BOOK OF ABSTRACTS

LIMSC 2025

May 14th-17th 2025
Leiden, The Netherlands

WELCOME TO LIMSC 2025

LIMSC

Leiden International (Bio) Medical Student Conference

CONTACT

ADDRESS

LEIDEN UNIVERSITY
MEDICAL CENTER
ALBINUSDREEF 2
2333 ZA LEIDEN
THE NETHERLANDS

POSTAL ADDRESS

M.F.L.S. FOR THE
ATTENDANCE OF LIMSC
K1-69
PO BOX 9600
2300 RC LEIDEN

SOCIALS

WWW.LIMSC.NL

LIMSC@LUMC.NL

INSTA: LIMSC.LEIDEN
FACEBOOK:
LIMSC.LEIDEN

LINKEDIN: LIMSC

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PREFACE

LIAM HUIZINGA

Dear participant of LIMSC,

It is a great honour to welcome you to Leiden for the fourteenth edition of the Leiden International (Bio)Medical Student Conference (LIMSC).

With the slogan 'Key to the Future', we want to present you the options for your future during the conference. Our scientific programme, consisting of guest lectures, oral presentations, poster presentations and workshops, gives you the opportunity to enrich your knowledge and to gain various new insights into the scientific research of today. Along side to our scientific program, LIMSC offers an extensive social programme, that gives you the opportunity to get in touch with fellow future doctors and researchers.

The slogan 'Key to the Future' finds its origin in the coat-of-arms of the city of Leiden, that consists of two red keys in an X-shape. Because of this, Leiden is often referred to as the 'Sleutelstad' (City of Keys). Another nickname for Leiden is 'the city of discoveries'. The founding of the Leiden University 450 years ago was the beginning of the era of discoveries in Leiden. During LIMSC and in Leiden, we hope you discover a passion, a friendship or a little bit more about yourself, as others in your position have done so themselves. At the venue of LIMSC, the Leiden University Medical Centre (LUMC), a considerable amount of discoveries have been done. Together, the internationally oriented Leiden University and the highly inventive LUMC are the perfect combination for a enriching global student conference.

Eighteen months ago, the Organising Committee started with the preparations for the fourteenth edition of LIMSC. One year later we were joined in our effort by the Head Crew. Together we've been an incredible journey, that would not have been possible without the tremendous effort of each committee member. I would like to take this opportunity to express my gratitude to the LUMC, Medical Faculty for Leiden Students, Committee of Recommendation, Advisory Committee, Scientific Committee, and Crew for their excessive support.

With great pride, we present to you: LIMSC 2025. I wish you all an inspirational and educational conference. Make sure to enjoy the coming few days to their fullest, and use all opportunities while you discover your keys to the future!

On behalf of the 14th LIMSC Organising Committee,
Liam Huizinga
President

LIAM HUIZINGA
PRESIDENT OF LIMSC

PREFACE

JEROEN KORSMIT

Dear Participant of LIMSC,
Welcome to the fourteenth edition of the Leiden International (Bio)Medical Student Conference!

It is an honor to formally welcome you to the Leiden University Medical Center (LUMC). We are excited for the upcoming days, filled with stimulating lectures, groundbreaking research, and engaging activities. The entire Organizing Committee (OC) and Head Crew (HC) have dedicated considerable effort to bring you an exceptional program, and we are thrilled to present it to you.

The LIMSC OC is a committee of the Medical Faculty for Leiden Students (M.F.L.S.), the student association of LUMC since 1912. Representing 3,500 members, we advocate for students' interests in education and organize a wide range of recreational activities. We are proud to host LIMSC for the fourteenth time and hope to inspire and connect with you throughout the event.

What makes LIMSC particularly special is the diversity of individuals who attend the conference. We firmly believe that diversity promotes knowledge, and that we can all benefit from each other's experiences and expertise. This conference features pioneering research, renowned guest speakers, and, above all, talented participants. We encourage you to take full advantage of this unique opportunity to connect with one another.

Lastly, I would like to express my gratitude to the Executive Board of LUMC for their continued collaboration, hard work, and trust. I would also like to extend my thanks to the entire LIMSC OC and HC for their hard work, we are very proud of your efforts.

On behalf of the 112th M.F.L.S. Board, I wish you an exciting, inspiring, and enjoyable time at LIMSC, in Leiden, and in the Netherlands.

Jeroen Korsmit
President M.F.L.S. Board 2024-2025

JEROEN KORSMIT
PRESIDENT OF M.F.L.S.

PREFACE

MARLIES REINDERS

Dear students,

It is with great pleasure that we warmly welcome you to the Leiden International (Bio)Medical Student Conference 2025. This event unites passionate students in medicine, biomedical sciences, pharmacy and clinical technology. This event will also offer you a unique opportunity to come together with experts and peers from around the world, who will inspire and challenge us in the pursuit of knowledge, innovation, and progress in our field of life sciences & health.

The importance of international collaboration cannot be overstated in a time when medical challenges are becoming increasingly complex. Our society is confronted with numerous health issues that cannot be solved by one country or region alone. Sharing knowledge, experiences and best practices is essential for developing effective solutions that have a global impact. This year's International Congress is dedicated to the power of AI, sharing innovative research results and understanding the relevance of academic medical centre's as a motor in the public-private collaboration with partners of the Leiden Bio Science Park. For you as students this congress presents a golden opportunity to not only learn about the latest developments but also to network with fellow students, professionals, and researchers from various countries. It is a chance to broaden our horizons, gain new insights, and perhaps even initiate international collaborations that will enrich our careers as future health professionals. We are proud to offer a platform for this invaluable exchange of ideas and knowledge.

We also want to take a moment to express our gratitude to the many speakers, organizers, and volunteers who have made this congress possible. Thanks to their dedication, time, and energy, we are able to come together and learn from some of the most prominent scientists and doctors in the field. Without their commitment, this event would not have been possible.

Over the next few days, we have assembled a diverse program, featuring a groundbreaking symposium on AI, renowned guest speakers, and a diverse array of stimulating workshops. Additionally, the scientific program provides excellent networking opportunities, including a tour of the Leiden Bio Science Park, visits to various LUMC departments and a Career & Internship Fair. Each program part promises to be engaging, innovative, and of great significance to the future of our profession.

Finally, we also want to emphasize that this congress is not just an academic event, but an opportunity for the community of medical students to come together, engage in discussions, and learn from one another. The strength of a student association lies in the bond we share and the way we support and challenge each other to bring out the best in ourselves.

We hope that you will find as much inspiration and enjoyment from this congress as we have had in organizing it. Let us face the challenges of medicine together and seize the opportunities that lie ahead.
On behalf of the organizers of the LIMSC, we wish you an inspiring and enriching experience.

Sincerely,
Marlies Reinders
Member of the board of LUMC / dean

MARLIES REINDERS
DEAN

PREFACE

HESTER BIJL

Freedom

First of all, I would like to extend a warm welcome to this conference to all who have travelled to our university from all over the world. We appreciate you coming and we are happy to do everything we can to make your trip worthwhile.

Here in Leiden we have been studying and researching for centuries under the motto Praesidium Libertatis, which means Stronghold of Freedom. After all, science always benefits from a diversity of views, which must be able to be exchanged in complete freedom. We are happy to offer that opportunity during this thirteenth edition of the Leiden International (Bio)Medical Student Conference.

I wish you a congress with interesting encounters, inspiration and perhaps new connections or - judging by the experience of previous participants - even friendships for life. I would like to remind you in this context of the words of the great Hippocrates:

Wherever the art of medicine is loved, there is also a love of humanity.

May you these days, in complete freedom, enrich each other's minds and find recognition in your shared love for humanity in general and for (bio)medical sciences in particular.

I hope that this unique collection with the latest insights from this field will find a place in your bookshelf, and will remind you of these inspiring days in our midst for a long time to come.

Prof.dr.ir. H. Bijl
Rector Magnificus of Leiden University

HESTER BIJL
RECTOR MAGNIFICUS

PARTNERS

ICoMS

MSC

ISCOMS
science beyond borders

ICCIMS
INTERNATIONAL STUDENT CONGRESS ON CLINICAL INNOVATION AND MEDICAL SCIENCES

MOSA 2025
MAASTRICHT | HASSELT

International Stroke Conference

iMED
CONFERENCE® 16.0

Lodz, POLAND
www.jpm.umed.pl

SKY MEETING
SURGICAL KNOWLEDGE FOR YOUTH

29th European Congress of Obstetrics and Gynaecology (EBCOG)

5–7 June 2025
Congress Center and Forum, Messe Frankfurt
Frankfurt am Main, Germany

PARTNERS


الجمعية السعودية لأمراض الروماتيزم
SSR
Saudi Society Of Rheumatology


ICMS
FOR STUDENTS
& YOUNG DOCTORS


MoKe
MED


AIMS
MEETING


LISSC


NeuRi
Student Congress
of Neuroscience


ICHAMS
International Conference for Healthcare and Medical Students


Plexus


CROSS

ORGANIZATION

ORGANIZING COMMITTEE

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Dylan Verfuurt
Treasurer and vice-president

Eric Cheung
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Friso Mulder
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2023-2024

Isabel Kollen
Board member
2023-2024

Jeroen Korsmit
Board member
2024-2025

Wouter Jalink
Board member
2024-2025

HEAD CREW

Hello everyone,

We are the Head Crew of LIMSC, and over the past few months, we have had the privilege to help organise the Leiden International (bio)Medical Student Conference. Together with the Organising Committee, it has been an amazing - and sometimes challenging - experience.

As a team of six, each of us took on a different role. Fleur was in charge of all administrative matters surrounding LIMSC. Benthe worked closely with the Treasurer and helped organise the C&I Fair. Rayan planned the social events where participants can connect, share ideas and experience Dutch culture.Tijmen focused on the scientific programme, including our amazing guest speakers and workshops. Xiao Xiao was responsible for creating the Book of Abstracts. And Celine managed the planning and logistics before and during LIMSC.

It has been an amazing journey so far, and we are looking forward to meeting all of you soon!

Kind regards,

Fleur Slot, Benthe Geuns, Rayan El Badmoussi, Tijmen Stalenberg, Xiao Xiao Huijbers and Celine Pham
Head Crew of LIMSC 2025

HEAD CREW LIMSC 2025

FLEUR SLOT - SECRETARY
BENTHE GEUNS - FINANCE
TIJMEN STALENBERG - SCIENTIFIC PROGRAM
RAYAN EL BADMOUSSI - SOCIAL PROGRAM
XIAO XIAO HUIJBERS - PR&DESIGN
CELINE PHAM - LOGISTICS

COMITTEE OF RECOMMANDATIONS

The Committee of Recommendation consists of four outstanding people with broad scientific networks. They are convinced of the importance of international student conferences like LIMSC.

Prof.dr.ir. H. Bijl
Rector Magnificus Leiden University

Prof.mr. C.J.J.M. Stolker
Former Rector Magnificus

P. Heijkoop
Mayor of Leiden

Dr. A.M.J. Langers
Vice-Dean of LUMC

ADVISORY COMMITTEE

The Advisory Committee consists of 7 professors of the LUMC, working in different fields, but all very enthusiastic about LIMSC. They function as ambassadors of LIMSC in the LUMC. The Advisory Committee has an active role in helping the Organising Committee to make LIMSC a success, by giving advice about guest speakers and organisation. Furthermore, they play an active role in the promotion of LIMSC.

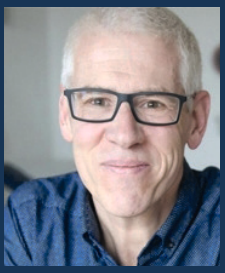
Prof. dr. Reinders
Dean of LUMC

Prof.dr. Vleggeert-Lankamp
Neuro surgeon

Prof. dr. Goumans
Department of cell- and chemical biology

Prof. dr. Van den Dobbelsteen
Professor in Medical Process Engineering and education director KT

Prof. dr. Swen
Professor clinical pharmacology



Prof. dr. Steendijk
Professor cardiovascular fysiology

SCIENTIFIC COMMITTEE

ACADEMIC PHARMACOLOGY

- Prof.dr. van Gelder
- Dr. M. van der Lee
- Prof.dr. J.J. Swen

CANCER

- Dr. P.J.K. Kuppen
- Dr. J. van der Hage
- Dr. Roeland Dirks

CARDIOVASCULAR

- Prof.dr. P.H.A. Quax
- Prof.dr. A.J van Zonneveld
- Dr. N. Ajmone Marsan

IMMUNITY

- Prof.dr. R. Arens
- Prof.dr. A.J. Lankester
- Prof.dr. C. van Kooten

INFECTION

- Dr. W. J. Hoepel
- Prof.dr. M. Yazdanbakhsh
- Dr. B. Everts

HEALTH, AGEING & SOCIETY

- Prof.dr. S. Mooijaart
- Prof.dr. J. Gussekloo
- Prof.dr. W.P. Achterberg

The Scientific Committee is a group of prominent professors, clinicians and researchers that supports the Organising Committee in the process of selecting the abstracts, after an initial evaluation by the Organising Committee.

MEDICAL GENOMICS

Prof.dr. D.J.M. Peters

Prof.dr. G.W.E. Santen

PREVENTION & LIFESTYLE

Prof.dr. H. Vos

Dr. J. de Wilde

BIOMEDICAL IMAGING

Prof.dr.ir. B.P.F. Lelieveldt

Prof.dr. L.F. de Geus-Oei

Prof.dr. S.A.R.B. Rombouts

Dr. H.E. Kan

NEUROSCIENCE

Dr. R. Fronczek

Prof.dr. A.M.J.M. Maagdenberg

Prof.dr. G.J. Lammers

REGENERATIVE MEDICINE

Prof.dr. I. Meulenbelt

Prof.dr. I.P.J. Alwayn

MEDICAL TECHNOLOGY

Prof.dr. J. van den Dobbelsteen

Prof.dr. D.E. Atsma

Prof. J. Dankelman

PROGRAM

SCHEDULE

MAY 14

10:30-12:30 MUSEUM TOUR
NATURALIS BIODIVERSITY CENTER

14:00-16:00 AI SYMPOSIUM
CZ6-LUMC EDUCATION BUILDING

21:00-00:00 PUB CRAWL
LEIDEN CITY CENTRE

MAY 15

8:00-15:00 REGISTRATION DESK
FOYER LUMC EDUCATION BUILDING

9:00-9:30 OPENING
BOERHAVEPLEIN-LUMC HOSPITAL

9:30-10:30 GUESTSPEAKER 1
CZ1-LUMC HOSPITAL

10:30-10:45 WORKSHOPS
DIVERS

12:30-13:45 LUNCH
BOERHAVEPLEIN-LUMC HOSP

14:00-15:00 POSTER PRESENTATION AND
ORAL SESSION 1
DIVERS

15.15-16:15 GUEST SPEAKER 2
CZ1-LUMC HOSPITAL

16:30-17:30 POSTER PRESENTATION AND
ORAL SESSION 2
DIVERS

17:45-18:45 OFFICIAL RECEPTION
FOYER LUMC EDUCATION BUILDING

19:30-23:00 LIMSC FESTIVAL
NATIONAL MUSEUM OF ANTIQUITIES

SCHEDULE

MAY 16

8:30-15:00 REGISTRATION DESK
FOYER-LUMC EDUCATION BUILDING

9:00-9:30 OPENING
CZ6-LUMC EDUCATION BUILDING

9:30-10:30 POSTER PRESENTATION AND ORAL SESSION - DIVERS

10:30-10:45 COFFEE
FOYER-LUMC EDUCATION BUILDING

11:00-12:15 WORKSHOP 2
DIVERS

12:30-14:15 LUNCH/C&I FAIR
BOERHAVEPLEIN-LUMC HOSPITAL

14:30-15:30 GUESTSPEAKER 3
CZ6-LUMC EDUCATION BUILDING

15:45-16:45 GUESTSPEAKER 4
CZ6-LUMC EDUCATION BUILDING

17:00-18:00 POSTER PRESENTATION AND ORAL SESSION - DIVERS

19:30-22:30 BLACK TIE DINNER
THE FACULTY CLUB - LEIDEN ACADEMY BUILDING

MAY 17

8:30-15:00 REGISTRATION DESK
FOYER-LUMC EDUCATION BUILDING

9:00-9:30 OPENING
CZ6-LUMC EDUCATION BUILDING

9:30-10:30 COFFEE
FOYER-LUMC EDUCATION BUILDING

11:00-12.15 WORKSHOP 3
DIVERS

12:30-13:45 LUNCH
BOERHAAVEPLEIN-LUMC HOSPITAL

14:00-15:00 POSTER PRESENTATION AND ORAL SESSION 5
DIVERS

15:15-16:15 POSTER PRESENTATION AND ORAL SESSION 6
DIVERS

16:30-17:30 DRINKS & SNACKS
FOYER-LUMC EDUCATION BUILDING

17:45-18:45 AWARDS & CLOSING CEREMONRY
CZ6-LUMC EDUCATION BUILDING

22:00-00:00 PARTY
TBD

GUEST SPEAKER

PROF. ANDRIES VAN DER MEER

Prof. Dr. Andries van der Meer is Full Professor of Microphysiological Systems at the University of Twente, The Netherlands. Van der Meer is the president of the European Organ-on-Chip Society (EUROoCS). He also served as chair of the Focus Group on Standardization for Organ-on-Chip of the European standardization body CEN CENELEC. He is a leading international proponent of standards-driven innovation in the field of organs-on-chips. Before joining the University of Twente in 2015, Dr. Van der Meer worked as a Senior Research Fellow at Harvard Medical School and the Wyss Institute of Harvard University, Cambridge, MA, USA. He has a PhD (University of Twente, 2010), and a MSc in Biology (University of Groningen, 2005). Organs-on-chips are advanced tissue culture models that can mimic organ-level functionality in a controlled, dynamic microsystem. They differ from other cell culture models in that they use microenvironment engineering to capture increasingly complex physiological functions. In the past years it has been shown that organs-on-chips can provide accurate and relevant data for preclinical studies, thereby potentially reducing the time and cost of drug development and clinical trials. Moreover, with their unique combination of person-specific human cells and high-level tissue function, organs-on-chips challenge the strong reliance on animal models in life sciences.

In this talk, Prof. Van der Meer of the University of Twente will provide examples of how organs-on-chips can be used to study drugs, taken from his group's work on vessels-on-chips, heart-on-chip and retina-on-chip. Moreover, he will address the central challenge in the field: how far can we push the realism of organ-on-chip models and how will we maximize their impact?

GUEST SPEAKER

PROF. DAME MOLLY STEVENS

Professor Dame Molly Stevens DBE FRS FREng is the John Black Professor of Bionanoscience at the University of Oxford and a part-time professor at Imperial College London and the Karolinska Institute. Molly's multidisciplinary research balances the investigation of fundamental science with the development of technology to address some of the major healthcare challenges. She is a serial entrepreneur and the founder of several companies in the diagnostics, advanced therapeutics, and regenerative medicine fields. Her work has been instrumental in elucidating bio-material interfaces. She has created a broad portfolio of designer biomaterials for applications in disease diagnostics and regenerative medicine. Her substantial body of work influences research groups around the world and she has been multiple times listed as Clarivate Analytics Highly Cited Researcher in Cross-Field research.

Molly holds numerous leadership positions, Deputy Director of the Kavli Institute for Nanoscience Discovery, Deputy Director of the UK Quantum Biomedical Sensing Research Hub, and Scientist Trustee of the National Gallery. She is a Fellow of the Royal Society and the Royal Academy of Engineering (UK), a Foreign Member of the National Academy of Engineering (USA), an International Honorary Member of the American Academy of Arts and Sciences, and she was recognised with the 2023 Novo Nordisk Prize and the 2024 Royal Society Armourers and Brasiers Company Prize, amongst many other accolades.

GUEST SPEAKER

PROF. KYPROS NICOLAIDES

Kypros Nicolaides, Professor of Fetal Medicine. Director of the Research Centre for Fetal Medicine of King's College Hospital and Founder and Chairman of the Fetal Medicine Foundation. He has been honoured with highest awards of excellence from many national and international professional bodies, including the Eardley Holland Gold Medal of the RCOG, International Society Ultrasound in Obstetrics & Gynaecology, National Grand Cross of the Order of Makarios III from the Republic of Cyprus, Gold Cross of The Order of the Phoenix from the Republic of Greece.

He is an elected member of the National Academy of Medicine (USA) and the recipient of Honorary Doctorates in Medicine from 14 Universities across the world. He published over 1600 peer-review papers in Scientific Journals.

GUEST SPEAKER

PROF. MICHELE DIANA

Prof. Michele Diana, MD, Ph.D, EMBA, obtained the Medical Degree in Rome, Italy, and specialized in General Surgery in Switzerland. He obtained a Ph.D in Medical Sciences and received the Venia Legendi at the University of Strasbourg (France). A

dditionally, he holds an Executive Master in Business Administration from INSEAD Business School. He is faculty member of leading scholar surgical societies, including the SAGES, the European Association of Endoscopic Surgery (EAES), the International Society of Fluorescence Guided Surgery (ISFGS) and the International Society of Medical Innovation and Technology (iSMIT). His main translational research interests include image-guided surgery, surgical robotics and surgical applications of machine and deep learning. He has authored more than 250 peer-reviewed papers and book chapters (h-index 47).

Current position(s) & affiliations:

- Director of Surgical Innovation, Geneva University Hospital, Switzerland
- Invited Professor, University of Geneva Medical School, Switzerland
- Faculty, ICube Lab, Photonics for Health, Strasbourg, France

Founder and Chief Medical Officer at ASTRANICE, Strasbourg, France

GUEST SPEAKER

MAX HODAK

Max Hodak is the founder and CEO of Science Corporation, a clinical stage medical device and neural engineering company developing advanced brain-computer interfaces and other technology applications for a range of unmet patient needs. Science Corporation is headquartered in the San Francisco Bay area, with additional offices in the Raleigh Durham Research Triangle and in Paris, France.

Max's training is in biomedical engineering and his primary research and professional focus for almost 20 years, beginning before college, has been on neural engineering and brain-computer interfaces.

Max was a cofounder of Neuralink, where he served as President from its inception through early 2021, helping to develop advanced brain-computer interfaces and other technology applications. Before Neuralink, he helped start Transcriptic, a robotic cloud laboratory for the life sciences, where he was CEO for the first five years.

Max believes that one of the essential goals of our generation is to understand the physics of consciousness and learn to engineer experience directly – a founding principle of the company.

In this Keynote Lecutre, Max will talk about "The Future of Neural Engineering."

WORKSHOPS

ANIMAL TESTING FACILITY

Curious about the role of animal research in medical advancements? Join us for an exclusive workshop at the LUMC Animal Testing Facility during LIMSC 2025. This session offers a behind-the-scenes look at how laboratory animals contribute to cutting-edge biomedical research. Learn about ethical considerations and how researchers ensure the highest standards of animal welfare. Engage in discussions with experts and gain insights into the future of biomedical research.

BENEATH THE WHITE COAT

Doctors and medical students frequently face mental health challenges, including burnout, anxiety, trauma, addiction, and depression. Despite these struggles, barriers such as stigma, time constraints, and fear of professional repercussions often prevent them from seeking the care they need. At LUMC Curium (department of child and adolescent psychiatry of the Leiden University Medical Center), we conducted a qualitative interview study with ten doctors who sought treatment at ArreA, a specialized mental health clinic for medical professionals in the Netherlands. The study focused on three key areas: 1) the factors contributing to mental health challenges among doctors, 2) their unique treatment needs, and 3) how their experiences with mental illness and recovery impact their professional functioning. Thematic analysis showed that Doctors' mental health challenges were shaped by workplace culture, high responsibility, emotional detachment, and lack of self-care. Hierarchical structures and a culture discouraging vulnerability further exacerbated these issues. Doctors reported benefiting most from non-verbal therapy, group sessions with other healthcare professionals, and specialized care with attention for the doctor identity. Recovery journeys increased empathy toward patients, enhanced emotional awareness, and encouraged self-care practices

EXPERIENCING AGEING

Are you curious about the challenges and opportunities of ageing in modern society? Join the master's program Health, Ageing, and Society for an engaging workshop during the LIMSC days hosted by MFLS in Leiden.

In this interactive session, you will:
Explore thought-provoking statements related to ageing and societal perceptions of older individuals.
Participate in a hands-on demonstration to experience what it feels like to grow older, using tools that simulate physical and sensory changes associated with ageing.
Discuss the implications of ageing on healthcare, policy, and daily life, guided by the themes of our courses

WORKSHOPS

EXOSKELETON PROJECT MARCH

As Project MARCH (Motor Assisted Robotic Chassis for Humans), we have the vision that we can improve the quality of life for people with paraplegia by using exoskeleton technology. An exoskeleton is a motorized robotic harness which enables people with paraplegia to stand up and walk again. Project MARCH develops a new exoskeleton each year. We want to stimulate the technological innovation of exoskeletons by developing a new exoskeleton each year, whilst always challenging ourselves to think of new solutions.
Project MARCH is a non-profit student team. Our team consists of people from various backgrounds and years of studies. All of us set aside our studies for a year, in order to fully commit ourselves to the development of an all-around and user-friendly exoskeleton. Project MARCH is located in the Dream Hall on the TU Delft campus. The Dream Hall strives to an ecosystem around robotics which attracts the best researchers, multinationals, and startups and through that plays a progressive role in the development of the next generation of robotics.

FORENSIC MEDICINE

Step into the world of forensic medicine and discover the intricate process of post-mortem examination. This hands-on workshop delves into the principles of forensic death investigation, guiding participants through the methods used to determine cause and manner of death. Led by an experienced forensic expert, you will explore and reveal the story hidden within the body.

MASTERING ORGAN PERFUSION

Have you ever wondered how organs are kept alive outside the body during transport for transplantation? In this immersive workshop, you will work with a pig kidney to explore the fascinating world of organ perfusion. From cannulating and flushing the kidney to assembling and priming a functional perfusion setup, you will dive into the mechanics of organ preservation. Guided by our hospital's experts, you and your team will take on the challenge of creating a fully operational system.

ORTHOPEDIC SURGERY - GAMMA NAIL FIXATION

Step into the fascinating world of Orthopaedic Surgery with this hands-on workshop, where you will explore the intricacies of fracture management using the cutting-edge Gamma Nail technique. Combining surgical precision with engineering innovation, this session offers a unique opportunity to delve into the mechanics and clinical impact of intramedullary fixation. Explore the science behind the tools and witness how advanced techniques are transforming orthopaedic trauma care.

WORKSHOPS

PERSONALIZED MEDICINE IN ACADEMIC PHARMACY

Step into the future of healthcare with our Personalized Medicine Workshop, hosted by the Department of Academic Pharmacy. During this hands-on session, you'll get an exclusive look at your own DNA and compare it with your classmates'! Learn how genetics influence drug responses and explore how personalized medicine is revolutionizing treatments

SIMULATOR SESSIONS ANESTHESIOLOGY

This workshop combines an interactive lecture by an expert specialist with a hands-on session in the state-of-the-art simulation centre at the Skillslab of LUMC. Dive into a real-time anesthesiology case simulation, designed to refine your skills and decision-making in a realistic environment.

SPINE SURGERY

Have you ever wanted to know what it feels like to be a neurosurgeon? In this workshop you get the opportunity to perform a spine surgery together with one of the neurosurgeons from the LUMC

TOUR OF ANATOMICAL MUSEUM

On this tour, you will explore the Anatomical Museum of Leiden, the winner of the European Museum of the Year Award 2009. The museum showcases fascinating artifacts spanning over 450 years of the Leiden Medical Faculty's history.

VIRTUAL REALITY IN THORACIC SURGERY

An increasing number of applications are available to study medicine or biomedical sciences in Virtual Reality (VR) or Augmented Reality (AR). At LUMC we developed multiple VR apps to aid medical education. In this workshop, you will experience a VR application as an educational tool for thoracic surgery.

WORKSHOPS

AMBOSS

Medical doctors from AMBOSS, the leading medical learning platform, will host an informative and interactive workshop for medical students to find out how to study smarter and score higher. Designed and curated by over 70 international physicians, AMBOSS uses intelligent learning features to guide students and physicians through their medical careers. Explore the AMBOSS platform, including the comprehensive Library with over 1,400 articles and the Qbank with over 9,000 clinical case-based questions

LAPAROSCOPY AND SUTURING

Surgical precision begins with practice. This workshop provides a unique opportunity to develop essential laparoscopic and suturing skills in a hands-on setting. Under expert guidance, you will work with real surgical instruments and practice essential techniques for the operating room. Experience what it takes to perform delicate procedures with accuracy and control.

MASTERING ORGAN PERFUSION

Have you ever wondered how organs are kept alive outside the body during transport for transplantation? In this immersive workshop, you will work with a pig kidney to explore the fascinating world of organ perfusion. From cannulating and flushing the kidney to assembling and priming a functional perfusion setup, you will dive into the mechanics of organ preservation. Guided by our hospital's experts, you and your team will take on the challenge of creating a fully operational system.

ROBOTIC SURGERY WITH DA VINCI ROBOT

Discover the future of surgery in this hands-on workshop featuring the Da Vinci Surgical System and image-guided techniques. Learn how robotic assistance enhances precision, practice basic controls, and explore how real-time imaging improves surgical accuracy.

SURGICAL NAVIGATION IN ROBOTIC SURGEY

In this surgical navigation workshop, you will explore cutting-edge technology that enhances precision and outcomes in orthopedic procedures. This workshop will provide an in-depth understanding of how surgical navigation systems assist surgeons in planning, guiding, and executing complex surgeries with greater accuracy. Participants will gain hands-on experience with advanced navigation tools, learn about their benefits in improving patient safety, and discuss the latest advancements shaping the future of orthopedic surgery.

WORKSHOPS

TOUR OF THE 7-TESLA ULTRA LOW FIELD MRI SCANNERS

MRI is an important diagnostic tool, as it can non-invasively image different parts of the body. The strong 7-Tesla MRI of the Gorter Center provides many new opportunities, both in terms of diagnostic power as in technical developments. On the other side, new ultralow-field MRI-scanners are bringing unprecedented flexibility at low cost to the clinical setting. At the Gorter Center, we are building such a low-field MRI-system. In this workshop, we will first present some of the frontiers of the research in MRI, followed by a demo of the 7-Tesla and the low-field MRIs.

ANATOMICAL PREPARATION/DISSECTION

Embark on an extraordinary journey into human anatomy in this hands-on workshop, led by the esteemed professors of anatomy from the LUMC. Held in the Dissecting Laboratory of the LUMC, this experience offers you the rare opportunity to work with real human anatomical preparations. Guided by experts, you will gain unparalleled insights into the intricacies of the human body, exploring its structures in a setting designed for advanced learning and discovery. This is a unique chance to deepen your understanding of anatomy like never before!

