India

Introduction
It is commonly believed that if a person loses one of their basic senses like sight or hearing, other senses will be amplified to compensate the loss. It has been proven that this amplification does indeed help the person up to an extent, but this increase in the senses as compared to other individuals, who have all senses intact, has not been quantified.

Material & Methods
A Cross Sectional Case-control Pilot Experimental Study was carried out using a method that has been developed by the authors, wherein a pure tone sound at a specific intensity was brought inwards towards the subject from multiple directions and the distance was measured where the participant could hear the sound and was noted. The same experiment was carried out in Normal Individuals with normal 6/6 vision and these measurements were compared. Positon of nose in respect to the direction of sound source was used to denote the results in angles made by the two. A pure tone of 256 Hz , of 30db was used as the sound source and the distance from the subject was measured in meters.

Results
Out of total 60 individuals in the study, 45 had some degree of blindness. In both groups, the highest sensitivity is at 0° followed by 45°- 315°, then comes 90°-270° and 135°- 215° to put nose position of 180° at least amount of sensitivity. A 10% amplification in the distance is present between any and all type of visually impaired individuals and normal individuals whereas totally blind individuals have around 20% amplification compared to normal individuals in the distance to appreciate the sound.

Conclusion
A visible difference can be seen in the distance where a total blind person can hear, which is higher than the distance at which a normal individual can hear. High loss of vision, low loss of vision and one eye blind individuals come in the range between these two. Although, the results are not statistically significant, they are clinically present, and a with a larger sample size, a better assessment of this amplification can be done.

Paediatrics
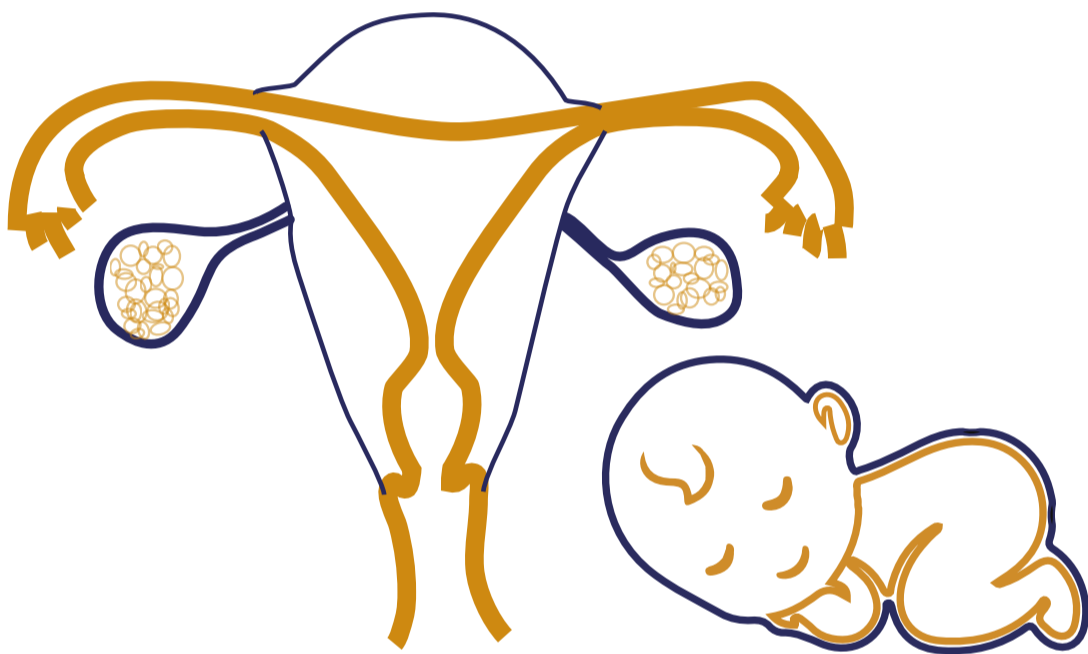
Presenters:
Adel Sadeghdoust
Karolina Markusiewicz
Victoria Koval
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Ilyas Kairgaliyev
Yttsje-Anne Mosselaar
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Sarafraz device, an innovative instrument for safe rhinoplastys

Zahra Sarafraz Zanjani
Iran

Introduction

Rhinoplasty is one of the most common surgeries in the field of beauty, which is performed for aesthetic and functional purposes. Nasal dorsum is one of the most important parts of the nose in this surgery and hump removal is one of the important goals in rhinoplasty. Hump removal is currently done by osteotome and rasp. Complications of surgery on this part include irregularities, excessive removal of the nasal bone (saddle nose deformity), and damage to the skin and soft tissue. Changes in traditional surgical methods and new tools can reduce the risk of tissue damage and complications. The purpose of this study is to compare the common rhinoplasty device (Osteotome-Rasp) with the innovative surgical device (Sarafraz device) in hump removal in terms of complications and surgical outcomes.

Material & Methods

In this 10-years multicentric clinical trial 500 patients who underwent hump removal with 2 different surgical instruments (osteotome-rasp and Sarafraz Device) involved. Patient's satisfaction and complications were evaluated by NOSE, ROE, QOL questionnaires, digital photography and surgical time.

Results

A total of 500 patients underwent rhinoplasty (247 patients in Sarafraz device and 253 patients in osteotome-rasp group). Min age was 26 years and 78% of subjects were female. Skin and soft tissue complications(subcutaneous cysts, swelling, hematoma, telangectasia,..) were significantly higher in the osteotome-rasp group (P value< 0.05). There was not any significant difference in surgical time between two groups (P >0.05).

Conclusion

Rhinoplasty is one of the popular surgeries with minor and major complications. Skin and soft tissue damage is one of the them. Adjusting techniques and using new surgical tools can reduce these complications. Sarafraz device is an innovative surgical tool, which is a combination of drill and aufricht and made of stainless steel, which has promising results in reducing postoperative complications by protecting the skin during the surgery and removes the hump carefully.

Ventriculoperitoneal shunt: catheter placement and malfunction.

Karolina Markusiewicz
Poland

Introduction

Ventriculoperitoneal shunt (VP) insertion is the gold standard procedure to manage hydrocephalus (HCP). VP drains the excess of the cerebrospinal fluid (CSF) from the ventricular system into the peritoneal cavity. Ventricular catheter blockage is the most common cause of VP malfunction. The ventricular catheter may be placed into the anterior horn of the lateral ventricle through the Kocher's point or through the parieto-occipital approach (Keen's point) into the trigone of the lateral ventricle. The aim of this study was to assess the safety and efficacy of VP placement and determine the risk of shunt malfunction depending on the place of the insertion of the ventricular catheter.

Material & Methods

The retrospective analysis was based on the data of 176 patients under the age of 10 months (39% female, 61% male), collected over a period of 6 years (2017-2022). 145 patients (n=145), who had undergone VP placement using either frontal ($n_1 = 91$) or parieto-occipital ($n_2 = 54$) approach, were involved. From the frontal horn group, 24,2% of patients required a replacement of the catheter, and from the parieto-occipital group – 40,7%. A null hypothesis ($H_0: p_1 - p_2 = 0$), which stated that there was no difference in the outcome in two corresponding groups, was established and tested against an opposite one ($H_1: p_1 - p_2 \neq 0$). The z-test ($(p_1 - p_2 - 0)/(DSED\_pooled(p_1 - p_2))$) was performed to conclude whether to reject or confirm the null hypothesis.

Results

The value of the calculated Z-test was -2.0975, hence the p-value of the results was 0.03572 which led us to reject the null hypothesis at a significance level of 0.05. There was enough evidence to conclude that there is a statistically significant difference between the outcomes in those two populations.

Conclusion

The patients that had a placement of ventriculoperitoneal shunt performed through a parieto-occipital approach to the ventricular system were more likely to need a replacement of the catheter later in the future because of the ventricular catheter blockage. Based on the results of the study, it should be advised to choose the frontal approach to the ventricular system, when possible.

CLINICAL ASSESMENT OF DAMAGE MARKERS OF BLOOD–AIR BARRIER IN CHILDREN WITH ACUTE LEUKEMIA

Victoria Koval
Ukraine

Introduction

Blood–air barrier (BAB) is a functional part of the lungs with epithelial, interstitial and endothelial components. Determination of its damage markers will allow studding of pulmonary complications in children with acute leukaemia (AL). The purpose of the study is to assess the level and clinical significance of damage markers of epithelial (IL-6), interstitial (TGF-β) and endothelial (VEGF) components of BAB in children with AL.

Material & Methods

We examined 51 children aged 6-18 years with AL at Kharkiv City Children's Hospital№16 and 15 healthy children for control group. Children with AL were divided into 2 groups: 1st group – during induction phase of chemotherapy (n = 24), 2nd group – in remission (n= 27). The level of IL-6 and TGF-β in exhaled breath condensate (EBC), VEGF in blood serum were investigated by ELISA. We used STATISTICA 7.0 for data processing.

Results

Pulmonary complications were diagnosed in 84.31% of children with AL: acute bronchitis (58.82%), wheezing (19.60%), bronchial asthma (5.88%), pneumonia (47.06% (24/51), interstitial pneumonia- in 1.96%, pleurisy (3.92%), pneumothorax (3.92%), pulmonary fibrosis (1.96%), leukemic infiltration (1.96%). 29.63% of children had pulmonary complications during the period of remission. In children of group 1, the level of IL-6 was 52.71 (48.28; 60.71) pg/ml, TGF-β 30.46 (22.90; 40.65) pg/ml, VEGF - 164.12 (150.18; 197.08) pg/ml, in children of 2 groups: IL-6 - 20.98 (18.57; 24.64) pg/ml, TGF-β – 18.55 (14.91; 22.14) pg/ml, VEGF – 169.11 (132.15; 198.66) pg/ml, in children of the control group: IL-6 8.12 (7.02; 9.45) pg/ml, TGF-β – 15.22 (13.88; 16.00) pg/ml, VEGF 130.65 (129.45; 132.15) pg/ml. The levels of all studied markers were higher in both AL groups than in control group (p1-K<0.05, p2-K<0.05). The level of VEGF in children of groups 1 and 2 had no significant difference(p>0.05). The level of IL-6 and TGF-β was significantly higher in 1st group than in 2nd group (p1-2<0.05).

Conclusion

Children with AL have significant increased levels of IL-6, TGF-β and VEGF and high incidence of lung complications (84.31%). Even during remission, damage markers of BAB are increased. Therefore, children with AL, including remission, can be classified as a group of high risk at developing lung complications.

Frequency of C-reactive protein test requests in children presenting at ambulatory care settings

Mohammed Alkhmees
Nederland

Introduction

C-reactive protein (CRP) is an important biomarker that could be used to detect infections in children at ambulatory care settings. However, the evidence of CRP is scares in this population and it is unknown how this test is actually used in clinical practice. Therefore, we aimed to describe the frequency of CRP test requests in British general practices (GP) and emergency (A&E) departments. We aimed also to evaluate referral patterns following these CRP test.

Material & Methods

This was a retrospective cohort study using the Infections in Oxfordshire Research Database (IORD). We included children younger than 18 years old visiting a GP and/or A&E departments in Oxfordshire between 2006 and 2021. All subjects had at least one CRP test at the first presentation. We used descriptive statistics.

Results

During a 16 year period, 110,594 CRP tests were requested in 73,631 children, whereof 42,863 (58.4%) children at GP and 30,498 (41.6%) children at A&E. Furthermore, we observed a rising trend of test requests, reaching its peak in 2019 (+44% at GP and +177% at A&E, compared to 2006). In most cases at the GP office (64,012 (91%)), CRP test results were < 20 mg/L, of which (59,531 (93%)) episodes did not require a second evaluation in the hospital. In addition, 1906 (0.3%) of all test results were > 80 mg/L and only 953 (50%) episodes from this group were re-evaluated in the hospital. While 28,708 (72%) of the CRP test results at A&E were < 20 mg/L, the number of admitted children in this group was higher than non-admitted children (16,651 (58%) vs. 12,057 (42%)). Furthermore, 3884 (10%) of all children have a CRP > 80 mg/L, of which 3030 (78%) were also admitted.

Conclusion

CRP test is increasingly requested in children at ambulatory healthcare settings and most test results were < 20 mg/L. At the GP office, the vast majority of these children were not referred to the hospital, whereas at the A&E department, CRP outcomes were less predictive for admission to the hospital. More studies are needed evaluating whether CRP test actually have an impact on clinical decision making in ambulatory care setting.

Caustic injuries in children: our 5-year experience.

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Kazakhstan

Introduction

Caustic ingestion among children is one of the most common problems worldwide, and has serious consequences for a child's health. The aim of the study was to analyze the results of the treatment of children with caustic injuries and compare the results of early and late dilatations in the treatment of post-burn esophageal strictures.

Material & Methods

A retrospective single-center study was conducted, which included the medical records of 327 children admitted to our clinic in the period from 2017 to 2022. The inclusion criteria were patients with ICD-10 diagnosis codes T28.6, X49, and K22.8. An analysis was carried out by gender, mean age, degree of injury, complications, ingested substance, and an assessment of the outcomes after early and late esophageal dilatations.

Results

Out of 327 children, 62.12% (n=203) were boys and 37.88% (n=124) were girls. The mean age was 2 years and 7 months. After endoscopic examination according to the Zargar classification system: I degree (83%, n=271), IIA degree (11%, n=36), IIB degree (5%, n=16), III degree (1%, n=3). 55 patients underwent dilatation procedures (bougies, balloons). 42 patients (IIa st.-27, IIb st.-13, III st.-2, average age 2 years. 6m.) underwent early dilatation on the 7th-10th day from the moment of caustic ingestion. 13 patients (IIb st.-11, III st.-2, mean age 2y.9m.) underwent late dilatation on the 3rd-4th weeks (due to the late visit to the clinic). The most common types of complications after dilatation were the formation of an artificial pouch (1%, n=3) and perforation of the esophagus (0.6%, n =2). The proportion by the type of agent ingested was alkali (78%, n=255) and acid (22%, n=72).

Conclusion

Due to the widespread use of chemicals in our daily lives and the lack of special protective mechanisms (locks) for children, there is an increase in the incidence of chemical burns of the esophagus, which leads to the growth of childhood disabilities. During the analysis, no significant difference was found between the early and late dilatations. Nevertheless, a comparison of the results and outcomes of early and late dilatations requires further research in multicenter and multistage studies.

Evaluation and optimization of the use of emergency letters by patients with inborn errors of metabolism causing fasting intolerance

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Introduction
Fasting intolerance is a serious feature of several inborn errors of metabolism (IEM), including fatty acid oxidation disorder (FAOD) and glycogen storage disease (GSD). Metabolic decompensations can lead to 'metabolic emergencies' for patients with fasting intolerance because of the risk of hypoglycaemia. For these metabolic emergencies, most patients use emergency letters. The emergency letters describe the steps patients need to take when the risk of decompensation is factual to prevent an emergency. Physicians should also be able to use the emergency letter. The aim of this research is twofold. First, we evaluate the use of emergency letters to further optimize the emergency care for these patients. Second, we want to create a pocket card with important information about the patient and a QR code which leads to the most recent emergency letter for that specific patient.

Material & Methods
A single-centre, observational, retrospective study using surveys and interviews. Inclusion criteria were patients with GSD or FAOD, treated in the University Medical Centre Groningen (UMCG) and who have an emergency letter. Pediatricians working in the north-eastern part of the Netherlands, who work in collaboration with the UMCG and have experience with the emergency letter, were also included. The data of the interviews were analyzed using tables and the surveys via google forms.

Results
During this study we performed a mirror meeting (12 attendees), patient interviews (n=3) and physician interviews (n=7). There were also patient surveys collected (n=37). The main points of improvement that emerged from the survey were: make the emergency letter available as an application/ QR code, clarify the severity of the disease more, use easier language for parents and improve lay-out to highlight important things. Most respondents were interested in a pocket card with a QR code that leads to the emergency letter.

Conclusion
Parents and physicians are pleased with the existence of emergency letters. However, emergency letters are not always up to date and, in the majority of cases, the emergency letter was not used prior to hospitalization. By improving the (ease of) use of emergency letters, critical events can be treated more efficiently and subsequent hospitalization can be prevented.

Single-Dose Thymoglobulin Achieves Higher Efficacy than Basiliximab Induction without Compromising Safety in Pediatric Kidney Transplant Recipients

Antonio Malheiros
Brazil

Introduction

Since there are still uncertainties about the best induction therapy in pediatric transplantation, the purpose of this study was to compare the efficacy and safety of thymoglobulin (ATG) single dose versus basiliximab (BAS) in pediatric kidney transplantation during 12 months of follow-up.

Material & Methods

This is a single-center natural experiment including consecutive kidney transplant recipients <18 years (PKT). Exclusion criteria: PRA > 50%, retransplants, children included in other studies and those who lost follow-up. All PKT used BAS as induction therapy from May 2013 until April 2016, and a 3mg/kg single-dose of ATG from May 2016 to April 2018. In both groups, all patients received calcineurin inhibitor, prednisone and azathioprine or mycophenolic acid as maintenance therapy. Anti-CMV preemptive strategy was used.

Results

In the study period, 266 PKT were performed, and 227 patients (85%) were included for analysis (BAS group = 113 and ATG group = 114). The 12-month composite endpoint of survival free from acute rejection, allograft loss and recipient death were superior in ATG versus BAS group (78 vs. 61%, p=0.003). ATG group had lower incidence of treated and biopsy-proven acute rejection compared to BAS (19% vs. 34%, p=0.014, and 18% vs. 32%, p=0.002, respectively). The overall incidence of the CMV infection was similar (33% vs. 37% p=0.500), although there was a lower rate of CMV events after treatment of acute rejection in the ATG group (6% vs. 14%, p=0.04). Patients in the ATG group also had a lower rate of EBV infection (1% vs. 7%, p=0.020). There was no difference in readmission rate in the first month (24 vs. 23%, p=0.847) or incidence of PTLD at one year (1 vs. 3%, p=0.280). At 12 months, the mean allograft function was 86 ± 29 mL/min/1.73m2 in the ATG group and 84 ± 30 mL/min/1.73m2 in the BAS group (p=0.614). One-year patient and graft survival rates were, respectively, 100% vs. 97% in the ATG group (p=0.154) and 98% vs. 94% in the BAS group (p=0.347).

Conclusion

These data suggest that a single-dose 3mg/kg ATG induction, when compared to BAS, improves efficacy without compromising the safety in low-risk pediatric kidney transplant recipients.

Psychiatry
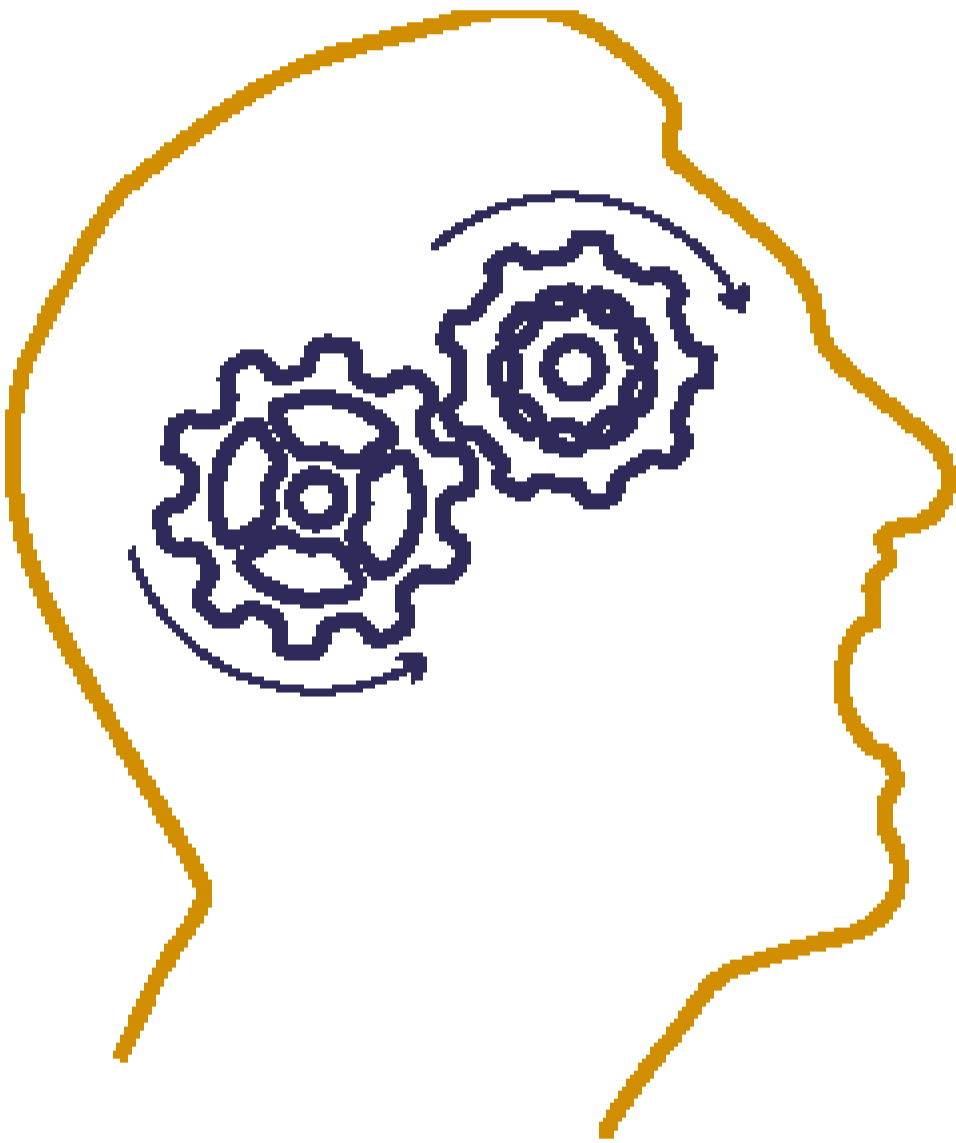
Presenters:
Rawan Mustafa Suliman Babiker
Jomar Jay Pucan
Esraa Alfadul
Mary Elizabeth Amalia
Mohamed Gbreel
Samson Ojedokun
Dhairrya Diwan
Akanksha Mahajan

EFFICACY OF FLOUROMETHOLONE EYE DROP IN POST LASEK WITH CONJUNCTIVITIS ; A DOUBLE-BLIND RANDOMIZED CLINICAL TRIAL STUDY

Masoumeh Rezaeiasl
Iran

Introduction

The prevalence of myopia is much higher in Asians than in Caucasians , and appears to be increasing in urbanised Asian communities. Presently, LASIK continues to be the dominant refractive surgery procedure for myopia ;However, LASEK has been shown to affect the health of the ocular surface by decreasing corneal sensation, tear secretion, tear quality, corneal and conjunctival epithelial integrity, and conjunctival goblet cell density. The aim of the present study was to investigate the effect of flourometholone eye drop on improvement of clinical symptoms in post-LASEK patients, also in this study were used the FML® eye drop as flourometholone active pharmaceutical ingredient .

Material & Methods

This prospective, double-blind, randomized, single-center comparative study comprised 86 subjects (50 men, 36 women; range 17-60 years) in patients of post-LASEK with conjunctivitis. Dosing of flourometholone eye drop for adults was: for first 48 hours period 2 drops be poured into the affected eye q 2 hr; for second 48 hours period 2 drops be poured into the affected eye q 4 hr; for third 48 hours period 2 drops be poured into the affected eye q 6 hr; for fourth 48 hours period 2 drops be poured into the affected eye q 8 hr; finally 2 drops be poured into the affected eye q 12 hr up to end of duration. The Patients were examined by an ophthalmologist before and after of treatment and clinical symptoms were recorded in a special form. Improvement of clinical symptoms evaluated based on VAS(Visual Analog Scale) and ophthalmologist assessment.

Results

The evaluation of the results showed that flourometholone eye drop in improvement clinical symptoms such as dry eyes(p-value=0.000), eye redness(p-value=0.008), eye itching improve(p-value=0.004), eye irritation(p-value=0.000), improve blurred vision(p-value=0.000), foreign body sensation in the eye(p-value=0.000) were significant . But in some factors include the fluctuating vision(p-value=0.326), pain relief improve(p-value=0.288), the SPK(p-value=0.235), itching of the eyelids improve(p-value=0.069), the papill form(p-value=0.098), the cemosis(p-value=0.326) In the study groups before and after treatment were not significant.

Conclusion

The results of this study showed that FML® eye drop was significantly effective in improving symptoms of patients of post lasek such as dry eyes, eye redness, eye itching improve, eye irritation, improve blurred vision, foreign body sensation in the eye.

MORPHOMETRIC AND GENETIC PROFILE OF PATIENTS WITH NANOPHTHALMIA FOLLOWED AT HC-FMUSP

Pedro Pires
Brazil

Introduction

Nanophthalmos is a disease of ocular development characterized by a functional eye with some specific alterations such as the curvature of the cornea, the axial length, and the anterior chamber deep. Thus, due to the different phenotypes of this disease, this study aims to identify the morphometric and genetic profiles of those patients.

Material & Methods

This is a cross-sectional, descriptive, and non-interventionist study carried out in patients diagnosed with nanophthalmos in at least one eye, followed at HC-FMUSP. Patients were invited to undergo ultrasonic biometry, IOL Master, or Pentacam. In total, the study was able to analyze 64 eyes of 32 patients. Some of these agreed to have their genetic material collected and sequenced in search of patterns to be correlated to the phenotype. For the study, patients with an axial length of less than 21mm and/or corneal diameter of less than 11mm, who had other symptoms, such as high hypermetropia, were considered nanophthalmos.

Results

On average, an axial length (AXL) of 17.56 mm and a horizontal corneal diameter (WTW) of 11.17 mm were verified. As for the corneal curvature profile, K1, and K2 average, respectively, 46.64D and 48.17D. Regarding the anterior chamber depth (ACD), the study divided the phakic and pseudophakic profiles, which had, respectively, an average of 2.2 mm and 2.54 mm. Additionally, a higher dispersion was verified between the axial lengths concerning the corneal diameters, with the first having a standard deviation of 2.52, while the WTW, of 0.89, demonstrating that these eyes not only have reduced volume, but also other disproportionalities related to the pathology. Four patients had their exome sequenced. Three of them had pathogenic mutations in PRSS56 two homozygosis and one heterozygosis. In the patient who presented heterozygosity, another mutation of still unknown importance was found in this same gene. The fourth patient had heterozygous pathogenic mutations in the ABCA4 and NR2E3 genes, related to Retinitis Pigmentosa.

Conclusion

After the study, it was possible to verify not only the morphometric distribution of the eyes of the HCFMUSP patients but also to find some genes that cause this condition in our population, serving as a basis for future analyses

Prevalence of eating disorders among undergraduate medical students in Government Medical College, Amritsar

Akanksha Mahajan
India

Introduction

According to National Eating Disorders Association, America, 70 million people internationally live with eating disorders. About one person dies every hour due to an eating disorder. (Eating Disorders Coalition, 2016). However, in India, eating disorders are one of the most under-researched areas. College years are known to coincide with the typical age of onset for EDs. Therefore, this study aims at assessing prevalence of eating didorders amongst MBBS students in GMC Amritsar.