MASS DISASTER VICTIM IDENTIFICATION THE DUTHC APPROACH

Join us for an eye-opening and impactful workshop on Mass Disaster Identification! This is your chance to gain hands-on experience, learn from top experts, and play a crucial role in disaster response. This workshop will equip you with essential skills to help bring closure to families in times of crisis.

ARTIFICIAL INTELLIGENCE IN BRONCHOSCOPY

In this workshop on Artificial Intelligence in Bronchoscopy, innovation meets clinical precision. In this session, we will explore how cutting-edge AI technologies are transforming the landscape of pulmonary medicine, by enhancing diagnostic accuracy, streamlining procedures, and shaping the future of bronchoscopic interventions.

WORKSHOPS

EPIDEMIOLOGY AND STATISTICS IN RESEARCH

Discover how epidemiology and statistics shape biomedical research! This workshop covers study designs, data analysis, and key methods to interpret results accurately, essential for evidence-based research in medicine and life sciences.

CHIPS ON ORGANS - WIRELESS POWER TRANSFER

Join us for an exciting workshop on Wireless Power Transfer (WPT), a groundbreaking technology used to power optogenetic implants. The session will begin with an introduction to WPT and how it is applied to energy supply in advanced medical devices. Afterward, you will have the opportunity to dive into hands-on work, where they will collaborate in groups to build a simplified version of a WPT-powered implant. This workshop offers a unique chance to explore cutting-edge technology and gain practical experience in a rapidly advancing field.

EMERGENCY MEDICINE

Don’t miss the hands-on workshop on ABCDE assessment in an emergency setting. This session will provide an in-depth exploration of the ABCDE approach, a critical framework for prioritizing patient care during emergencies. You will work through realistic clinical scenarios, applying the ABCDE principles to assess and manage patients in a fast-paced environment. It’s a great opportunity to sharpen your practical skills and enhance your ability to make quick, life-saving decisions under pressure.

FETAL MEDICINE

Presentation on fetal therapy, including a demonstration and the opportunity to practice with the digital laser. To conclude, a demonstration of placental injection by Prof. Lopriore.

MICROSCOPY

Pathologists look under the microscope daily to find life-saving discoveries. Here you will learn important microscopy skills that will help you along the way in medical school.

WORKSHOPS

MICROSCOPY

Pathologists look under the microscope daily to find life-saving discoveries. Here you will learn important microscopy skills that will help you along the way in medical school.

FERTILITY PROBLEMS AMONG FEMALE MEDICAL SPECIALISTS

Fertility problems can deeply impact the lives and careers of medical professionals, yet it's a topic often surrounded by silence. In this interactive workshop, we will explore fertility issues specifically among doctors. Together, we will break down the challenges, share insights, reflect on the history of how we ended up in today's system and look for solutions to better support ourselves and each other.
What will we discuss?
Open discussion in a safe environment
Analysis of the personal and systemic factors involved
Building awareness and resilience within the medical community

WORKSHOPS

DAY 1	DAY 2	DAY 3
ANIMAL TESTING FACILITY	AMBOSS	ANATOMICAL PREPERATION
BENEATH THE WHITE COAT	BENEATH THE WHITE COAT	BENEATH THE WHITE COAT
EXOSKELETON PROJECT MARCH	EXOSKELETON PROJECT MARCHT	MASS DISASTER VICTIM IDENTIFICATION
EXPERIENCING AGEING	EXPERIENCING AGEING	MASTERING ORGAN PERFUSION
FORENSIC MEDICINE	LAPAROSCOPY AND SUTURING	TOUR ANATOMICAL MUSEUM
MASTERING ORGAN PERFUSION	MASTERING ORGAN PERFUSION	VIRTUAL REALITY IN THORACIC SURGERY
ORTHOPAEDIC SURGERY GAMMA NAIL FIXATION	PERSONALIZED MEDICINE IN ACADEMIC PHARMACY	FERTILITY PROBLEMS AMONG SPECIALISTS
PERSONALIZED MEDICINE IN ACADEMIC PHARMACY	ROBOTIC SURGERY DA VINCI ROBOT	
SIMULATOR SESSIONS ANESTHESIOLOGY	SIMULATOR SESSIONS ANESTHESIOLOGY	
SPINE SURGEY	SURGICAL NAVIGATION - ORTHOPEDIC SURGERY	
VIRTUAL REALITY IN THORACIC SURGERY	TOUR 7-TESLA AND MRI SCANNER	
ARTIFICIAL INTELLIGENCE IN BRONCHOSCOPY	EMERGENCY MEDICINE	
EPIDEMIOLOGY & STATISTICS IN RESEARCH	VIRTUAL REALITY IN THORACIC SURGERY	
	CHIPS ON ORGANS - WIRELESS POWER TRANSFER	
	FETAL MEDICINE	

SOCIAL PROGRAM

NATURALIS MUSEUM TOUR

On Wednesday, participants are invited to explore the renowned Naturalis Biodiversity Center. Discover awe-inspiring exhibits on evolution, dinosaurs, and the incredible diversity of life on Earth. As the first event of the conference, this visit offers a perfect opportunity to get acquainted with Leiden's Bioscience Park and start making meaningful connections with fellow attendees in a unique museum setting.

PUBCRAWL

Get to know Leiden by night during the LIMSC Pubcrawl on Wednesday evening! Hop between some of the city's most iconic bars with fellow participants and experience the vibrant student atmosphere Leiden is known for. Whether you're in the mood for dancing or just a casual drink and chat, Leiden's student pubs have it all.

LIMSC FESTIVAL

Join us on Thursday for the LIMSC Festival, a lively evening dedicated to discovering Dutch culture. Enjoy hands-on workshops including blind tastings of classic Dutch snacks, a crash course in the Dutch language, and traditional games. The evening begins with dinner at Wooping, a beloved local Chinese restaurant, and continues at the stunning Rijksmuseum van Oudheden — a historic gem in the heart of Leiden, home to one of the Netherlands' most impressive archaeological collections.

BLACK TIE DINNER

The Black Tie Dinner will be held on Friday evening at the Faculty Club of the Academy building, Leiden's oldest and most stunning university building, dating back to 1516. It promises to be a unique event, in which a fine dining experience is brought to you in a truly exceptional setting, where you will get to spend time getting to know fellow participants.

SOCIAL PROGRAM

CLOSING PARTY

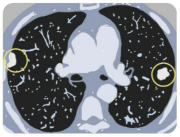
Celebrate the end of an inspiring conference week at the LIMSC Closing Party on Saturday night, together with your new friends! Join us for an unforgettable evening filled with music and dancing, featuring sounds from all around the world.

RESEARCH THEMES

Academic Pharma

Cancer

Cardio vascular



(Bio)Medical Imaging

Immunity

Infection

Life- Course

Medical genomics

Medical Technology

Neuroscience

Prevention & Lifestyle

Regenerative Medicine

ACADEMIC PHARMACOLOGY

Effect of hydroalcoholic extract of clover plant on insulin secretion from pancreatic beta cell line

N. Goodarzi[1]

[1]Ahvaz Jundishapur University of Medical Sciences

Introduction: Herbal medicines are one of the best options used to treat diabetes. Trifolium pratense (T. pratense) has been suggested in traditional medicine to treat some diseases such as cough, asthma and eczema. The aim of this study is to investigate the protective effects of pratense hydroalcoholic extract on the toxicity caused by streptozotocin (STZ), which is a diabetes-inducing drug, and insulin secretion from RIN 5F pancreatic beta cells.

Methods: The possible protective effect of T pratense extract was evaluated by using pre-treatment program, simultaneous treatment and post-treatment against STZ with a concentration of 25 mM using MTT test. The effect of the extract on insulin secretion in low and high glucose concentrations was investigated. Data were analyzed using one-way ANOVA statistical test and 0.05 was considered significant

Results: The survival results of RIN 5F cells in doses of 5, 10, 15, 20 and 30 µg/ml of T pratense extract showed a significant increase compared to the control group (p=0.001). T. pratense extract at doses of 10, 15, and 20 µg/ml had a significant protective effect (p=0.01) on STZ toxicity, and this effect is greater in simultaneous treatment. Treatment with T. pratense extract also increased insulin concentration in the cell culture medium.

Conclusion: T. pratense has anti-diabetic properties and protective function by increasing cell viability and increasing insulin secretion.

Key words: Insulin, Extract

Preparation and Characterization of Thermo-Sensitive In Situ Gel Nano-Emulsion of Antiviral Agent for Ocular Drug Delivery

Z. Mansouri[1], M.M Mahboobian[1]

[1]Hamadan University of Medical Sciences, Hamadan, Iran

Introduction: Ocular herpes simplex infection is a major cause of visual morbidity worldwide. It may be treated by acyclovir (ACV); however, the bioavailability of ACV to the ophthalmic epithelium is low. ACV in the form of an ophthalmic ointment must be applied every 4 hours. The aim of this study is to prepare an in situ gel nano-emulsion (NE) of ACV as an ocular drug delivery system to improve its bioavailability and enhance pre-corneal residence time.

Methods: The solubility of ACV in various components was measured. Based on the solubility results, pseudo-ternary phase diagrams were developed using oil (triacetin), surfactant (poloxamer 188, poloxamer 407), and co-surfactant (transcutol P). These diagrams were constructed at different surfactant/co-surfactant weight ratios (1:1, 2:1, 1:2) using the water titration method. Oil-in-water (O/W) NEs of ACV were prepared by the spontaneous emulsification method. The gelation temperature, at which the physical state of the NEs changed, was determined. Based on initial release studies, formulations with the slowest release characteristics underwent further physicochemical investigations, including particle size, polydispersity index, pH, refractive index, osmolality, and viscosity. Accelerated stability tests were conducted, including heating-cooling cycles, freeze-thaw cycles, and centrifugation. The optimized formulation was selected for excised bovine corneal permeation studies, hen's egg test-chorioallantoic membrane (HET-CAM), and modified Draize tests to evaluate ocular permeation and irritation.

Results: The optimized in situ gel NE formulations exhibited a sustained release pattern compared to the marketed product. Particle size analysis showed that all samples were in the nanometric range (below 100 nm) with a suitable polydispersity index. Physicochemical evaluations, including pH, refractive index, osmolality, and viscosity, demonstrated that all formulations were acceptable for ophthalmic use. Stability studies confirmed no physical instabilities, such as creaming, cracking, or phase separation. Permeation studies revealed that drug permeation from the optimized formulation was approximately 2.8 times higher than the control solution. Irritation tests indicated that the optimized in situ gel NE was well tolerated by the eye.

Conclusion: The results demonstrated that the in situ gel NE formulation provided a superior alternative to ophthalmic ointments by enhancing bioavailability and prolonging pre-corneal residence time for ACV.

Investigating the effect of sertraline consumption in pregnant rats on the development of the lungs of newborns.

M.H. Amnieh1, A.F. Marvast[1]

[1]Department of Toxicology and Pharmacology, School of Pharmacy and Pharmaceutical Sciences, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.

Introduction: Antidepressant use is common during pregnancy, with selective serotonin reuptake inhibitors (SSRIs) being the major medicines used to treat depression disorder. Sertraline (Zoloft), is one of the most frequently used SSRIs in this regard. This study was designed to assess the histopathological impacts of sertraline exposure on the pulmonary development of fetal rats.

Methods: In this investigation, 20 virgin adult Wistar breed rats were employed. To aid in mating, each female rat was housed with a male for a day and night. Upon the observation of vaginal plaques confirming pregnancy, the rats were separated into two groups of ten using a randomized table. From the onset of pregnancy until delivery, the treated group received 21 mg/kg Zoloft (Pfizer Sertraline) once daily via gavage, with a gavage volume of 5 ml. The second group, serving as the negative control, received a daily gavage of 5 ml of distilled water. Immediately following birth, three neonatal rats from each group (totaling 60 rat neonates) underwent anesthesia and surgical procedures. Subsequently, the left lung of each neonate was excised and stained with Hematoxylin and Eosin for histological evaluation.

Results: When compared to the control group, the mean values of neonatal parameters such as the number of offspring, body weight, lung weight, kidney weight, heart weight, count of bronchioles and vessels, inner diameter of the terminal bronchus, and inner diameter of the respiratory bronchus were significantly lower in the sertraline-exposed group. Conversely, the average internal diameter of vessels, muscular thickness of vessels, odonticia, bronchi, bronchial wall, and alveolar sac wall were significantly elevated in the sertraline group in comparison to the control group.

Conclusion: Sertraline therapy shows a considerable effect on lung development in newborn rats. It also creates anatomical and functional abnormalities in the pulmonary systems of the newborns. This study highlights the need for consideration regarding the use of sertraline to minimize adverse effects on fetal lung development.

Keywords: Sertraline, lung development, SSRI, Pregnancy, Rat model, Histopathological effect

Protective Effects of Dapsone on Acute Aluminum Phosphide Toxicity: A Preclinical Study

F. Bargharary[1], Y.A.T Ahmaditabatabaei[1], A Maleki[1], A. Dehpour[1], R. Mohammad Jafari[1]

[1]Tehran University of Medical Sciences

Introduction: Aluminum phosphide (ALP), commonly known as "rice tablet" in Iran, is a highly toxic pesticide that causes severe acute poisoning. Upon exposure to moisture or stomach acid, ALP releases phosphine gas (PH3), a mitochondrial toxin that induces oxidative stress, cellular apoptosis, and multi-organ failure. Dapsone, an antibiotic with potent anti-inflammatory and antioxidant properties, has shown potential in mitigating oxidative damage and restoring cellular homeostasis. This study investigates the protective effects of dapsone against acute ALP toxicity in male rats.

Methods: A total of 72 male Albino Wistar rats (180–250 g) were divided into six groups: control, ALP(12 mg/kg) only, and ALP + dapsone at doses of 1, 3, 10, 20 mg/kg. ALP toxicity was induced via oral gavage at the LD50 dose(12 mg/kg), while dapsone was administered intraperitoneally(IP) one hour post-ALP exposure. ECG parameters (QRS, QT, ST segments), oxidative stress markers (ROS, MDA), and antioxidant enzyme activities (SOD, CAT, GPx) were assessed. Statistical analysis was conducted using one-way ANOVA followed by Tukey's post hoc test.

Results: Dapsone significantly reduced oxidative stress markers (ROS, MDA) and improved antioxidant enzyme activities in a dose-dependent manner. At 10 mg/kg, dapsone restored ECG parameters, reduced cardiac arrhythmias, and attenuated myocardial damage compared to the ALP-only group. Histopathological analysis revealed reduced necrosis and apoptosis in cardiac tissues treated with dapsone.

Conclusion: This study highlights dapsone's therapeutic potential in mitigating acute ALP toxicity by reducing oxidative damage, improving cardiac function, and attenuating cellular apoptosis. These findings pave the way for further preclinical and clinical investigations into dapsone's role in managing ALP poisoning.

Keywords: Aluminum phosphide, dapsone, oxidative stress, ECG, antioxidant enzymes, apoptosis

Ascorbic Acid Reduces the Blood Boss After Total Knee Arthroplasty: Insights from a Randomized Controlled Trial

P. Hosseini-Monfared[1], A. Mirahmadi[1], S.M Kazemi[1]

[1]Bone Joint and Related Tissues Research Center, Shahid Beheshti University of Medical Sciences

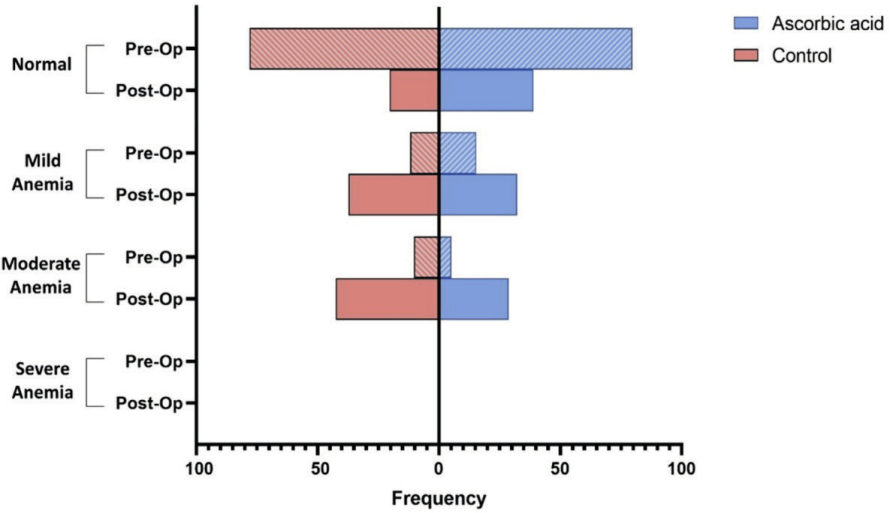
Introduction: Blood loss is among the main complications of total knee arthroplasty (TKA) and oxidative stress, and hemolysis caused by reactive oxygen species (ROS) are one of the causes of hemoglobin (Hb) drop. Ascorbic acid is a potent antioxidant that can protect against ROS. In this study, we aim to explore the antioxidant effect of ascorbic acid on blood loss and patientreported outcomes following outpatient TKA.

Methods: Patients scheduled for outpatient primary TKA were enrolled in this randomized, double-blind clinical trial and were assigned to one of the two groups. The patients in the ascorbic acid group received intravenous vitamin C perioperatively. Patients in the placebo group received only normal saline. We calculated the blood loss using the Hb drop. Patient-reported outcomes such as Oxford Knee Score, WOMAC, KOOS, and FJS were used to evaluate the postoperative pain and function in the six-month follow-up.

Results: After considering the exclusion criteria, 118 patients were included in this study, 59 in each group. The two groups' demographic features, preoperative Hb level, and functional scores did not show any statistically significant difference (p-values>0.05). The patients who have received ascorbic acid had lower Hb drop (g/dL) (p-value<0.001) and total blood loss in the first postoperative day (p-value<0.001). None of the patients in our study required a blood transfusion. Fewer patients who received ascorbic acid reached the minimum clinically important difference (MCID) for Hb drop (2 g/dL) than patients in the control group (15.3% compared to 52.5%, p-value<0.001). Furthermore, the continuous fragility index (CFI) of the Hb drop and TBL were 18 and 19 respectively. Ascorbic acid reduced the incidence of postoperative anemia, and multivariate logistic regression analysis demonstrated that being male, having lower preoperative Hb, and not using ascorbic acid were associated with an increased likelihood of postoperative anemia.

Conclusion: Our findings demonstrated that perioperative use of ascorbic acid can reduce blood loss by nearly 36% on the first postoperative day and should be considered as an effective bloodpreserving agent in conjunction with tranexamic acid during TKA.

Keywords: Blood Loss, Antioxidants, Total Knee Arthroplasty, Ascorbic Acid


Ascorbic acid
Control
Normal
Pre-Op
Post-Op
Mild Anemia
Pre-Op
Post-Op
Moderate Anemia
Pre-Op
Post-Op
Severe Anemia
Pre-Op
Post-Op
100
50
0
50
100
Frequency

Effectiveness of Sublingual Immunotherapy in Reducing Asthma Severity in Allergic Patients.

A. Falahati Marvast[1]

[1]Shahid Sadoughi University of Medical Sciences, Yazd, Iran

Introduction: Asthma associated with allergic sensitization remains a major public health concern. Sublingual immunotherapy (SLIT) has gained attention as a non-invasive approach to desensitize patients to allergens and improve respiratory function. However, its long-term efficacy in asthma control needs further investigation.This study evaluates the effectiveness of SLIT in reducing asthma severity and medication dependency in patients with allergic asthma over a 24-month period.

Methods: A total of 250 patients with moderate allergic asthma, confirmed by skin prick tests and elevated specific IgE levels, were enrolled in a randomized controlled trial. The treatment group (n=125) received daily SLIT for house dust mite allergens, while the control group (n=125) received a placebo. The Asthma Control Test (ACT) scores, forced expiratory volume (FEV1), and medication usage were recorded at 6, 12, and 24 months.

Results: Patients receiving SLIT showed a 42% improvement in ACT scores ($p<0.001$), a 15% increase in FEV1 ($p=0.005$), and a 28% reduction in medication use ($p=0.002$) compared to the control group. No serious adverse effects were observed.

Conclusion: Sublingual immunotherapy significantly improves asthma control, lung function, and reduces medication dependency, highlighting its potential as a long-term treatment for allergic asthma.

Keywords: Sublingual Immunotherapy, Allergy, lung function

Sensitivity and specificity of anti-VEGF therapy as a criterion for predicting postoperative complications in patients with secondary neovascular glaucoma

D.O. Denysenko[1], M.I. Kovtun[1]

[1]Karazin Kharkiv National University

Introduction: It is known that secondary neovascular glaucoma (NVG) is based on pathological vascular neoplasms in the iris at the angle of the anterior chamber of the eye. The trigger for progressive neovascularization of the anterior vascular tract is retinal ischemia, which occurs against the background of impaired blood circulation. The aim of our study was to determine the sensitivity and specificity of the surgical treatment of NVG, which includes a gradual reduction in intraocular pressure against the background of the use of anti-VEGF therapy.

Methods: 24 patients (women) with type 2 diabetes mellitus for over 10 years, visual acuity 0.01 - 0.3 in order to determine the sensitivity and specificity of anti-VEGF drugs on the results of treatment were divided into 2 groups: Group I patients (n = 12) - underwent filtering operations, in Group II in addition to surgical treatment, anti-VEGF therapy (aflibercept) was performed.

Results: The ability to compensate for intraocular pressure with local antihypertensive agents in patients of Group II after surgery was statistically proven. The introduction of an additional anti-VEGF drug to patients of Group II after 4 weeks, according to ROC analysis, demonstrated the prognostic significance of reducing the frequency of NVG attacks in the postoperative period (95% CI: 0.70 - 0.74, $p<0.05$) and contributed to improving vision by 0.09±0.02 (95%CI: 28 - 20%).

Conclusion: The use of anti-VEGF drugs in the treatment of VNG on the background of type 2 diabetes mellitus for more than 10 years significantly improves the functional results of treatment of patients and reduces the risk of postoperative complications.

Keywords: Secondary Neovascular Glaucoma, Anti-VEGF Therapy, Diabetes Mellitus, Postoperative Complications

Application of Immobilization Method to Enhance the Stability and Bioavailability of a Combined Drug Based on Serratiopeptidase and Ibuprofen

R.R. Babaeva[1], G.U. Tillaeva[1], U.M. Tillaeva[1]

[1]Tashkent Pharmaceutical Institute, Uzbekistan

Introduction: Long-term use of NSAIDs like ibuprofen is associated with gastrointestinal and nephrotoxic risks. Combining ibuprofen with serratiopeptidase, an enzyme with anti-inflammatory and fibrinolytic properties, may mitigate these effects. However, serratiopeptidase's instability in gastric conditions necessitates immobilization strategies to enhance therapeutic efficacy. To develop a combined ibuprofen-serratiopeptidase drug using chitosan and calcium-alginate carriers, evaluating stability, release kinetics, and bioavailability to optimize delivery.

Methods: Two immobilization systems were tested: 1. Chitosan complexes: Electrostatic interaction between chitosan's amino groups and drug carboxyl groups. 2. Calcium-alginate particles: Gelation with sodium alginate. Stability and release profiles were analyzed via HPLC (FarmHPLC system with DAD: 227, 223, 232 nm; FLD: Ex=230 nm, Em=460 nm). Formulations included MKTS (calcium-alginate), MKTS paxta (with stabilizer), and Entrotsel (purified).

Results: Gastric protection: Chitosan released ≤18% of drugs at pH 1.2 vs. 22% for alginate. Intestinal release: Chitosan enabled 85% serratiopeptidase release over 8 h (pH 6.8), 7% higher than alginate. Bioavailability: Chitosan increased serratiopeptidase AUC by 40% (18.5 ± 1.2 vs. 13.1 ± 0.9 μg·h/mL). Stability: Entrotsel showed optimal purity (single peak at 0.672 min; no impurities), while MKTS paxta exhibited partial release (secondary peak at 1.041 min). Prolonged action: Ibuprofen's Tmax extended to 4 h, reducing gastric exposure.

Conclusion: Chitosan's superior mucoadhesion (+25 mV zeta potential) and thermostability (denaturation temperature: 78°C vs. 65°C for free enzyme) confirm its potential for targeted delivery. Entrotsel, with maximal stability, is prioritized for preclinical trials. Immobilization synergistically enhances efficacy while lowering ibuprofen doses, reducing toxicity risks. Future work includes animal studies, clinical trials, and exploring pH-sensitive hydrogels for personalized delivery.

Keywords: Drug immobilization, serratiopeptidase, ibuprofen, chitosan, calcium-alginate, controlled release.

Development of a Recombinant Yeast Expression System for Enhanced Insulin Production

E. Gholami[1]

[1]Islamic Azad university, Shahrud branch

Introduction: Insulin is a critical treatment for diabetes, and its production in recombinant systems has revolutionized diabetes care. Yeast-based expression systems offer several advantages, such as cost-effectiveness and scalability. However, optimizing insulin production remains a challenge. The aim of this study is developing a recombinant yeast expression system capable of efficiently producing human insulin and to optimize growth and fermentation conditions for enhanced yield.

Methods: The yeast strain Saccharomyces cerevisiae was transformed with a plasmid containing the human insulin gene. The growth conditions (temperature, pH, and nutrient concentration) were optimized using response surface methodology (RSM). Insulin quantification was performed using HPLC and ELISA techniques. The recombinant yeast was cultured in batch fermentation for 72 hours, with insulin production monitored at regular intervals.

Results: The optimized system yielded 120 mg/L of insulin after 72 hours of fermentation, a 50% increase over baseline production. The highest yield was achieved at a fermentation temperature of 30°C, pH 6.5, and glucose concentration of 30 g/L. Insulin purity was 92%, and the protein exhibited bioactivity as measured by its ability to activate insulin receptor signaling.

Conclusion: The recombinant yeast expression system successfully produced human insulin with improved yield and purity. This system holds potential for large-scale production of insulin at a lower cost, supporting its application in the biopharmaceutical industry.

Keywords: Yeast, Insulin, Bioactivity

Evaluating the Role of Clinical Pharmacists in Preventing Drug-Drug Interactions in Oncology Patients

N. Pashanezhad[1]

[1]Shiraz university of medical sciences

Introduction: Drug-drug interactions (DDIs) are a significant cause of morbidity and mortality, especially in oncology patients who are often prescribed multiple medications. Clinical pharmacists are well-positioned to identify and manage DDIs, improving patient safety. However, the impact of clinical pharmacy interventions on preventing DDIs in oncology patients remains underexplored. This study investigates the role of clinical pharmacists in identifying and preventing drug-drug interactions in oncology patients receiving chemotherapy.

Methods: A prospective cohort study was conducted over a 6-month period at ABC Cancer Center. A total of 200 oncology patients were included, and clinical pharmacists performed daily medication reviews to identify potential DDIs. The pharmacists then provided recommendations to the prescribing oncologists to adjust drug regimens accordingly. The number and severity of DDIs before and after pharmacist interventions were recorded.

Results: Before intervention, 55% of patients had at least one clinically significant DDI. After intervention, 80% of the identified DDIs were resolved, and only 15% of patients had DDIs after the pharmacist's recommendations ($p<0.01$). The most common DDIs involved chemotherapeutic agents and supportive medications, such as antiemetics and antibiotics.

Conclusion: Clinical pharmacists play a crucial role in identifying and preventing DDIs in oncology patients, leading to improved patient safety. This study underscores the importance of incorporating clinical pharmacists into oncology teams to optimize medication therapy and reduce adverse drug reactions in cancer patients.

Evaluating the Synergistic Effect of Withania Somnifera and Metformin in Type 2 Diabetes Management

S. Lashani[1]

[1]Tabriz university of medical sciences

Introduction: Type 2 diabetes mellitus (T2DM) is a growing global health concern characterized by insulin resistance and hyperglycemia. While metformin remains the first-line treatment, herbal medicine offers potential complementary benefits. Withania Somnifera (Ashwagandha) is a medicinal plant known for its adaptogenic and hypoglycemic properties. Combining it with metformin may enhance glycemic control and reduce complications. The aim of this study was investigating the synergistic effect of Withania Somnifera and metformin in reducing blood glucose levels and improving insulin sensitivity in diabetic rats.

Methods: Fifty Wistar rats were randomly divided into five groups: Control (saline), Diabetic control, Metformin (500 mg/kg), Withania Somnifera extract (300 mg/kg), and Combination therapy (Metformin + Withania Somnifera). Diabetes was induced by streptozotocin (STZ, 40 mg/kg). Fasting blood glucose (FBG), insulin levels, HbA1c, and lipid profile were measured at baseline and after 8 weeks.

Results: The combination therapy resulted in a 57% reduction in FBG, significantly higher than metformin alone (38%) or Withania Somnifera alone (30%) ($p<0.001$). HbA1c levels improved by 24%, and insulin sensitivity increased by 33% compared to diabetic controls. The combination also improved lipid profiles, with a 15% reduction in LDL cholesterol and a 22% increase in HDL.

Conclusion: Withania Somnifera enhances the glucose-lowering effects of metformin, suggesting a potential adjunct therapy for diabetes management. Further clinical studies are required to validate these findings in human subjects.

Keywords: Diabetes, Metformin, Withania Somnifera

Development and Characterization of a Nanoemulsion-Based Drug Delivery System for Poorly Soluble Drugs

S. Lashani[1]

[1]Tabriz university of medical sciences

Introduction: Poor aqueous solubility remains a major challenge in drug formulation, limiting bioavailability and therapeutic efficacy. Nanoemulsions have gained attention as efficient drug delivery systems due to their ability to enhance solubility, stability, and absorption of lipophilic drugs. This study aims to develop and characterize a nanoemulsion-based drug delivery system for curcumin, a poorly water-soluble drug, to enhance its bioavailability and therapeutic potential.

Methods: A self-emulsifying nanoemulsion was formulated using a combination of caprylic/capric triglycerides, Tween 80, and polyethylene glycol 400 as oil, surfactant, and co-surfactant, respectively. The formulation was optimized using pseudo-ternary phase diagrams and evaluated for droplet size, polydispersity index (PDI), zeta potential, drug loading efficiency, and in vitro drug release. The stability of the formulation was assessed over three months under different storage conditions.

Results: The optimized nanoemulsion exhibited a droplet size of 85.2 nm, a PDI of 0.18, and a zeta potential of -32.1 mV, indicating good stability. Drug loading efficiency was 92.4%, and in vitro release studies demonstrated a 4.8-fold increase in curcumin dissolution compared to the pure drug. The formulation remained stable over three months with no significant changes in physicochemical properties.