Material & Methods

A randomised sample of 100 students was taken who participated in an offline survey conducted in GMC Amritsar using 3 standardised questionnaires, i.e., EAT-26,(eating disorders assessment test), BSQ-8,(body shape questionnaire), PSS-10 (perceived stress scale)

Results

67% of the participants were found to be at a risk of developing eating disorders, as they obtained score above 20 on EAT-26 questionnaire. A significant association was found between EAT-26 scores with gender, year of study, BSQ score and PSS score with $p < 0.05$ in chi-square tests.

Conclusion

The study sheds light on the fact that a great proportion of the undergraduate medical student population is at a risk of developing eating disorders. Stress and a negative body image emerged as the two most important risk factors, thus, emphasising the need to introduce certain interventions in the curriculum itself to enable the students to manage stress effectively and at the same time, develop a healthy body image.

Medication Adherence among Psychiatric Patients in Tigani El-Mahi Outpatient Clinic, Omdurman Locality, Khartoum State, Sudan, 2019

Rawan Mustafa Suliman Babiker
Sudan

Introduction
Poor-adherence among patients diagnosed with psychiatric illness is associated with poor clinical outcomes and high economic and human resource utilisation all over the world. However, in Sudan, where this study has been conducted, there is a shortage of studies and data regarding the prevalence of non-adherence and its associated factors among psychiatric patients. Therefore, this study was aiming to determine the magnitude of medication non-adherence and associated factors among patients with psychiatric disorders.

Material & Methods
This was a descriptive cross-sectional hospital based study in which 105 participants with diagnosis of a psychiatric disorder were randomly interviewed at the outpatient clinic of Tigani El-Mahi psychiatric hospital, Omdurman, Sudan. An anonymous socio-demographic questionnaire and the 8-item Morisky Medication Adherence Scale (MMAS-8) were used for data collection. And SPSS was used for the analysis.

Results
Of the 105 participants, 57.1% had low-adherence, 29.5% had medium adherence and only 13.3% had high adherence to psychiatric medications. Medication -adherence among psychiatric patients is strongly associated with the type of medications currently taken by the patient (P-value = 0.010), the frequency of medication intake (P-value = 0.028), type of psychiatric illness (P-value = 0.041) and the side-effects caused by the medications (P-value = 0.043).

Conclusion
Multiple factors related to the diseases and medications are associated with non-adherence in psychiatric patients. There's no association between the socio-demographic factors and the medication non-adherence. (P-value>0.05)

Association of screen media exposure and burnout among adolescents enrolled in different online curricula in Metro Manila: analytic cross-sectional study

Jomar Jay Pucan
Philippines

Introduction
Due to the COVID-19 pandemic, it became imperative for the education sector to shift to full online curriculum and eventually hybrid education, which utilized both synchronous and asynchronous teaching-learning activities with the use of internet-enabled devices. However, this new educational policy posed several challenges to educators and students, such as increased workload, prolonged screen time, and burnout. This study determined the association of online screen media exposure and burnout among adolescent senior high school students enrolled in different online curricula in Metro Manila.

Material & Methods
This analytic cross-sectional study identified adolescent senior high school students from different high schools in Metro Manila who were recruited via non-probability convenience sampling. The level of online screen media exposure was assessed based on the cut off value of four (4) or more hours of internet usage related to online academic work, and participants answered the Copenhagen Burnout Inventory to ascertain presence or absence of said mental health condition. Data analysis included cross-tabulation for prevalence rate ratio, and Chi-square test was used to determine statistical significance.

Results
Of the 117 respondents, most had significant online screen media exposure (88, 75.21%). In relation to Copenhagen Burnout Inventory, the majority scored less than 50 (66, 56.41%) which comprised those without burnout. The prevalence rate ratio (PRR) was calculated 3.9 (p-value 0.002).

Conclusion
Among adolescent senior high school students with significant online screen media exposure of four hours or more, there was 3.9 higher risk of exhibiting burnout symptoms, and this was statistically significant.

Burnout and its associated factors among healthcare workers in Khartoum's COVID-19 isolation centers: A cross-sectional study

Esraa Alfadul
SUDAN

Introduction

Burnout prevalence and its consequences on healthcare workers during the Coronavirus Disease 2019 pandemic are not well investigated in Sudan. This study aims to assess the prevalence of burnout and its associated factors among doctors and nurses during the omicron wave in Khartoum isolation centers.

Material & Methods

A multi Centre facility-based cross-sectional study was conducted between 20th February and 10th April 2022 during the last wave of Coronavirus Disease 2019. A total of 306 doctors and nurses filled out the questionnaire, with a response rate of 64.8 . They were recruited from 5 isolation centers scattered in the three localities of Khartoum. The level of burnout was assessed using an online semi-structured questionnaire based on the Oldenburg Burnout Inventory questionnaire.

Descriptive statistics were used for continuous variables and frequencies with percentages for categorical variables. The Chi-square test and Fisher exact test were used to identify variables associated with burnout. Logistic regression was used to determine the factors associated with burnout, and the p-value of $\leq .05$ is considered statistically significant.

Results

Results: The prevalence of burnout was 45.7%. Multivariate logistic regression showed doctors were more likely to have burnout than nurses (OR:1,982, CI 95% 1,2173,228 p=0,006). Also, engaged healthcare workers were less likely to suffer from burnout than single healthcare workers (OR: 1.982, CI 95% 1.217 – 3.228; p =.006). A low number of household members (p= .017) was associated with burnout among participants.

Conclusion

There is a high prevalence of burnout among healthcare workers in Khartoum Isolation Centers, which is more apparent among doctors. Significant relations show a positive effect on burnout

Factors associated with burnout among medical students of St. Luke's Medical Center- College of Medicine William H. Quasha Memorial

Mary Elizabeth Amalia
Philippines

Introduction
Burnout in medical students was found to be higher than the general population. This study aimed to determine the factors associated with burnout and its prevalence among medical students of St. Luke's Medical Center College of Medicine-William H. Quasha Memorial (SLMCCM-WHQM) enrolled during A.Y. 2021-2022.

Material & Methods
This is an analytic cross-sectional study. Stratified random sampling was used wherein 420 students were selected. A total of 205 students responded to the online questionnaire for the assessment of sociodemographic characteristics, morbidities, extracurricular activities, burnout (Oldenberg Burnout Inventory - Student version), social support (Multidimensional Scale of Perceived Social Support), physical activity (The Godin-Shephard Leisure-Time Physical Activity Questionnaire- GSLTPAQ), and impact of COVID-19 (questionnaire adapted from the study of Harries et al.,2021). The online questionnaire was emailed to the selected participants. Chi-square test of independence was used to determine the association of burnout with extracurricular activity. Spearman rank order correlation was used to determine the relationship of year level, physical activity, and social support with burnout. Univariate analysis using Odds Ratio and confidence intervals was done. Ordinal logistic regression analyses were carried out to control for the confounders. A p-value of less than 0.05 was considered statistically significant.

Results
From the 205 participants, the majority have moderate burnout (72.20%), 22.4% have high burnout, and 5.37% have low burnout. Year level, physical activity, social support and extracurricular activity showed no significant association with burnout. However, burnout showed a weak positive correlation with year level (r=0.0835) and a weak negative correlation with physical activity
(r=-0.0707) and social support (r=-0.1255). Mental health disorder (p-value=0.036) and impact of COVID-19 (p-value=0.001) showed significant association with burnout. Second year students were twice as likely to develop burnout, OR=2.21, 95% CI [0.70,7.03], compared to first years. Students with high physical activity, OR=0.69, 95% CI [0.34,1.42], and social support, OR=0.65, 95%CI [0.31,1.36] were less likely to develop high burnout, while students with no extracurricular activity were less likely to develop high burnout, OR= 0.69 , 95% CI [0.32, 1.49]

Conclusion
The study shows high prevalence of moderate and high burnout among the medical students of SLMCCM-WHQM. High levels of negative impact of COVID-19 and presence of mental health disorders are significantly associated with burnout, which may be due to increased cynicism and mental health deterioration during the pandemic.

THE COMPARISON OF ENT DISORDERS IN COVID-19 PREGNANT AND NON-PREGNANT WOMEN AT MATARAM UNIVERSITY HOSPITAL: A STUDY IN RURAL AREAS

Belva Bhadranitya Buana
Indonesia

Introduction

West Nusa Tenggara is the Province in Indonesia which has an ANC visit rate below the national average (67.7%), this condition exacerbated by the pandemic and positive cases in pregnant women tend to rise. COVID-19 is associated with more severe infection-related complications in pregnant women, compared to non-pregnant women. Extrapulmonary symptoms of COVID-19 which manifest through various disorders of the ENT are being recognized gradually. Given the low awareness of ENT disorders during pregnancy in rural areas, this study aims to compare the characteristics of ENT disorders in pregnant and non-pregnant women positive for COVID-19 for early detection to prevent long-term effects in pregnant women.

Material & Methods

This is a quantitative descriptive study with a cross sectional design, using total sampling. The research subjects were medical record files from pregnant and non-pregnant RT-PCR positive COVID-19 female patients at Mataram University Hospital from May 2020-May 2021 according to the inclusion and exclusion criteria, with the primary outcome; Chemosensory symptoms, URTI, Auditory Disorder, Vestibular Disorder. The standard mean differences (SMDs) with 95% confidence intervals (CIs).

Results

There were 79 samples of positive RT-PCR women for COVID-19, 36 (45%) of whom were pregnant and 43 (53.1%) were not pregnant. The mean age of the non-pregnant group was 46.67 ± 2.34 years [(41.95-51.40); range: 20-75; $p<0.709$]. The pregnant group was 28.06 ± 1.05 years [(25.92-30.19); range: 19-44; $p<0.768$]. The data is normally distributed, that age deviation can be ignored. There was no significant relationship ($p=0.062$) between pregnancy status and chemosensory symptoms ($p>0.05$). There was a significant relationship ($p=0.002$) between pregnancy status and symptoms of upper respiratory tract infection ($p<0.05$). There were no symptoms of auditory disturbances in the entire study population. Pregnancy has a significance ($p=0.010$) for vestibular disorders ($p<0.05$).

Conclusion

To conclude, pregnancy has statistical significance for several variables of ENT disorders.

Public Health II

Presenters:
Humphrey Beja
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Clinical Efficacy of SARS-CoV-2 Vaccination in Hemodialysis Patients

Eduardo Villa
Chile

Introduction
The COVID-19 pandemic is a global public health problem. Patients with end-stage renal disease on hemodialysis are at a higher risk of infection and mortality than the general population. Worldwide, a vaccination campaign has been developed that has been shown to reduce severe infections and deaths in the general population. However, there are currently limited data on the clinical efficacy of vaccinations in the hemodialysis population.

Material & Methods
A national multicenter observational cohort was performed in Chile to evaluate the clinical efficacy of anti-SARS-CoV-2 vaccination in end-stage renal disease patients on chronic hemodialysis from February 2021 to August 2021. In addition, the BNT162b2 (Pfizer-BioNTech) and CoronaVac (Sinovac) vaccines were evaluated. The efficacy of vaccination in preventing SARS-CoV-2 infection, hospitalizations, and deaths associated with COVID-19 was determined.

Results
A total of 12,301 patients were evaluated; 10,615 (86.3%) received a complete vaccination (2 doses), 490 (4.0%) received incomplete vaccination, and 1196 (9.7%) were not vaccinated. During follow-up, 1362 (11.0%) patients developed COVID-19, and 150 died (case fatality rate: 11.0%). The efficacy of the complete vaccination in preventing infection was 18.1% (95% confidence interval [CI]:11.8-23.8%), and prevention of death was 66.0% (95% CI:60.6-70.7%). When comparing both vaccines, BNT162b2 and CoronaVac were effective in reducing infection and deaths associated with COVID-19. Nevertheless, the BNT162b2 vaccine had higher efficacy in preventing infection (42.6% vs. 15.0%) and deaths (90.4% vs. 64.8%) compared to CoronaVac.

Conclusion
The results of our study suggest that vaccination against SARS-CoV-2 in patients on chronic hemodialysis was effective in preventing infection and death associated with COVID-19.

Predicting elastography parameters for hepatic steatosis via spectroscopic analysis of raw broadband ultrasound data acquired with a handheld device

Jakob Schäfer
Deutschland

Introduction
Nowadays, the prevalence of diffuse liver diseases is steadily increasing. Their degree has so far been determined by liver MRI or Elastography by Fibroscan® devices. In recent years, quantitative evaluation of radiofrequency (RF) ultrasound signals has shown promising results in this area. This study aimed to predict elastography parameters as a measure of the degree of steatosis using frequency spectroscopic analysis of ultrasound signals recorded with a handheld device.

Material & Methods
RF and B-mode images from 45 patients in different stages of diffuse liver disease were analysed. Liver elastography was used as a reference standard. Different bandwidths were generated by recordings of a high-frequency (5-15 MHz) and a low-frequency (2-6 MHz) transducer. The ultrasound signals were split into frequency and space components using a short-time Fourier transformation and then normalised with a reference phantom. From these, the attenuation was calculated and plotted against the controlled attenuation parameter (CAP) from the Fibrosan® which is used to predict grades of liver steatosis. This was done both for all frequencies averaged and for individual frequencies.

Results
For the low-frequency transducer, Pearson correlation coefficients for correlation with CAP were 0.44 (p=0.003) for all frequencies and 0.51 (p<0.001) for the best frequency (0.28 MHz), respectively. For the high-frequency transducer, Pearson correlation coefficients were 0.67 (p<0.001) for all frequencies and 0.70 (p<0.001) for an optimal frequency of 5.2 MHz.