Conclusion: Nanoemulsions are a promising approach to improve the solubility and bioavailability of poorly water-soluble drugs. This study highlights their potential in enhancing therapeutic efficacy and pharmaceutical stability.

Keywords: Drug delivery, Nanoemulsions

Pharmacokinetics of Cardiovascular Drugs in Patients with Heart Failure: Impact of Altered Drug Metabolism and Clearance

S. Eghbalkharazi[1]

[1]University of Milan

Introduction: Patients with cardiovascular diseases, particularly heart failure (HF), often experience altered pharmacokinetics due to changes in drug absorption, distribution, metabolism, and excretion. Factors such as reduced hepatic blood flow, renal impairment, and altered plasma protein levels can significantly affect drug efficacy and toxicity. This study aims to evaluate the pharmacokinetic variations of commonly prescribed cardiovascular drugs in HF patients and assess their clinical implications.

Methods: A prospective observational study was conducted on 150 HF patients (NYHA class II-IV) and 50 age-matched healthy controls. Plasma concentrations of metoprolol, digoxin, and rivaroxaban were measured using high-performance liquid chromatography-mass spectrometry (HPLC-MS) at predefined time points after drug administration. Pharmacokinetic parameters, including maximum plasma concentration (Cmax), time to peak concentration (Tmax), half-life (t1/2), and clearance (CL), were analyzed. Correlations between drug levels and hepatic/renal function markers (eGFR, ALT, albumin) were assessed using multivariate regression models.

Results: Compared to healthy controls, HF patients exhibited significantly altered pharmacokinetics for all three drugs: Metoprolol: Increased Tmax (3.2 ± 0.8 vs. 2.1 ± 0.6 hours, $p < 0.01$) and prolonged half-life (8.4 ± 2.3 vs. 5.7 ± 1.6 hours, $p < 0.01$), suggesting reduced hepatic clearance. Digoxin: Higher Cmax (1.8 ± 0.5 vs. 1.2 ± 0.4 ng/mL, $p < 0.01$) and increased accumulation in patients with eGFR < 50 mL/min/1.73m², indicating impaired renal clearance. Rivaroxaban: Increased interindividual variability in plasma levels, with patients having eGFR < 60 mL/min showing 30% higher drug exposure, raising concerns for bleeding risk.

Conclusion: This study highlights significant pharmacokinetic alterations in HF patients, emphasizing the need for individualized dosing strategies. Reduced hepatic and renal clearance impacts drug exposure, increasing the risk of adverse effects. Clinicians should consider therapeutic drug monitoring and dose adjustments, particularly for renally cleared drugs. Future research should explore personalized dosing algorithms based on patient-specific pharmacokinetic profiles.

Keywords: Pharmacokinetics, cardiovascular drugs, heart failure, drug metabolism, renal clearance, hepatic impairment, precision dosing.

The Importance of Drug Solubility in Enhancing Antidepressant Efficacy and Bioavailability

M. Parchianloo[1], S. Eghbalkharazi[2]

[1]Zanjan university of medical sciences
[2]University of Milan

Introduction: Depression is a widespread mental health disorder requiring long-term pharmacological treatment. The efficacy of antidepressants is highly dependent on their solubility and subsequent bioavailability, influencing absorption, onset of action, and therapeutic outcomes. Poorly soluble drugs exhibit delayed absorption, variable plasma concentrations, and reduced clinical effectiveness. This study explores the impact of solubility on the pharmacokinetics and therapeutic efficacy of commonly prescribed antidepressants.

Methods: A comparative pharmacokinetic analysis was conducted on fluoxetine (low solubility), sertraline (moderate solubility), and venlafaxine (high solubility) in 100 patients diagnosed with major depressive disorder. Plasma drug concentrations were measured at 1, 3, and 6 hours post-administration using high-performance liquid chromatography (HPLC). Key pharmacokinetic parameters, including Cmax (maximum plasma concentration), Tmax (time to peak concentration), and bioavailability, were analyzed. Clinical outcomes were assessed over 8 weeks using the Hamilton Depression Rating Scale (HAM-D).

Results: Venlafaxine (high solubility): Rapid absorption (Tmax = 1.5 ± 0.4 hours), higher bioavailability (87%), and significant symptom reduction (HAM-D score improvement: 52%). Sertraline (moderate solubility): Intermediate absorption (Tmax = 2.8 ± 0.6 hours), bioavailability of 44%, and moderate symptom reduction (HAM-D improvement: 42%). Fluoxetine (low solubility): Delayed absorption (Tmax = 5.1 ± 0.9 hours), lower bioavailability (24%), and slower symptom relief (HAM-D improvement: 30%). Statistical analysis confirmed a significant correlation between solubility and both pharmacokinetic parameters ($p < 0.01$) and clinical efficacy ($p = 0.02$).

Conclusion: Drug solubility plays a crucial role in the absorption and therapeutic efficacy of antidepressants. Poorly soluble drugs demonstrate delayed onset and variable clinical response, emphasizing the need for solubility-enhancing formulations such as nanoemulsions, solid dispersions, or prodrug strategies. Optimizing solubility could lead to faster symptom relief and improved patient adherence. Future research should focus on formulation advancements to enhance antidepressant bioavailability.

Keywords: Solubility, antidepressants, bioavailability, pharmacokinetics, depression, drug absorption, formulation science.

Development and Preclinical Evaluation of a Novel Neuroprotective Agent Targeting Oxidative Stress in Parkinson's Disease

M.D. Bazamfare[1]

[1]European University of Lefke

Introduction: Oxidative stress is a key pathological mechanism in Parkinson's disease (PD), leading to neuronal degeneration in the substantia nigra. Current treatments primarily focus on symptom management rather than neuroprotection. This study investigates a novel small-molecule antioxidant, NPX-107, designed to mitigate oxidative stress and improve dopaminergic neuron survival in PD models.

Methods: A 6-hydroxydopamine (6-OHDA)-induced rat model of PD was used to evaluate NPX-107. Animals were divided into three groups: control, NPX-107 (10 mg/kg, i.p.), and a standard levodopa-treated group. Motor performance was assessed using the rotarod test and apomorphine-induced rotations. Oxidative stress biomarkers (malondialdehyde, superoxide dismutase, and glutathione) were measured in the striatum, while tyrosine hydroxylase (TH)-positive neurons were quantified using immunohistochemistry.

Results: NPX-107 significantly improved motor performance (rotarod retention time: +35%, $p < 0.05$) and reduced rotational asymmetry compared to untreated PD rats. Biochemical analysis revealed a reduction in malondialdehyde levels (-42%) and increased antioxidant enzyme activity (+50%, $p < 0.05$). Immunohistochemistry confirmed a 30% increase in TH-positive neurons in the substantia nigra, suggesting neuroprotection.

Conclusion: NPX-107 demonstrates significant antioxidant and neuroprotective effects in a PD model, suggesting its potential as a disease-modifying therapy. Further studies are warranted to assess long-term efficacy and clinical translatability.

Keywords: Parkinson's disease, oxidative stress, neuroprotection, antioxidants, small molecules

Determination of water-soluble vitamins in the leaves of Isatis Tinctoria

E.S. Saidjalolova[1], Sh.O Khakimjanova[1], G.U. Tillayeva[1]

[1]Tashkent Pharmaceutical Institute, Tashkent, Republic of Uzbekistan

Introduction: Alcoholic and aqueous extracts and dry extracts were obtained from the leaves. In both extracts, vitamins were determined by HPLC. Woad (Isatis tinctoria) is a representative of the cabbage or cruciferous family. Modern scientific studies have proven anti-inflammatory, antitumor, antimicrobial, antiviral, antidiabetic and antioxidant activities. The analysis of water-soluble vitamins was conducted by HPLC method. Also, calculations of the quantitative content of vitamins were carried out.

Methods: Water-soluble vitamins in the sample were detected using the method of high-performance liquid chromatography (HPLC). Chromatography conditions: Agilent-1200 chromatograph (equipped with an auto-dispenser); Eclipse XDBC 18 column (reverse-phase), 5 microns, 4.6 x150 mm; Detector with diode array (DAD), identification was carried out at 204 nm, 254 nm, 290 nm; Flow rate of 1ml/min; Eluent acetate buffer: acetonitrile (0-5 min 96:4; 6-8 min 90:10; 9-15 min 80:20; 15-17 min 96:4); The temperature of the thermostat is 250C, -5 µl.

Results: It follows from table 1 that the alcoholic extract of leaves of Isatis tinctoria contain the most vitamin B6, B2 and C. Aqueous extract contains the most vitamin C and B3 (PP).

Conclusions: Vitamin B6 is a water-soluble vitamin that your body needs for several functions. It has health benefits for the body, including promoting brain health and improving mood. Health benefits of vitamin B2 include supporting cellular functions that provide the body with energy, allowing it to work efficiently. Vitamin C is an antioxidant that helps protect your cells against the effects of free radicals. So, it is possible to use leaves of Isatis tinctoria for the development of biologically active additives.

Keywords: Isatis Tinctoria, Leaves, Aqueous and Alcoholic Extracts, Vitamins

Vitamins	Water extract	Alcohol extract
	Quantitative content, mg/g	Quantitative content, mg/g
B1	-	0,136
B2	0,91	16,229
B6	-	28,602
B3 (PP)	1,71	0,925
C	5,65	2,382

Evaluation of the Toxicity of Environmental Pesticides in Rat Liver and Kidney Tissues

M. Barari[1]

[1]Department of Pharmaceutical Sciences, Islamic Azad University

Introduction: Environmental pesticides are widely used in agriculture, but their potential toxicity poses significant risks to human and animal health. Recent studies have highlighted the toxic effects of chronic pesticide exposure on liver and kidney function, yet comprehensive toxicological evaluations remain limited. The aim of this study was assessing the hepatic and renal toxicity of common environmental pesticides in Wistar rats after prolonged exposure.

Methods: Fifty adult Wistar rats were randomly divided into five groups: control (saline), low dose (10 mg/kg), medium dose (50 mg/kg), high dose (100 mg/kg), and pesticide combination group (low dose of 3 pesticides). Pesticides were administered for 30 consecutive days. Liver and kidney functions were evaluated by measuring serum ALT, AST, urea, and creatinine levels. Histopathological analysis of liver and kidney tissues was conducted to identify structural damage. Oxidative stress markers such as malondialdehyde (MDA), superoxide dismutase (SOD), and glutathione (GSH) were assessed.

Results: Rats exposed to higher doses (50-100 mg/kg) exhibited significant elevations in ALT (35%) and AST (28%) compared to control, indicating liver damage. Kidney function was impaired, with urea levels increasing by 40% and creatinine by 30% in the high-dose group ($p<0.01$). Histopathological analysis revealed hepatocellular necrosis and glomerular damage in the high-dose and combination pesticide groups. Oxidative stress markers were significantly elevated in these groups ($p<0.05$).

Conclusion: Prolonged exposure to environmental pesticides leads to significant hepatic and renal toxicity, with oxidative stress contributing to the damage. These findings underscore the need for stricter regulatory controls and the exploration of safer alternatives.

Keywords: Pesticides, Toxicity, Oxidative stress

BIOMEDICAL IMAGING

Detection and classification of lung cancer in histopathology images using deep learning

F. Aghajanloo[1]

[1]Zanjan University of Medical Sciences

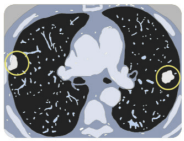
Introduction: Lung cancer is one of the most malignant types of cancer, having the highest mortality rate among all other cancers. Due to the poor prognosis of this disease, most patients are diagnosed in the final stages of the cancer. Therefore, early diagnosis of this disease can lead to the recovery of a higher percentage of patients suffering from lung cancer. Histopathology images that provide detailed insight into lung tissue are a valuable asset in this effort. The aim of this study is to use the EfficientNetB0 model of deep learning, to detect lung cancer in histopathology images.

Method: We initiated our study by collecting a comprehensive dataset of 10,000 histopathology images, carefully selected from diverse medical institutions, ensuring a balanced representation of benign and malignant lung tissue cases. EfficientNetB0 model was used for model development. Data were divided into training and test sets with a 1 to 3 ratio. Model performance was assessed using key metrics, such as accuracy, sensitivity, specificity, and F1 score.

Results: EfficientNetB0 deep learning model results in lung cancer detection and classification using histopathology images were impressive with an overall accuracy of 94%, F1 score of 0.95 with a sensitivity, and a specificity of 93%, and 97%, respectively for the test sets. Moreover, our model correctly classified 90% of the cases into two groups of benign and malignant, showing its capability in detection of lung cancer.

Conclusions: Our findings show the EfficientNetB0 model ability in histopathology-based lung cancer classification, emphasizing the significance of meticulous feature representation in image analysis. This study opens up a new and promising strategy for improving diagnostic tools, having a great impact on the early stages of detection.

Keywords: Deep learning, Lung cancer, EfficientNetB0



(Bio)Medical Imaging

Impact of radioiodine therapy on the oxidative-antioxidative status in subclinical hyperthyroidism

W. Dobkowska[1], N. Zyśkowska[1], M. Obrycka[1]

[1]Department of Nuclear Medicine, Medical University of Białystok, Poland

Introduction: Subclinical hyperthyroidism is an asymptomatic or oligosymptomatic condition, nevertheless it is important to prevent progression to overt hyperthyroidism. Oxidative stress plays a significant role in hyperthyroidism induced– tissue damage. We aimed to determine whether radioiodine therapy (RIT) has a beneficial effect on the oxidative/antioxidative status in subclinical hyperthyroidism.

Methods: We studied 157 patients with untreated subclinical hyperthyroidism, aged 23–78 years; 68 patients with multinodular goiter, 89 patients with autonomous nodules and twenty adults volunteered as a control group. Before the treatment all the patients had normal levels of serum fT3, fT4, low levels of serum TSH (<0.1 mU/l) and effective half-life was more than 3 days. Malignant changes were excluded in all nodules by fine-needle aspiration biopsy. In the investigated groups, we evaluated malondialdehyde (MDA) as a marker of oxidative stress, glutathione (GSH) and glutathione peroxidase (GPx) activity as a parameter of antioxidant system before and 6 months after RIT. The serum fT4, fT3 and TSH were evaluated before and monthly up to 12 months after RIT. Thyroid ultrasound, and thyroid scan were done before and after 12 months of 131I therapy. The activity dose was calculated by Marinelli's formula and ranged between 200 and 600 MBq. The absorbed dose ranged between 160 and 280 Gy.

Results: Thyroid volume reduced to 45% (average); 118 patients were in euthyroidism, 39 patients received a second dose of RIT. 10 patients were in hypothyreosis. Subclinical hyperthyroidism caused a significant increase in MDA level ($P<0.05$) as well as a significant decrease in GPx activities ($P<0.05$) and GSH level ($P<0.05$) compared to euthyroid controls subject. Achievement of euthyroidism after 6 months of radioiodine administration resulted in a significant decrease of MDA, significant increase of GSH and non-significant increase in GPx activities.

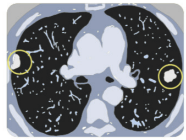
Conclusions: Our results confirm the imbalance of the oxidative/antioxidative status in subclinical hyperthyroidism. The effectiveness of RIT in oxidative/antioxidative status has been confirmed.

Keywords: Radioiodine, Subclinical Hyperthyroidism

Radioactive iodine - treatment of subclinical hyperthyroidism. Fiveyear evaluation study

N. Zyśkowska[1], W. Dobkowska[1], M. Obrycka[1]

[1]Department of Nuclear Medicine, Medical University of Białystok, Poland



(Bio)Medical Imaging

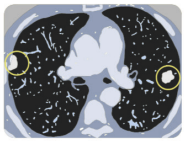
Introduction: Subclinical hyperthyroidism (SCH) is a condition characterized by low TSH level meanwhile T4 and T3 levels are normal. Although subclinical hyperthyroidism does not give any symptoms, it may be dangerous to a patient, because it can progress to symptomatic hyperthyroidism. If subclinical hyperthyroidism is detected early, it can be treated very successfully, but unfortunately official guidelines are purely defined. Most patients are recommended to wait and monitor hormon levels, which is problematic, because not all of them are aware that their condition may proceed.Our reaserch was done to investigate a five year effect of radioactive iodine therapy in patients with subclinical hyperthyroidism.

Methods: We treated 1656 patients aged 32–76. 54% had multinodular goiter (MNG), and 46% had autonomous nodules (ATN). Malignancy was excluded via fine needle aspiration biopsy. All patients had serum TSH <0.1 mU/l and effective half-life >3 days (T24/T48). Marinelli's formula determined activity doses (200–600 MBq). Absorbed doses: MNG 150–260 Gy, ATN 200–300 Gy. Follow-ups occurred every 6 weeks in year 1, then biannually for 4 years.

Results: After 1 year, 97% of patients with ATN and 91% with MNG succeeded in therapy and achieved euthyroidism. Only 3% of ATN and 8% of MNG patients developed hypothyroidism, while 1% of MNG required a second dose of I-131. After 3 years, 96% of ATN and 91% of MNG patients achieved euthyroidism, and after 5 years, 97% of ATN and 91% of MNG patients maintained it. Moreover, quality of life improved for all patients with reduced palpitations, tachycardia, atrial fibrillation, better exercise tolerance, and stabilized blood pressure.

Conclusions: Early diagnosis and treatment with radioactive iodine is very beneficial for patients. It can lead to a full recovery and highly improve the quality of life. That is the reason why we would like to emphasize the need to include this method of treatment in official guidelines for all patients.

Keywords: radioactive iodine; subclinical hyperthyroidism; endocrinology; nuclear medicine



(Bio)Medical Imaging

Investigation of the Detection Rate of Machine Learning Models in Recognition and Classification of Colorectal Polyps

A. Hajialigol[1], S. Shayesteh[1]

[1]Alborz University of medical sciences

Introduction: Colorectal polyps are diagnosed and treated with colonoscopy. There are two challenges in the discussion of colorectal polyps. First, the rate of undetected polyps in colonoscopies, where 25% of polyps are not detected, which can be due to poor bowel preparation, lesions located in areas that are difficult to evaluate, lack of experience or distraction of the endoscopist, the appearance of the polyp, and inappropriate techniques. The second challenge is to distinguish different types of polyps, especially adenoma and hyperplastic types. Because adenomas are preferred for polypectomy due to the risk of malignancy compared to hyperplastic polyps. In this study, we intend to use recorded images of polyps and diagnostic algorithms to produce an artificial intelligence platform for quick detection and classification of polyps.

Methods: In this study, our sample size was 250, and colonoscopy was performed using the 170-cv OLYMPUS system. The imaging parameters were set by the endoscopist and the required number of images was recorded for each polyp. The sample removed by the endoscopist was sent to the pathology laboratory. The criterion for diagnosing the type of polyp was the sample pathology report.

Results: The experimental data set contains 250 complete colonoscopy images from 250 different patients. The ratio of males to females was 1.43, the average age was 61.25 (interquartile range: 54-70), the overall accuracy of CNN in detecting visible tools in the test dataset was 86.12%, and the loss bonding box was close to zero (0.04) for the class. “Adenoma”, precision was 0.86, recall was 0.92, and F1 score was 0.89. For the “Non Adenoma” class, precision was 0.86, recall was 0.73, and F1 score was 0.78.

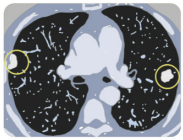
Conclusions: In conclusion, our study shows that instrument detection using artificial intelligence technology is reliable and has high sensitivity and specificity. Therefore, the new artificial intelligence system can be useful to reduce distracting CAde diagnoses during conoscopy procedures. Although the clinical benefits of the new AI system require further evaluation, our study demonstrates the great potential of AI technology beyond superficial evaluation.

Keywords: Colorectal Polyps; Artificial Intelligence; Convolutional Neural Network (CNN)

Analysis of nasal septum deviation and nasal pyramid based on computed tomography (CT) scans

A. Jovanović[1], Prof. dr D. Mašulović[1]

[1]Centre for radiology University Clinical Centre of Serbia



(Bio)Medical Imaging

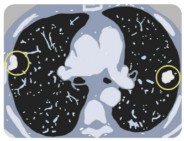
Introduction: Among all radiological diagnostic methods for assessing nasal function, multi-detector computed tomography (MDCT) of paranasal and nasal cavities has the highest sensitivity. The Aim: The aim of our research was to describe different types and types of deviation of the nasal septum and their influence on the size of nasal passages in relation to the concha and nasal mucosa, by analyzing computed tomographic (CT) images.

Methods: The study included 50 patients aged 21 to 65, 28 were women and 22 were men. On CT scans, we measured the flow of the nasal passages, the degree and type of the curvature of nasal septum, the size and ratio of the nasal shells in relation to the nose and their influence on the size of nasal passages, the curvature (deviation) of the cartilaginous and bony parts of the nasal septum and described their relationship and the relationship with nasal passages and nasal concha.

Results: Through our research and statistical analysis, we found there are 7 types of nose deviation. In 46 examinees (92% of cases) with septal deviation, we found the mucosa was more thickened and hypertrophic on the side opposite to septal deviation ($p<0.05$).

Conclusions: We found that there are seven types of deviation of the nasal septum, and that the patency of nasal passages directly depends on the ratio of the curvature of nasal septum, the thickness of mucosa and their mutual relationship with lower concha.

Keywords: nasal septum deviation; CT computed tomography of the nasal pyramid; hypertrophy of the nasal mucosa



(Bio)Medical Imaging

Muscle Ultrasonography in Costello Syndrome: unveiling new clinical insights of a complex muscular phenotype

L. Mondelli[1], Dr. Leoni, Dr. Zampino[1], Dr. Viscogliosi[1], Dr. Trevisan[1], Dr. Viscogliosi[1]

[1]Università Cattolica del Sacro Cuore/ Fondazione Policlinico Universitario Agostino Gemelli/ IRCCS

Introduction: Costello syndrome is a rare genetic disorder within the spectrum of RASopathies, caused by mutations in the HRAS gene, leading to the dysregulation of the RAS/MAPK signaling pathway. A more severe musculoskeletal involvement, including reduction in muscle force and impaired mobility, has been described as part of the syndrome phenotype. This study aims to evaluate these features using ultrasonography, a widely recognized technique for its diagnostic value in neuromuscular disorders. Despite its established role in muscle health assessment, it has never been conducted in RASopathies to date.

Methods: Notably, ultrasonography is a radiation-free technique that visualizes muscle architecture, particularly fibroadipose infiltration (FAI), which appears as increased echogenicity due to pathological remodeling. Additionally, the study explored associations between muscle involvement, metabolic factors, and nutritional parameters.The research cohort consisted of 20 individuals (13 females, 7 males, median age of 19 years) with molecularly confirmed CS diagnoses. Ultrasonographic evaluations were conducted using a Samsung RS85 Prestige machine equipped with a 7–11 MHz linear transducer. Muscles assessed included paravertebral muscles, rectus femoris, vastus medialis and lateralis, and gastrocnemius. FAI was graded according to the Heckmatt scale (1-4), whereas nutritional assessments included macronutrient intake analysis and measurements of resting energy expenditure.

Results: The analysis revealed that FAI was identified in 100% of participants, with the lumbar paravertebral muscles being the most commonly affected ones, showing grade II involution (<30%) in almost the entire cohort (85%). In addition, a higher percentage of patients showed FAI in vastus lateralis (70%). No significant association was found between FAI and age, biochemical parameters and nutritional profile of the patients.

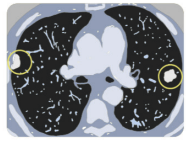
Conclusions: Consequently, we speculate that FAI in individuals with CS may be predominantly linked to the underlying molecular background rather than modifiable factors. Despite its strengths, the study is limited by the small cohort size, reflective of the rarity of CS, and the operator-dependent nature of ultrasonographic imaging. Therefore, prospective studies involving larger cohorts are crucial to validate these findings, monitor disease progression and assess the efficacy of targeted interventions. In conclusion, this study underscores the potential of ultrasonography to enhance clinical management in individuals with CS and related RASopathies.

Keywords: Costello Syndrome; Fibroadipose Infiltration (FAI); Ultrasonography

Effectiveness of 3D visualization of liver compared to 2D CT scan or MRI on decision making of a multidisciplinary tumor board: a crossover randomized trial.

V. Pas[1], prof. dr. H. Eker[1], prof. dr. N. Rashidian[1]

[1]Belgium; Ghent University; Department of general and hepato-biliary surgery and liver transplantation



(Bio)Medical Imaging

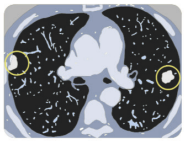
Introduction: This study explores the effectiveness of three-dimensional visualisation compared to traditional two-dimensional (2D) CT and MRI imaging in the decision-making process of multidisciplinary teams (MDTs) for liver malignancies. The aim is to determine whether 3D rendering (3DR) can enhance understanding and impact clinical decision-making within MDTs.

Methods: A randomized crossover trial was conducted with eight physicians from Ghent University Hospital. The study involved discussing 20 liver tumor cases using both 2D and 3D imaging modalities. The 'Synapse 3D' software by Fujifilm was used to create the 3D models. The trial consisted of two MDT meetings, with a one-month washout period between them to minimize memory bias. The primary endpoint was clinical decision-making, while secondary endpoints included the quality of MDT teamwork and user experience with the 3D software.

Results: The introduction of 3DR impacted the decision for local treatment (i.e. surgery or ablation) in 25% of the cases. In 60% of the cases, there was a change in the overall treatment approach. In four cases, 3DR resulted in a shift towards non-invasive (i.e. systemic, rather than local) treatments, with some patients initially considered for local therapy being deemed inoperable upon 3D evaluation. The user experience feedback indicated indifference about the software's usability.

Conclusions: Incorporating 3D visualization into MDT meetings for liver tumors has the potential to alter treatment recommendations. The study highlights the broader influence of 3D models on treatment strategy, including the choice for local therapy modality and consideration of liver transplantation. Further research could assess the impact of these changes on patient outcomes.

Keywords: 3D Visualization; Multidisciplinary Team (MDT); Liver Tumors; Clinical Decision-Making



(Bio)Medical Imaging

Reference Relaxation Time Values in T1- and T2-Weighted Sequences for Myocardial Mapping Using Magnetic Resonance Imaging

N. Ostruszka[1], Y. Dubna[1]

[1]Jagiellonian University Collegium Medicum

Introduction: T1- and T2-weighted mapping techniques have become essential tools for assessing myocardial tissue characteristics in cardiac magnetic resonance imaging (MRI). However, the range of reference values for these techniques is strictly dependent on the magnetic field strength and the data acquisition software. Accurately determining the reference relaxation time values in T1- and T2-weighted sequences is crucial for diagnosing heart diseases such as myocarditis, amyloidosis, and Fabry disease, which lead to characteristic changes in relaxation times.

Methods: A total of 51 healthy volunteers aged 20 to 43 years were included in the study. All participants underwent cardiac MRI using a 1.5T scanner, assessing ventricular volume and systolic function. Mapping sequences were analyzed in the end-diastolic phase of the left ventricle in three long-axis projections (four-chamber, three-chamber, and two-chamber views) and three short-axis segments (basal, midventricular, and apical). Image analysis was performed by a single operator. For each participant, the mean relaxation time in T1- and T2-weighted sequences was calculated, and the normal reference range was defined as the mean ± 2 standard deviations. Statistical analyses were conducted using Statistica software, version 13.3 (TIBCO Software, CA, USA). The study was approved by the Bioethics Committee of Jagiellonian University, and all participants provided written informed consent.

Results: The mean relaxation time in the T1 mapping sequence was 993.1 ms, with the lower limit of normal at 930.3 ms and the upper limit at 1055.9 ms. Similarly, for T2 relaxation time, the mean value was 45.6 ms, with the lower limit at 40.3 ms and the upper limit at 50.9 ms.

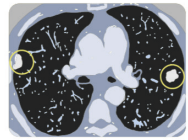
Conclusions: The obtained reference values are consistent with literature data, confirming their validity as a reference point for future clinical studies. Establishing reference values for a specific population and equipment is crucial for the accurate interpretation of results and the diagnosis of cardiac pathologies, such as inflammatory and infiltrative diseases.

Keywords: T1, T2-weighted, relaxation time, mapping sequences, reference values, magnetic resonance imaging

Shear Wave Elastography for Diagnosing and Managing Thyroid Nodules in Paediatric Patients

M. Skorupska[1], F. Bossowski[1]

[1]Poland, Medical University of Bialystok, Department of Pediatrics, Endocrinology and Diabetes with a Cardiology Unit



(Bio)Medical Imaging

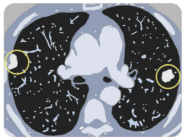
Introduction: Shear wave elastography (SWE) is a novel ultrasound imaging technique that can quantitatively measure tissue stiffness and thus help distinguish between benign and malignant thyroid nodules in adults. It is a non-invasive method that offers additional information on tissue elasticity beyond conventional ultrasonography. However, its utility in the paediatric population remains underexplored, and standardized SWE cut-off values for distinguishing benign from malignant thyroid nodules in children have yet to be established.

Methods: This retrospective study analyzed 116 paediatric patients aged 7.5 to 18, including 168 thyroid nodules. All patients underwent both SWE and fine-needle aspiration biopsy (FNAB). SWE was conducted in real-time using the Philips Epiq Elite ultrasound system equipped with a 22 kHz–2 MHz linear transducer. Elastographic findings were presented as colour-coded histograms and quantified using Young's modulus, expressed in kilopascals (kPa). FNAB cytology results were categorized according to the Bethesda System for Reporting Thyroid Cytopathology. Statistical analyses assessed the relationship between SWE measurements and cytological classification.

Results: A statistically significant difference in mean SWE values was observed between benign nodules and those classified under Bethesda categories III, IV, and V ($p = 0.0004$). A positive correlation between SWE measurements and Bethesda classification was also noted, with higher SWE values associated with increasing cytological atypia. These findings suggest that SWE can be a valuable non-invasive marker for predicting the malignancy risk of thyroid nodules and may help avoid unnecessary FNAB in low-risk cases.

Conclusions: As a non-invasive complementary tool for evaluating thyroid nodules in paediatric patients, SWE shows potential and improves conventional ultrasonography in risk stratification. If SWE can identify nodules with a higher likelihood of malignancy, it may help determine the need for invasive diagnostic procedures. The ability to reliably distinguish benign from malignant nodules through elastographic assessment could improve clinical decision-making and reduce the burden of unnecessary biopsies in children.

Keywords: Shear wave elastography; paediatric thyroid nodules; adolescents; ultrasound imaging



(Bio)Medical Imaging

Combining multiplex-staining and artificial intelligence-based image analysis for histological endometriosis sections

S. Korman[1], Prof. Dr. G. Vissers[1], Prof. Dr. M.A.J. Gorris[1], Prof. Dr. K. Verrijp[1], Prof. Dr. W.W.P. Verdurmen[1], Prof. Dr. M. Simons[1], Prof. Dr. S. Taurin[1], Prof. Dr. M. Sater[1], Prof. Dr. A. Nap[1], Prof. Dr. R. Brock[1]

[1]Radboud University

Introduction: Endometriosis is characterized by the complex interplay of various cell types and exhibits great variation between patients and its subtypes. In cancer research, multiplex immunochemistry and artificial intelligence-based image analysis advance our understanding of cellular interactions. Both types of neoproliferative disorders resemble each other in ectopic lesion growth, immune response induction, and high cell density. We introduce an endometriosis-specific multiplex panel, perform tissue segmentation, and cell-identification using the cancer specific ImmuNet algorithm.

Methods: A 6-plex immunofluorescence panel in combination with a nuclear stain was established. Nine endometriosis samples were stained and regions of interest were manualy pre-selected from whole-slide images. The widely used inForm Tissue Analysis Software was used to segment epithelial, stromal and fibrotic tissue compartments. We employed our in-house developed cancer specific ImmuNet algorithm to identify immune-cells and their proliferative status in relation to the specific tissue structures.

Results: An endometriosis-specific multiplex panel comprising of PanCK, CD10, SMA, calretinin, CD45, Ki67 and DAPI enabled the distinction of tissue structures in endometriosis. Whereas inForm enabled a reliable segmentation of tissue substructures, for cell identification, the segmentation-free ImmuNet algorithm was superior. This combined approach allowed us to compare the proportions of the tissue compartments between lesions, as well as their respective abundance of proliferating immune cells.

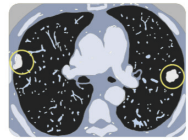
Conclusions: We demonstrate the great potential of combining multiplex staining and cell phenotyping for endometriosis research. Our multiplex panel visualises endometriosis lesion architecture and immune cell distribution. With the employment of ImmuNet we show that it is capable of performing cell phenotyping on tissue types that were not part of the training set, underlining the potential of the method for heterogenous endometriosis samples.

Keywords: Endometriosis, Multiplex Immunofluorescence

Artificial Intelligence in Detecting Pulmonary Nodules on Chest CT Scans

M. Ti[1]

[1]Tabriz uinversity of medical sciences



(Bio)Medical Imaging

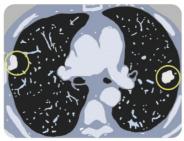
Introduction: Pulmonary nodules are frequently detected on chest CT scans, and early identification of malignant nodules is crucial for timely intervention. Traditional radiologic assessment is time-consuming and prone to inter-observer variability. Artificial intelligence (AI)-assisted detection has emerged as a potential tool to enhance accuracy and efficiency. This study evaluates the effectiveness of an AI-based model in detecting pulmonary nodules compared to radiologists.

Methods: A retrospective study was conducted on 500 anonymized chest CT scans from a tertiary hospital's imaging database. A deep learning AI model was trained using 300 annotated scans, while 200 scans were used for testing. AI results were compared with findings from three experienced thoracic radiologists. Sensitivity, specificity, and false-positive rates were analyzed using statistical methods.

Results: The AI model demonstrated an overall sensitivity of 92.1% and a specificity of 89.4% in detecting nodules >6 mm in size. Radiologists had a mean sensitivity of 87.5% and specificity of 91.2%. The false-positive rate of the AI model was 8.2%, which was slightly higher than radiologists (6.9%). AI-assisted readings reduced reporting time by an average of 22% per scan.

Conclusions: AI-assisted pulmonary nodule detection demonstrated high sensitivity and specificity, comparable to expert radiologists. Integration of AI in radiology could enhance diagnostic efficiency while maintaining accuracy. Further studies are required to refine AI algorithms and assess their real-world clinical impact.

Keywords: Artificial intelligence, pulmonary nodules, chest CT, deep learning, radiology automation



(Bio)Medical Imaging

The Role of Dynamic Contrast-Enhanced MRI in Early Detection of Breast Cancer in High-Risk Patients

M. Ti[1]

[1]Tabriz uinversity of medical sciences

Introduction: Mammography remains the standard for breast cancer screening, yet its sensitivity is limited in high-risk populations, particularly in dense breast tissue. Dynamic contrast-enhanced MRI (DCE-MRI) offers superior sensitivity but is underutilized. This study assesses the diagnostic accuracy of DCE-MRI in detecting early-stage breast cancer among high-risk women.

Methods: A prospective study was conducted on 250 high-risk women (BRCA1/2 mutation carriers or family history of breast cancer) undergoing annual screening. Each participant underwent both digital mammography and DCE-MRI. Lesion detection rates, sensitivity, specificity, and positive predictive values were calculated and compared between modalities.

Results: DCE-MRI identified 32 malignant lesions, while mammography detected 19. MRI sensitivity was 95.6% compared to 68.4% for mammography ($p < 0.01$). Specificity remained comparable (MRI: 88.2%, mammography: 91.5%). MRI detected an additional 13 malignancies that were missed on mammography, leading to earlier intervention in 9 cases.

Conclusions: DCE-MRI significantly improves early detection rates in high-risk populations, outperforming mammography alone. Its routine use in high-risk patients could facilitate earlier diagnosis and improved treatment outcomes. Further research is needed to evaluate cost-effectiveness and integration into current screening protocols.

Keywords: Breast cancer, MRI, mammography, early detection, high-risk screening

CANCER

Effect of melatonin in the treatment of hot flashes and sex problems caused by hormone therapy in patients with breast cancer: a randomized, double-blind, placebo-controlled clinical trial

P. Sattari[1], A.Falahati Marvast[2]

[1]Esfahan University of Medical Sciences, Esfahan, Iran.[2]Shahid Sadoughi University of Medical Sciences, Yazd, Iran

Introduction: Menopausal complications have been reported in women with hormone-positive breast cancer such as hot flashes, decrease in libido, mood changes, and decrease in quality of life as a result of anti-hormonal drugs administration. To manage these side effects, various drugs such as serotonin receptor inhibitors or GABA receptor antagonists have been used, which will lead to other severe side effects in these patients. Melatonin has been considered as a prominant antioxidant controlling drug-induced side effects recent years. Melatonin has been shown to be effective in treating mood changes and sleep disorders in cancer patients, and its effects on psychosomatic complications from antihormone therapy appear to be possible. Therefore, in this study, for the first time, we aimed to investigate the effect of melatonin consumption on the prevention of menopausal complications such as hot flashes, sexual function and quality of life due to hormone therapy in breast cancer patients.

Methods: This study was a randomized, placebo-controlled clinical trial. The patients participating in the study were selected from the hematology-oncology clinic of Al-Zahra and Seyed AlShohada hospitals in Isfahan, Iran. Adults with breast malignancy were divided into two groups of intervention and placebo. The subjects in the intervention group received 3 mg of melatonin tablets twice a day for 4 weeks, and patients in the placebo group received the identical placebo. Finally, after completing the study, they were compared in terms of study variables. Patients before and after 4 weeks of follow-up with the intervention were evaluated with questionnaires such as Menopause rating scale, Female sexual function index and finally the quality of life of patients with Menopause-specific quality of life questionnaire in comparison with the placebo group.

Results: This study showed that melatonin is able to reduce the number and severity of hot flashes and mean menopause score, quality of life score during menopause, and sexual function score (excluding satisfaction) have improved in intervention group in comparison with placebo group. Also, all the criteria in both groups improved significantly compared to baseline after 4-week follow-up.

Conclusion: Due to the positive effect of melatonin on improving the parameters of menopausal symptoms such as severity and number of hot flashes, patients sexual function and also improving the quality of life during treatment with anti-hormone drugs in patients with breast cancer, melatonin can be suggesting to treat breast cancer patients who are suffering from menopusal symptoms.

Keywords: Melatonin, Menopausal symptoms, Breast cancer, Sexual dysfinction, Hot flashes

Comparison of overall survival of local recurrence and distant metastasis of breast conserving surgery with modified radical mastectomy in Iranian women with stage one and two breast cancer

N. Pashanezhad[1]

[1]Shiraz university of medical sciences

Introduction: Breast cancer in Iran has a lower age of onset and a higher severity, which can affect the effectiveness of breast conserving surgery (BCT) and modified radical mastectomy (MRM) as common treatments. The purpose of this study is to compare survival of overall local recurrence and distant metastasis of these two surgical methods were in women with stage one and two breast cancer.

Methods: This study was conducted on female patients with stage 1 and 2 breast cancer undergoing MRM or BCT referred to Imam Reza hospital in Tabriz from 2020-2023. Patient characteristics, tumor information, treatment method, distant metastasis and overall survival of patients were collected. The data was entered into SPSS software and subjected to statistical analysis.

Results: A total of 506 patients were included in the study. Eighty percent of the patients were in stage 2 and the rest of the patients were in stage 1. In terms of local recurrence, the two groups did not differ significantly ($p = 0.83$). The overall survival in BCT and MRM was 105.43 ± 2.06, and 96.26 ± 2.16 months, respectively, which indicates that the overall survival was higher in the BCT group ($p = 0.002$).

Conclusion: The findings of the study showed that metastasis in women undergoing MRM is more and their overall survival is less. Also, there was no significant difference in local recurrence in two groups. According to the results, BCT treatment can probably be suggested as the treatment of choice.

Keywords: survival, metastasis, breast cancer, mastectomy

Comparative analysis of follicular cell- derived thyroid carcinoma: assessing the impact of high-grade features in an advanced disease cohort

Mariana Caldeira[12], Sule Canberk[123], Sofia Macedo[23]

[1]University of Porto (FMUP), Portugal. [2]Instituto de Investigação e Inovação em Saúde (i3S), University of Porto, Portugal. [3]Institute of Molecular Pathology and Immunology of the University of Porto (Ipatimup), Portugal.

Introduction: In the latest 5th WHO's Classification of Tumors of Endocrine Organs [1], a new term was created to identify those cases, at the time of pathological evaluation, which have a worse prognosis within differentiated follicular cell-derived thyroid carcinomas (DF-CDTC): Differentiated High Grade Thyroid Carcinoma (DHGTC). In our work, we aimed to evaluate its frequency and clinicopathological features within a series of advanced follicular cell-derived thyroid carcinoma (AdvTC).

Methods: We gathered several clinicopathological characteristics from a retrospective cohort of 138 patients with AdvTC submitted to total thyroidectomy, followed by therapy with radioactive iodine (131I). We reclassified them according to 5th WHO's criteria; compared DHGTC to non-high grade differentiated follicular cell-derived thyroid carcinomas (non-HGDTC), and DHGTC to Poorly Differentiated Thyroid Carcinoma (PDTC). We also performed survival analysis for disease-specific survival (DSS).

Results: We found that DHGTC's prevalence is higher in AdvTC than what is described in studies without prior clinical selection. In comparison to non-HGDTC, DHGTC cases were significantly associated to several adverse clinicopathological features: age ranges of ≤18 and ≥55 years old; presence of distant metastasis; lung metastasis; synchronous metastasis; higher median tumor size and in the range of >2 cm; tall-cell subtype of PTC; higher median mitotic index and in the range of ≥5/2 mm2; tumor necrosis; angioinvasion; high AJCC 8th edition pT stage (pT3/T4) and submission to additional therapies, including tyrosine kinase inhibitors (TKI). PDTC, in comparison to DHGTC, displayed higher tumor size, a lower mitotic count and more frequent necrosis. Independent prognostic factors for worse DSS, in the whole series, were higher age (≥55 vs <55 years old) [p=0,005, HR=19,625, 95% CI (2,479-155,372)], coherent with AJCC's new cutoff value for risk stratification, and male sex [p=0,029, HR=7,441, 95% CI (1,231-44,965)], coherent with the knowledge that male patients have more aggressive disease at presentation. DHGTC cases show worse clinical outcomes compared to non-HGDTC cases, namely more cases with persistence of disease at the end of follow-up.

Conclusions: Our results support the usefulness of subgrouping DHGTC tumors, as proposed in the 5th WHO classification, since they more frequently display aggressive features and poor outcomes.

Keywords: Thyroid Carcinoma, Differentiated Thyroid Carcinoma, Differentiated HighGrade Thyroid Carcinoma, Poorly Differentiated Thyroid Carcinoma

Bridging the Gap: Breast Cancer Awareness and Self-Examination Knowledge in Tertiary Care Centre

V.V. Kale[1]

[1]Dr. Pdmmc Amravati affiliated to Maharashtra University of Health Sciences, Nashik, Maharashtra, India

Introduction: Breast cancer remains the leading cancer diagnosis among women globally. In India, the burden of breast cancer is rising, but awareness and preventive practices, such as self-breast examination (SBE), are limited. Understanding awareness levels and knowledge gaps in populations can guide targeted educational interventions. To assess the knowledge and awareness of breast cancer and self-breast examination among women attending a tertiary care centre. The objectives are: 1. To assess participants' knowledge of breast cancer risk factors and symptoms; 2. To evaluate knowledge and practice of self-breast examination among participants; 3. To assess participants' knowledge of breast cancer risk factors and symptoms.

Methods: This cross-sectional study involved 193 women attending outpatient services at a tertiary care centre at Amravati, Maharashtra, India. Data were collected using a structured questionnaire covering demographics, knowledge of breast cancer risk factors, symptoms, and awareness and practice of SBE.

Results: The findings revealed that 75.5% of participants lacked adequate knowledge about breast cancer, and 80% were unaware of SBE. Additionally, 90% of the participants had no understanding of risk factors or treatment options for breast cancer. A significant positive correlation was observed between higher education levels and increased knowledge of breast cancer risk factors ($p < 0.05$).

Conclusions: The study highlights a substantial knowledge gap in breast cancer awareness and SBE practices among women in this tertiary care setting. The results underscore the urgent need for targeted cancer literacy programs at national and state levels, as well as community involvement to promote awareness. Integrating SBE training as part of regular hospital care may empower women to take preventive action.

Keywords: Breast Cancer, Awareness, Self-Breast Examination, Tertiary Care, Women's Health

From pH Testing to Colposcopy: A Comparative Analysis of Sequential Screening Tools for Cervical Cancer in Low-Resource Settings

V.V. Kale[1]

[1]Dr. Pdmmc Amravati affiliated to Maharashtra University of Health Sciences, Nashik, Maharashtra, India

Introduction: Cervical cancer remains a leading cause of cancer-related mortality in women globally, with disproportionate impacts in low-resource settings. Conventional screening methods like cytology and HPV testing are resource-intensive, making them inaccessible in underserved areas. This study explores the utility of a sequential cervical cancer screening strategy, integrating PrePap QR (pH testing), VIA (Visual Inspection with Acetic Acid), cytology, and colposcopy, as a feasible and cost-effective model for early detection in tribal populations.

Methods: This prospective, cross-sectional study was conducted in the tribal regions of Khapri District, Nagpur. A total of 154 women aged 30–60 years were recruited during organized cervical screening camps. Trained health workers, including ANMs and ASHAs, conducted sequential screening: PrePap QR (cervical pH testing) as the initial tool, followed by VIA, cytology (Pap smear), and on-site colposcopy for further evaluation of suspicious cases. Sensitivity, specificity, and feasibility were assessed for each method individually and as a combined strategy.

Results: PrePap QR identified abnormal pH levels in 25% of participants, of which 80% correlated with abnormal findings in subsequent tests. VIA showed acetowhite lesions in 20% of cases, and cytology detected precancerous changes in 15% of participants. Colposcopy confirmed high-grade lesions in 10% of cases. The combined sequential approach improved detection rates, reduced unnecessary colposcopies, and proved feasible in the low-resource setting.

Conclusions: The sequential cervical cancer screening model using PrePap QR, VIA, cytology, and colposcopy demonstrated high accuracy and feasibility for early detection in tribal populations. Training local health workers ensured effective implementation and scalability, offering a cost-effective alternative for cervical cancer screening in underserved areas. This study highlights the potential of integrating innovative tools like PrePap QR into cervical cancer screening programs in resource-constrained settings. The scalable approach can significantly reduce cervical cancer mortality globally by addressing gaps in early detection and timely intervention.

Keywords: Cervical cancer, PrePap QR, pH testing, VIA, cytology, colposcopy, low-resource settings, public health, tribal populations, early detection

From Needle to Diagnosis: Correlation Between Fine Needle Aspiration and Parotid Tumour Histopathology

K. Markusiewicz[1], B. Wisniewski[1]

[1]Medical University of Warsaw, Poland

Introduction: This study assesses the efficacy of fine-needle aspiration biopsy (FNAB) in diagnosing parotid gland tumours by comparing fine needle aspiration biopsy (FNAB) results with postoperative histopathology, which is the gold standard procedure.

Materials: The study included 179 patients who underwent parotidectomy between January 2019 and December 2022, with both pre-operative FNAB and post-operative pathology results available.

Results: The most common benign tumour identified in histopathology was Warthin's tumour (66 patients, 46%), while squamous cell carcinoma was the most frequent malignant lesion (11 patients, 8%). Malignant tumours comprised 22% of the cases. FNAB demonstrated a diagnostic accuracy of 73.10%, with a sensitivity of 62.50% and a specificity of 76.11%. The positive likelihood ratio was 2.62, meaning a positive FNAB result moderately increases the likelihood of malignancy, while the negative likelihood ratio was 0.49, indicating a negative result substantially reduces the likelihood of cancer.

Conclusions: The findings suggest that FNAB is a valuable diagnostic tool, particularly effective at identifying benign lesions, making it useful in pre-operative planning. However, the study also emphasises the importance of integrating FNAB with clinical and radiological evaluations to improve diagnostic accuracy and minimise false-positive and false-negative outcomes. FNAB's high specificity and accuracy support its continued use in the diagnostic workup of parotid gland tumours, aiding in the differentiation between benign and malignant lesions and informing surgical decisions.

Keywords: FNAB, salivary gland, histopathology, biopsy, parotid gland tumours

The Predictive Significance of Determining The Neutrophil-To-Lymphocyte Ratio In Patiens With NSCLC Treated With Atezolizumab In The Second Therapeutic Line

K Femić[1]

[1]Faculty of Medicine, University of Novi Sad

Introduction: Neutrophil-to-lymphocyte ratio (NLR) has previously been established as a prognostic factor for chemotherapy response in patients with NSCLC. As immunotherapy is increasingly taking a prominent place in the treatment of NSCLC, NLR becomes interesting as a cheap and reproducible predictive factor for response on immunotherapy. This study aimed to determine whether NLR can serve as a predictive factor for immunotherapy response for NSCLC.

Methods: This is a retrospective study including number of 40 patients who received atezolizumab as immunotherapy in the second line of treatment. NLR was determined in all patients included in the study according to the formula (absolute number of neutrophils/absolute number of lymphocytes) x 100, where the normal ratio value is 1-3, elevated value is 6-9, and high value is above 9. (evaluated radiologically - as stable disease, partial regression, or complete regression). Demographic characteristics of patients, clinical and pathological characteristics of the tumor, type of previous therapy, and NLR were considered, and their correlation with the type of response to therapy was analyzed. The differences in the values of numerical variables were tested using Student's t-test for two data groups or one-way analysis of variance (ANOVA) with an appropriate post hoc test for three or more data groups. In addition to descriptive statistical methods, Spearman's correlation was used. In the interpretation of results, statistical significance of $p<0.05$ was considered the minimum level of significance.

Results: Based on statistical analysis of the data, a correlation between the NRL value and gender, tumor type according to pathohistological diagnosis, stage of the disease and PFS was not established. Despite the small number of patients and lack of statistical significance, our research also found that patients with calculated NLR within reference values had a longer period without disease progression.

Conclusion: Considering the lack of statistical significance, it cannot be confirmed with certainty that NLR can serve as a predictive factor for immunotherapy response. If further research confirms the assumption that NLR represents a good prognostic factor for response to immunotherapy, its use in everyday clinical practice would enable better and higher-quality selection of patients for specific therapies.

Keywords: neutrophil-to-lymphocyte ratio; bronchial carcinoma; immunotherapy; atezolizumab

Metatarsal Aneurysmal Bone Cysts Treated With En Bloc Resection and Reconstruction With Fibular Allograft

M. Mohammadi[1]

[1]Iran University of Medical Sciences

Introduction: Treatment of Primary metatarsal aneurysmal bone cyst (ABC) with curettage and bone grafting unfortunately has a high recurrence rate, particularly in short tubular bones. This study presents a 16-year experience treating ABCs in the bones of the foot at an orthopaedic oncology referral center. Treatment involved en bloc resection and reconstruction of the defect with fibular allograft in all cases. Retrospectively collected data were used to document the outcomes.

Methods: This retrospective review includes patients with primary metatarsal ABC treated en bloc resection at a single center between 2004 and 2020. Information on the diagnosis, treatment, complications, and outcomes was collected from our database for all eligible patients. Radiologic healing was used as our primary outcome measure. The patient's function was assessed using the Toronto Extremity Salvage Score (TESS) and Musculoskeletal Tumor Society (MSTS) score.

Results: The study included 19 subjects (11 women, 8 men) with a mean age of 18 years (SD 11-35). The average resected length was 4.24 cm (3-6 cm). The mean follow-up time was 79.26 months (28-160 months). The mean TESS score and MSTS were 94.52 and 28.42, respectively. The average healing time was 10.2 weeks. No patient had local recurrence. Arthrodesis was performed in 3 patients because of joint involvement. Repeat surgery was performed for 2 patients, debridement for one because of infection and bone graft for another because of nonunion. One patient had experienced an allograft fracture.

Conclusion: Based on the Enneking classification, our experience has shown that a reasonable surgical approach for primary active and invasive metatarsal ABC is en bloc resection and reconstruction with fibula allograft. This method has a low risk of recurrence and does not result in significant functional impairment.

Keywords: Primary metatarsal aneurysmal bone cyst, bloc resection, TESS, MSTS

The Role of Vitamin D Deficiency in Breast Cancer Risk and Progression

I Khan[1], J. Hakeem[1]

[1]Department of Biochemistry and Molecular Biology, Faculty of Medicine, Bukovinian state medical university chernivtsi Ukraine

Introduction: Vitamin D3 (VD) exhibits immunomodulatory and anticancer properties, primarily mediated through the activation of vitamin D receptors (VDRs) on breast cancer cells. Breast Cancer cells have vitamin D recepters these recepters are activated by vitamin D that can make the cancer cells slow down their growth.This activation initiates pathways that inhibit tumor growth, promote apoptosis, and reduce metastasis. However, global vitamin D deficiency, especially in regions with low sunlight exposure such as Canada, some Europe countries and the US, has raised concerns regarding its potential role in breast cancer risk and severity. To evaluate the association between vitamin D deficiency and breast cancer risk, disease progression, and severity, and to investigate the anticancer effects of vitamin D3.

Methods: This study involved 1,200 women (600 breast cancer patients and 600 healthy controls) aged 30–65 years. Serum 25-hydroxyvitamin D [25(OH)D] levels were classified as deficient (<20 ng/mL), insufficient (20–29 ng/mL), or sufficient (≥30 ng/mL). Tumor size, grade, and receptor status were analyzed in breast cancer patients. In vitro experiments assessed the impact of vitamin D3 on cancer cell proliferation and apoptosis. Statistical models accounted for confounders such as age, BMI, lifestyle, and menopausal status.

Results: Vitamin D deficiency was prevalent in 75% of breast cancer patients versus 40% of controls. In vitro, vitamin D3 treatment reduced tumor cell proliferation by 40% and increased apoptosis by 30% ($p<0.01$). Clinically, sufficient vitamin D levels correlated with smaller tumors and lower grades. Vitamin D deficiency was most prevalent in Canadian participants (70%), followed by the UK (65%) and the US (55%).

Conclusion: The study demonstrates a strong link between vitamin D deficiency and breast cancer risk and progression. Adequate vitamin D levels may reduce tumor aggressiveness through mechanisms that inhibit growth and promote apoptosis. Public health initiatives should prioritize addressing widespread deficiency via supplementation and lifestyle changes. Further studies are needed to clarify causal relationships and optimal therapeutic dosages.

Keywords: Vitamin D, breast cancer, tumor progression, apoptosis, cancer prevention

Highlighting the Potential of Cold Atmospheric Plasma Therapy in Reducing the Growth of Cancer-Derived 3D Organoids

S. Esbati[1], J. Baroen[2], A. Privat Maldonado[2], E. Smits[2], A. Bogaerts[2]

[1]University of Hasselt, [2]Department of oncology, University of Antwerpen

Introduction: Cancer remains a leading challenge in the 21st century. Conventional therapies still suffer from limitations, including lack of selectivity, resistance to treatment, and severe side effects. Recent research highlights the potential of cold atmospheric plasma (CAP) to address current challenges. CAP, an ionized gas enriched with reactive species, induces oxidative stress in cancer cells, leading to cellular function disturbance, growth inhibition, apoptosis, and immunogenic cell death (ICD) activation, thereby eliciting anti-tumor responses, which are selective. However, most of the scientific evidence is derived from two-dimensional cell cultures, which cannot accurately capture the complex interactions between cells and their environment. By contrast, three-dimensional (3D) organoids provide a more accurate model of human tumor biology, preserving the heterogeneity and morphology of patient tumors. This study aims to evaluate the impact of CAP on 3D organoids derived from head and neck squamous cell carcinoma (HNSCC) and pancreatic ductal adenocarcinoma (PDAC), two of the most aggressive and lethal cancers.

Methods: Organoids derived from up to five HNSCC and five PDAC candidates are treated with the kINPen MED plasma jet. Growth rates are monitored over time, with and without treatment. Measurements are performed with the Tecan Spark Cyto and analyzed with Orbits. Reactive species, including Nitrate/Nitrite and hydrogen peroxide, are quantified using fluorometric assay kits. ICD is evaluated by measuring three markers: Calreticulin (flow cytometry), high mobility group box one (enzyme-linked immunoassay), and adenosine triphosphate (bioluminescence assay). Statistical analyses are performed using GraphPad Prism v10.

Results: Our preliminary data demonstrate that the growth rate of organoids derived from a patient with PDAC and HNSCC is diminished following CAP treatment. Consequently, we intend to monitor the growth rate of organoids using a larger sample size to elucidate how CAP interacts with various complex tumor structures across different patients. Moreover, we will assess the concentration of reactive species and investigate ICD induction following CAP treatment.

Conclusion: The observed reduction in organoid growth rates following CAP treatment suggests its potential effectiveness in targeting cancer cells in a realistic tumor model. Collectively, this study enhances our understanding of the mechanisms and alterations induced by CAP in cancer cells.

Keywords: cold atmospheric plasma, HNSCC, PDAC, kINPen MED plasma jet

Re-evaluating Existing Drugs and Molecular Docking for FLT3 Mutation in Acute Myeloid Leukemia Before Clinical Trials

A.Shayanrad[1], A. Haghi[23], M. Reza Eghdami[4], H. Poustchi[1], M. Nikbakht[23]

[1]Digestive Diseases Research Institute, Tehran University. [2]Research Institute for Oncology, Hematology and Cell Therapy Tehran University. [3]Cell Therapy and Hematopoietic Stem Cell Transplantation Research Center
[4]Department of social services and head of biological anthropology lab. University of Guilan. Rasht. Iran

Introduction: Driver mutations in the FLT3 receptor tyrosine kinase, a class III receptor, are present in approximately one third of acute myeloid leukemia (AML) patients. These mutations, known as FLT3 internal tandem duplication (FLT3-ITD) and tyrosine kinase domain (TKD) mutations, lead to the constant activation of FLT3 and its downstream signaling pathways, such as PI3K/AKT/mTOR, RAS/MAPK. Despite the initial high response rates, the use of FLT3 inhibitors as monotherapy is limited due to the development of resistance, resulting in leukemia relapse within a few weeks to months.

Methods: In this study, we focused on pre-clinical drug repositioning strategies and utilized molecular docking to evaluate 112 unique drugs that have been tested in clinical trials and clinics for the treatment of leukemia. This computer-based approach not only reduces costs but also saves time and energy. Since FLT3 mutation are both prevalent and effective in the treatment process, we investigated its binding affinities to the selected agents. Subsequently, AML cells were treated with the agents identified through molecular docking, and the expression of FLT3 gene was analyzed using real-time PCR.

Results: Our objective was to identify common pre-clinical characteristics that may determine the success or failure of drugs in patients. Our findings revealed that Fludarabine and Dasatinib exhibited strong binding affinities and have the potential to be anti-cancer candidates that target FLT3.

Conclusion: Although our analysis was limited to AML, similar investigations could provide valuable insights for drug discovery campaigns targeting other subtypes of leukemia. This knowledge can be confirmed with NGS analysis for further studies.

Keywords: Leukemia, FLT3, Drug Repositioning, Molecular docking

Efficacy of Probiotics in Alleviating Gastrointestinal Symptoms in Gastric Cancer Patients

S. S. Hoseininejad[1], N. Rahmani[1], A. Amirabadi[1]

[1]Iran/ Mashhad University of Medical Sciences

Introduction: Gastric cancer (GC) patients frequently endure debilitating gastrointestinal (GI) symptoms, which can persist even after treatment. This study aims to evaluate the efficacy of a probiotic supplement including Lactobacillus acidophilus, Bifidobacterium lactis, and Bifidobacterium longum, in alleviating these symptoms and enhancing patient's quality of life.

Materials & Methods: In this randomized clinical trial, 60 GC patients were assigned to either a probiotics group (receiving daily probiotic capsules for 2 weeks) or a placebo group (receiving daily placebo capsules for 2 weeks). participants rated the severity of their GI symptoms they on a visual analogue scale (VAS), where 0 indicated no pain and 10 represented the worse possible pain, at baseline, and at four and eight weeks post-intervention. The average VAS score for each symptom were compared between the two groups at each time point using the Mann-Whitney test. Additionally, VAS scores within each group were analyzed across different time points using Greenhouse-Geisser test.

Results: The probiotics group exhibited a significant reduction in VAS scores for upper abdominal pain and heartburn at eight weeks post-intervention compared to baseline (P value = 0.001). Furthermore, they reported significantly lower severity scores for constipation after eight weeks of treatment (P value < 0.001). No significant improvements were observed for other GI symptoms in this patient population.

Conclusion: Two weeks of probiotic supplementation significantly alleviate upper abdominal pain, heartburn, and constipation in GC patients. These findings indicates that probiotics may serve as a beneficial adjunctive treatment for managing gastrointestinal symptoms in this patient population.