Conclusion
The results show that a correlation between the CAP value of the Fibrosan® and the ultrasound attenuation can be established using raw data from handheld ultrasound devices. It is worthwhile to look at them on a frequency-specific basis, since optimized frequencies lead to better results than summarized ones. Better results were produced with the high-frequency transducer, which could indicate that consideration of higher-frequency signals is advantageous for this question.

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.

Barriers and facilitators to successful intensive adherence counseling in rural- northern Uganda: an exploratory interview with HIV-positive clients using the COM-B- framework

Humphrey Beja
Uganda

Introduction
Intensive adherence counseling (IAC) was introduced as a strategy to enhance adherence to antiretroviral therapy (ART) among HIV clients with non-suppressed viral loads. There has been sub-optimal viral load suppression among HIV clients in Uganda enrolled in IAC. However, there is a scarcity of literature on the barriers and facilitators of successful IAC. We aim to explore the barriers and facilitators to successful IAC among HIV-positive clients seeking care in public health facilities in rural northern Uganda.

Material & Methods
This was an exploratory qualitative study conducted among 15 purposively sampled HIV-positive clients enrolled in IAC in public health facilities offering ART services in northern Uganda. We conducted in-depth interviews using semi-structured interview guides based on the capability, opportunity, motivation, and behavior (COM-B) framework for behavior change. Data were analyzed using the deductive thematic approach of Braun and Clarke following the COM-B framework.

Results
The majority of the participants were females (60%), married (53%), and attained primary education (47%). Barriers to successful IAC were Capability – alcoholism and promiscuity, Opportunity – stigma and discrimination, delayed viral load result, shortage of food, and heavy workload; and Motivation – deteriorating health and lack of incentives. Facilitators to successful IAC were Capability – good knowledge of ART, good memory, and reminder alerts; Opportunity – availability of ART, social support, availability of ART, prolonged ART refill, and good counseling; and Motivation – desire to live longer and healthy and the desire to fulfill dreams and goals.

Conclusion
Successful implementation of IAC needs to consider the context of the person in care thus the need to strengthen individualized IAC sessions. HIV care providers can adopt the COM-B framework to perform individualized IACs and use the information to strengthen the counseling sessions.

Evaluation and Prevention of Medical Errors through training of Healthcare Professionals in Tertiary Care Hospital

Dr Zeeshan Ali
Pakistan

Introduction

This study objective was to evaluate the medical errors i.e., documentation errors, medication errors, discharge summary errors, readmission rates and noncompliance of surgical safety checklist in a tertiary care hospital and to find out significance of quality improvement training of doctors and nurses on prevention and reduction of these errors.

Material & Methods

It is a retrospective and prospective observational study in a tertiary care hospital. The retrospective patients medical record was reviewed as pre training assessment for the month of January to March 2021. The Prospective data was reviewed as post training assessment for the month of April 2021 to June 2021. Three quality improvement training sessions on clinical documentations and prevention of medical errors were conducted after the pre training assessment. A total of 700 medical records were reviewed 350 during pre-training assessment and 350 after the training of doctors ands nurses.

Results

Five categories of medical record were reviewed: medical documentation errors, discharge summary errors, medication errors, noncompliance of WHO safety checklist and readmission rates. 66 out of 68 KPIs of clinical documentation showed a statistically significant improvement in clinical documentation after the quality improvement training. There was significant improvement in medical documentation errors and medication errors, after the training the p-value was less than 0.0001 in all the key performance indicators (KPI) of medical documentation and medication errors. Readmission rates among medicine patients were decreased from 14.7% to 9.1% and 15.9% to 5.5% in surgery patients. A significant improvement in discharge summary errors was also seen after the training except for the KPI follow-up instruction which was non-significant after training with p-value 0.0955. The compliance of WHO safety checklist was also significantly improved in all KPI's with p-value less than 0.001 except for antibiotic prophylaxis information which was non- significant with p-value 0.230.

Conclusion

The study demonstrated that medical errors can be prevented with comprehensive and continuous quality improvement team trainings of doctors and nurses.

Readiness of managers and health care providers for eHealth at Primary Health Care centers in Khartoum state, 2022

Rofida Salah Asmally
Sudan

Introduction

eHealth is defined as "the use, in the health sector, of digital data— transmitted, stored and retrieved electronically—for clinical, educational and administrative purposes, both at the local site and at a distance. In Primary Health Care (PHC), the role of eHealth in promoting PHC systems defines its need for achieving the PHC aims. This literal work aims to study the readiness of managers and health care providers for eHealth at Khartoum state PHC centers.

Material & Methods

This was a facility based cross sectional study. A sample size of 327 was calculated and multi-stage cluster sampling was used. A validated questionnaire was used and generated data was analyzed using the statistical package for social sciences (SPSS). Variables were described as n (%) and mean ± SD. Non-parametric tests and spearman's correlation were used to investigate the association of readiness scores with different categorical and numerical variables, respectively Hierarchical multiple regression model was used to model the associations.

Results

A total of 262 forms were filled. Cronbach's alpha values for all questionnaire categories were above 0.90. The overall readiness score for managers was 114/216 (52.7%). And for health care providers it was 110/200 (55%). Factors associated with eHealth readiness included occupation, doctors level of expertise, PHC center, and PHC center type.

Conclusion

Effective eHealth implementation cannot be achieved if healthcare providers are not ready for such a change. This study found that the majority of healthcare providers at PHC centers across Khartoum state are not ready for eHealth implementation. The findings of this study can be considered by decision makers to enhance readiness of the providers for electronic transformation plans in PHC centers nationally.

Prevalence and factors associated with needle-stick injuries and mucocutaneous splashes among health profession students in Uganda.

Dianah Rhoda Nassozi
Uganda

Introduction
Occupational hazards like needle-stick injuries and mucocutaneous splashes are a significant contributor to the risk of acquiring blood-borne infections including HIV among healthcare workers, including medical students. However, its true burden and risk factors among medical students in Uganda is not well understood.

Material & Methods
A cross-sectional study using quantitative techniques was carried out between July and August 2022 among health profession students pursuing Bachelor of Medicine and Surgery (MBChB), Bachelor of Dental Surgery (BDS), and Bachelor of Science in Nursing (BSN) who are in clinical years at Makerere University. Simple random sampling was used to send online self-report questionnaires to eligible participants using KoBo Toolbox. Data analysis was performed using STATA 17.0.

Results
A total of 217 medical students with a mean age of 24 years, the majority being male (n=152, 70.1%), participated in the study. The majority (n=170, 78.3%) were pursuing MBChB. Nearly three-quarters (75.7%) were vaccinated against the Hepatitis B vaccine, and of these, 75.7% (n=128) were completely vaccinated against Hepatitis B. Overall, 44.7% (n=97) and 25.3% (n=55) had sustained mucocutaneous splashes and needle-stick injuries, respectively, with 13.4% (n=29) having sustained both occupational hazards. One-third (33%) of the needle-stick injuries occurred during the obstetrics and gynecology (OBGY) rotation, mainly while recapping needles (34.7%), assisting in surgery (30.9%), and withdrawing blood (30.1%). Female students were 19% more Blood (78.1%) and amniotic fluid (54.2%) were the most frequent body fluid splashes, and these mostly occurred during the OBGY rotation (61.5%). Female students were 19% and 30% more likely to sustain NSI and BFS, respectively but these were not statistically significant. The bivariate analysis also showed that religion (p=) and sponsorship were significantly associated with needle- stick injuries. At binary logistic regression, only private sponsorship was significantly associated with needle-stick injuries (adjusted odds ratio: , 95% CI: , 9=0.034).

Conclusion
Needle-stick injuries and mucocutaneous splashes are common among medical students. Preventive strategies must be implemented to protect to reduce the risk of acquiring blood-borne infections in the future of health workforce.

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 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 5% at the end of treatment, high bacterial load and lack of sputum conversion correlate with unsuccessful treatment outcome.

Surgery and Transplantation
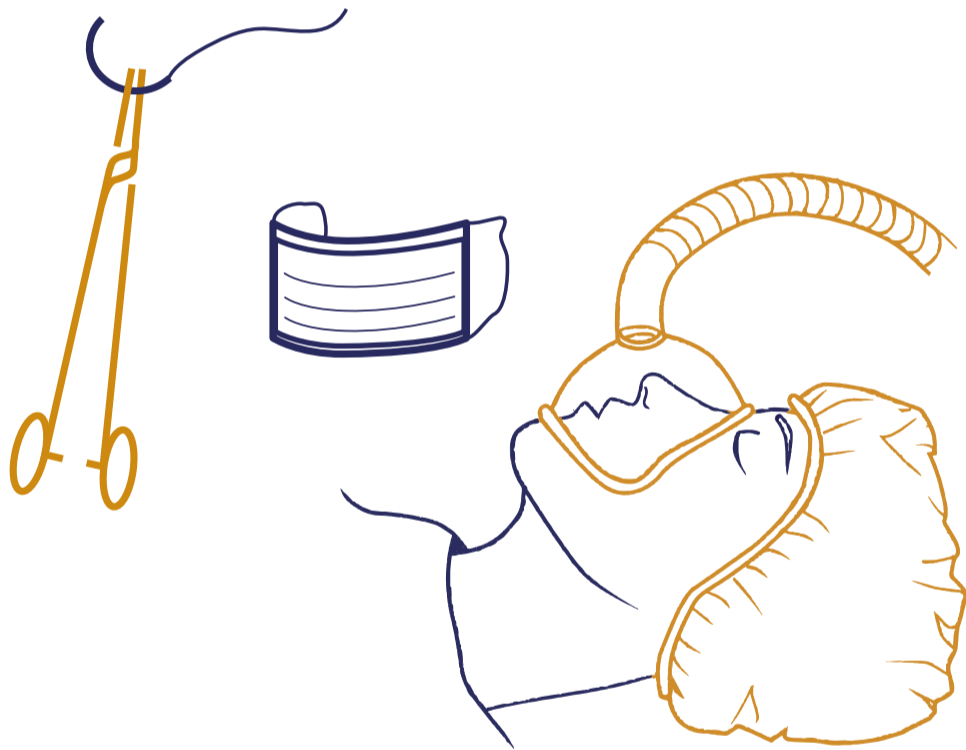
Presenters:
Seyed Ali Moosavi
Mayara Munhoz de Assis Ramos
Tessa Ferwerda
Nathália Franchon Marques Tejada
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Evaluation the relation between coronary artery calcium score in CT angiography and patients' lipid profile with possible coronary artery disease

Pegah Nekooeizadeh
Iran

Introduction
Coronary heart disease is known as a life-threatening factor that makes a person susceptible to atherosclerosis and coronary heart disease. Therefore, identifying these risk factors is still a challenge.The diagnosis and identification of risk factors for coronary heart disease, including the role of impaired lipid profile, is considered in this study. The purpose of this study is to investigate the relationship between lipid profile and atherosclerosis of the coronary arteries as a risk factor and the importance of its control and treatment in Cardiovascular diseases.

Material & Methods
In this study, 120 patients with possible coronary artery disease without previous history who referred to the CT angiography center participated. For these patients, HbA1c and blood lipid profile tests, which include: triglyceride (TG),Total cholesterol, low density cholesterol (LDL) and high density cholesterol (HDL) were measured. Also, in the findings of their CT angiography , the amount of calcium in their coronary arteries was checked and measured, and the information was analyzed with statistical methods. We divided people into two groups based on the amount of calcium in their coronary arteries. And we divided people with calcium levels above zero.

Results
The level of triglyceride, total cholesterol, low-density cholesterol and hemoglobin A1C in group A is lower than group B, and the difference in triglyceride, total cholesterol and low-density cholesterol is significant ($P<0.05$).) and in hemoglobin A1C it is close to significance ($P=0.065$). On the other hand, the density with high cholesterol in group A is higher and close to significance ($P=0.055$).

Conclusion
We divided the data into two groups: the group that had zero calcium level in CT angiography and the group that had calcium level above zero. Based on the results of triglyceride level, total cholesterol and low-density cholesterol in the group with zero calcium level was lower than the other group, and high-density cholesterol in the group with zero calcium level was higher than the other group.

Utilization of HCM-AF Risk Score in forecasting occurrence of atrial fibrillation - 5- year observation

Agata Suleja
Poland [4,5,6]

Introduction
Hypertrophic cardiomyopathy (HCM) is a genetic disease causing numerous life-threatening complications. Atrial fibrillation (AF) in HCM population constitutes an important step in progression of the disease. Recently developed American tool – HCM-AF Risk Calculator allows accurate prognosis of AF occurrence in HCM patients. Our aim was to assess clinical application of HCM-AF Risk Score in the prediction of 2 and 5-year clinical outcome of Polish patients with HCM.

Material & Methods
Retrospective cohort study included 92 consecutive patients with HCM (50% female, median age 53.5) and baseline sinus rhythm diagnosed at the 1st Chair and Clinic of Cardiology, Medical University of Silesia in Katowice in 2013-2018. Analysis involved clinical characteristics, laboratory tests, echocardiography, Holter monitoring, 2- and 5-year clinical outcome (total mortality, re-hospitalization, ICD implantation, heart failure) regarding the baseline HCM-AF Risk Score.