Keywords: Gastric cancer, gastrointestinal symptoms, probiotics, Upper abdominal pain, Heartburn, constipation

“CHEKing” Functional Impact: Functional analysis of alternative transcripts of CHEK2

J. Federman Hoffer[1]

[1]Department of Human Genetics and Cancer, Leiden university, LUMC

Introduction: Checkpoint kinase 2 (CHEK2), is a gene that encodes for the serine-threonine kinase CHK2 protein, that is activated in response to DNA damage (1,2). CHK2 regulates cell cycle progression by inducing cell cycle arrest, allowing time for DNA repair, and promoting apoptosis to eliminate genomically unstable cells (1,3). Multiple studies have validated the tumor-suppressive role of CHK2, demonstrating that truncating variants in the CHEK2 gene, such as c.1100delC, are associated with a moderate risk of breast cancer (1, 3, 4, 5).

There is a strong need to identify which CHK2 variants are most intimately associated with an increased breast cancer risk (5). Not only because breast cancer is the most common malignancy in women world-wide, but also because it has an undeniable heritable component, and the risks associated with moderate or rare variants are not well estimated (4). Further, current variant classification guidelines disregards the possibility of encoding (partially) functional protein isoforms from alternative mRNA transcripts generated by CHEK2 variants. Therefore, we aim to implement quantitative functional characterization of alternative transcripts for CHEK2 to unravel the impact of its variants to the expression of these transcripts.

Materials & Methods: In this project, we will analyze the naturally-occurring in-frame CHEK2 transcripts and the transcripts that emerge following single exon deletions. To this end, we engineered a CHEK2 knock-out mouse ES (mES) cell line expressing full-length human CHEK2 gene from a bacterial artificial chromosome (BAC). We will perform CRISPR-Cas9 based assay by introducing dual gRNAs that facilitates incision of single exons. In order to assess the functional impact of single exon deletions that lead to expression of different alternative transcripts, KAP1 phosphorylation level at p.S473 will be analyzed. KAP1 phosphorylation, which has been shown to impair in Chek2KO mES cells upon DNA damage induction (5), will be used as a readout for CHK2 function. Furthermore, the expression of these alternative transcripts will be investigated from the barcoded BAC transcripts via PacBio-based sequencing and western blot analysis.

Results: Collectively, this systematic analysis will uncover the functionality of naturally occurring inframe transcripts as well as those generated by the deletion of individual exons at the DNA level.

Keywords: Checkpoint kinase 2, breast cancer, mES, bacterial artificial chromosome, PacBio-based sequencing

Improving cancer risk analysis: making a distinction between pathogenic and benign BRCA1 splicing variants

M.L. Constandse[1]

[1]Leiden University, LUMC

Introduction: BRCA1 is a high penetrance gene in breast cancer development. When we look at the odds ratio of BRCA1 loss of function variants, we see a 10-fold increase in breast cancer development risk when someone has a BRCA1 mutation (1). The best established function of Brca1 is its function in DNA damage repair through HR where it works together with other DNA damage response proteins, and executes its function as a tumour suppressor in this way (2). Functionality of Homologous Recombination proteins is directly linked to breast cancer risk, and therefore, germline mutations in BRCA1, BRCA2 and PALB2 that result in complete loss of protein function significantly increase the risk of breast cancer development.

There are a few important domains in the Brca1 protein of which we know that if they contain a mutation in the encoding exon, it alters protein function (3). In addition to this, there are also still many exon mutations of which we do not know the functional consequences, which are referred to as Variants of Uncertain Significance. Identifying these variants is needed because mutations in the acceptor or donor site of an exon almost always results in (partial) exon skipping and gets coded as pathogenic (4). Once a variant is identified as pathogenic it can be referred to in the clinic.

Materials & Methods: In order to assess the pathogenicity of BRCA1 splicing variants, mouse embryonic stem cells are transfected with a Bacterial Artificial Chromosome (BAC). From this, we can measure the functional consequences of the variant on HR by introducing a broken GFP gene which can only be expressed if BRCA1 is functional. Furthermore, we assess the PARPi sensitivity and survival rate of these variants. Besides performing functional assays with the BACs, we establish an RNA profile from which we can determine BRCA1 isoforms expressed, and could potentially be a rescue transcript for functional HR. To further look into these rescue transcripts, we transfect the mESCs with a cDNA construct of the same variant with which we study HR functionality of a specific isoform.

Results: With this pipeline of VUS functionality testing, cancer risk analysis can be improved in the clinic.

Keywords: Breast cancer, BRCA1, mES, Bacterial Artificial Chromosome, PARPi sensitivity

Single Strand Annealing: potential for new therapy targets for BRCA1 deficient cancer cells?

N.A. Schilder[1]

[1]Biomedical sciences, Leiden University, LUMC

Introduction: In 2022 2.3 million people were diagnosed with breast cancer worldwide, of which 5-10% had BRCA1 deficient tumors.1,2 These tumors have a high mutation rate and a poor prognosis due to the role of BRCA1 in the repair of double strand breaks (DSBs). DSBs are extremely toxic lesions that represent a major challenge for genomic integrity. To overcome these DSBs, cells have evolved four mechanisms to repair these genetic insults.2 Currently, these tumors are treated with PARP1 inhibition. These inhibitors block the repair of single strand breaks, leading to more DSBs. Moreover, PARP1 inhibition also leads to impairment of Microhomology- Mediated End Joining (MMEJ), since PARP1 also functions upstream within this DSB repair pathway. This deficiency of two out of four DSB repair pathways will result in a rapid accumulation of DSBs that is too much to overcome, ultimately leading to cancer cell death.3

However, 40 - 70% of patients develop resistance against PARP-inhibitors, thus new therapies are needed to treat these patients.3 Previously, we identified that EXO1 is important for the survival of BRCA1-deficient cells and that this survival is dependent on the role of EXO1 is single-strand annealing (SSA) repair. SSA is dependent on homology of at least 40 base pairs. However, these homologies can be up to 28kb apart and therefor SSA requires extensive trimming of the broken DNA-ends by EXO1 to expose single-stranded DNA. Next, these exposed strands are used by RAD52 for the homology search and strand annealing. After which the flaps are removed and the gaps are filled. Nevertheless, upon knock-down of RAD52 there was still SSA activity, suggesting a second parallel pathway to RAD52.

Methods: A CRISPR-based screen was performed to identify new proteins associated with the SSA pathway, many belonging to the Fanconi anemia protein family, which are known to be essential in crosslink-repair and HR.4 Subsequently, we validated the role of these FA proteins in SSA. In this study we aim to determine the essentiality of these proteins in BRCA1 knock-out cells, by performing competition assays in different cell lines and creating stable knock-out cells for rescue experiments.

Keywords: BRCA1, CRIPSR, PARP-inhibitors, DBS repair pathway. Knock-out cells

Pancreaticoduodenectomy (Whipple Procedure) for Ductal Pancreatic Adenocarcinoma in an 80-Year-Old Patient with Multiple Comorbidities

A. Mahmudov[1], I. Iliyaz[1], P. Chernopolsky[2]

[1]Medical University, Varna, Bulgaria. [2]UMHAT" Saint Marina", Varna, Bulgaria

Introduction: Pancreatic adenocarcinoma is a highly aggressive cancer, with poor prognosis often due to late-stage diagnosis. Pancreaticoduodenectomy, commonly known as the Whipple procedure remains the only potentially curative treatment for tumors located in the head of the pancreas. The procedure involves resection of the pancreatic head, duodenum, bile duct, and parts of the stomach, followed by complex reconstruction. Despite advancements in surgical techniques, it is associated with significant morbidity. This case describes the clinical presentation, surgical management, and outcomes in a patient with pancreatic adenocarcinoma, providing insight into the management of this challenging condition.

Methods: Patient Information: An 80-year-old male with type 2 diabetes, hypertension, ischemic heart disease, and chronic atrophic gastritis was admitted with jaundice and upper abdominal pain. Chief Complaint: The patient reported progressive jaundice, dark urine, pale stools, and sharp pain in the right hypochondrium. He also exhibited symptoms of acute cholecystitis. History of Present Illness: Symptoms started one month prior, with intermittent episodes of jaundice and worsening pain. No history of weight loss or vomiting was reported. Physical Examination: Physical examination revealed scleral icterus, right upper quadrant tenderness, and mild hepatomegaly. No palpable masses were identified. Investigations: CT scan: Cholecystitis, Dilated intrahepatic bile ducts and ductus choledochus. MRCP: Showed dilated intrahepatic and extrahepatic bile ducts, with a suspected tumor in the pancreatic head or uncinate process. Laboratory Findings: Elevated liver enzymes (ALT, AST), direct hyperbilirubinemia, and mildly elevated tumor marker CA 19-9. Diagnosis: Ductal pancreatic adenocarcinoma (T2N1M0, G2) with associated obstructive jaundice and cholecystitis.

Discussion: Given the patient's age, comorbidities, and tumor resectability, a pancreaticoduodenectomy (Whipple procedure) was performed, including removal of the head of the pancreas, duodenum, gallbladder, and part of the bile duct. Postoperatively, the patient was monitored in the intensive care unit, receiving insulin therapy for diabetes management and antibiotics for cholecystitis. Postoperative recovery was uneventful, with gradual resolution of jaundice and improvement in liver function. The patient was discharged on postoperative day 12 with follow-up for adjuvant therapy consideration.

Conclusion: This case highlights the feasibility of a Whipple procedure in an elderly patient with multiple comorbidities and a moderate differentiated pancreatic adenocarcinoma, demonstrating satisfactory outcomes with appropriate perioperative management.

Keywords: Pancreatic adenocarcinoma, pancreaticoduodenectomy, Whipple procedure

Prognostic factors and the Impact of Adjuvant Therapy on Survival Outcomes in ypT0-T2N0M0 Esophageal Squamous Cell Carcinoma

S. Hannah Abraham[1], S. Agouzzal[1], K.Y. Jiang[2], T. Dong[3]

[1]West China School of Medicine, Sichuan University, West China Hospital. [2]Tohoku University, Department of Surgery, Graduate School of Medicine, Sendai. [3]Sichuan University, West China Hospital, Department of Thoracic Surgery

Introduction: While neoadjuvant therapy has transformed outcomes for esophageal squamous cell carcinoma (ESCC), the post-surgical role of adjuvant therapy in ypT0-2N0M0 cases sparks ongoing debate, leaving clinicians seeking clarity on its necessity and impact on survival. We aimed to evaluate the prognostic factors influencing the survival outcomes of patients with ypT0-2N0M0 stage ESCC and to determine the necessity of adjuvant therapy in such cases.

Methods: Patients that were enrolled in the study were those with ypT0-2N0M0 stages who underwent neoadjuvant therapy followed by radical esophagectomy between 2011 and 2024. Overall survival (OS) was assessed using the Kaplan-Meier method and compared using the log-rank test. Independent prognostic factors for OS were evaluated by univariate and multivariate Cox proportional hazards model analyses. Additionally, a nomogram model was constructed and evaluated by the area under the receiver operating characteristic curve and calibration curve.

Results: Cohort study of 363 patients, of which 67 received adjuvant therapy. The median age was 63 years, with predominantly male population (80.2%), and comprising mostly of advanced cTNM stage III (49.3%). Patients without adjuvant therapy demonstrated better OS compared to those who received it (P=0.002). Multivariate analysis showed age (HR=1.04, 95% CI: 1.01-1.08, P=0.016), BMI (HR=0.85, 95% CI: 0.78-0.94, P<0.001), vascular invasion (HR=2.82, 95% CI: 1.02-7.84, P=0.047) and adjuvant therapy (HR=2.32, 95% CI:1.37-3.94, P=0.002) were independent OS prognostic factors. The nomogram demonstrated good discrimination, with an area under the receiver operating characteristic curve of 0.664. The calibration curve indicated that the predicted survival probability aligned well with the actual survival probability.

Conclusion: Older age, low BMI, greater tumor invasion, and adjuvant therapies, particularly radiotherapy, are associated with worsening of OS in ESCC patients. Neoadjuvant therapy (particularly radiotherapy and immunotherapy combinations), surgical approach (McKeown), and ypTNM stage are key factors in predicting adjuvant therapy efficacy, which may reduce survival in low-risk patients (ypT0/TisN0M0) while providing no significant benefit to ypT-1N0M0 and ypT2N0M0 patients. This highlights the potential for tailored treatment, avoiding adjuvant therapy in low-risk patients to prevent toxicity and reduced survival, with the study's nomogram aiding risk-based individualized decisions.

Keywords: Esophageal Squamous Cell Cancer, ypTNM, prognostic factors, adjuvant therapy, nomogram

Mediastinal Mass Diagnosed as Seminoma: A Rare Differential Diagnosis

A. Ožanić[1], L. Maričević[1], L. Nikić1, T. Nadarević[12]

[1]University of Rijeka, Faculty of Medicine. [2]Department of Diagnostic and Interventional Radiology, Clinical Hospital Center Rijeka (CHCR), Rijeka, Croatia

Introduction: Seminoma is a rare extragonadal germ cell tumor, accounting for only 4% of all mediastinal tumors. Due to its rarity, mediastinal seminoma is frequently overshadowed by more prevalent and aggressive diagnoses. This case report presents a 24-year-old male with progressive dyspnea and a mediastinal mass, initially suspicious for mediastinal lymphoma. A definitive diagnosis of seminoma was established after extensive diagnostic work-up, most importantly the patohistological analysis of a tissue specimen acquired by CT guided transthoracic needle biopsy.

Case presentation: A 24-year-old male presented to the Emergency Department at Clinical Hospital Center Rijeka (CHCR) complaining of chest pain and breathing difficulties. The patient reported a fivemonth history of dyspnea, initially triggered by exertion, but later occurring at rest, worsened by lying on his side, and accompanied by a persistent dry cough. A chest radiograph revealed a lobulated, dense mass in the middle and anterior mediastinum. A subsequent computed tomography (CT) scan of the chest, abdomen, and pelvis confirmed an expansive, homogeneous soft tissue mass compressing dorsal mediastinal structures. Further evaluation included a transthoracic biopsy and immunohistochemical analysis, which determined the mass to be an extragonadal seminoma. Based on these findings, the patient started treatment with four cycles of chemotherapy following the Bleomycin-Cisplatin-Etoposide (PEB) protocol at the Department of Radiotherapy and Oncology. The patient was regularly followed up, and the final chest CT scan showed a significant, almost complete reduction of the mediastinal mass. Consequently, patients' initial symptomes relieved.

Conclusion: Mediastinal seminoma is a rare malignant tumor, predominantly affecting males between the ages of 20 and 40. With advancements in diagnostic modalities and treatment protocols, high cure rates are achievable. This case emphasizes the critical need for a thorough diagnostic work-up, as the final diagnosis was only confirmed by tissue sampling and pathological analysis. Such an approach is essential to correctly identify rare conditions and guide effective treatment strategies.

Keywords: Biopsy, Needle; Extragonadal Germ Cell Tumors; Germ Cell Tumors; Mediastinal Neoplasms; Seminoma

Apoptotic Effects of Linarin and Its Derivatives on MDA-MB-231 Breast Cancer Cells: A Molecular and Cellular Investigation

Y. Ahmaditabatabaei[1], S.N. Ostad[1], F. Bargharary[1], S. Tavajohi[1]

[1]Tehran University of Medical Sciences, Department of Pharmacology and Toxocology

Introduction: Triple-negative breast cancer (TNBC) is an aggressive subtype of breast cancer with limited therapeutic options due to the absence of hormone receptors and HER-2 expression. Linarin, linarygenin, and propargyl linarin—flavonoids extracted from the hydroalcoholic extract of *Salvia* species—exhibit antioxidant, anti-inflammatory, and pro-apoptotic properties. This study investigates the apoptotic effects of these compounds on MDA-MB-231 cells, focusing on key molecular mechanisms and potential therapeutic pathways.

Methods: MDA-MB-231 cells were cultured in DMEM supplemented with 10% FBS and antibiotics. Cytotoxicity of linarin, linarygenin, and propargyl linarin was assessed using the MTT assay, and IC50 values were determined. Apoptosis was evaluated through Annexin V/PI staining followed by flow cytometry, while cell cycle arrest was analyzed at the IC50 concentration using PI staining. Western blotting was performed to assess the inhibitory effect of these compounds on STAT3 phosphorylation and the expression of apoptotic markers such as Bax, Bcl-2, and Caspase-3.

Results: Linarin, linarygenin, and propargyl linarin exhibited IC50 values of 610 µM, 18 µM, and 15 µM, respectively. Treatment with these compounds significantly reduced cell viability in a dose- and time-dependent manner. Flow cytometry revealed increased early and late apoptotic cells post-treatment, particularly with linarygenin and propargyl linarin. Western blot analysis confirmed upregulation of pro-apoptotic proteins (Bax, Caspase-3) and downregulation of anti-apoptotic proteins (Bcl-2). Additionally, all compounds inhibited STAT3 phosphorylation, highlighting their role in disrupting cell survival pathways.

Conclusion: This study demonstrates the potent apoptotic effects of linarin and its derivatives on MDA-MB-231 cells through modulation of intrinsic apoptotic pathways and STAT3 inhibition. The findings suggest these compounds, especially linarygenin and propargyl linarin, as promising candidates for TNBC therapy, warranting further preclinical studies.

Keywords: Linarin, linarygenin, propargyl linarin, triple-negative breast cancer, apoptosis, STAT3 inhibition, Bax, Bcl-2, MDA-MB-231

Case report: Malignant Granular Cell Tumor in Tracheobronchial Tree

J. Krup[1], D. Tegeltija[12]

[1]Faculty of Medicine, University of Novi Sad. [2]Institute for Pulmonary Diseases of Vojvodina, Serbia

Introduction: Pulmonary granular cell tumors (GCTs) are rare neoplasms derived from Schwann cells, with only 2–6% occurring in the tracheobronchial tree. These tumors can be benign or malignant and often present with nonspecific radiological findings, such as pneumonia, mucoid impaction, atelectasis, or an endobronchial mass. A definitive diagnosis requires histopathological and immunohistochemical analysis. Management depends on tumor size and location, with treatment options including bronchoscopic excision, laser therapy, or surgical resection when necessary.

Case Report: A 68-year-old former smoker with a history of hypertension, diabetes mellitus, and chronic obstructive pulmonary disease was admitted to our hospital with progressive dyspnea, fever, and a productive cough persisting for six days. His physical examination was unremarkable. Chest computed tomography (CT) revealed a 19 × 16 mm cavitary mass in the left upper lobe. Bronchoscopy identified multiple small, polypoid, yellow tumors in the right upper lobe bronchus. These lesions were successfully excised via endoscopic resection. Histopathological analysis revealed a submucosal tumor composed of large polygonal cells with eosinophilic granular cytoplasm, prominent nucleoli, a low nuclear-to-cytoplasmic (N/C) ratio, and no necrosis. The tumor cells were separated by delicate fibrovascular stroma, and immunohistochemical staining was positive for S100, NSE, and CD68, confirming the diagnosis of a granular cell tumor. After multidisciplinary discussion, the patient underwent a left upper lobectomy. The procedure was successful, with no complications. Pathohistological examination of the mass detected on CT confirmed it as acinic adenocarcinoma (pT1cN0MX; IA3). Postoperatively, the patient was monitored with daily physical examinations and chest X-rays. Follow-up evaluations over the past seven months showed no signs of recurrence or metastasis.

Conclusion: A granular cell tumor in the lung is rare and requires a thorough examination for an accurate diagnosis. Management depends on tumor size and location, with endoscopic resection and surgery both proving effective in this case. Regular follow-ups are essential to monitor recovery and detect any potential complications early.

Keywords: Pulmonary granular cell tumors, tracheobronchial tree, left upper lobectomy, acinic adenocarcinoma

Evaluation of clinical, morphological and pathohistological characteristics of thymoma

L. Ljubotin[1], Jelena Amidžić[1], Bosiljka Krajnović[1]

[1]Faculty of Medicine , University of Novi Sad

Introduction: Thymomas are the most common tumors of the thymus that origin from epithelial cells responsible for maturation of T-lymphocytes. They have a benign course and they grow slowly. The aim of the work is to determine gender and age of patients with thymoma, most frequent symptoms, localization of thymoma, stage and most common histological subtypes, as well as accompanying diseases.

Methods: The scientific research work represents a retrospective study of the Institute for Pulmonary Diseases of Vojvodina (IPBV). The data were obtained from the information system IPBV, Integrated Health Information System of the Republic of Serbia. The research included 51 patients with a pathohistological diagnosis of thymoma.

Results: Of the 51 patients diagnosed with thymoma, 35 (68.6%) were women and 16 (31.4%) were men. The average age was 56 years. Out of total number of patients, 34 (66.7%) had no symptoms. In 50 (98%) patients, tumor was localized in anterior mediastinum and only 1 in middle mediastinum. Of total number of patients, 25 (49%) had no accompanying diseases, while 10 (19.6%) had myasthenia gravis. Timoma in 29 (56.9%) patients was in stage I. Type B1 (16) and AB (16) were equally represented in study.

Conclusion: Thymoma was most present in adult women. Most patients with thymoma were asymptomatic. Thymoma was most often localized in anterior mediastinum. Most of the patients with thymoma had no associated diseases. Thymoma was most often diagnosed in stage I, while B1 and AB were the most common histological subtypes.

Keywords: thymus; tumors of the thymus; Masaoka-Koga classification; myasthenia gravis

Evaluation of cytotoxicity effect of stevia rebaudiana Bertoni plant extract on liver (Hep G2), clone, (HT29), breast (MCF7) cancer cell lines

P. Sattari[1], M. Hassanpour amnieh[2], A. Falahati Marvast[2]

[1]Esfahan University of Medical Sciences, Esfahan, Iran. [2]Shahid Sadoughi University of Medical Sciences, Yazd, Iran

Introduction: Since cancer is considered one of the most important causes of death in the world, compounds that show anti-cancer effects seem to be valuable, one of the plants that has many pharmacological effects, and in recent years of research Stevia plant (Stevia rebaudiana Bertoni) has been studied in order to discover its cytotoxic effects.

Methods: In this research, the cytotoxicity activity of the active ingredient of stevia plant, which is mainly steviaside and ribodioside A, has been evaluated as an anti-cancer agent. The cytotoxic effects of this compound on Hep 2 MCF7, HT29 and Hep G2 cell lines were evaluated by MTT assay method at 48 and 72 hours and at six concentrations. To determine the viability of cells, ELISA reader was used at a wavelength of 570 nm. IC50 values were also calculated for each cell line using the sigmoid dose-response curve and non-linear regression analysis using GraphPad PRISM software.

Results: Based on the results of biological evaluations, stevioside, which is the active substance of stevia plant leaves, has growth enhancing effects on Hep G2 liver cancer cell line and weak growth inhibition on MCF7 breast cancer cell line and on clone cancer cell line (HT29) did not show cytotoxic effect.

Conclusion: According to the results of this study, the active ingredients of stevia plant have different cytotoxic effects in different human cancer cell lines.

Key words: Stevia, growth inhibition assessment, MTT assay

Engineering a Monoclonal Antibody for Targeted Drug Delivery in Cancer Therapy

S. Shakarami[1]

[1]Shiraz University of Medical Sciences, Iran

Introduction: Monoclonal antibodies (mAbs) are increasingly used in targeted cancer therapies due to their ability to specifically bind to tumor antigens. However, the efficiency of drug delivery can be limited by insufficient binding affinity and selective targeting.The aim of this study was to engineer a monoclonal antibody against the HER2 receptor for enhanced targeted drug delivery in breast cancer cells, improving therapeutic efficacy and reducing side effects.

Methods: A humanized monoclonal antibody targeting the HER2 receptor was developed using phage display technology. The antibody was conjugated to Doxorubicin, a chemotherapy drug, through a cleavable linker. Binding affinity and specificity were evaluated using flow cytometry and confocal microscopy. The therapeutic efficacy was assessed in HER2-positive breast cancer cell lines (MCF-7) using MTT assays and cell cycle analysis.

Results: The engineered mAb showed a binding affinity of 3.2 nM to the HER2 receptor. Conjugation with Doxorubicin resulted in a 50% increase in cellular uptake compared to free Doxorubicin. The combination therapy showed 48% reduction in tumor growth in in vivo xenograft models compared to controls ($p<0.01$). No significant toxicity was observed in non-cancerous tissues.

Conclusion: The engineered HER2-targeting monoclonal antibody conjugated to Doxorubicin significantly improved drug delivery and therapeutic outcomes in HER2-positive breast cancer models. This strategy shows promise for personalized cancer treatment by reducing systemic toxicity and enhancing tumor-targeted drug delivery.

Keywords: HER2 receptor, Drug delivery, Doxorubicin

Case Report on Von Hippel-Lindau Syndrome Manifested as Multiple Retinal Capillary Hemangioblastomas

N. Khukhunaishvili[1]

[1]Tbilisi State Medical University, Medical Sciences, Georgia

Introduction: Von Hippel-Lindau Syndrome (VHL) is a rare, autosomal dominant, familial neoplastic disease that affects multiple organs such as the kidneys, eyes, liver, adrenals and brain. Mutations in the tumor suppressor gene VHL cause the disease, which commonly manifests as a variety of tumors such as hemangioblastomas of the retina and brain as well as renal cell carcinoma. Its prevalence is estimated to range from 1 in 36000 to 1 in 50000.
This case highlights the surgical management of advanced retinal hemangioblastomas associated with VHL. Generally retinal hemangioblastomas are treated with intravitreal injections (anti-VEGF) and laser photocoagulation. However due to advanced complications, this patient required top-tier retinal surgery, which concluded with excellent results.

Discussion: In 17.12.2024 22 year old male patient presented with a progressive decline in central vision. A routine eye examination showed impaired vision, Funduscopy revealed three peripheral hemangioblastomas with well-defined boundaries and feeding vessels. In the macular zone fibrous proliferation with retinal traction was detected. Retinal Optical Coherence Tomography confirmed retinal detachment . Angiography showed leakage from the vessels. The patient was scheduled for retinal surgery to remove the tumors. All the tumors were successfully removed. After the surgery the retina reattached and eyesight is gradually improving. Retinal hemangioblastoma is associated with Von Hippel-Lindau syndrome. Moreover the patients family history is positive for multiple cysts in the kidney and liver hemangioma. The patient was recommended to undergo an MRI scan of the brain, spinal cord, liver and kidneys and to have an ultrasound on internal organs. Ultrasound confirmed a liver hemangioma.

Conclusion: Early diagnosis, surgical removal, and regular surveillance are essential for managing VHL-related retinal hemangioblastomas, to preserve eyesight and prevent other systemic diseases. This patient is recommended to undergo regular check-ups to stay ahead of his genetic disease and detect potential hemangiomas in different organs at an early stage.

Keywords: Von Hippel-Lindau syndrome, retinal hemangioblastoma, familial neoplastic disease

Enhancing Cancer Treatment Efficacy through Hyperthermia Therapy: An Investigation into Electric Current Control and Blood Flow Effects

N. Bolandi[1]

[1]Tabriz university of medical sciences, Iran

Introduction: Cancer is referred to as the uncontrolled growth and proliferation of cells, which can lead to the formation of tissue masses known as tumors, metastases, or the spread of cancer cells to other organs in a process called metastasis. The primary methods for treating cancer include surgery, chemotherapy, radiotherapy, and the increasingly prevalent approach of hyperthermia.This study focuses on investigating the treatment of tumors and cancerous tissues through hyperthermia therapy.

Methods: The research method involves assessing the impact of blood flow within vessels on tumor tissue, as well as examining the influence of parameters such as the electrode's shape and power in hyperthermia therapy. The study utilizes COMSOL simulator software to model and analyze these factors.

Results: The results of the study demonstrate that increasing the thermal power of the electromagnetic source applied to tumor tissue can bring the maximum injury position closer to the tissue, thus reducing the time required for tumor tissue destruction. Additionally, the presence of a blood vessel within the tumor tissue can mitigate damage to healthy tissue by providing a cooling effect. Furthermore, the study reveals that the distance from the electrode's center inversely affects treatment time, with greater distances reducing the time required for tumor destruction.

Conclusion: In conclusion, hyperthermia therapy, in conjunction with the precise control of electric current, the utilization of COMSOL simulator software, and the consideration of blood flow effects, holds promise for more effective and efficient cancer treatment.

Keywords: Hyperthermia, Electric current, COMSOL simulator software, Effect og blood flow transfer

Early Detection of Lung Cancer Using a Multiplex CRISPR-Cas13 Assay for Circulating Tumor DNA Mutations

S. Eghbalkharazi[1]

[1]Department of Pharmacy, University of Milan, Italy

Introduction: Lung cancer remains the leading cause of cancer-related deaths globally, largely due to late-stage diagnosis. Current diagnostic methods, such as tissue biopsy and next-generation sequencing (NGS), are invasive, costly, and time-consuming. Circulating tumor DNA (ctDNA) in liquid biopsies has emerged as a promising non-invasive biomarker for early cancer detection. This study evaluates a novel CRISPR-Cas13-based multiplex assay for rapid and highly sensitive detection of key lung cancer driver mutations in plasma ctDNA.

Methods: A CRISPR-Cas13 detection system was designed to target frequently mutated genes in lung cancer, including EGFR (L858R, T790M), KRAS (G12C), and TP53 (R248Q, R273H). Plasma samples were collected from 180 lung cancer patients (stages I–III) and 60 cancer-free controls. ctDNA was extracted and analyzed using a fluorescence-based CRISPR-Cas13a platform. Sensitivity, specificity, and detection limits were compared with PCR and NGS.

Results: The CRISPR-Cas13-based assay detected lung cancer-associated mutations with a sensitivity of 97.2% and specificity of 99.1%, outperforming PCR (sensitivity: 91.5%, specificity: 96.8%) and approaching the accuracy of NGS ($p < 0.01$). The assay identified mutations in early-stage (I–II) patients with high accuracy (AUC = 0.92). Detection time was under 60 minutes, significantly faster than PCR (4 hours) and NGS (48 hours). The assay also demonstrated a low detection limit of 3 copies per reaction, making it suitable for early-stage screening.

Conclusion: This study demonstrates the potential of a CRISPR-Cas13-based multiplex assay as a rapid, highly sensitive, and non-invasive tool for early lung cancer detection. Its high accuracy and low turnaround time could significantly improve lung cancer screening and personalized treatment strategies. Further validation in large-scale clinical trials is needed before implementation in routine diagnostics.

Keywords: Lung cancer, gene detection, CRISPR-Cas13, circulating tumor DNA, liquid biopsy, early diagnosis, precision medicine

Assessing the viability of an LC-MRM-MS assay for protein quantification in cancer liquid biopsies

I.E. van der Voort[1], W. E. Mesker[1], Y.E.M van der Burgt[1]

[1]Clinical Chemistry and Laboratory Medicine, University of Leiden, LUMC. Netherlands. [2]Department of Surgery, University of Leiden, LUMC. Netherlands

Introduction: Colorectal cancer (CRC) is one of the prevalent cancers worldwide, occurring in aggressive and less aggressive forms. Pancreatic ductal adenocarcinoma (PDAC) is a highly aggressive tumour type associated with poor survival. These cancers are commonly classified according to the tumour-node-metastasis (TNM) system. However, the TNM is rather limited in its ability to predict treatment outcome or survival. Recently, a complementary prognostic tool was developed within the LUMC, namely the tumour stroma ratio (TSR). This tool assesses the proportion of stroma in and around tumour tissue – it was found that these values correlate with disease outcome. The principle of the test is based on tumour associated stroma – one of the central components of the tumour microenvironment. One inherent drawback of the TSR is that it requires tissue samples. To overcome this, a less invasive liquid chromatography multiple reaction monitoring mass spectrometry (LC-MRM-MS) assay has been designed. This assay consists of a panel of 13 proteins that are quantified using 32 peptides. The focus of this project is to assess the viability of the designed assay with regard to correlation with the TSR.

Methods and Results: The technical variation of the assay was evaluated as well as the reproducibility of the peptide quantifications using standard serum pools and stable-isotope labelled peptides. It was found that the LC-MRM-MS method allows for detection of the proteins AAT, C4BPA, CO3 and HEP2 above the limit of quantification (LoQ). The interpeptide agreement was assessed, since each protein was quantified with multiple peptides. Additionally, nine proteins were observed above the limit of detection (LoD), but below the LoQ. These nine proteins are still relevant for downstream experiments as these may be upregulated in tumour stroma.

Conclusion: All 13 proteins will be investigated in patient serum samples – to determine whether these proteins correlate with TSR of corresponding tissue PDAC and CRC samples.

Keywords: Colorectal cancer, tumour stroma ratio, LC-MRM-MS method

Optimizing patient selection for PIPAC in Peritoneal Carcinosis: Insights from a Single-Institution Experience

P. Catania[1], A. Di Giorgio[1], F. Pacelli[1]

[1]Italy, Università Cattolica del Sacro Cuore, Policlinico Universitario A. Gemelli

Introduction: Pressurized intraperitoneal aerosol chemotherapy (PIPAC) is an innovative method to deliver intraperitoneal chemotherapy in patients with either peritoneal metastases or primary peritoneal tumors who are not eligible for cytoreductive surgery (CRS). The current standard treatment (ST) reccomends at least three PIPAC once every 6-8 weeks, combined with systemic chemotherapy when indicated. However, many patients are unable to complete the full cycle of treatment, limiting the benefits of PIPAC. The aim of this study is to evaluate patient selection criteria to ensure that all individuals undergoing PIPAC can successfully complete the full ST, resulting in survival advantages. Additionally, the study shows how the improved patient selection over time has contributed to enhanced clinical outcomes.

Methods: This is a retrospective, single-institution study based on a prospectively managed database, which enrolled patients with gastrointestinal and gynecological cancers with non resectable peritoneal metastases treated beetwen January 2017 and March 2023.

Results: We analized a total of 226 patients for a total of 434 PIPACs at our center. The analysis revealed that only 29% of patients completed the ST during the study period. Multivariate analysis identified preoperative ascites >500 mL and a prior history of bowel obstruction as significant predictors of discontinuation. Over the years, improvements in patient selection and the increased procedural expertise have led to significant advancements. Specifically, the median overall survival increased from 8 months to 14 months, and the completion rate of the standard treatment regimen improved from 13% in 2017 to 42% in 2023.

Conclusion: These findings highlight that patient selection is crucial to ensure successful PIPAC treatment completion. Consequently, we speculate that key pretreatment factors, such as ascites and a history of prior intestinal obstructions can significantly impact the likelihood of completing the treatment regimen, influencing patient outcomes. However, larger studies are needed to validate our criteria and support their implementation in routine clinical decision-making process.

Keywords: PIPAC, Peritoneal Metastases, Surgical Oncology

Worse Prognosis for Breast Cancer in the Second and Third Trimesters and Shortly Postpartum: An Update of the Dutch Pregnancy-Associated Breast Cancer Cohort

C.F.J. Bakhuis[12], C.van Dooijeweert[12], E. van der Wall[2]

[1]Department of Pathology, University Medical Center Utrecht, Utrecht, the Netherlands. [2]Department of Medical Oncology, University Medical Center Utrecht, Utrecht, the Netherlands

Introduction: Pregnancy-Associated Breast Cancer (PABC) is often defined as breast cancer during pregnancy (PrBC) or in the first year postpartum (PPBC). In earlier research, we observed adverse disease characteristics and a worse prognosis for PABC. We now updated and expanded our nationwide Dutch PABC Cohort, also including patients with a breast cancer diagnosis after an abortion (AABC). Here, we studied the histopathology and prognosis of PrBC, PPBC and AABC patients to further explore the potential differences between these specific PABC subgroups.

Methods: All pathology reports of invasive breast carcinoma between January 1st 1988 and July 1st 2022 were screened for pregnancy-related keywords to find all patients diagnosed with PrBC (subdivided per gestational trimester at diagnosis), PPBC or AABC within one year after childbirth or an interrupted pregnancy. The different PrBC, PPBC and AABC subgroups were compared for tumor characteristics and survival.

Results: A total of 787 patients were included, of whom 60% were pregnant during their diagnosis. We observed two distinct groups based on histopathology and prognosis, with the best prognosis for patients diagnosed during the first trimester, after six months postpartum or after an interrupted pregnancy ("Group A"). When compared to patients diagnosed later in pregnancy (i.e., second and third trimester) or within six months postpartum ("Group B"), patients in Group B more often had high grade tumors (73% grade III vs. 60%, P=0.002), which were more often of the triple negative subtype (43% vs 28%, P<0.001). Also, the five-year overall survival of patients in Group B was significantly worse than in Group A (67% vs. 88%, P<0.001), a difference that also upheld in multivariable analysis.

Conclusions: With this extensive update of our nationwide Dutch PABC cohort, we show that especially PrBC patients diagnosed in the second and third trimesters and PPBC patients within six months after childbirth exhibit unfavorable tumor characteristics, with an associated worse prognosis. This highlights the need for in-depth analyses in these specific groups of PABC patients to elucidate the etiologic mechanisms involved.

Keywords: breast cancer, pregnancy, pregnancy-associated breast cancer

NK cells in the glioblastoma tumor microenvironment

N.V. Faaij[1], A. Cleven[1], P.A.J.T. Robe[2]

[1]Department of neuro-oncology, University Medical Center Utrecht, Utrecht, the Netherlands. [2]Department of Neurosurgery, University Medical Center Utrecht, Utrecht, the Netherlands

Introduction: Natural killer (NK) cells serve as the first line of defense against infected and malignantly transformed cells. However, recent studies have shown that NK cells can adopt an immunosuppressive, tumor-supporting role in various solid malignancies. We assessed whether these alterations also occur within glioblastoma multiforme (GBM), a rapidly proliferating and highly aggressive type of brain cancer for which no curative treatment currently exists.

Methods: To address this, we isolated, expanded and characterized NK cells from healthy donors, peripheral blood (PB) of GBM patients, as well as the GBM tumor-infiltrating NK (TINK) cells using flow cytometry. Next, we analyzed their ability to target GBM tumor samples, their effect on GBM proliferation and, the effect of different patient-derived GBM tumor samples on the phenotype and functionality of the NK cells using short-term and long-term live-imaging of cocultures.

Results: We found GBM tumor-infiltrating NK cells to be scarce and the in vitro expansion capacity of all GBM patient-derived NK cells inferior to healthy donor-derived NK cells. Additionally, co-culturing NK cells (both patient- and donor-derived) with GBM cells led to an increased proliferation rate of tumor cells. GBM patient-derived NK cells, both TINK and PB, displayed altered cytotoxic functionality compared to healthy donor NK cells in co-culture with GBM tumor cells.

Conclusion: Our findings indicate that GBM tumors may selectively alter or reprogram infiltrating NK cells to support tumor growth, potentially influencing NK cells in peripheral circulation as well. Future studies with a much larger sample size are needed to validate our results, minimize heterogeneity and determine the significance of NK cell involvement in GBM progression.

Keywords: Brain tumor, GBM, NK cells, tumor growth, proliferation

Elucidating cancer-associated fibroblast (CAF)-mediated immune modulation in melanoma

D. Kholodniuk[1], B. Aschenbrenner[1], B.M. Lichtenberger[1]

[1]Austria, Medical University of Vienna, Department of Dermatology

Introduction: Cancer-associated fibroblasts (CAFs) are crucial elements within the tumor microenvironment (TME), showing significant diversity based on the tissue of origin. Recent studies categorize CAFs into inflammatory CAFs and myofibroblastic CAFs, characterized by distinct phenotypes and secretomes. In non-melanoma and melanoma skin cancer, further subgroups emerge: immunomodulatory CAFs (iCAFs), matrix-CAFs (mCAFs), and RGS5+ CAFs. Intriguingly, iCAFs, which express proinflammatory and immunomodulatory factors, are highly abundant in aggressive skin tumors and serve as the major source of chemokines in the TME, indicating that they play a key role in immune cell recruitment and activation. This study aimed to elucidate the interplay between iCAFs and immune cells, focusing on T cell activation and macrophage polarization in melanoma.

Methods: A protocol was developed to transform healthy skin-resident fibroblasts into CAFs with an iCAF-like phenotype in vitro. Primary melanoma-derived CAFs and in vitro-induced iCAFs were assessed for their capacity to stimulate naïve CD4+ and CD8+ T cell activation and proliferation using a T cell activation assay. Additionally, we evaluated the impact of CAF-derived conditioned media on macrophage polarization. The iCAF gene signature was established via qPCR and scRNAseq.

Results: Both primary melanoma CAFs and induced iCAFs promoted CD4+ and CD8+ T cell activation and proliferation while conditioned media from iCAFs drove macrophages toward an M2-like phenotype. Importantly, we revealed that melanoma cells inhibited the proliferation of activated CD4+ and CD8+ T cells, while iCAFs sustained high levels of T cell proliferation. Furthermore, we could show that the secretome of melanoma cells is capable of transforming healthy dermal fibroblasts into cytokine-producing iCAF-like cells in vitro, likely in an IL1β-dependent manner.

Conclusion: These findings underscore the immunomodulatory role of iCAFs in melanoma, revealing their dual capacity to sustain T cell responses while fostering an immunosuppressive macrophage phenotype. The ability of melanoma cells to induce an iCAF-like state in fibroblasts suggests a dynamic tumor-stroma crosstalk. Targeting iCAF-mediated pathways could offer novel therapeutic strategies to enhance melanoma immunotherapy.

Keywords: Cancer-associated fibroblasts, melanoma, immune crosstalk, T cell activation, macrophage polarization, tumor microenvironmen

Detecting and differentiating benign and malignant lesions in gastric cancer using electrical impedance spectroscopy

E.Keshtkar[1], A. Keshtkar[2], M.H. Somi[3]

[1]Medicine and Surgery Department, University of Bologna, Italy. [2]Medical Physics Department, Tabriz University of Medical Sciences, Iran
[3]Internal Medicine Department, Tabriz University of Medical Sciences, Iran

Introduction: Gastric cancer is a significant global health concern, ranking as the fourth most common cancer and the second leading cause of cancer-related deaths worldwide. While gastroscopy remains the gold standard for the diagnosis of primary gastric cancer, limitations exist in the early detection of flat lesions, such as the selection of a suitable biopsy site during endoscopy, which relies on a subjective visual inspection. Electrical impedance spectroscopy is a minimally invasive diagnostic technique that can help differentiate between normal, benign, and malignant tissues in the stomach, and also allows for a more objective selection of biopsy sites during endoscopy.

Methods and Results: A total of 70 impedance data points from 34 patients were collected during endoscopy at frequencies ranging from 2 KHz up to 1 MHz. The instrument used was the Tabriz Mark1system, which is composed of a 2 mm diameter probe with four gold electrodes at its tip. A10μA current is passed between two of the electrodes, while the other two electrodes measure the voltage. Following impedance measurement, biopsies were taken from the same sites. We compared the results obtained from our method with the histopathological reports obtained from biopsies. It was observed that an increase in frequency leads to a reduction in impedivity for both normal and abnormal tissues. Additionally, the impedivity values measured at each frequency demonstrated a clear distinction between normal, benign, and malignant gastric tissues. Normal tissues exhibited the highest values of impedivity, while benign lesions showed moderately decreased impedivity, and malignant lesions had significantly lower impedivity.

Conclusion: The significant differences in impedivity between malignant and non-malignant gastric tissues can help provide a better clinical picture for the medical team in the diagnosis. While gastroscopy remains the gold standard, we highlight the potential of electrical impedance measurements as a minimally invasive diagnostic tool for the detection and differentiation of benign and malignant lesions in gastric cancer, and also its capability to enhance existing diagnostic techniques by offering a more objective approach to identifying optimal biopsy sites during endoscopy.

Keywords: Electrical impedance spectroscopy, Gastric cancer, Minimally invasive diagnosis

A Delayed Diagnosis: B-Cell Non-Hodgkin Lymphoma of the Epipharynx Initially Misdiagnosed as Chronic Sinusitis-case report

L. Nikić[1], A. Ožanić[1], I. Kučić-Mirković[1], M. Klapan (Mentor)[2]

[1]University of Rijeka, Faculty of Medicine, Rijeka, Croatia. [2]Clinic for Otorhinolaryngology and Head and Neck Surgery, Clinical Hospital Center Rijeka (CHCR), Rijeka, Croatia

Introduction: B-cell Non-Hodgkin Lymphoma (B-NHL) is a malignant lymphoid neoplasm rarely occurring in the epipharynx. Due to nonspecific symptoms like nasal congestion, headaches, and auditory disturbances, it may be misdiagnosed as chronic sinusitis, delaying diagnosis and treatment. This case highlights the importance of early recognition of atypical lymphoma presentations in pediatric patients with persistent upper respiratory symptoms.

Case Presentation: A 12-year-old male presented in December 2023 with persistent cough, rhinorrhea, and dyspnea unresponsive to amoxicillin. Weeks later, he developed left-sided facial headaches (7/10 intensity), otalgia, and progressive hearing loss with tinnitus. A painless submandibular swelling appeared soon after. Despite repeated antibiotic therapy, symptoms persisted for three months. Ear, Nose, and Throat (ENT) evaluation revealed a nasal mass, prompting hospitalization. Magnetic Resonance Imaging (MRI) and Computed Tomography (CT) confirmed an epipharyngeal lesion. Surgical biopsy confirmed high-grade B-cell Non-Hodgkin Lymphoma (B-NHL) of peripheral B lymphocytes, classified as stage II and treated under the B-NHL Berlin-Frankfurt-Münster (BFM) 2012 protocol. Treatment included a pre-phase regimen, chemotherapy (A4 block), and supportive care. During treatment, Clostridium difficile-associated gastroenteritis and oral candidiasis developed but resolved with therapy. Psychological support and prophylaxis were provided. At discharge, he was afebrile and in good condition.

Conclusion: This case emphasizes the need for thorough evaluation in pediatric patients with persistent sinus-related symptoms. Misdiagnosis can delay treatment, worsening outcomes. Clinicians should maintain suspicion for malignancy in cases with atypical progression. Improved diagnostic protocols may enhance early detection and management.

Keywords: Lymphoma, Non-Hodgkin, Medical Oncology, Nasopharyngeal Neoplasms, Sinusitis

Level of Serum Tumour Markers in Obese and Non-Obese individuals: a Case-Control Study among Indian population

S.K. jasu[1], S. Dey1, S. Bhattacahrya[1]

[1]Department of Biochemistry, Calcutta National Medical College & Hospital (CNMCH), West Bengal University of Health Sciences (WBUHS), India

Introduction: This study investigates the levels of serum tumour markers—CA 19-9, CEA, CA 125, and PSA—in obese and non-obese individuals. These markers are often elevated in various cancers but can also be found within the normal range in healthy individuals. Previous studies suggest an inverse correlation between obesity and these markers due to hemodilution. The aim of this study is to explore the impact of obesity on these tumour markers in the Indian population, which has not been extensively studied. As cancer rates rise globally and obesity becomes a major concern in India, understanding the relationship between obesity and tumour markers can help in early diagnosis and treatment.

Methods: The study involved 120 subjects (60 males, 60 females) from an outpatient department. Participants with metabolic disorders or a history of cancer were excluded. BMI and waisthip ratio were measured, and four tumour markers—CEA, CA 19-9, PSA (for males), and CA 125 (for females)—were assessed using the CLIA method. Statistical analyses, including mean, standard deviation, p-values, etc., were performed.

Results: Previous research indicates an inverse relationship between obesity and serum tumour markers, possibly due to hemodilution. The current study found similar results for CA 19-9 and CEA in males, as well as CEA in females. However, contradictory findings were observed for CA 19-9 and CA 125 in females and PSA in males. Obese females had higher mean levels of CA 19-9 and CA 125, with CA 19-9 showing mean values of 23.28 ± 13.07 (obese) vs. 18.49 ± 11.32 (non-obese), and CA 125 showing 13.38 ± 11.43 (obese) vs. 10.99 ± 5.33 (non-obese). In obese males, PSA levels were higher, with means of 1.467 ± 1.234 (obese) vs. 1.095 ± 0.836 (non-obese).

Conclusion: The study suggests that hemodilution in obese individuals may lead to an underestimation of tumour marker levels. Abdominal obesity, appreciably common in India, may contribute to these contradictory results, with factors like smoking and age also playing a significant role. Recent studies indicate obesity increases the risk of ovarian and pancreatic cancers in females, which aligns with the study's findings.
This research emphasizes the need to consider obesity's impact on tumour marker levels, especially in the context of early cancer detection and treatment strategies.

Keywords: Hemodilution, Abdominal Obesity, Waist-Hip ratio, CLIA, Standard Deviation

Intra-tumor heterogeneity of Ki-67 and PR are predictors of recurrence risk in HR+ breast cancer: an AI based digital imaging analysis approach

L. Cox[1], C. De Bie[1], F. Haentjens[1]

[1]Department of Medicine, University of Antwerp

Introduction: Hormone receptor-positive (HR+) breast cancer (BC) has a better prognosis than HR− BC. However, it still carries a long-term recurrence risk. This study aims to investigate whether intra-tumor heterogeneity of ER, PR, HER2 and Ki-67 can predict recurrence in HR+ BC.

Methods: We included 79 HR+ BC patients, classified as high-risk (n = 49) or low-risk (n = 30) based on their genomic expression profile (GEP) score. Tumor samples were stained (ER, PR, Ki-67, and HER2) and digitized for Digital Image Analysis (DIA) using QuPath. Using AI, individual tumor cells were recognized and classified in four regions of interest based on the highest tumor-cell density. Subsequently, heterogeneity was quantified using the Morisita-Horn (MH) index for which every tumor-cell was mapped using XY-coordinates and square tessalation (100 mcm) was applied. Logistic regression models with the significant variables in univariate analysis were generated and performance was evaluated with the Akaike Information Criterion (AIC).

Results: High-risk patients had a significantly higher tumor grade (p = 0.037) and Ki-67 score (> 10%) (p = 0.026). A higher Ki-67+ cell density correlated with increased recurrence risk (OR: 5.77, 95%CI 1.44 - 26.23, p = 0.016), while no significant correlation was found for ER, PR, or HER2-positive cell density. Patients with greater Ki-67 heterogeneity (MH index ≥ 0.23) had a fivefold higher probability of being high-risk (OR: 5.08, 95%CI 1.22 - 23.19, p = 0.028). Conversely, greater PR heterogeneity (≥ 0.03) was linked to a lower recurrence score (OR: 0.20, 95%CI 0.04 - 0.87, p = 0.036). The logistic regression model using DIA-derived Ki-67 scoring showed a slightly better fit (AIC = 70.4) than the conventional method (AIC = 73.3), though the Vuong test found no statistically significant difference (p = 0.226).

Conclusion: Both a high Ki67+ density and heterogeneity (indicating spatial variation in proliferation) are linked to increased recurrence risk in HR+ BC. In contrast, PR heterogeneity correlates with a lower recurrence score, possibly due to a more homogeneous presence of PR-negative cells. Furthermore, our findings suggest that a DIA analysis using AI provides a reliable alternative to traditional scoring methods.

Keywords: Breast cancer, tumor heterogeneity, Ki-67, genomic expression profile (GEP), digital image analysis (DIA), artificial intelligence (AI)

The Impact of DNA Methylation Dynamics on CD8+ T Cell Fate and Function

R.A. Wagensveld[1], A.M. van der Leun[2]

[1]Biomedical Sciences, University of Leiden, LUMC, Leiden, The Netherlands. [2]Cancer Biology, Dana-Farber Cancer Institute, Harvard medical School, Boston, Massachusetts, United States

Introduction: CD8+ T cells are critical mediators of the anti-cancer immune response, recognizing and eliminating malignant cells. Establishing an effective anti-tumor T cell response requires a diverse repertoire of tumor-reactive T cells in functional states. Recent studies indicate that DNA methylation is a key epigenetic mechanism in regulating CD8+ T cell differentiation and function. Interestingly, upon antigen recognition, CD8+ T cells undergo rapid proliferation, leading to loss of DNA methylation across large genomic regions (unpublished). Our study investigates the impact of this proliferation-associated global DNA methylation on CD8+ T cell viability, phenotype, and function. The insights gained could enhance fundamental understanding of T cell regulation and support novel epigenetic engineering strategies to improve T-cell-based immunotherapies.

Methods and Results: To assess the effects of global hypomethylation, we employed CRISPR-Cas9 gene editing to knock-out DNA methylation maintenance proteins DNMT1, HELLS and CDCA7 in CD8+T cells. These KO cells display loss of DNA methylation that reflects the global DNA hypomethylation observed in fast-proliferating CD8+ T cells. Hypomethylating CD8+ T cells were tracked over 14 days, with assessments at days 0 and 14. Key analyses included two 18-color flow cytometry panels for phenotypic characterization, Nanopore sequencing to profile DNA methylation patterns, and a multitox viability assay to measure cell viability. Preliminary results indicate decreased viability in DNMT1 KO cells, and to a lesser extent in HELLS and CDCA7 KO cells. Additionally, early observations suggest that DNMT1 and CDCA7 KO cells may exhibit a shift in phenotype, highlighting potential alterations in CD8+ T cell functionality. To further dissect the effects of DNA hypomethylation on T cell state and function, we employ bulk RNA sequencing to identify dysregulated pathways.

Conclusion: Our investigations suggest a link between global DNA hypomethylation and reduced viability. In addition, preliminary data also hint at potential phenotypic shifts in hypomethylated CD8+ T cells. We are currently validating these effects, as well as investigating the mechanisms that underly reduced cell growth and altered functionality of hypomethylating CD8+ T cells. Ultimately, these findings may contribute to developing novel epigenetic engineering strategies for enhancing T-cell-based immunotherapies.

Keywords: T cell epigenetics, DNA methylation, tumor immunology

Concurrent Paraneoplastic Syndromes in Lung Cancer: Hypertrophic Osteoarthropathy and Deep Vein Thrombosis in a Patient with Pre-existing Coronary Stent – A Case Report

M. Vahedi[14], N. Shabib[2], A.M. Mohamadi Kamal[3], A. Mobini[3], S. Shabib[34]

[1]Department of Internal Medicine, Arak University of Medical Sciences, Arak, Iran
[2]Department of Medicine and Surgery, Parma university, Parma, Italy
[3]School of Medicine, Arak University of Medical Sciences, Arak, Iran
[4]Amir Al-Momenin University Hospital, Arak University of Medical, Sciences, Arak, Iran

Introduction: Lung cancer, a leading cause of cancer-related mortality worldwide, is frequently associated with paraneoplastic syndromes such as hypertrophic osteoarthropathy (HOA) and deep vein thrombosis (DVT).

Case: This case report describes a 66-year-old man with a history of coronary stent placement who presented with a 3-month history of cough, hemoptysis, dyspnea, fatigue, and bilateral leg pain. \Diagnostic evaluation, including chest CT, bronchoscopy, bone scan, and Doppler ultrasound, confirmed squamous cell carcinoma of the lung with concurrent HOA—evidenced by digital clubbing and periostitis—and DVT in the right popliteal vein. The patient was initiated on anticoagulation therapy with apixaban to manage the DVT and referred to oncology for treatment of the underlying malignancy.

Conclusion: This case highlights the rare simultaneous presentation of HOA and DVT as paraneoplastic syndromes in a patient with squamous cell carcinoma, a less typical association than with adenocarcinoma. It emphasizes the complexity of managing such conditions in individuals with pre-existing cardiovascular disease, which requires a multidisciplinary approach.

Keywords: Hypertrophic Osteoarthropathy (HOA), Deep Vein Thrombosis (DVT), Squamous Cell Carcinoma, Paraneoplastic Syndromes, Lung Cancer

Microsurgical Reconstruction of a Craniofacial Defect Using a Free Latissimus Dorsi Flap: A Surgical Approach

K. Petkov[1]

[1]Bulgaria, Medical University, Sofia, Uni Hospital , Panagyurishte

Background: Basal cell carcinoma is the most common skin malignancy, with a tendency for local invasion and recurrence in aggressive cases. When it invades critical anatomical structures such as the external acoustic meatus, orbit, and craniofacial bones, radical excision is necessary, often leaving complex three-dimensional defects requiring advanced reconstructive techniques. Free tissue transfer is essential in cases where local flaps or skin grafts provide insufficient coverage.

Case Presentation: A 62-year-old female presented with a recurrent, locally invasive basal cell carcinoma, affecting the temporal, parietal and right frontal regions, lateral canthus of the orbit and eyebrow, with full invasion of the external acoustic meatus. The patient had undergone previous temporal bone reconstruction with a titanium plate, which was removed during this procedure. A radical excision was performed, including total parotidectomy, 1 cm tumor margin resection, and debridement of the skull defects to the level of the dura, preparing the bleeding edges with sterile wax. Given the extensive soft tissue loss and exposure of vital structures, a free latissimus dorsi myocutaneous flap was selected for reconstruction due to its large surface area, robust vascularity, and reliability in covering complex defects. Microvascular anastomoses were performed between the thoracodorsal and facial arteries (end-to-end, 9-0 Ethilon), with venous anastomoses to branches of the external jugular system. The muscle component was skin-grafted with a split-thickness graft from the left thigh.
Results: The flap demonstrated excellent perfusion with immediate capillary refill, and postoperative recovery was uneventful. Histopathology confirmed clear surgical margins, and no major complications occurred. The patient retained orbital integrity and showed progressive wound healing.

Conclusion: This case highlights the critical role of free flap microsurgery in advanced head and neck oncologic reconstruction. The latissimus dorsi flap provides durable soft tissue coverage and aesthetic restoration, making it a preferred option for large, multi-layer defects. Such cases require multidisciplinary collaboration to optimize both oncologic and functional outcomes.

Key words: basal cell carcinoma, free flap, myocutaneous flap, split-thickness skin graft

Unusual Presentation of Multiple Myeloma in a Younger Patient- a Case Report

N. Hudej[1], K. Bolte[1], D. Pulanić[12]

[1]University of Zagreb, School of Medicine, Zagreb, Croatia
[2]Division of Hematology, Department of Internal Medicine, University Hospital Centre Zagreb, Zagreb, Croatia

Introduction: Multiple myeloma (MM) is a plasma cell malignancy primarily affecting older adults, often presenting with anemia, renal insufficiency, hypercalcemia, and osteolytic lesions. This case report describes an atypical presentation of MM in a young adult male with pulmonary embolism, deep venous thrombosis, acquired hypofibrinogenemia, and inherited thrombophilia, posing significant diagnostic and therapeutic challenges.

Case presentation: A previously healthy 34-year-old male patient was hospitalized with clinically unprovoked pulmonary embolism, confirmed by CT angiography. Initial treatment included low-molecular-weight heparin (LMWH) with bridging to warfarin. Laboratory analysis revealed inherited thrombophilia (prothrombin G20210A heterozygous mutation). One month later, he developed deep venous thrombosis (DVT) of the left lower leg, complicated by nephrotic syndrome and hypofibrinogenemia (0.4-0.6 g/L). Further diagnostic work-up confirmed IgA kappa MM, stage 3B, with nephrotic-range proteinuria, and multiple osteolytic lesions. Treatment was initiated with the VCD (bortezomib, cyclophosphamide, and dexamethasone) protocol, leading to complete remission (CR) of MM and normalization of fibrinogen after four cycles, while continuing warfarin for secondary thromboprophylaxis. He then underwent high-dose cyclophosphamide and pegylated filgrastim mobilization for autologous stem cell collection, which was successful. The initial autologous stem cell transplantation (ASCT) procedure was uneventful; however, on day +8 post- ASCT, during aplasia, he developed sepsis and septic shock, requiring intensive care unit (ICU) admission. Hematological recovery occurred by day +13 with clinical improvement, but he subsequently developed an ischemic stroke with left-sided hemiplegia and motor aphasia. Treatment included LMWH, acetylsalicylic acid, and physical therapy, resulting in neurological improvement. He later received consolidation therapy with another four cycles of VCD, followed by maintenance therapy with interferon for five years, remaining in CR of MM.

Conclusion: This case highlights the importance of considering paraproteinemia in young patients with unusual thrombotic events or unexplained systemic manifestations. Early multidisciplinary management is essential for optimizing outcomes, even in complex cases with severe complications.

Keywords: Multiple myeloma, pulmonary embolism, deep venous thrombosis, thrombophilia, acquired hypofibrinogenemia

Concurring Invasive Micropapillary Carcinoma of the Breast and Follicular Lymphoma: Is there more than meets the eye? - A case report

M.C. Simian[1], I.M. Rusu[1], R. Pintican[12]

[1]Faculty of Medicine, "Iuliu Haţieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania. [2]"Prof. Dr. Ion Chiricuţă" Institute of Oncology, Cluj-Napoca, Romania

Introduction: Breast cancer is a significant global health concern, impacting millions annually. Invasive micropapillary carcinoma (IMPC) is a rare type of breast cancer, displaying distinctive morphological features along with aggressive biological behaviour. Follicular lymphoma (FL) is a low-grade, indolent B-cell lymphoma thought to arise from follicular lymphocytes. The association between the two conditions constitutes an exceedingly rare occurrence, with almost no documentation in the current literature. This paper aims to underline the diagnosis process of an unprecedented case of right mammary IMPC and grade 1/2 FL.