Results
According to HCM-Risk Score stratification 11 patients (11.9%) from analyzed cohort had low, 17 patients (18.5%) had intermediate, and 64 patients (69.1%) had high risk of AF. In patients from low-risk cohort mortality was 18.2% whereas AF incidence was 9.1% and 18.2% in 2- and 5-year follow-up respectively. However, in the intermediate-AF-risk cohort mortality was 11.8% and AF incidence was 17.7% and 25.5%. In high-risk group AF has been detected in 25 (43.9%) patients within 2-year-follow-up and 32 (56.1%) within 5 year-follow-up, total mortality was 43.9% and HF progression was significant.

Conclusion
HCM-AF Risk Score seems to be useful in both prediction of AF occurrence and clinical outcome in HCM patients. Polish HCM population is characterized by relatively high HCM-Risk Score coexisting with high AF occurrence thus AF screening should be obligatory in this group.

Community Awareness and the Prevalence of Active Urinary Schistosomiasis: A cross- sectional study among the Under-privilged Rurals of North Kordofan, Sudan, 2022

Lina Hemmeda
Sudan

Introduction
Schistosomiasis is a water-borne parasitic disease caused by trematode worms of the genus Schistosoma. It is one of the neglected tropical diseases (NTD) with Africa accounting for at least 90% of those seeking treatment for schistosomiasis. This study intends to evaluate the prevalence of active Schistosomiasis in school children, as well as their awareness, attitude, and behavior toward the illness in El-Rahad province; which is situated in North Kordofan state, the absence of rivers in the region renders inhabitants dependent on the freshwater lake (Al turaa), a man-made reservoir that collects rainwater.

Material & Methods
This is a facility-based analytical cross-sectional study among 424 primary school children aged seven to 13 in five villages recruited through stratified sampling method, as this is the highest age group of schistosomiasis prevalence in children according to WHO; structured and pre-tested questionnaires were used to collect the data in face-to-face interviews In addition, urine samples were collected from each pupil and then assessed microscopically for S. Haematobium eggs Presence. Data was then analyzed using SPSS version 25.0

Results
A total of 424 primary school students, from five villages; participated in the study. Almost all the students (96%) had poor knowledge about urinary schistosomiasis, causative agent, transmission, presentation, complications and prevention. 94% of students was found to have positive attitude regarding seeking medical help and receiving treatment of schistosomiasis. Regarding practices, the most frequent poor practice was fetching water from ponds/streams (89%), followed by swimming or bathing, washing clothes or utensils in water sources (75.1%). In general, 100% of the students had poor practices. Attitude revealed that females have lower chance of having the infection than their male counterparts, p-value 0.01 About 27% (n=115) of them had active urinary schistosomiasis infection at the time of the study.

Conclusion
The study revealed poor level of awareness and knowledge, positive attitude, and poor practices among primary school students. There was also high level of active infection in aligns with the poor practicing behaviours. Moreover, being a female and resident of particular villages such as Tendelti was found to to be significantly associated with the active infections.

Characteristics of liver transplant recipients with prope tolerance and comparing with their control group on full immunosuppression regimen

Seyed Ali Moosavi
Iran

Introduction

Liver transplant recipients are often subjected to excessive therapy by immunosuppressive drugs, which produce several complications. Minimization or even withdrawal of immunosuppression in selected patients is an attractive alternative. Tolerance is an immunologic unresponsiveness to particular donor tissues. Several kinds of tolerance are defined, such as full immunological tolerance, operational tolerance, or immunosuppressive drug minimization, sometimes referred to as prope tolerance. We investigated the frequency and characteristics of these near (or prope from Latin) tolerance in liver transplant recipients in Shiraz Organ Transplant Center.

Material & Methods

We reviewed the medical records of over 3800 adult liver transplant recipients to select a group treated with a low-dose tacrolimus monotherapy (n = 90) between 1994 and 2017 in our transplant center. The patients with the best liver function parameters were selected; then, the clinician arbitrarily decided to withdraw steroids first and then mycophenolate mofetil and maintain each patient on low-dose tacrolimus. We compared the characteristics of prope tolerant recipients on low-dose tacrolimus with those on standard immunosuppression, namely full-dose tacrolimus plus steroids and mycophenolate mofetil (n = 233).

Results

Out of over 3800 liver transplant patients, 90 (2.34%) recipients were treated with a minimum dose of tacrolimus monotherapy. These recipients were compared to a selected group of 233 (6.1%) recipients treated with full-dose tacrolimus plus steroids and mycophenolate mofetil. In a prope tolerant group, there were 55 males (61.1%) and 35 females (38.9%) recipients. The mean age at the time of transplant was 39.92 ± (SD = 13.40) years, with an average time from the transplantation time to completed weaning from triple immunosuppression to low-dose monotherapy of 41.35 months (SD = 17.27). The most common etiology of liver disease among both groups was viral hepatitis.

Conclusion

The achievement of prope (almost) immune tolerance was possible only in some liver transplant recipients with a relatively low risk of rejection. Our analysis suggests a difference in the underlying diseases and recipients' age and the number of rejections between the two groups.

TRANSLATIONAL RAT MODEL OF DONATION AFTER CIRCULATORY DEATH FOLLOWED BY NORMOTHERMIC REGIONAL LUNG PERFUSION

Mayara Munhoz de Assis Ramos Brazil

Introduction

The transplantation of organs donated after circulatory death (DCD) is an option to treat end-stage lung diseases, additionally normothermic regional perfusion is an alternative to ex-vivo lung perfusion (EVLP).Therefore, this study aimed to develop and evaluate a new rat model for the regional perfusion.

Material & Methods

Male Wistar rats were submitted to circulatory death (19.1% KCl solution, i.v.), underwent 30 minutes of warm ischemia being ventilated (VP) or not (NVP) and then were openly perfused in situ for 2h with Perfadex® at 37oC. Perfusate was collected after circulating the lungs via pulmonary artery and leaving through the left ventricle. Gas and perfusate samples were collected at the beginning (15 min) of the perfusion and at the end (120 min).

Results

The first surgeries were done without previous administration of heparin, simulating a patient who had a cardiac arrest outside the hospital. However, it was not possible to perform the perfusion properly due to clotting. A flush with cold PBS and 5% bovine albumin, after the ischemia time, was added improving the flow, but it still led to pulmonary edema. Finally, 500UI of heparin was added 1 min before the cardiac arrest and a flush with cold Perfadex® was performed right after ischemia. Partial O_2 pressure did not alter due to ventilation during ischemia or after the perfusion, while partial pressure of CO_2 indicates a slight acidosis in the group ventilated during ischemia VP (15min=10.1±1.6; 120min= 7.9± 1.4 p=0.0213). Perfusate pH did not vary significantly during the experiment. The perfusates increased in TNF-α: V(15 min= 7.5±2.5; 120 min=63.2±43.9 pg/mL; p=0.1424) and NV (15min=6.4±2.0;120 min=69.7±25.4 pg/mL p=0.1424) and IL-10: V(15 min= 1.7±1.0; 120min=6.1±3.2 pg/mL; p=0.1510) and NV(15 min= 0.7±0.6; 120min=5.2±2.7 pg/mL; p=0.1510).

Conclusion

A new model was developed indicating the need to use heparin and flush right before the normothermic in situ lung perfusion with Perfadex®. The model can be successfully used to gather molecular data and analyse DCD lungs followed by normothermic regional perfusion.

Cardiovascular Risk Factors in Living Kidney Donors and Recipient Kidney Function

Tessa Ferwerda
The Netherlands

Introduction

Transplantation with a kidney from a living donor is the best treatment for most patients with end- stage kidney disease. Because of a shortage of donor organs, selection criteria for living kidney donors have been liberalised towards allowing for donors with increased cardiovascular risk. This may reduce donor organ quality and function. While donor kidney function and age are known to affect recipient kidney function, this is unknown for cardiovascular risk factors of the donor.

Material & Methods

In a longitudinal cohort study of n=713 living kidney donor-recipient pairs, we measured donor cardiovascular risk factors and glomerular filtration rate (GFR) during the screening moment. Recipient GFR was measured one year after transplantation by means of iothalamate infusion. In univariable and multivariable linear regression analyses, we studied the associations of donor age, sex, GFR, body-mass index, smoking, blood pressure, HbA1c, and cholesterol levels, with recipient GFR.

Results

Living donors were 52 ± 11 years old, 54% were female and their pre-donation GFR was 101 ± 16 mL/min/1.73m2. The recipients were 48 ± 15 years old, 40% were female and their GFR one year after transplantation was 54 ± 15 mL/min/1.73m2. We found an association between donor age (St. β -0.31, P<0.001), donor GFR (St. β 0.31, P<0.001), systolic blood pressure (St. β -0.19, P<0.001), HbA1c (St. β -0.12, P=0.003) and cholesterol levels (St. β -0.10, P=0.010) with recipient GFR. In a multivariable model donor age (St. β -0.20, P<0.001), GFR (St. β 0.21, P<0.001) and systolic blood pressure (St. β -0.13, P<0.001) were associated with recipient GFR, determining 18% of the recipient GFR variance.

Conclusion

We show that living kidney donor age, donor GFR and systolic blood pressure are independent determinants of recipient GFR at one year after transplantation. These results indicate that the selection of living kidney donors may influence recipient kidney function, underlining the importance of adequate donor screening.

Comparison of Lymphoscintigraphy and reverse mapping in the identification of axillary sentinel nodes in patients with breast cancer

Sevil Ghasemi
Iran

Introduction

Breast cancer is the most common female-specific cancer and is responsible for 15% of cancer-related deaths in women. The status of the axilla lymph nodes is the most important prognostic factor for determining the treatment of invasive breast cancers .in recent decades axillary node dissection has been replaced by sentinel node biopsy in determining the status of axillary nodes. Although morbidities caused by ALND , such as lymphedema, has been decreased after routinely used SLNB but some other methods are needed to reduce such complications .One of these methods is Axillary Reverse Mapping (ARM). The purpose of this study is to investigate the concordance of lymphoscintigraphy and reverse mapping with blue dye in identifying the sentinel lymph node in the axilla region in breast cancer patients and candidates for sentinel lymph node biopsy (SLNB) so we can avoid dissection of uninvolved ARMnodes and prevent post operative lymphedema of ipsilateral upper limb.

Material & Methods

In this study, which was designed in a cross-sectional manner, 70 patients with breast cancer and candidate for SLNB were included in the study as available sampling. Then all patients participating in the study underwent both lymphoscintigraphy and reverse mapping with blue dye , then we compared the result of these two methods in the identification of sentinel lymph nodes in the axilla and cross over between them was calculated.

Results

In this study, the average age of the patients was 52.86 ± 8.35. 12 patients had blue nodes in surgical field , among which 9 cases of cross over was recognised between reverse mapping with blue dye and lymphoscintigraphy. Based on the statistical analysis of the available results, the percentage of crossover in identifying the sentinel lymph node was 12.8 % between two methods . Findings of lymphoscintigraphy and reverse mapping with blue dye were significantly different from each other in the identification of sentinel lymph nodes in the axilla area, $P=0.001$. Also, the average tumor size in the examined patients was 1.76 ± 0.35. There was no significant relationship between the tumor size and the result of reverse mapping with blue dye in identifying the sentinel lymph node $P=0.86$

Conclusion

In this study, we found that with usage of available injectable blue dyes in our country (Trypan blue), only few percentage of ARM nodes (17.1%) were detectable among which 12.8% cross over rate was reported. Which means the findings of lymphoscintigraphy and reverse mapping with blue dye in the identification of sentinel nodes are not consistent with each other.

Vascular Medicine and Radiology
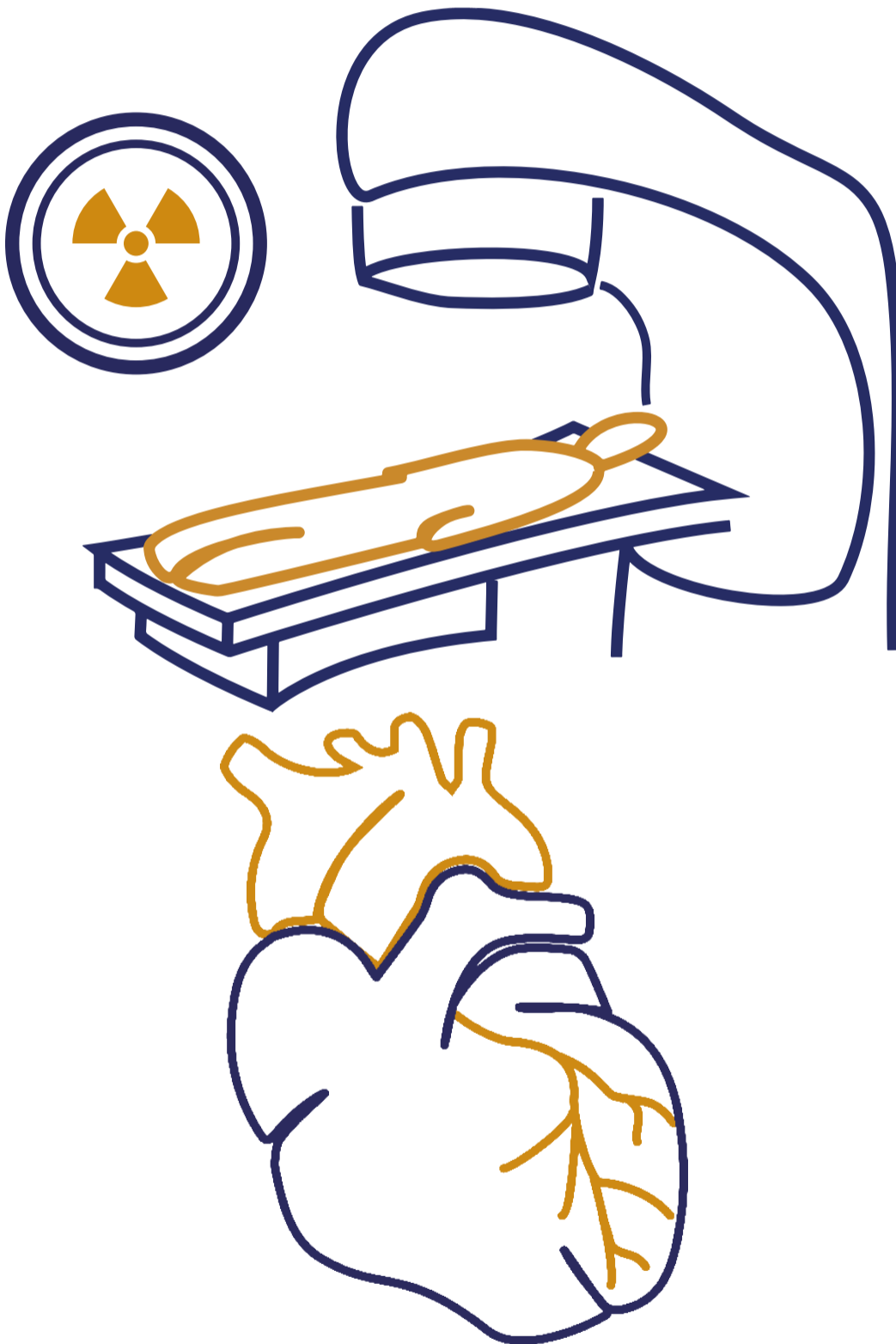
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Isabel Dieleman
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Yulia Busygina
Karol Stępniak
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Knowledge, attitude, perception and practice of self-medication among future drug prescribers in the University of Ibadan, Nigeria: a cross-sectional study