Case presentation: We introduce the case of a 46-year-old woman who presented to the hospital for gradual enlargement of the right breast observed over a period of four months prior to the consultation. The affected breast presented Celsus' signs, squamous lesions and erythema, suggesting carcinomatous mastitis. Moreover, palpable axillary lymph nodes were found bilaterally. Mammography of both breasts was performed, revealing microcalcifications in all quadrants of the right breast, substantial tegumentary and interstitial oedema, with numerous bilateral axillary adenopathies, although the left breast was presumed to be clean. Ultrasound further highlighted the adenopathies and indicated an additional suspect left intramammary ganglion whilst finding extensive, ill-defined, and intensely vascularised hypoechoic areas of the right breast, containing echoic focuses representing the microcalcifications. MRI investigation strengthened the mentioned results, while CT TAP revealed adenopathies as well, this time at the level of the abdomen and pelvis. The right mammary mass was diagnosed as cT4bNx-Mx IMPC of the breast, concurred after also performing a biopsy. Histopathological exam of the left axillary adenopathies revealed lymphoid follicles of various dimensions, positive for CD20, bcl-2, bcl-6, CD10, and a Ki of 15-20%, accompanied by monoclonal populations of IGK rearrangements, thus confirming the second diagnosis of grade 1/2 follicular lymphoma. The patient is currently under treatment and observation.

Conclusion: This case underlines the utmost importance of thorough patient examination, especially regarding imagistic investigations. As stated above, the chance of concurrence of the two presented types of cancer is extremely low. However, the medical team overseeing the case provided rigorous analysis, leading to an astounding final diagnosis, which allowed subsequent adequate management.

Keywords: Invasive micropapillary carcinoma (IMPC), Follicular lymphoma (FL), carcinomatous mastitis, adenopathy

Cutaneous metastasis from gastric cancer – a rare finding in the oncological sphere: a case report

I.M. Rusu[1], Rebeca Ioana Rus[1], Claudia Cristina Burz[12]

[1]Faculty of Medicine, "Iuliu Haţieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania. [2]"Prof. Dr. Ion Chiricuţă" Institute of Oncology, Cluj-Napoca, Romania

Introduction: Gastric cancer is the fifth most common cancer worldwide, with adenocarcinomas making up 95% of cases. While this type of tumor is not uncommon, it can give rise to less typical metastases, posing diagnostic and therapeutic challenges. Cutaneous metastasis is one example, with estimates of prevalence around 0.7%. Herein, we present a case in which skin lesions, later confirmed as metastases decided therapeutic course and dominated the initial presentation of a patient with gastric cancer.

Case presentation: A 58-year-old male patient presented to the oncology department accusing epigastric pain, nausea and loss of appetite. An erythematous lesion covered an important area of the right hemithorax. CT-TAP scan showed an ill-defined multilobed area in the deep plane of the anterior thoracic wall and thickening of the skin, with diffuse infiltration in the soft tissues of the left axilla, alongside vascular and nodular tracks in the adjacent muscles, all presenting characteristics of malignancy. Soft tissue echography strengthened suspicions of malignant infiltration. Based on symptomatology, an esogastroduodenoscopy was performed, identifying an infiltrative-ulcerative lesion in the antrum of the stomach. A biopsy was collected and histopathological analysis confirmed the diagnosis of G3 poorly differentiated tubular adenocarcinoma. The cutaneous lesion was later confirmed as a metastasis through a biopsy. Considering the advanced stage of the disease and a negative HER2 testing, first-line protocol chemotherapy (FOLFOX) was initiated. Irradiation of the cutaneous tumor plaque was also employed, aiding in reducing plaque size. However, the following evaluation revealed nodules had appeared on the erythematous background. This unfavorable evolution of the tumor plaque decided the switch to treatment with Ramucirumab and Paclitaxel. Six rounds have been administered so far, with progressive remission of the cutaneous plaque as the main indicator of treatment effectiveness. The team continues to monitor the evolution of the patient.

Conclusion: This report describes an atypical presentation of gastric cancer, in the form of skin lesions of metastatic nature. Moreover, as most centers worldwide encounter few cases of skin metastasis from gastric cancer, cohort studies are difficult to accomplish, making case reports a valuable source of data for larger analyses.

Keywords: Gastric cancer, cutaneous metastasis, Ramucirumab

Biomarker Heterogeneity and Its Clinical Implications in HER2-Positive and Triple-Negative Breast Cancer

J. Dupont[1], L. Eykens[1], E. Lecour[1], C. Van Berckelaer[1]

[1]Faculty of Medicine, University of Antwerp, Belgium

Introduction: Intra-tumor heterogeneity is associated with poorer outcomes in breast cancer (BC). However, heterogeneity can be defined in various ways. In this proof-of-concept study, we evaluated the heterogeneity of four commonly used predictive markers (ER, PR, HER2, and Ki67) using an AI-based digital image analysis (AI-DIA) approach and correlated this receptor heterogeneity with pathological complete response (pCR) after neoadjuvant chemotherapy (NACT).

Methods: We included 45 BC patients who received NACT. Pre-treatment biopsy samples were stained according to validated protocols for ER, PR, Ki-67, and HER2. Subsequently, slides were digitized and uploaded into QuPath software for AI-DIA. The AI detected four regions of interest on each slide with the highest tumor/stroma ratio, identified individual tumor cells in these regions, and classified the tumor cells according to staining intensity. XY-coordinates of tumor cells were extracted, and after applying a raster with individual square sizes of 100x100 mm, we calculated a Morisita-Horn Index (MHI) for each staining.

Results: Out of 45 patients, 26 (58.8%) had HER2+ and 19 (42.2%) had triple-negative (TN) breast cancer. Almost half of the patients achieved a pCR (21/45, 46.7%). A negative PR status (P=0.005), a negative ER status (P=0.055), and a higher Ki67 (P=0.040) correlated with pCR. Using the AI-DIA method, the density of ER (P< 0.001) and PR (P< 0.001) was also inversely correlated with pCR, while a higher density of KI67 (P=0.025) was associated with more pCR. A better response to NACT was observed in patients with greater heterogeneity of Ki67 (higher MHI, P=0.002) and less heterogeneity of PR (P=0.002). After constructing a multivariate logistic regression model, the only factor that remained significantly associated with pCR was greater Ki67 heterogeneity (OR: 7.14, 95%CI 1.04 – 48, P=0.045). In this model, the AI-DIA method for quantifying the density of ER, PR, and Ki67 performed comparably to the traditional scoring method.

Conclusion: Spatial localization of Ki67+ tumor cells appears to play a significant role in tumor biology. Using novel AI-DIA based method, we demonstrated that patients with greater heterogeneity of Ki67+ tumor cells, possibly indicating distinct areas of higher proliferation, are more likely to achieve a pCR after NACT.

Keywords: breast cancer, heterogeneity, AI-DIA, Ki67, HER2

The Impact of Cellular Biological Factors and Tumor Size on Predicting Axillary Lymph Node Involvement in Breast Cancer Patients

R. Mansouri[1], M. Javadi[2], S. Alipour[2]

[1]Hamadan University of Medical Sciences, Iran. [2]Department of Surgery, Hamadan University of Medical Sciences, Iran

Introduction: Axillary lymph node involvement is a crucial prognostic factor in breast cancer patients and significantly influences the choice of systemic treatment. Typically, determining whether the axillary lymph nodes are involved or not requires sampling and dissection of these nodes. This study investigates how various biological factors and tumor size affect axillary lymph node involvement.

Methods: This study retrospectively included 124 cases of breast cancer patients referred to the pathology laboratory of Besat Hospital in Hamedan from January 2018 to September 2023. According to postoperative pathological results, 87 cases (70.16%) had axillary lymph node metastasis, and others did not. The cell biology, tumor size, and grade, distant metastasis, pathological results included lymphovascular invasion (LVI), and the expression of estrogen receptor (ER), progesterone receptor (PR), HER-2, and Ki-67 were collected between two groups with or without lymph node metastasis. The relevant data were extracted from the patient's medical records and recorded in a data sheet. Subsequently, the data were analyzed using SPSS-26 software at a 95% confidence level.

Results: There was no significant difference in general demographic information between the two groups. (P=0.937) In patients with and without involvement of axillary lymph nodes, respectively, the mean and standard deviation of tumor size were 39.58(95% CI:35.67,43.49) and 34.27(95% CI:25.24,43.30) mm (P=0.003), and the frequency of KI 67 ≥10% was 37.5% and 87% (P=0.028). In addition, the proportion of LVI in the group with involvement of axillary lymph nodes was significantly higher (37.50% vs. 6.10%, P< 0.001). A statistically significant relationship was also observed between axillary lymph node involvement and tumor grades (P=0.02), as well as distant metastasis (P = 0.03). However, no significant differences were found between the two groups in the positive rates of HER-2, ER, and PR (P< 0.05).

Conclusion: The factors of larger tumor size, high grade of tumor, KI-67 ≥10%, distant metastasis, and LVI positivity are predictors for axillary lymph node metastasis in patients with breast cancer. They might be helpful for a detailed preoperative assessment of the patient's condition.

Keywords: Breast cancer, lymphatic metastasis, biological factor

Thoracic surgery dataset to predict post-operative life expectancy in lung cancer patients

A. Farshid[1], P.A. Dadkhah[2], M. Asadi Anar[3]

[1]Students Research Committee, School of Medicine, Ardabil University of Medical Sciences, Ardabil, Iran. [2]School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran. [3]College of medicine, university of Arizona, Tucson, AZ, USA

Introduction: Lung cancer survival rates remain low post-surgery, regardless of the cancer type. Thoracic surgery data provides critical insights into the outcomes of lung cancer patients. Machine learning (ML) has emerged as a powerful tool for predicting post-operative life expectancy in these patients. This study evaluates the performance of ML classification systems, focusing on the Random Forest Classifier, to predict survival outcomes after thoracic surgery.

Methods: The study utilized the Thoracic Surgery Data Set, collected retrospectively from the Wroclaw Thoracic Surgery Centre (2007–2011), comprising 470 patients who underwent major lung resections. The dataset was preprocessed, and feature selection was performed using gain ratio and information gain ranker methods. The Random Forest Classifier was employed, and model performance was evaluated using stratified 5-fold cross-validation.

Results: The model achieved an AUC score of 0.53, indicating a limited ability to distinguish between positive and negative classes. However, it demonstrated 100% accuracy, with no false positives or false negatives, correctly classifying all instances. These results highlight the potential of the Random Forest Classifier in predicting post-operative survival, while also suggesting the need for further refinement to improve its discriminative power.

Conclusion: This study demonstrates the potential of ML algorithms, particularly the Random Forest Classifier, in achieving high accuracy for predicting one-year survival outcomes for lung cancer patients following thoracic surgery. The findings underscore the importance of feature selection and cross-validation in enhancing model performance, offering valuable insights for clinical decision-making and patient care.

Keywords: Thoracic Surgery, Post-operative Life Expectancy, Lung Cancer, Machine Learning, Random Forest

Expression of SLC6A9 amino acid transporter and clinical features of endometrial cancer

M. Szczygieł[1], L. Ciecierski[2], M. Zaborowski[23]

[1]Scientific Society of Poznan University of Medical Sciences, Poznan, Poland. [2]European Center for Bioinformatics and Genomics, Institute of Bioorganic Chemistry, Polish Academy of Sciences, Poznan, Poland
[3]Department of Gynecology, Obstetrics and Gynecologic Oncology, Division of Gynecologic Oncology, Poznan University of Medical Sciences, Poznan, Poland

Introduction: EC is currently the most common gynecological cancer in high-income countries. The Cancer Genome Atlas (TCGA) distinguishes four molecular subtypes of EC: POLE ultramutated (POLEmut), microsatellite instability hypermutated (mismatch repair deficient, MMRd), copy-number low (no specific molecular profile, NSMP), and copy-number high (p53 abnormal, p53abn) subtype. Response to therapy and prognosis differs between the molecular subtypes. TCGA molecular classification was incorporated into a new FIGO staging system. Tumor cells utilize amino acids as important structural and energetic substrates. The SLC6A9 gene encodes sodium- and chloride-dependent glycine transporter. According to The Human Protein Atlas high expression of SLC6A9 prognoses unfavorable outcome in EC. The current study aimed to define the association between the expression of SLC6A9 and clinical EC features.

Methods: The expression of eighteen amino acid transporters was assessed based on transcriptomic, proteomic, and clinical data of 373 EC tumors retrieved from TCGA. Kruskal-Wallis test, followed by pairwise Dunn's tests, was used for multiple group comparisons.
Results: SLC6A9 levels were significantly higher in grade 3 compared to grades 1 and 2 ($p = 1{,}59 \cdot 10\text{-}4$; $p = 1{,}96 \cdot 10\text{-}3$, respectively). SLC6A9 expression was higher in p53abn tumors as compared to NSMP ($p = 2{,}26 \cdot 10\text{-}6$) and MMRd ($p = 3{,}50 \cdot 10\text{-}5$). In addition, SLC6A9 expression was significantly lower in MMRd than in the microsatellite stable ($p=8{,}20 \cdot 10\text{-}3$) and microsatellite instability low group ($p=0{,}03$).

Conclusion: Expression of SLC6A9 is associated with copy-number high subtype features. Grade 3 copy-number high subtype without POLE mutation present a high-risk behavior. Expression of SLC6A9 emerges as a potential marker of high-risk EC.

Keywords: amino acid transporter, endometrial cancer, tumor marker

CARDIOVASCULAR

86 mm ascending aortic aneurysm rupture risek: size as a key Indicator for surgical management

P. Cristiana-Olivia[1]

[1]Medical student at ”Iuliu Hatieganu” University of Medicine and Pharmacy, Cluj-Napoca, Romania

Cardio vascular

Introduction: Ascending Aortic Aneurysm (AAA) is a life-threatening cardiovascular condition with a high risk of dissection and rupture, requiring complex surgical intervention. Factors such as aneurysm growth rate and patient-specific risk factors like hypertension and atherosclerosis further increase rupture risk. This case highlights the impact of aneurysm size on rupture risk and the need for timely surgical management.

Case Description: A 68-year-old female patient with a history of pulmonary embolism and AAA diagnosed four
years earlier presented with anterior chest pain. Imaging examinations confirmed an 86/85mm AAA, without dissection but with moderate coronary atherosclerosis.
Surgical intervention was performed to replace the ascending aorta and aortic arch with two segments of tubular graft. The brachiocephalic arteries were reimplanted, and the graft’s distal anastomosis was completed with a stable postoperative course.
On the 10th postoperative day, the patient developed complete thrombosis of the left subclavian and internal jugular veins. Heparin and vitamin K antagonists treatment was initiated, follow-up assessments showing partial recanalization of the veins.

Discussion: This case highlights the high rupture risk associated with large AAAs, particularly those exceeding 80mm. The patient’s 86mm aneurysm placed her in a high-risk category. Large thoracic aneurysms have an annual rupture risk above 30%, making elective surgery essential for survival (Davies et al., 2006). Despite known risks, the patient postponed surgery for years, underscoring the variability in aneurysm progression and the need for timely intervention. Additional factors like coronary atherosclerosis, hypertension and pulmonary embolism history exacerbated the pressure on the aortic wall.
Surgical decisions require balancing perioperative risks with rupture likelihood. While emergency repair carries a 50% mortality rate, elective surgery has significantly lower mortality. Guidelines recommend intervention for asymptomatic AAAs≥5.5cm and symptomatic or rapidly growing aneurysms, while smaller aneurysms monitoring is essential, as most of them eventually require surgery.(Gupta et al., 2011)

Conclusion: Timely surgical repair is essential to prevent aneurysm rupture. While elective repair carries risks, they are far lower than the risks associated with rupture. Decisions should consider individual risk factors, aneurysm size, and growth rate to ensure repair before complications develop. Regular monitoring and patient education are critical for improved outcomes.

Keywords: Ascendent aortic aneurysm, Complications, Rupture, Risk factors

Cardio vascular

Advancing Cardiac Fibrosis Research: a hiPSC-Derived Cardiovascular Model

J. Bos[1], R. P. Davis[12], L. Yiangou[1]

[1]Department of Anatomy and Embryology, Leiden University Medical Center, The Netherlands, [2]The Novo Nordisk Foundation Center for Stem Cell Medicine, reNEW, Leiden University Medical Center

Introduction: Cardiac fibrosis plays a prominent role in multiple diseases, such as diabetes, myocardial infarction, and hypertension. Fibrosis is characterised by the abnormal and excessive extracellular matrix (ECM) deposition within the tissue which causes permanent loss of function of the heart. This ECM deposition is primarily driven by fibroblast-to-myofibroblast conversion, which is mainly stimulated by TGF-β signaling and marked by increased α-smooth muscle action (α-SMA) expression. Rodent models of fibrosis often fail to mimic human physiology, highlighting the need for human-specific models. Primary adult human cardiomyocytes providing physiological models, are not only difficult to isolate, but also lack key cell types involved in fibrosis, such as cardiac fibroblasts, vascular, and immune cells. This limits their ability to replicate the complex cellular crosstalk within heart tissue. Human induced pluripotent stem cells (hiPSCs) offer a solution by providing multiple cardiovascular cell types. Yet, current models such as engineered heart tissues are hampering therapy development, as they are low-throughput and require specialised equipment.

Methods: Here, we developed a 3D cardiac fibrosis model using hiPSC-derived cardiac fibroblasts, cardiomyocytes, and endothelial cells to generate cardiac microtissues (cMTs). We induced a fibrotic phenotype by treating the cMTs with the pro-fibrotic cytokine TGF-β1.

Results: TGF-β1-treated cMTs were smaller in size and showed increased expression of fibrosis markers such as ACTA2, CCN2, POSTN, COL1A1 and FN1. Moreover, the TGF-β1-treated cMTs showed increased deposition of the ECM component Collagen. Functional assessment of cMTs, showed altered contraction parameters, indicating contractile dysfunction.
In addition, we observe an expansion of vimentin+/α-SMA+ cells in these cMTs, indicating conversion of fibroblasts to myofibroblasts. As a proof of principle, we inhibited the TGF-β1 pathway and demonstrated that the fibrotic phenotypes were ameliorated. Lastly, we showed that the fibrotic phenotype is maintained after removal of the TGF-β1 sΘmulus, mimicking the irreversible damage in vivo. We are currently validating this fibrosis model in multiple cell lines and in hiPSC-derived cardioids.

Conclusion: In summary, we describe a reproducible hiPSC-derived fibrosis model that more accurately mimics human heart tissue, providing a feasible plaŋorm for investigating the cellular and molecular mechanisms of the disease.

Keywords: cardiac fibrosis, hiPSC-derived models, microtissues

High-risk pulmonary embolism: effectiveness and safety of catheter-directed embolectomy compared to systemic thrombolysis, a two-centre experience.

M. Karnaś[1], P. Kurczyna[1], J. Stępniewski[1]

[1]Jagiellonian University Medical College

Cardio vascular

Introduction: High-risk pulmonary embolism (HR-PE) poses an immediate threat to life being related with 30-50% short-term mortality. The HR-PE patients may present with heterogenous symptoms such as persistent hypotension, obstructive shock or cardiac arrest. Systemic thrombolysis (ST) is the guideline-recommended life-saving treatment although associated with significant risk of bleeding complications. Thus catheter-directed embolectomy (CDE) has emerged as an alternative life-saving treatment strategy.
Aim: The study aimed to evaluate the early outcomes and complications among HR-PE treated with ST or CDE.

Methods: We evaluated medical records of HR-PE patients, defined in line with the current European Society of Cardiology Guidelines, from prospectively conducted registries of Pulmonary Embolism Response Teams (PERT) ran in the St John Paul II Hospital in Krakow and the University Hospital of the Lord's Transfiguration in Poznan. Clinical profile, treatment strategies and outcomes defined as in-hospital mortality, International Society of Thrombosis and Hemostasis (ISTH) major bleeding and a need for bailout therapy due to primary treatment strategy failure were compared.

Results: We identified 111 HR-PE patients (67 [52-74] years old; 48.6% females). There were 41 (36.9%) individuals who presented with cardiac arrest, and the remaining with obstructive shock or refractory hypotension. Absolute contraindications to ST were detected in 29 (26.1%) patients. All patients received pharmacological circulatory support and 4 (3.6%) also mechanical, all from CDE group. 53 (47.7%) patients were treated with ST and 58 (52,3%) with CDE. There were 26 (24.5%) in-hospital deaths. Patients treated with CDE had lower in-hospital mortality rate as compared to those treated with ST [4 (6.9%) vs 22 (45.8%) respectively, $p<0.001$]. The risk of major bleedings was greater in the ST group than in the CDE [9 (22.5%) vs 3 (5.1%) respectively, $p=0.03$]. Failure of the ST was reported in 4 (7.8%) patients.

Conclusions: HR-PE is a severe medical condition associated with highly increased risk of early death. The use of CDE as a primary reperfusion strategy was associated with favourable outcome and less frequent bleeding complications as compared to the ST

Keywords: venous thromboembolism, transcatheter interventions, reperfusion therapy

Cardio vascular

Pulmonary Embolism Presenting as Syncope with Underlying Family History: A Rare Case Report

A. Chavhan[1]

[1]Datta Meghe Institute of Higher Education and Research, Wardha, India

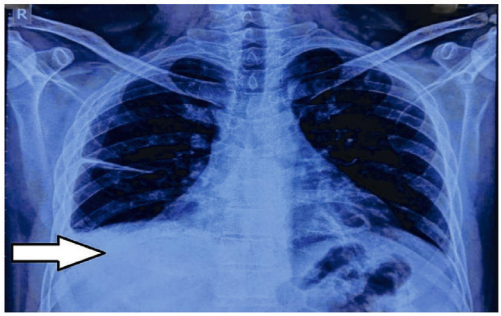
Introduction: An embolism occurs when a foreign body blocks a blood vessel, potentially leading to severe conditions like stroke or pulmonary embolism (PE). PE results from blockage in the pulmonary artery, often caused by deep vein thrombosis (DVT). It is life-threatening and difficult to diagnose, especially when symptoms are non-specific. Syncope is a relatively easy symptom to detect but rarely associated with PE. In cases without clear risk factors, family history becomes vital for diagnosis.

Methods and results: Patient Profile: A 38-year-old male presented with sudden syncope without prior symptoms or medical history of thromboembolic conditions. Initial Examination: Vital signs revealed mild tachycardia, hypotension, and marginally decreased oxygen saturation. A pleural rub was noted, but no overt signs of DVT were present.

Diagnostic Workup: Clinical findings and investigations supported PE. Key findings included pleural rub, a family history of stroke, RV dilatation, IVC congestion, anemia, elevated D-dimer, and pleural effusion confirmed by CTPA. Based on ESC/ERS guidelines, anticoagulation therapy was initiated, and further monitoring was advised.

Conclusion: This case highlights the diagnostic challenge of PE when syncope is the sole presenting symptom. It underscores the importance of considering PE in the differential diagnosis of syncope, particularly in patients with a family history of thromboembolic events.

Keywords: Pulmonary embolism, genetic history, syncope.



Respiratory Distress in (Near-)Term Newborns Delivered by Elective Caesarean Section: A Retrospective Observational Study

P.J.M. Smits[1], S.J.E. Cramer[1], A.B. te Pas[1]

[1]Willem-Alexander Children's Hospital, department of pediatrics, division of Neonatology, Leiden University Medical Center, Leiden, the Netherlands

Cardio vascular

Introduction: This study aimed to assess the incidence and severity of respiratory distress in (near-)term newborns delivered by elective caesarean section (ECS) at the Leiden University Medical Center (LUMC) based on the respiratory interventions that are provided post-delivery.

Methods: We conducted a retrospective observational study of newborns (≥36 weeks gestation)
born at the LUMC by ECS between July 1st 2016 and December 31st 2020. Inclusion criteria involved all NICU admissions after ECS, excluding congenital defects or admission due to non-respiratory problems. To determine the incidence and severity of respiratory problems, data was extracted from NICU records and the extent of respiratory interventions was used to stratify according to a severity classification (GR0-GR4).

Results: Of 1200 newborns delivered by ECS, 132 (11%) were admitted to the NICU, of which 80 (6.7%) were due to respiratory problems. Among these, 4 (5%) newborns had a normal transition without respiratory support but were admitted to the NICU for continuous monitoring, 4 (5%) newborns only received short-term respiratory support at birth but were admitted to the NICU for continuous monitoring, 62 (77.5%) newborns were admitted to the NICU for non-invasive respiratory support for ≤24 hours, 7 (8.75%) newborns were admitted to the NICU for respiratory support for >24 hours and/or surfactant therapy, and 3 (3.75%) newborns were admitted to the NICU because of persistent pulmonary hypertension of the newborn (PPHN) confirmed on ultrasound and received oxygen and/or nitric oxide (NO) therapy.

Conclusions: Newborns delivered by ECS have a higher rate of NICU admissions compared to those delivered vaginally, of which a substantial proportion consists of respiratory-related admissions. Most newborns required short-term non-invasive respiratory support for less than 24 hours. Detailed stratification of respiratory outcomes and required care enhances understanding of post-ECS neonatal care, emphasizing the need to reduce ECS rates and develop interventions to minimize respiratory complications and associated social and healthcare burdens.

Keywords: Respiratory distress; elective caesarean section; NICU admission; perinatal transition

Cardio vascular

Melatonin as a reactive treatment for post-operative delirium in patients in the cardiac ICU: a retrospective cohort study

A. Clarke[12], J. Hinchion[12]

[1]Department of Cardiothoracic Surgery, Cork University Hospital, Wilton, Cork, Ireland. [2]University College Cork, College Road, Cork, Ireland.

Introduction: ICU delirium is a significant problem in post-operative cardiothoracic patients, contributing to prolonged ICU and hospital stays and increased mortality. Current pharmacological treatments, such as benzodiazepines and antipsychotics, have notable adverse effects, leading to interest in safer alternatives. A systematic review has shown melatonin's effectiveness as a prophylactic agent for delirium in surgical and ICU patients. This study aims to assess the use of melatonin as a reactive therapeutic agent in post-operative delirium in cardiac ICU patients.

Methods: This retrospective cohort study analysed data from 127 patients diagnosed with delirium, confirmed through a positive CAM-ICU score. Patients were divided into two groups: one that received melatonin (n=57) as part of their delirium management and another that did not (n=70). The primary outcome was delirium regression, measured by a negative CAM-ICU score during the ICU stay. Secondary outcomes included ICU length of stay, hospital length of stay, and duration of mechanical ventilation. Statistical analyses included the Mann-Whitney U test for continuous variables, the Chi-square test for categorical variables, and binomial regression analysis to determine predictors of delirium regression.

Results: Delirium regression was slightly lower in the non-melatonin group (23/57, 32.9%) compared to the melatonin group (24/70, 42.1%), though this difference was not statistically significant (p=0.356). Binomial regression revealed an odds ratio of 0.845 (95% CI: 0.329-2.172, p=0.727) for melatonin's effect on delirium regression. Statistically significant predictors of delirium regression included ICU length of stay (1.126, 95% CI: 1.041-1.219, p=0.003) and mechanical ventilation (0.897, 95% CI: 0.833-0.965, p=0.004).

Conclusion: Melatonin showed a loose association with delirium regression but did not demonstrate significant effectiveness as a reactive treatment for post-operative delirium in cardiac ICU patients. Larger studies with more controlled environments are needed to better assess its potential as a treatment for ICU delirium.

Keywords: ICU Delirium; Melatonin; Post-operative Delirium; Cardiac ICU; Delirium Regression

Influenza B-Associated Myopericarditis Leading to Cardiogenic Shock: A Case Report

A. Ožanić[1], L. Nikić1, P. Baumgartner[2], T. Jakljević (supervisor)[2]

[1]University of Rijeka, Faculty of Medicine, Rijeka, Croatia, [2]Clinic for Cardiovascular Diseases, Clinical Hospital Center Rijeka (CHCR), Rijeka, Croatia

Cardio vascular

Introduction: Myopericarditis, an inflammatory condition affecting both the myocardium and pericardium, is often triggered by viral infections. While less commonly linked to cardiovascularccomplications than Influenza A, Influenza B can cause severe myocarditis, potentially resulting in cardiogenic shock and multi-organ failure. Early detection and aggressive treatment are crucial for improving patient outcomes. This case highlights the transition from Influenza B-associated myopericarditis to cardiogenic shock, underscoring the need for rapid diagnosis and intervention.

Case report: A 35-year-old female was transferred from Ogulin General Hospital to Clinical Hospital Center Rijeka (CHCR) for invasive cardiac evaluation due to suspected acute myocardial infarction. Three days before admission, she developed high fever, dry cough, generalized malaise, and neck and interscapular pain, worsening in the evening. An electrocardiogram (ECG) at the referring hospital showed inferolateral ST-segment elevation, prompting urgent transfer. Upon arrival at CHCR, the patient was hemodynamically stable. Emergency coronary angiography ruled out obstructive coronary artery disease. Given her febrile illness and respiratory symptoms, polymerase chain reaction (PCR) testing confirmed Influenza B infection. Initial transthoracic echocardiography (TTE) showed a preserved left ventricular ejection fraction (LVEF) of 55% and minimal circumferential pericardial effusion, suggesting myopericarditis. Antiviral therapy with oseltamivir was initiated. On the second day, acute decompensated heart failure developed and despite diuretic therapy and medical management, her condition deteriorated into cardiogenic shock. Repeat TTE showed an LVEF of 15–20%, necessitating mechanical circulatory support. The patient was subsequently transferred to the Cardiac Intensive Care Unit.

Conclusion: This case highlights the rapid progression of myopericarditis to cardiogenic shock,
emphasizing the importance of early diagnosis, aggressive therapy, and multidisciplinary management. It also reinforces the need for preventive measures like vaccination to mitigate severe outcomes.

Keywords: Cardiogenic Shock, Extracorporeal Membrane Oxygenation (ECMO), Influenza B, Myocarditis, Pericarditis

Cardio vascular

Correlation between obesity and diabetic nephropathy among patients with type 2 diabetes, Kyrgyzstan.

M. Uzair[1], A. Moldobaeva Z.[1]

[1]International higher school of medicine, Bishkek, Kyrgyzstan

Introduction: Approximately 1.5 million deaths are directly caused by diabetes each year. Obesity is a risk factor for CKD-related disability and mortality after adjusting for diabetes and hypertension. It is yet unknown how obesity relates to diabetic nephropathy (DN), despite the fact that it is a major risk factor for type 2 diabetes. The aim is to study correlation between obesity and diabetic nephropathy in patients with type 2 diabetes mellitus.