Samuel Olawale
Nigeria

Introduction
Antibiotic resistance is an imminent threat to global health. Due to a decline in the current treatment regimens' efficacy coupled with a low rate of development of new ones, predictably, infectious disease morbidity and mortality, especially those resulting from drug resistance will drastically increase around the world, Nigeria included. Self-medication contributes significantly to antibiotic resistance, and physicians can use antibiotics amiss. Therefore, we survey the knowledge, attitude, perception and practice of self-medication among future drug prescribers at the University of Ibadan.

Material & Methods
We conducted a cross-sectional web-based survey among 386 undergraduate Medical, Dental and Veterinary students at the University of Ibadan, Nigeria, using a structured self-administered questionnaire. Data were analysed using IBM SPSS version 23 and the Chi-squared test was used to test for association between variables. The level of significance was set at $p < 0.05$

Results
Out of the 380 responses that fit for analyses, 63.7% (IQR 13 - 15) of participants have adequate knowledge of antibiotic use and resistance, and 96.6% (95% CI 94.7 – 98.4) identified self-medication as a major cause of antibiotic resistance. The level of study was significantly associated with knowledge ($p<0.0001$). Although 74% (n=242; p=0.000931) of those that have adequate knowledge have self-medicated at some point, only 27.7% (n=242; p=0.623025) have self- medicated in the last six months, and 71.5% (n=242; $p<0.0001$) would educate people about antibiotic resistance. Although 48.7% (n=380) of the respondents think people should be taking drugs with a prescription, it is reassuring that the majority of the respondents, 77.1% and 72.1% believe that self-medication is wrong and consider it not appropriate to self-medicate on antibiotics respectively.

Conclusion
The prevalence of self-medication is high among the respondents. The level of study was significantly associated with knowledge, and only about two-thirds of the respondents have adequate knowledge. This could be due to students' exposure to antibiotic stewardship later in their academic year. Therefore, it is imperative to include antibiotic stewardship in the curriculum across all levels of study.

Determination of the proximal sealing zone of thoracic endografts after debranching of the left subclavian artery

Isabel Dieleman
The Netherlands

Introduction
For descending thoracic aortic aneurysms (TAA) in proximity of the aortic arch, debranching the left subclavian artery (LSA) may be necessary to extend proximal sealing in zone 2. The aim of this study was to determine the added proximal apposition length gained from LSA debranching during thoracic endovascular aortic repair (TEVAR).

Material & Methods
This multicenter retrospective study (2010–2020) included patients who underwent elective TEVAR in zone 2 for a degenerative TAA where the LSA was surgically debranched. The endograft (ap)position on the first postoperative computed tomography angiography (CTA) scan was assessed, including the shortest apposition length (SAL), tilt, and distance from the left carotid artery. Clinical end points (neurologic complications/endoleaks) at 30 days were also reported.

Results
Twenty-two patients were included. The median interval between TEVAR and the first postoperative CTA was 3 days (2-10 days). Median SAL was 9.2 mm (1.3-26.4 mm), of which 8.6 mm (1.3-16.2 mm) was gained proximal of the LSA, including the LSA orifice. In 10 patients (45.5%) the SAL was >10 mm, and the median tilt was 18.3° (13.9°-22.2°). Seven endoleaks were reported on the first CTA: 1 type Ia, 2 type Ib, 3 type II, and 1 type III.

Conclusion
Debranching the LSA adds valuable sealing length in zone 2, but the SAL was still relatively short in many patients, putting these patients at risk for a future type Ia endoleak. Accurate assessment of the circumferential apposition on postoperative CTA follow-up in these high-risk patients with short, complex landing zones seems mandatory.

Development of a multi-dimensional segmentation model and software platform for detecting small lesions in the nervous system

Xicheng Chen
China

Introduction

The detection and segmentation of small targets in the nervous system is the focus of clinical diagnosis and treatment, but segmentation is difficult in clinical practice, and it is very easy to miss diagnosis. There have been few studies on automatic segmentation of small targets in the past. A multi-dimensional and automatic image segmentation system based on deep learning is developed, which can detect and segment small lesions in nervous system MRI images, laying the groundwork for auxiliary disease diagnosis and treatment.

Material & Methods

We combine features extracted from 2D and 3D networks, introduce the joint loss function, and then construct a 2.5D deep learning automatic segmentation network. The method was trained and tested on a small set of nervous system focus data, and its performance was compared to that of various dimensional methods, classical methods, and advanced research. We have also created a visually appealing and low-barrier software platform to encourage clinical application and promotion.

Results

When compared to 2D and 3D models, the 2.5D model combining 2D and 3D features achieves the best segmentation performance in all evaluation indicators, with 80% DSC and 83% SEN. In comparison to traditional methods and advanced research, the 2.5D model achieves the best segmentation performance across all evaluation indicators. The 2.5D model is useful for locating many small lesions that are difficult to detect using existing methods.

Conclusion

To address the issue of small target detection in the nervous system, we created a 2.5D feature fusion image segmentation model and a visual decision support system, which provides an effective solution for nervous system disease diagnosis and prognosis guidance.

Evaluation of risk factors for delayed cerebral ischemia in patients treated with endovascular embolization of intracranial aneurysm

Zorka Joksimovic
Serbia

Introduction
Aneurysmal subarachnoid hemorrhage is a type of spontaneous hemorrhagic stroke which is caused by a ruptured cerebral aneurysm. The main treatment option for ruptured aneurysm is neuroendovascular procedure called endovascular coil embolization. Thanks to technological advances in devices used for endovascular coiling, this procedure is constantly developing, and remains most feasible and effective treatment. After the procedure, nearly one-third of survivors develop delayed cerebral ischemia, which is caused by narrowing of cerebral blood vessels and decreased cerebral blood flow. The main objective of this study was to examine the risk factors associated with delayed cerebral ischemia, after endovascular embolization of cerebral aneurysm.

Material & Methods
The study was designed as a cross-sectional study. The study included all patients, 18 and older, who were for the first time diagnosed with aneurysmal subarachnoid hemorrhage detected on CT and treated with endovascular embolization, at our institution, from January 2017-2022. The following variables were examined: socio-demographic data, clinical manifestations, scales (Hunt- Hesse-Scale, Fischer-Scale, Glasgow-Coma-Scale), initial CT findings, aneurysm features and procedure characteristics (use of coils, stents, flow diverters and/or ballon assisted techniques).
The impact of these variables on the main outcome (delayed cerebral ischemia) was investigated by univariate and multivariate logistic regression.

Results
In total, 50 patients (male/female:30%/70%) were enrolled. In relation to the hospitalization length of each patient, incidence of delayed cerebral ischemia was 0.66 per 100 patients-days of hospitalization. The frequency of CT hypodense zones, whose size was graded in three groups by VAS scale, were: 71.2% (small), 18.2% (medium) and 10.6% (large). The multivariate analysis showed that the intraventricular hemorrhage and patient age before endovascular embolization increase the chances of delayed cerebral ischemia 14.7 and 1.12 times, respectively, while use of flow diverters has protective effect of 1.5.

Conclusion
It was determined that intraventricular hemorrhage on initial head CT is a strong predictor of delayed cerebral ischemia, while use of flow diverters in treatment has protective effect.

The variation of the descending aorta morphology with age and sex in a South African sample

Pheladi Mokoena
South Africa

Introduction
The descending aorta is an important component of the cardiovascular system, and its morphological variation is associated with demographic and cardiovascular risk factors. The aim of this study was to determine the dimensions of the descending aorta and its association with age and sex in a South African sample.

Material & Methods
The descending thoracic aorta (DTA) and descending abdominal aorta (DAA) segments were measured on 97 computed tomography angiography (CTA) scans of an adult South African population (54 male and 43 female), mean age 48.5 ± 17.2 (range: 23-79) years. The sample was stratified by sex and age into six decade-long groups. The length of the DTA was measured from between T6 and T7 to the superior border of T12, and the length of the DAA was measured from the coeliac trunk to the bifurcation point. The lumen diameters were measured at six aortic landmarks: level between T6 and T7, midpoint of DTA, superior border of T12, coeliac trunk, left renal artery and the bifurcation point of the DAA. Tortuosity of the DA was quantified with the tortuosity index (TI) and assessed by phenotype description.

Results
The descending aorta tapered inferiorly from the DTA to the DAA bifurcation point at a ratio 1.59. Males had larger lengths and lumen diameters than females and the differences were significant only for DTA length ($p < 0.001$). The length of the DTA showed significant differences between age groups ($p < 0.001$). Mean diameters of both the DTA and the DAA had a significantly strong positive correlation to age and there were significant differences between age groups ($p < 0.001$). There was a strong positive correlation between age and tortuosity ($p < 0.001$). A tortuous c-shaped-curve was found only in the DAA in 8.2 % of the whole study sample, with a 7:1 male to female ratio.

Conclusion
The dimensions and tortuosity prevalence of the descending aorta differ between sexes and vary significantly with age. The results obtained from this study may be informative in the clinical setting for aortic disease management.

Specificity of preparing the chest X-rays reference dataset with pulmonary nodules for artificial intelligence assessments

Yulia Busygina
Russia

Introduction
Artificial intelligence(AI) is finding applications in healthcare, especially in radiology. However, to resolve the issue of the advisability of allowing AI algorithms into clinical practice, it is necessary to investigate the average diagnostic accuracy of radiologists. Chest X-rays(CXR) are one of the most common studies in radiology, which can detect pulmonary nodules. In which differential diagnosis with lung malignancies, including lung cancer, is required. We aimed to prepare a reference dataset for CXR with and without pulmonary nodules confirmed by chest CT.

Material & Methods
Out of all radiological examinations performed in Moscow from 2020 to 2022 using a time delta filtering code(CXR and chest CT were made in 14 days inclusive) and filtering for keywords in the "Impression" section("Consultation of an oncologist", etc.) were received study pairs(CXR and CT). Then they were manually assessed for the textual "Impression" section. An image review of 103 pairs of studies was conducted, according to the Glossary of Fleischner Society "pulmonary nodule", and 50 CXR were obtained that met the conditions. To balance the dataset, 50 CXR without pathology were added(25 "mild" norm(no changes) and 25 "complex" norm(changes that simulated pathology, with confirmation of the absence of pathological changes on the chest CT). Ethics committee approved.

Results
A total of 203 study pairs were selected and reviewed by 3 radiologists. As a result of the review, 100 CXR studies were selected, of which 50 with pathological changes(lung nodules): more than 6 mm, but less than 30 mm, located in the lung parenchyma; and 50 studies without pathological changes.

Conclusion
This dataset will help evaluate the diagnostic accuracy of radiologists(target pathology – "pulmonary nodules"), as well as AI algorithms participating in the Experiment(mosmed.ai). The peculiarity of the study was the division of CXR with no pathology into mild and complex(according to radiologists).
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The effect of antiatherosclerotic therapies on plaque vulnerability in CEUS assessment

Karol Stępniak
Poland

Introduction
In carotid ultrasound, a standard parameter evaluating the risk of ischemic stroke is the degree of stenosis. However, atherosclerotic plaque that does not cause hemodynamic changes can also cause a stroke. Intraplaque neovascularization and surface ulceration are features associated with plaque vulnerability and symptomatic disease. Contrast-enhanced ultrasound (CEUS) is a technique that allows accurate assessment of the surface of plaque and its neovascularization by injecting contrast media. The study aimed to evaluate the effect of antiatherosclerotic therapies on plaque vulnerability in CEUS assessment.

Material & Methods
The prospective study included 21 patients having carotid ultrasound examinations. Inclusion criteria were echolucent atherosclerotic plaque (Type 1-2 Gray Weale scale) with a thickness >2.5 mm. 24 suitable plaques were identified and evaluated in terms of echogenicity, location, and degree of stenosis. Subsequently, SonoVue (Bracco, Italy) contrast was administered intravenously as a 1.5 mL bolus flushed with 10 mL of 0.9% saline. CEUS evaluation was performed in longitudinal and/or transverse scans. From the moment of appearance of contrast in the carotid artery, the atherosclerotic plaque was assessed for contrast enhancement and surface area. The examination was performed with a Mindray Resona I9. Patients had a medical history taken in terms of the medications they were taking. Statins, antiplatelet drugs, and renin- angiotensin- system-acting agents were included in the analysis.

Results
Among the investigated plaques 10 were uniformly echolucent (type 1) and 14 were predominately echolucent (type 2). Eccentric plaques were found in 15 cases and concentric in 9. The localization of plaques was common carotid artery (14) and internal carotid artery (10). In 6 cases the plaque did not show any contrast enchantment, in 14 it was weakly enhanced and in 4 cases significant enhancement was found. The ulcerated surface was found in 6 plaques, in 9 cases the plaque surface had irregularities and the remaining 9 plaques were smooth. There were no statistically significant differences in intraplaque enhancement as well as surface changes dependent on antiatherosclerotic medications taken (p>0.05).

Conclusion
CEUS provides valuable information indicating the vulnerability of atherosclerotic plaque. However, there was no effect of the antiatherosclerotic drugs used on the characteristics of atherosclerotic plaques.

Vascular characterization of the pig lung as a healthy model to study the vasculature of lung cancer.

Maryelit Castro-González
Colombia

Introduction

Knowledge about vascular adaptation to cancer contributes to developing strategies for its treatment. Since it is not possible to obtain healthy human pulmonary arteries to assess the pathophysiology of vascular adaptation, we propose to characterize pig pulmonary arteries as a healthy model to be compared with human arteries that supply lung cancer. We have studies showing that the pig is better than other animal models to compare with the function of human mesenteric arteries in colon cancer. We are extending these studies to lung cancer.

Material & Methods

In organ bath, vascular reactivity (-VR- maximum effect "Emax"; sensitivity, "pD2") of porcine pulmonary arteries to contractile agonists and vasodilators was measured. The contractile response is normalized to a response to 40 mM KCl (% KCl). Hematoxylin-eosin staining was performed. In addition $\alpha 1$, $\beta 2$ and thromboxane-prostanoid (TP) receptors are quantified by fluorescence microscopy in each tunic.

Results

RV: KCl (Emax: $131.4\pm35\%$KCl; pD2: 1.52 ± 0.08), epinephrine (Emax: $96.7\pm11\%$KCl and PD2: 5.78 ± 0.09), ET- 1 (Emax: $74.12\pm16\%$KCl and pD2: 5.74 ± 0.06), bradykinin (Emax $116.1\pm11\%$ and pD2: 7.18 ± 0.09), sodium nitroprusside (Emax: $71.09\pm5\%$ and pD2: 5.64 ± 0.1), carbachol (Emax: $68.17\pm18.85\%$KCl; pD2: $6.00\pm0.3\%$), Isoproterenol (Emax: 57, $42\pm12.24\%$KCl; pD2: $6.59\pm0.42\%$) and U46619 (Emax: $120.6\pm15.11\%$KCl; pD2: $6.07\pm0.56\%$). Preliminary human pulmonary VR results would also be shown. In receptor expression, pig arteries differ from human arteries only in the tunica media for $\alpha 1$ (human intima: 1 ± 0.08, median: 1 ± 0.18; adventitia: 1 ± 0.17; intima of pig: 1.27 ± 0.15, mean: 1.5 ± 0.3, adventitia: 1.36 ± 0.2, p=0.001) and $\beta 2$ (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: $1.13\pm0, 14$, adventitia: 1.07 ± 0.11).

Conclusion

The complete characterization of the porcine artery will be presented, and eventually a comparison with arteries from patients with lung cancer. This characterization is the basis for identifying mechanisms affected by cancer and could serve as a model for evaluating drugs.
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Miscelleanous II

M I
S C

Presenters:
Pratyush Kumar
Omid Reza Tamtaji
Youssef   Soliman
Eva Kicker
Dhruv Vajipayajula
Akriti Kumari Gupta
Fereshteh Asgharzadeh
André Almeida
Eduardo Villa
Jakob Schäfer

A novel prognostic scoring system combining the revised Tokuhashi Score and the New England Spinal Metastasis Score for spinal metastases

Dionisia Mavritsakis
Ireland

Introduction

Numerous scoring systems have been developed in order to determine the prognosis of spinal metastases. Predicting as accurately as possible the life expectancy of patients with spinal metastatic disease is very important, as it is the decisive factor in selecting the most optimal treatment for the patient. The Revised Tokuhashi score (RTS) and the New England Spinal Metastasis score (NESMS) are popular scoring systems used to determine the optimal treatment modality. However, they sometimes provide conflicting results. We propose a novel prognostic scoring system, which combines the (RTS) and the (NESMS) to predict with greater accuracy the prognosis.

Material & Methods

We retrospectively reviewed the data of 64 patients with spinal metastasis enrolled between 2012 and 2021 in the Department of Orthopedic Surgery-Spine, Hôpital Maisonneuve-Rosemont, Montréal, Que. The new score per patient was then calculated as a combination of the RTS of each patient and the patient's corresponding NESMS score and then compared to the actual patient survival period in order to assess its adequacy in predicting the survival of patients with spinal metastases. The patients were divided into three groups: Low, Moderate or Good Prognosis.

Results

In the Low Prognosis group, the reliability of predicting the prognosis was 55.6% in 27 patients. In the Moderate Prognosis group, the reliability of predicting the prognosis was 95.8% in 24 patients. In the Good Prognosis group, the reliability of predicting the prognosis was 100% in 13 patients.

Conclusion

This study demonstrates that a new prognostic scoring system, which would combine the RTS and the NESMS, is promising in providing an improved accuracy for predicting the actual patient survival especially for the moderate and good prognosis patients. An appropriate prospective investigation with a larger sample size should be conducted to further investigate the validity of this novel scoring system and its overall predictive value.

Optogenetic tool kindling Pyroptosis in glioma through Calcium / Caspase-1/GSDMD pathway

Ruicheng Fan
China

Introduction

Glioma accounts for over 40 per cent of cancers in central neural system. Due to the lack of effective therapy, the median survival time of Glioblastoma multiforme (GBM) is less than one and a half years. Therefore, it is upon urgent request to discover a new way of treatment against GBM. Pyroptosis, a programmed cell death, has the characteristics of cell swelling and membrane pore formation. Recent studies have suggested that Pyroptosis might exert a negative impact on the vitality of GBM. Blue light sensitive protein LOV2 is a widely used optogenetic tools which modifies its structure when exposed to 470 nm blue light. By combining LOV2 with a calcium channel protein STIM1, it could be realized to switch on calcium channel and cause Pyroptosis in GBM cells with blue light stimulation (BLS).

Material & Methods

Human GBM cell lines U87, U118 and normal astrocytes cell line HA1800; immune deficiency nude mice; plasmid with LOV2-STIM1-mCherry; cell counting kit-8; Matrigel; DMEM cell cultivation medium; fetal bovine serum (FBS); antibodies of STIM1/cleavage Caspase-1/GSDMD-N terminal; fluorescence probes of calcium and reactive oxygen species (ROS).

Results

LOV2-STIM1 as an optogenetic tool was established in GBM cell lines and normal astrocytes cell line. After blue light stimulation, the proliferation, migration and metastasis ability of GBM cells crucially receded yet astrocytes remained a physiological standard. Similarly, the tumor size of xenograft in nude mice critically reduced by receiving blue light stimulation, compared to that of control group. The elevation of intracellular calcium, ROS and Pyroptosis related protein was also observed using flow cytometry and western blot.

Conclusion

Blue light stimulation could induce elevation of calcium and ROS, upregulation of Pyroptosis related protein Caspase-1/GSDMD in GBM cells. Pyroptosis caused by optogenetic tool in our study has negative effects on GBM both in vitro and in vivo, thus offers a potential therapeutic approach for GBM patients.

Music as an adjunct cost-effective therapeutic innovation for Management of Pain in Trauma Patients: A Systematic Review and Meta-analysis

Pratyush Kumar
India

Introduction

Music therapy reduces pain perceived, alleviates mood and promotes relaxation, regular breathing and rest. Being a readily available and inexpensive therapy, its efficacy for Management of Chronic Pain, such as that experienced by Trauma patients needs further exploration in low resource settings.

Material & Methods

PubMed (n=175), Trip Medical Database (n=278) and ClinicalTrials.Gov (n=28) were searched for 'Trauma', 'Music' & 'Pain'. Studies identified from inception were imported to EndNote X9 Library and duplicates removed. Only completed RCTs (Pubmed; n-16, TMD; n=2, CT.Gov; n=6) were screened using Title, Abstract and full text (n=41). Data extracted from 12 studies, was analyzed in Review Manager 5.4.

Results

Due to significant heterogeneity (Chi^2 = 365.17, P < 0.00001; I^2 = 97%), inverse variance random effect meta-analysis was done. Scores of the various pain measurement scales from a total of 852 patients from 12 studies revealed a pooled Standard Mean Difference of 0.31 [-0.61, 1.22]. Test for overall effect Z = 0.66 (P = 0.51) indicates that there is no significant difference in pain outcomes between Music Adjuvant therapy (MAT) Vs. Conventional Analgesic care. Subgroup analysis reveals a significant favor [Z = 1.18 (P = 0.24)] to MAT in patients of non-malignant pain of traumatic origin while in burn trauma patients it has no significant benefit [Z = 2.23 (P = 0.03)]. Similarly, as per pooled evidence, MAT is highly effective in the pediatric age group [Z = 1.00 (P = 0.32)] while no significant benefit in the adult age group [Z = 1.11 (P = 0.27)].

Conclusion

The pooled evidence suggests that both interventions significantly improve pain outcomes but Music therapy does not have any significant benefit over conventional therapy when compared as a whole. Evidence from the meta analysis indicates high efficacy of MAT in children while non such benefit can be proven in adult age group.

Neuroprotective effects of probiotics mixture on memory function and oxidative stress in 6- hydroxydopamine- induced Parkinson's disease rat model

Omid Reza Tamtaji
Iran

Introduction
Parkinson's disease (PD), the second most common neurodegenerative disorder, is characterized by selective loss of substantia nigra pars compacta (SNpc) dopaminergic neurons and accumulation of α-synuclein and ubiquitin in Lewy bodies, which are intracytoplasmic inclusions. The involvement of oxidative stress and dysbiosis in PD has been confirmed, and probiotics also have the ability to regulate the aforementioned mechanisms. Here, we studied the effects of probiotic supplementation on the experimental model of Parkinson's disease

Material & Methods
Thirty male Wistar rats were divided into three groups for a 14-day treatment. Probiotic group (pretreated with oral administration of probiotics followed by injection of 6 µg 6-OHDA dissolved in 2µL 0.2% saline with ascorbic acid into the right SNpc), Parkinson's disease group (oral administration of distilled water followed by injection of 6 µg 6-OHDA dissolved in 2µL 0.2% saline with ascorbic acid into the right SNpc) and sham group (oral administration of distilled water followed by injection of 2µL 0.2% saline with ascorbic acid into the right SNpc) groups. The probiotic mixture consisted of Lactobacillus acidophilus, Lactobacillus reuteri, Bifidobacterium bifidum and Lactobacillus fermentum. Then, a PD model was induced in rats by injection of 6-hydroxydopamine (6-OHDA). After 7 days, spatial memory and rotational behavior were assessed using the Morris water maze and apomorphine tests, respectively. In addition, lipid peroxidation and neuronal damage were assessed by the reactive thiobarbituric acid (TBARS) method and Nissl staining, respectively.

Results
Treatment with probiotics significantly prevented the increase in the number of contralateral rotations in the apomorphine test ($P < 0001$). In addition, administration of probiotics resulted in a decrease in escape latency and an increase in time spent in the target quadrant compared with PD rats in the Morris water maze test ($P < 0.0001$). Moreover, administration of probiotics resulted in a decrease in midbrain MDA levels ($P=0.026$). In the probiotic group, the number of damaged neurons after injection of 6-OHDA was significantly lower than in the PD group ($P=0.009$).

Conclusion
Taken together, Our findings revealed a neuroprotective effect of probiotics supplement against PD.

Efficacy of silver nanoparticles containing sulfasalazine on colitis

Fereshteh Asgharzadeh
Iran

Introduction
Ulcerative colitis (UC) is an inflammatory disease with a high incidence globally. The conventional treatment for UC includes sulfasalazine, used to control the pathogenic complication of the inflammatory and immune responses, although this is not very effective. To overcome the side effects and improve the therapeutic outcomes, novel therapeutic agents are warranted. Silver nanoparticles have been found to have potent therapeutic and anti-inflammatory properties in the management of inflammatory diseases

Material & Methods
The therapeutic potency of silver nanoparticles containing sulfasalazine (SSZ-AgNPs) was investigated by assessing a pathological score, histological staining and real time PCR methods in DSS- induced colitis in a murine model.

Results
SSZ-AgNPs was found to improve the disease activity index, colon shortening and body weight loss. SSZAgNPs was also found to reduce histopathological evidence of injury, by reducing inflammatory responses in colonic tissues. Additionally, treatment with SSZ-AgNPs resulted in downregulation of pro-fibrotic and proinflammatory factors such as: Col 1a1, Col 1a2, TNF-α, and INF-γ.

Conclusion
In our preclinical study we found evidence for the anti-inflammatory and anti-fibrotic activity of SSZAgNPs as a potential therapeutic

Molecular interference with SARS-CoV-2 replication by the antiviral peptide TAT-I24

Eva Kicker
Austria

Introduction
The recent SARS-CoV-2 pandemic highlights the urgent medical need for antiviral therapeutics in addition to an immunisation with vaccines. At the moment, only a few safe and effective antivirals are available for the treatment of v infections. Experimental peptides might be a future treatment option, as these peptides can act as entry-inhibitors that block or alter virus entry into the cell. The peptide TAT-I24, composed of I24, a 9-mer that inhibits gene expression from "foreign"- nucleic acids, might be such a candidate. This 9-mer sequence is linked to a TAT-peptide (residue 48-60 from HIV transactivator protein). This residue facilitates cell penetration and supports the transport of I24 into the cytosol in parallel with virus capsids. In this study, interactions of TAT-I24 with SARS- CoV-2 virus replication are investigated.

Material & Methods
In-vitro neutralization assays in VeroE6 cells were used to study the interaction of TAT-I24 as viral replication interfering substance with SARS-CoV-2 virus variants (Wuhan, Delta, Omicron). Experimental read-out was dual: qRT-PCR & specific staining (Anti-SARS-CoV-2 and Anti-TAT). Viral copy numbers were determined from supernatants, genomic and subgenomic SARS-CoV-2 transcripts from cell lysates.

Results
In previous studies, TAT-I24 has shown a broad range antiviral activity against DNA viruses, but also an inhibitory effect against the RNA virus SARS-CoV-2 could be observed in recent in-vitro neutralization experiments (unpublished data). We observed a dose dependant reduction of virus particles in the presence of TAT-I24 in VeroE6 cells when infected with SARS-CoV-2, although differences in the sensitivity to the peptide was observed for individual virus variants (Wuhan, Delta, Omicron). Considering differences on viral gene expression levels, preliminary data suggest a delayed assembly of virus particles and a reduced release, when cells are infected in the presence of TAT-I24.

Conclusion
TAT-I24 has interfering activity, the definite mode of action is not yet clear. Further evaluation of the effects on host gene expression as well as intracellular localization and virus uptake studies (virus and peptide specific antibody staining) are currently ongoing. In addition, air-liquid interface cultures with human alveolar cells are planned as in-vitro models to mimic a possible future therapeutic target region.

Evaluation of Signaling Events by Activated Protein C Cleavage of Protease Activated Receptor 1 on Human Platelets.

Dhruv Vajipayajula
United States

Introduction

Activated Protein C (APC) regulates blood coagulation by cleaving cofactors in the coagulation cascade. APC can cleave the Protease Activated Receptor (PAR1) on endothelial cells – this elicits cytoprotective effects and protection from endothelial dysfunction. Thrombin, another protease involved in coagulation cleaves PAR1 at a different site than APC, resulting in pro-inflammatory cellular responses. Although PAR1 is also expressed in human platelets, it is shown that platelets are not activated by APC, in contrast to marked activation by Thrombin.

Material & Methods

Here, we seek to investigate differences in APC/PAR1 mediated signaling in human platelets. A tethered peptide TR47 based on the cleavage site of PAR1 by APC has been designed and shown to cause similar effects as APC on endothelial cells. We investigated whether the tethered peptide causes platelet activation and triggers signaling events in human platelets. Platelet activation was traced through Born Aggregometry, and precipitated proteins were analyzed by Western blotting.
SFLLRN, another tethered peptide mimicking the action of Thrombin on PAR1, was used as a control agonist.

Results

SFLLRN caused human platelet aggregation, ADP secretion, and downstream signaling events such as ERK phosphorylation. TR47, on the other hand, did not cause any platelet activation, nor was ERK phosphorylation observed.

Conclusion

These preliminary results suggest that other factors or pathways in endothelial cells might contribute to cytoprotective signaling events and mitigation of dysfunction. It is reaffirmed that APC and Thrombin elicit different PAR1-mediated responses in human platelets as well. We anticipate finding evidence that TR47 might be working on other proteins to cause signaling events and protection from endothelial dysfunction, which is the target for further study

Health-Promoting lifestyle among elderly and their association with social capital and sense of coherence

Akriti Kumari Gupta
India

Introduction

With demographic change, the proportion of elderly in the population is increasing rapidly. With this, the health-promoting lifestyle practices among the elderly become very important to maintain and improve their quality of life. Health-promoting activities seek to strengthen the host through a variety of approaches in the form of health education, lifestyle modification, behaviour change, environment modification and nutrition intervention. The present study aimed to assess the health promoting lifestyle practices among the elderly and to understand its relationship with social capital and sense of coherence among the elderly.

Material & Methods

A cross section study was done in the nearby village of the medical college of Central India. The study was conducted among 123 participants above 65 years of age. Their Health Promoting Lifestyle Profile (HPLP), Sense of Coherence (SoC) and Social Capital was analysed using standard questionnaires via interviews and the score data were analysed using Pearson's product moment correlation, and also multiple linear regression analysis.

Results

Mean HPLP, SoC and Social Capital scores were 50.8 ± 5.4, 45.7 ± 11.1 and 18.2 ± 6.2 respectively. The scores on the HPLP II subscales of interpersonal relations and spiritual growth (65.3 ± 9.0 and 62.0 ± 7.7 respectively) was high and for stress management it was moderate (56.9 ± 7.4), while for health responsibility and nutrition it was low (47.2 ± 8.3 and 43.7 ± 7.6 respectively) and for physical activity it was very low (27.7 ± 4.2). Correlation coefficient of HPLP total lifestyle score was positively correlated with the Social capital score ($r=0.521$) and with the Sense of Coherence score ($r=0.241$).

Conclusion

There is a huge gap in understanding the lifestyle practices of the elderly and the factors which affect it. Less years of schooling, poverty, female sex, presence of chronic illness -adds as important additional factors leading to poor health promoting lifestyle practices. A better social capital of the elderly will lead to better health promoting lifestyle practices and is likely to improve the quality of life and happiness of the older adults.

Efficacy of silver nanoparticles containing sulfasalazine on colitis

Fereshteh Asgharzadeh
Iran

Introduction
Ulcerative colitis (UC) is an inflammatory disease with a high incidence globally. The conventional treatment for UC includes sulfasalazine, used to control the pathogenic complication of the inflammatory and immune responses, although this is not very effective. To overcome the side effects and improve the therapeutic outcomes, novel therapeutic agents are warranted. Silver nanoparticles have been found to have potent therapeutic and anti-inflammatory properties in the management of inflammatory diseases

Material & Methods
The therapeutic potency of silver nanoparticles containing sulfasalazine (SSZ-AgNPs) was investigated by assessing a pathological score, histological staining and real time PCR methods in DSS- induced colitis in a murine model.

Results
SSZ-AgNPs was found to improve the disease activity index, colon shortening and body weight loss. SSZAgNPs was also found to reduce histopathological evidence of injury, by reducing inflammatory responses in colonic tissues. Additionally, treatment with SSZ-AgNPs resulted in downregulation of pro-fibrotic and proinflammatory factors such as: Col 1a1, Col 1a2, TNF-α, and INF-γ.

Conclusion
In our preclinical study we found evidence for the anti-inflammatory and anti-fibrotic activity of SSZAgNPs as a potential therapeutic agent, and further investigations in clinical studies are warranted.

Anti-HLA sensitization is not associated with an increased risk of acute rejection among kindney transplant recipients without donor- specific antibodies

André Almeida
Brasil

Introduction

For many decades, anti-HLA sensitization has been recognized as a marker of immunological risk for kidney transplant recipients (KTRs). However, after the broad use of solid phase assays to identify anti-HLA antibodies, the risk stratification throughout calculated anti-HLA panel reactive antibody (cPRA) in KTRs in the absence of preformed donor-specific antibody (DSA) has been questioned. Thus, this study aimed to evaluate the impact of the cPRA on clinical outcomes of KTRs with no preformed DSA.

Material & Methods

Single-center cohort study enrolling sensitized (cPRA≠0) KTRs with no preformed DSA transplanted between 2015-19 (n=486). The primary outcome was biopsy-proven acute rejection (BPAR), while the secondary was 1-yr graft function (GFR, CKD-Epi). Multivariable analysis for BPAR was performed by Cox regression, and the cPRA performance to predict BPAR was estimated by the area under ROC (AU-ROC).

Results

All KTRs received a 3 mg/kg single-dose of thymoglobulin and steroids, followed by tacrolimus and mycophenolate (TAC+MPS) in 70.4%. There were no differences in KRTs characteristics regarding cPRA >0-50% (n=287), >50-80% (n=121), and >80% (n=78) strata, respectively, excepting frequency of females (48 vs. 76 vs. 78%, p<0.001) and retransplantation (10.8 vs. 17.4 vs. 32.1, p<0.001), time on dialysis (36 vs. 34 vs. 58 months, p=0.001), the frequency of zero MM in the HLA locus A (22 vs. 28.9 vs. 41.0%, p=0.009), B (19.2 vs. 25.6 vs. 42.3%, p<0.001), and DR (71.7 vs.
83.5 vs. 91.0%, p=0.001), and the frequency of TAC+MPS use (58.9 vs. 88.4 vs. 84.6, p<0.001). The overall incidence of BPAR was 11.5%, similar in the three cPRA strata: 10.5 vs. 12.4 vs. 14.1% (p=0.63). In a multivariable Cox regression, the BPAR was not associated with the higher cPRA strata, nor when included as a linear independent variable. The cPRA AUC-ROC to predict 1-yr-BPAR was 0.53 (95%CI= 0.46-0.45; p=0.46). The 1-yr-GFR was similar in the three cPRA strata: 48.4 vs. 43.8 vs. 46 mL/min/1.73m2 (p=0.23).

Conclusion

Among sensitized KTRs in the absence of preformed anti-HLA DSA, the level of sensitization assessed by cPRA was not associated with the risk of BPAR or a lower 1-yr-GFR.

Postscripts

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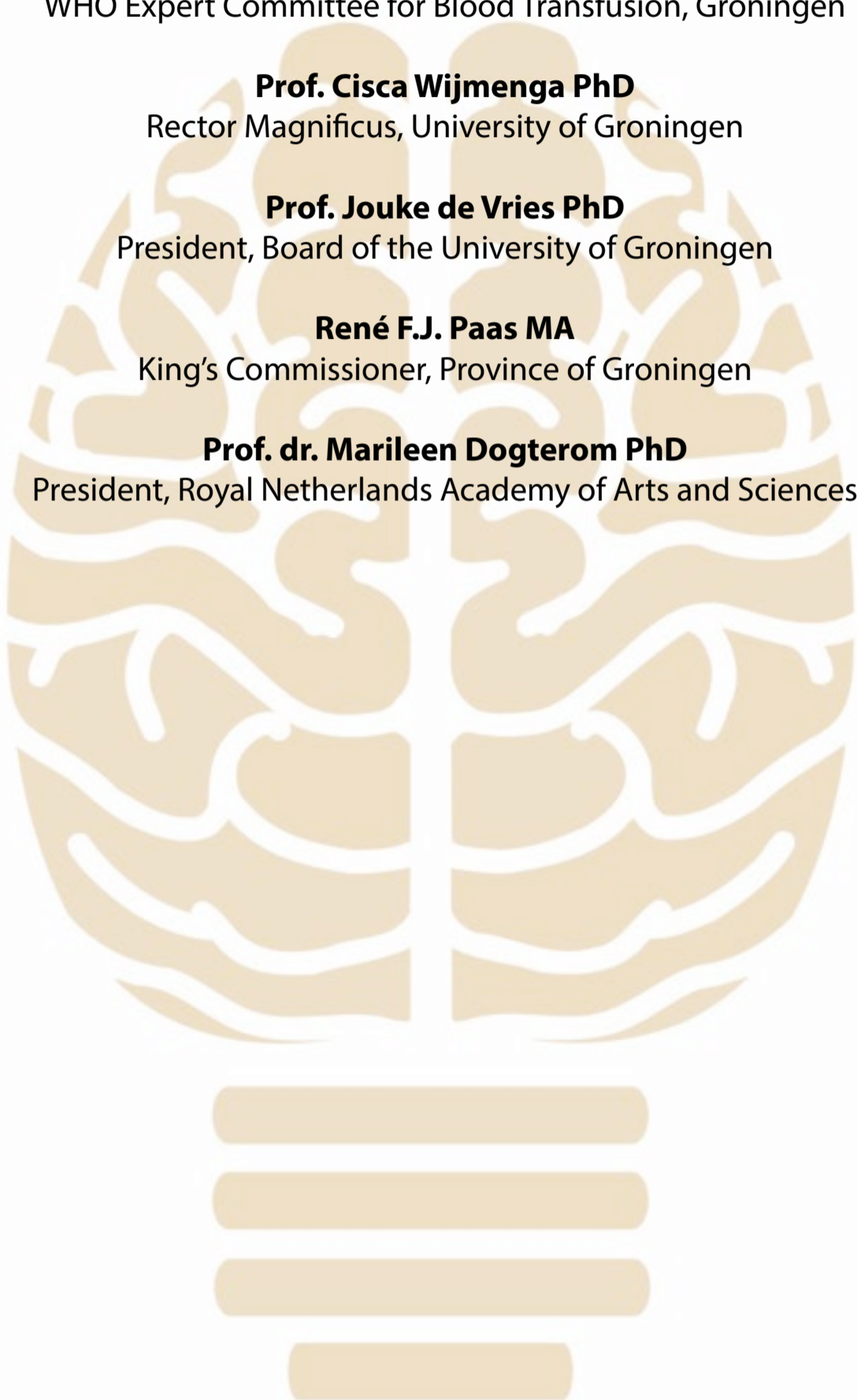
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Huntington's disease: fascinating insights in a fascinating disease
Prof. Berry Kremer MD PhD
Chairman Dept. of Neurology at UMCG

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.