Methods: Study design: cross-sectional retrospective. The data was obtained between 2023 and 2024 from Vedanta University Hospital in Bishkek, Kyrgyzstan. Our study included 60 patients with T2DM (-32 men and -28 women) of age between 44 to 86 year (mean age -62,0±10,0 years). Our criteria is to take patient who have T2DM more than a five year. Anthropometric parameters measured included body mass index (BMI), blood pressure (Bp), blood test include glucose, HbA1c, total cholesterol, triglycerides, high density lipoprotein (HDL) and low density lipoprotein (LDL) were determine. Severity of diabetic nephropathy was assessed by the level of microalbumin in urine excretion. The patients were categorized into 2 groups: with obesity (BMI≥30 kg/m2) and without it (BMI<30 kg/m2).

Results: The prevalence of microalbuminuria increased ($p<0,05$) in type 2 diabetic patients with a BMI ≥30 kg/m2. We frequently observe elevated blood pressure, triglycerides, total cholesterol, and high and low density lipoproteins in patients with type 2 diabetes whose BMI is greater than 30 kg/m2 compared to less than 30 kg/m2.

Conclusion: Type 2 diabetes mellitus and hyperglycemia are the two main mechanisms of kidney damage in diabetes mellitus, along with obesity and hypertension both have a major impact on the development of diabetic nephropathy.

Key words: obesity, type 2 diabetes mellitus, diabetic nephropathy, microalbumin, body mass index (BMI), glycohemoglobin, hypertension.

Normotensive shock in a patient with acute pulmonary embolism – dangerous, yet still overlooked state. A case report.

W. Chaba[1], M. Karnaś[1]
Supervisor: J. Stępniewski MD, PhD

[1]Jagiellonian University Medical College, Cracow, Poland

Cardio vascular

Introduction: Normotensive shock (NS) is defined as a decreased cardiac index (CI) ≤2.2 l/min/m2 without hypotension (SBP≥90 mmHg). Detection of that state in patients with acute pulmonary embolism (APE) has been recently gaining recognition as it may indicate the need for a reperfusion treatment approach.

Case presentation: We report a case of a 78-year-old male with bilateral, central APE who was admitted to the Pulmonary Circulation Centre in the St. John Paul's II Hospital Krakow, Poland from a peripheral hospital. Upon arrival, he presented with dyspnoea at rest, respiratory compromise with 79% oxygen saturation on room air, tachycardia of 120 bpm, and blood pressure of 110/90 mmHg. Echocardiography revealed right ventricle overload with the right-to-left ventricle ratio of 1.6. His NT-proBNP (2402 pg/mL), cardiac troponin (304 ng/L) and lactate (2.3 mmol/L; norm).

Discussion: The prevalence of NS in patients with APE may reach up to 34%. Patients with NS usually present with right ventricle overload and signs of peripheral hypoperfusion causing greater risk of deterioration. Early detection of NS is a key to decide on catheter-directed reperfusion treatment.

Keywords: catheter-directed embolectomy, PERT, reperfusion treatment

Cardio vascular

The Role of Novel Biomarkers in Predicting Early Cardiovascular Events: A Prospective Cohort Study

S. Shakarami[1]

[1]Shiraz university of medical sciences, Iran.

Introduction: Cardiovascular diseases (CVDs) remain the leading cause of morbidity and mortality worldwide. Early identification of individuals at risk is crucial for timely intervention. Recently, novel biomarkers such as myeloperoxidase (MPO) and soluble ST2 (sST2) have gained attention as potential predictors of cardiovascular events. This study aims to evaluate the predictive value of these biomarkers in assessing early cardiovascular risk.

Methods: A prospective cohort study was conducted on 250 patients aged 40–70 years with no prior history of cardiovascular disease but exhibiting at least one risk factor (hypertension, diabetes, or dyslipidemia). Blood samples were collected at baseline to measure levels of MPO, sST2, and traditional markers such as high-sensitivity C-reactive protein (hsCRP). Patients were followed for 24 months, with primary outcomes including the incidence of major adverse cardiovascular events (MACE) such as myocardial infarction, stroke, and cardiovascular death. Receiver operating characteristic (ROC) analysis was used to assess the predictive power of the biomarkers.

Results: During the follow-up period, 38 patients (15.2%) experienced MACE. Baseline levels of MPO and sST2 were significantly higher in those who developed cardiovascular events compared to those who did not ($p < 0.001$). ROC analysis revealed that sST2 had the highest predictive accuracy (AUC = 0.84), followed by MPO (AUC = 0.79) and hsCRP (AUC = 0.74). Multivariate regression analysis confirmed that elevated MPO and sST2 levels were independent predictors of MACE after adjusting for traditional risk factors ($p = 0.002$).

Conclusion: This study demonstrates that novel biomarkers such as MPO and sST2 can significantly enhance cardiovascular risk stratification. Their incorporation into routine clinical assessments may improve early detection of at-risk individuals and guide preventive strategies. Further large-scale studies are needed to validate these findings and establish standardized cutoff values for clinical use.

Keywords: Cardiovascular risk, biomarkers, myeloperoxidase, soluble ST2, myocardial infarction, prevention.

Exploring the Association Between the C-Peptide to Glucose Ratio and Cardiovascular Disease Risk Factors, Evidence from NHANES.

H. Ghasemirad[1]

[1]Shahid Sadoughi University of Medical Sciences,Yazd,Iran

Cardio vascular

Introduction: Cardiovascular disease (CVD) remains a leading cause of morbidity and mortality worldwide. Identifying biomarkers that correlate with CVD risk is essential for early detection and prevention. The C-peptide to glucose ratio has emerged as a potential biomarker of insulin resistance and metabolic dysfunction, which contribute to cardiovascular pathophysiology. However, the relationship between this ratio and cardiovascular risk factors remains underexplored. This study uses data from the National Health and Nutrition Examination Survey (NHANES) 2001-2002 to investigate the association between the C-peptide to glucose ratio and a composite cardiovascular history index.

Methods: We utilized two key datasets from NHANES 2001-2002: one containing cardiovascular risk factor data and the other containing biochemical measurements of C-peptide (pmol/mL) and glucose (mg/dL). A cardiovascular history index was created by aggregating responses to multiple cardiovascular-related questions, representing participants' reported cardiovascular symptoms. The C-peptide to glucose ratio was calculated by dividing C-peptide levels by glucose levels. Correlation analysis was conducted to examine the relationship between the cardiovascular history index and the C-peptide to glucose ratio.

Results: The correlation analysis revealed a weak positive correlation between the cardiovascular history index and the C-peptide to glucose ratio ($r = 0.133$, p-value < 0.05). While the correlation was modest, the findings suggest that individuals with higher cardiovascular risk, as indicated by the cardiovascular history index, tend to have a slightly elevated C-peptide to glucose ratio. This highlights the potential role of insulin resistance and metabolic dysfunction in cardiovascular symptomatology.

Conclusion: This study provides preliminary evidence of a weak positive association between the C-peptide to glucose ratio and cardiovascular disease risk factors in the NHANES 2001-2002 dataset. Although the correlation is modest, these findings suggest that the C-peptide to glucose ratio may serve as a useful biomarker for assessing cardiovascular risk, particularly in individuals with elevated BMI or advanced age. Further studies with larger, more diverse cohorts are needed to confirm these findings and explore the underlying mechanisms linking metabolic biomarkers to cardiovascular disease.

Cardio vascular

Prevalence, Prognosis, and Outcomes of Catheter Ablation in Patients with Premature Ventricular Complexes: A Retrospective Study from Afshar Hospital (2015-2020)

N. Ghasemirad[1]

[1]Shahid Sadoughi University of medical sciences , Yazd,Iran

Introduction: The aim of this study was to assess the prevalence, prognosis, and success rates of catheter ablation for PVCs (Premature Ventricular Complexes) in patients referred to Afshar Hospital in Yazd from 2015 to 2020.

Methods: A retrospective cohort study was conducted on 75 patients diagnosed with PVCs who underwent catheter ablation. Data was collected from medical records, including demographic information, risk factors, drug treatments, PVC origins, and follow-up outcomes. Statistical analyses were performed to assess the relationship between PVC origin, ablation success, recurrence, and complications.

Results: The cohort consisted of 56% males and 44% females, with a mean age of 47.01±13.7 years. The most common PVC origin was the Right Ventricular Outflow Tract (RVOT) (54.7%), followed by the Left Ventricular Outflow Tract (LVOT) (17.3%), and Mitral Ring (12%). Hypertension was present in 31% and diabetes in 11% of patients. The most frequently used medications were β-blockers (56%). Ablation was successful in 81.3% of cases, with a recurrence rate of 18%. The most common complications related to PVCs included palpitations (62.7%), chest pain (30.7%), and shortness of breath (20%). Among ablation-related complications, hematoma at the catheter insertion site occurred in 2.7% of patients, and thromboembolism in 1.3%. The success of ablation was significantly higher in PVCs originating from the Coronary Cusp and Epicardium (100% success rate).

Conclusion: Catheter ablation is an effective treatment for PVCs, with an overall success rate of 81.3%. PVC origin plays a critical role in determining the success of ablation and the likelihood of recurrence. The findings highlight the importance of identifying PVC origin for better clinical management and improving treatment outcomes.

Keywords: Premature Ventricular Complexes, Catheter Ablation, PVC Origin, Ablation Success, Recurrence, Risk Factors

“Two Tracks, One Station – A Heart at a Crossroad. A Clinical Case of Complete Transposition of the Great Arteries: Is Reaching the Destination Possible?”

W. Lisińska[1], Prof. I. Strzelecka PhD[1], Prof. M. Respondek-Liberska MD, PhD[1]

[1]Medical University of Lodz, Poland

Cardio vascular

Introduction: Complete transposition of the great arteries (dextro-transposition, d-TGA) is congenital heart disease, characterized by atrioventricular concordance (normal atrial and ventricular connections) and ventriculo-arterial discordance (the aorta arises from the right ventricle, while the pulmonary artery originates from the left ventricle). This anatomical abnormality disrupts normal blood flow, leading to life-threatening hypoxemia if untreated.

Case Report: A pregnant 29-years old patient was referred at 22 + 6 days of gestation to a Prenatal Cardiology Clinic following a second-trimester ultrasound that raised suspicion of a congenital heart defect. Her obstetric history included an early pregnancy complication at 6+2 weeks, when she was admitted for vaginal bleeding and diagnosed with a 3 cm subchorionic hematoma. A fetal echocardiogram confirmed the diagnosis of complete d-TGA with ventricular septal defect (VSD) and outflow congenital heart disease (CHD), along with good atrial communication (FO index = 33%) and preserved pulmonary circulation. Prenatal monitoring evaluations at 25, 28, 30, and 34 weeks of gestation confirmed stable fetal hemodynamics and normal growth. It was concluded that there was no immediate need for a Rashkind procedure (a balloon septostomy) postnatally, as the fetal heart had good atrial communication (FO index=27%). Delivery was performed via cesarean section, and the neonate was born with a birth weight of 3700 g with Apgar scores were 5/7/ 7. At two weeks of age, the neonate underwent planned corrective cardiac surgery, which involved connecting the proximal aorta to the pulmonary artery outlet, simultaneously reimplanting the coronary arteries into the “neo-aorta,” and connecting the proximal pulmonary artery to the aortic outlet. Postoperatively, the infant required intensive care with mechanical ventilation and catecholamine infusion, wound infection was managed with teicoplanin and ceftazidime. Follow-up echocardiography confirmed good myocardial contractility and no pericardial effusion.

Conclusion: The connections between the systemic and pulmonary circulations of blood in atrial septal defect, patent ductus arteriosus, or ventricular septal defect allows the neonate with TGA to survive until the arterial switch surgery.Early prenatal diagnosis of congenital heart defects, such as complete d-TGA, is crucial for optimizing outcomes.

Keywords: congenital heart disease, d-TGA, prenatal

Cardio vascular

Clinical significance of the coronary flow velocity reserve in prediction of cardiac mortality and heart failure in hypertrophic cardiomyopathy

D. Zdravkovic[1], M. Tesic[12]

[1]University of Belgrade, Faculty of Medicine. [2]Clinic for Cardiology, University Cinical Centre of Serbia

Introduction: Microvascular dysfunction is considered to be a major determinant of clinical deterioration and outcome in patients with hypertrophic cardiomyopathy (HCM). Nevertheless, long-term prognostic value of transthoracic Doppler echocardiography (TDE) coronary flow velocity reserve (CFVR) on cardiac mortality and heart failure requiring hospitalization is uncertain in HCM patients. The aim of our study was to evaluate long-term prognostic value of CFVR on clinical outcome in HCM patients.

Methods: The cohort of 196 HCM patients (100 woman; mean age 48±14 years) was included in the prospective study. Patients' clinical characteristics, echocardiographic and CFVR findings for left anterior descending (LAD) were
evaluated in all patients. The primary outcome was composite of HCM related cardiac death and heart failure requiring hospitalization. Patients were stratified into two subgroups depending on CFVR LAD value: Group 1 (CFVR LAD>2, (n=119)) and Group 2 (CFVR LAD≤2, (n=77)).

Results: During a median follow-up of 109 months, 40/196 (20.4%) patients had primary outcome. In Group 1, there were 4/119 (2.0%), whereas in Group 2 there were 36/77 (46.7%,p<0.001 vs. Group 1) events of the composite outcome. By Kaplan-Meier analysis, patients with preserved CFVR LAD had significantly higher cumulative event-free survival rate compared to patients with impaired CFVR LAD (98.3% and 97.0% vs. 75.2% and 55.3% at 5 and 8 years, respectively: log-rank 51.1, p<0.001), Multivariable analysis identified only CFVR LAD≤2 as an independent predictor for adverse cardiac outcome (HR 12.150; 95% CI 4.192-35.213, p<0.001), adjusted for the age, gender, family history of sudden cardiac death, maximal wall thickness, presence of moderate mitral regurgitation and left atrial volume indexed for body surface area >34ml/m2.

Conclusion: In patients with HCM, impaired CFVR LAD (≤2) is a strong, independent long term predictor of adverse cardiac outcome.

Keywords: hypertrofic cardiomyopathy; microvascular disfunction; CFVR.

Giant Ascending Aortic Aneurysm: A Life-Threatening Dilemma? – A case report

R. I. Rus[1], L. O. Rusu[1], P. Gocan[2]

[1]Faculty of Medicine "Iuliu Hațieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania, [2]"Niculae Stăncioiu" Heart Institute, Cluj-Napoca, Romania

Cardio vascular

Introduction: Giant ascending aortic aneurysms (AAo) are extremely rare due to advancements in diagnostic imaging, yet they remain a serious condition with high morbidity and mortality. Aneurysms exceeding 6 cm in diameter are associated with a significant risk of rupture or dissection, necessitating timely surgical intervention. However, the complexity of surgical repair and perioperative risks makes management challenging.

Case Report: We present a case of a giant AAo aneurysm in a 73-year-old woman with severe aortic insufficiency. The patient had a history of hypertension, and presented with worsening dyspnea. Electrocardiography (ECG) revealed an 86 bpm sinus rhythm, and chest X-ray indicated mediastinal widening and cardiomegaly. Transthoracic echocardiography (TTE) identified a severely dilated ascending aorta (95 mm), severe aortic insufficiency, and left ventricular dysfunction. Thoracoabdominal CT angiography confirmed a giant aneurysm of the ascending aorta, with a maximal transverse diameter of 96/97 mm, compressing the left atrium and extending to the aortic arch. A fusiform aneurysmal dilation of the descending thoracic aorta was also noted, but without signs of dissection or rupture. Due to the imminent risk of rupture, prompt surgical intervention was recommended, including prosthetic aortic valve replacement, AAo and aortic arch replacement, and supra-aortic trunk reimplantation ("elephant trunk" technique). The main risks include rupture, dissection, and compression of adjacent structures, leading to heart failure or life-threatening arrhythmias. The patient decided to postpone the procedure. On six-month follow-up, she remained in a stable condition, with only mild clinical symptoms, and imaging findings remained unchanged.

Conclusion: Giant ascending aortic aneurysms are uncommon due to improved early detection. However, they remain life-threatening, with a 31% risk of rupture or dissection when exceeding 6 cm in diameter. Surgical management is essential, despite its considerable technical complexity and elevated perioperative risk. This case highlights the delicate balance between surgical risks and disease progression, emphasizing the importance of vigilant monitoring in patients who delay intervention.

Keywords: Giant ascending aortic aneurysm; aortic insufficiency; thoracoabdominal CT angiography; surgical management.

Cardio vascular

Sensitivity and specificity of lactate clearance as a marker for the prognosis of acute kidney injury in patients with tourniquet syndrome

P. Kyiko[1]

[1]Kharkiv National Medical University

Introduction: The risk group in medical triage of victims is patients who have blood loss, but at the time of assessment are conscious without clinical changes in hemodynamic parameters. The aim of our study was to determine lactate clearance after achieving normovolemia as a criterion for restoring tissue perfusion and to analyze the correlation of its rate with the frequency of acute kidney injury (AKI).

Methods: 30 male patients with combat trauma, in whom a tourniquet was used on the lower limb for 41.2±18.1 minutes without conversion, were divided into 2 randomized groups (GCS - 14.2±0.4 points). The first 3 days of treatment were evaluated for the caval index, perfusion index (PI), indicators of acid-base status. Patients in group I (n=15) received a standard intensive care protocol, group II – similarly with the addition of a 4.2% sodium bicarbonate solution when reaching a caval index of < 0.5 with a dIVC of 2.4±0.2 cm – normovolemia, PI 3.8±0.2% and an average SaO2 level of 96.2±1.1%.

Results: All patients had an elevated venous blood lactate level of 3.3±0.4 mmol/l on the 103.6±22.9 minutes after injury. The infusion of 4.2% sodium bicarbonate starting from 103.6±22.9 minutes after injury, significantly reduced the blood lactate level, increased lactate clearance, and reduced the need for vasopressors to achieve the target levels of PI and SaO2 in capillary blood reference values. According to the ROC analysis, the predictive significance of the occurrence of AKI in the lactate clearance index (area under the ROC curve was 0.74, 95% CI: 0.72 - 0.76, $p<0.05$) was determined as high with the limit values of +/- 21%/4 hours (95%CI: 24 - 18%).

Conclusion: In further studies, it is important to determine the capillary lactate level in the field and/or during evacuation, to correlate the level of capillary and venous lactate upon admission to the clinic, which is an important point when triaging patients regarding the severity of injuries even with a preserved level of consciousness - 14.2±0.4 points on the GCS.

Determination of the nerves of the afferent pathway of the Holtz reflex

Z. Alizade[1]

[1]Azerbaijan Medical University

Cardio vascular

Introduction: The Holtz reflex is a cardiovascular reflex in which irritation of the peritoneum or abdominal organs causes a slowdown and sometimes cardiac arrest. The exact afferent pathways of this reflex are still a subject of debate. According to one hypothesis, afferent impulses are transmitted via the vagus nerve, however direct experimental evidence for this is scientifically insufficient. The study aims to experimentally identify the Holtz reflex afferent pathways and more precisely test the hypothesis that the vagus nerve solely carries impulses from the abdominal cavity to the brain.

Methods and Results: The experiment was conducted on three healthy rabbits under general anesthesia with the purpose of investigating the afferent pathways of the Holtz reflex. The experiment entailed preparation of the animals by shaving the abdomen and inserting ECG electrodes, then registering the background heart rhythm. The abdominal cavity was then opened, and electrical stimulation of the solar plexus was conducted, resulting in an extreme decrease in heart rate, confirming the stimulation of the Holtz reflex. The esophagus was subsequently ligated to completely block the vagus nerve, and the solar plexus was stimulated again, which caused a decrease in heart rate including asystole. Nevertheless the results revealed that even when the vagus nerve was blocked, the reflex continued unabated, suggesting that other neural pathways may be involved, possibly sympathetic nerves such as the splanchnic nerve. This means that the vagus nerve is not the only one transmitting afferent impulses for the Holtz reflex and requires searching for other pathways.

Conclusion: In the first stage of the study, it has been experimentally proven that the vagus nerve cannot be considered the only afferent pathway for the Holtz reflex. This contradicts the traditional hypothesis and indicates the need for further research in this direction. In the next stage of the study there will be examined the role of sympathetic nerves in the transmission of reflex impulses and studied the involvement of the spinal cord in this cardiovascular reflex.

Keywords: Holtz reflex, cardiovascular reflex, vagus nerve, celiac plexus, asystole

Cardio vascular

Anatomical and Pathophysiological Changes in the Early Post-TAVI Period

T. Wolf[1]

[1]The Third Faculty of Medicine, Charles University in Prague, Czechia

Introduction: Transcatheter aortic valve implantation (TAVI) is a well-established treatment for severe symptomatic aortic stenosis in high-risk patients and those over the age of 75. However, early post-procedural cardiac changes are not yet fully understood. This study aims to assess early echocardiographic and conduction changes following TAVI to provide insights into cardiac remodeling and its clinical implications.

Methods: This retrospective study analyzed the medical records and echocardiographic findings of 612 patients who underwent TAVI at University Hospital Královské Vinohrady in Prague between April 2018 and April 2024, using new-generation valves implanted by experienced operators. Data were collected at three time points: pre-TAVI, immediately post-TAVI, and 30 days after the procedure. Echocardiographic parameters, including left ventricular ejection fraction (LVEF), mitral regurgitation severity, and LV-to-aortic mean pressure gradient, were evaluated. Additionally, conduction abnormalities were assessed, with a particular focus on the development and resolution of left bundle branch block (LBBB) and third-degree AV block.

Results: Our analysis showed that LVEF improved from pre-TAVI to 30 days post-TAVI, with the interquartile range increasing from 50–60% to 55–65%, while the median remained stable at 60% ($p < 0.001$, Wilcoxon test). Similarly, mitral regurgitation severity decreased in individual patients, although the median remained unchanged (median: 2, IQR: 2–3, $p < 0.001$). The LV-to-aortic mean pressure gradient increased by more than 5 mmHg in 8% of patients between post-TAVI echocardiography and the 30-day follow-up. New-onset LBBB occurred in 23.7% of patients, with 38.6% resolving within 30 days. Third-degree AV block requiring permanent pacemaker implantation occurred in 10% of patients.

Conclusion: Our findings highlight an early improvement in LV function and a reduction in mitral regurgitation severity following TAVI. A mean gradient increase in a small patient subset suggests early subclinical leaflet thickening or thrombosis, warranting further investigation. Additionally, conduction disturbances, particularly new-onset LBBB and third-degree AV block, were common, with a notable proportion of LBBB cases resolving within 30 days. These insights enhance our understanding of early post-TAVI remodeling and may help refine early post-procedural patient monitoring and management.

Keywords: TAVI, early changes, ejection fraction, mitral regurgitation, conduction abnormality

The Impact of Hypoxia on Calcium Signaling in Adipocytes: The Role of TRPV1 in Lipid Metabolism

T. Wolf[1], L. Ryšková[1]

[1]The Third Faculty of Medicine, Charles University in Prague, Czechia

Cardio vascular

Introduction: Adipocyte hypoxia contributes to metabolic disorders such as obesity, yet the underlying molecular mechanisms remain unclear. Cytosolic calcium (Ca2+) plays a crucial role in the regulation of adipocyte metabolism, including adipogenesis, lipid storage, and lipolysis. However, how hypoxia affects Ca2+ homeostasis and plasma membrane calcium transporters remain largely unexplored. This study investigates hypoxia-induced changes in calcium transporter gene expression in murine and human adipocytes, with a focus on the TRPV1 calcium channel and its role in lipid metabolism.

Methods: 3T3-L1 preadipocytes were differentiated into adipocytes and maintained under normoxic (21% O2) or hypoxic (4% O2) conditions for 14 days. Human adipose tissue samples were obtained from patients with obstructive sleep apnea syndrome. Gene expression profiling targeted 42 plasma membrane calcium transporters. The role of TRPV1 was further assessed by treating hypoxia-exposed adipocytes with a TRPV1 agonist (1 μM capsaicin) or antagonist (1 μM capsazepine). Lipid accumulation, gene expression, and lipolysis were evaluated. Statistical significance was determined using t-tests or two-way ANOVA, with data presented as means ± SD (N = 6).

Results: Hypoxia significantly altered calcium transporter expression in both murine and human adipocytes, with TRPV1 showing a 30-fold reduction in gene expression under hypoxia (1.02 ± 0.08-fold to 0.03 ± 0.01-fold, $p < 0.001$) relative to normoxic conditions. Pharmacological modulation of TRPV1 during hypoxia influenced lipid metabolism: activation via capsaicin reduced lipid accumulation by 5% (1.89 ± 0.02 to 1.79 ± 0.02 OD492nm, $p < 0.01$), whereas inhibition with capsazepine increased lipid content by 8% (1.89 ± 0.02 to 2.05 ± 0.01 OD492nm, $p < 0.05$).

Conclusion: Hypoxia strongly suppresses TRPV1 expression, potentially altering adipocyte calcium signaling. Pharmacological modulation of TRPV1 directly affects lipid metabolism, highlighting its potential as a therapeutic target for metabolic regulation in adipose tissue. Future studies will explore its role in lipolysis and mitochondrial function to better understand its contribution to hypoxia-induced metabolic adaptations.

Keywords: TRPV1, hypoxia, adipocytes, lipid storage

Cardio vascular

Evaluation the effect of the start time of cardiac rehabilitation treatment on the functional outcome of myocardial infarction patients after Primary PCI

R. Mansouri[1], A. Dabiri[1], L. Madjidi[1]

[1]Hamadan university of medical science, Iran

Introduction: The time of starting cardiac rehabilitation after cardiac events or procedures may affect patients' functional outcomes. Due to concerns and conflicting findings about the start-time effectiveness of Cardiac rehabilitation (CR) on the cardiac function of ACS patients, this study will evaluate the short-term effects of CR in ACS patients who underwent primary PCI treatment.

Methods: This study involved forty patients with coronary syndrome who underwent successful primary PCI. They were randomly divided into two groups: Group A started rehabilitation one month after PCI, while Group B began two months later. Both groups completed an 8-week cardiac rehabilitation program, during which quality of life, maximum heart rate, heart rate recovery, metabolic equivalent of task (MET), and diastolic function were measured before and after. SPSS software version 25 was used for statistical analysis.

Results: After rehabilitation, in groups A and B, respectively: the average score of quality of life was 65.85 and 67.07 (P=0.192), with average LVEF changes compared to before the intervention 2.25 and 0.15% (P=0.305), grade 1 and 2 diastolic heart failure 15 and 15% (P=0.506), HR Max 107/45 and 115/20 (P=0.091), HR Recovery 22/50 and 23/10 (P=0.800) and MET change 6.60 and 6.20 (P=0.556). Regarding other echocardiography parameters, no significant difference was observed between the two groups (P>0.05).

Conclusion: It seems that the beginning of cardiac rehabilitation one month after Primary PCI compared to the beginning two months after Primary PCI has no significant difference in terms of the impact on the patient's quality of life, LVEF, diastolic failure, Heart Rate Max, MET, and Heart Rate recovery.

Keywords: Cardiac rehabilitation(CR); Myocardial infarction; PCI; Coronary Artery Bypass Grafting; RTC; Randomized Controlled Trial

Comparative Clinical Outcomes and Mortality Risk in Cardiac Surgery versus Percutaneous Interventions

S. Faizabadi[1], A. Farshid[2], N. Deravi[3]

[1]Shiraz University of Medical Sciences, Shiraz, Iran. [2]Ardabil University of Medical Sciences, Ardabil, Iran. [3]Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Cardio vascular

Introduction: Coronary artery disease and valvular heart disease are leading causes of mortality globally. This study aimed to investigate the correlation between expected mortality rates (EMRs) and observed mortality rates (OMRs) for common cardiac interventions using recent national data on percutaneous coronary intervention (PCI), coronary artery bypass grafting (CABG), and cardiac valve surgeries.

Method: This multi-institutional, retrospective observational study analyzed in-hospital/30-day mortality outcomes for 106,836 patients who underwent PCI, CABG, or cardiac valve procedures across 64 non-federal hospitals in New York State between December 2012 and November 2015. The procedures included emergency and non-emergency PCI, CABG, valve or valve-CABG surgeries, and transcatheter aortic valve replacement (TAVR).

Results: Among the 106,836 cases, a 3.21% 30-day mortality rate was observed (n=3,436). To assess the disparity between OMR and EMR, a one-sample t-test was performed. Effect sizes-were determined using Cohen's d and Hedges' correction. With a 95% confidence interval, the t-value for the OMR (mean difference = 2.037 ± 1.728, CI: 1.95–2.12) was 47.270, while the EMR (mean difference = 1.930 ± 1.284, CI: 1.86–1.99) yielded a t-value of 60.279. The OMR was significantly higher than the EMR ($p<0.001$).

Conclusion: The OMR was significantly higher than the EMR across all cardiac procedures, suggesting potential influences from patient demographics, comorbidities, and variations in hospital practices. Further research is needed to understand these factors and improve the quality of cardiac care.

Keywords: Percutaneous Coronary Intervention, Coronary Artery Bypass Graft, Valve Surgery, Coronary Artery Disease, Mortality Rate.

Cardio vascular

Reperfusion injury in patient with acute abdominal aortic occlusion due to gastric dilatation caused by pyloric stenosis: case report

M. Misiak[1], A. Maciejowska[1]

[1]Department of Vascular Surgery, National Medical Institute of the Ministry of the Interior and Administration, Warsaw, Poland

Introduction: Obstruction of blood flow in large arteries due to gastric distension is uncommon and mostly observed in visceral arteries in patients suffering from bulimia/anorexia following overeating episodes. We present a fatal case of acute aortic occlusion in a non-bulimic patient presenting with acute gastric dilatation due to pyloric stenosis.

Case presentation: A 62-year-old female was admitted to the emergency department with severe abdominal pain. Upon admission, her condition was critical, and the physical examination revealed a distended abdomen, pale and cold lower limbs, and absent femoral pulses. Acute bilateral limb ischaemia (Rutherford-IIB) was diagnosed. The general assessment revealed BP 109/55 mmHg, HR, severe acidosis (pH 7.184), elevated lactate level (13.3 nmol/l). Given the patient's critical condition, an ultrasound and abdominal CT scans were ordered, revealing an extremely distended stomach compressing and obstructing the abdominal aorta, inferior vena cava, and superior mesenteric artery. Attempts to place a nasogastric tube were unsuccessful, followed with laparotomy and gastric decompression, nasogastric tube placement with manual control, resulting in an immediate restoration of aortic flow and the reappearance of pulses in the femoral and superior mesenteric artery and leg reperfusionl. Due to the patient's critical condition, she was transferred to intensive care for conservative treatment, where, despite therapeutic efforts, she developed a multi-organ failure and acidosis, followed by further decrease in pH(7.037), and lactate elevation to 28 nmol/L, resulting in circulatory arrest and patients death, 7h post-admission.

Conclusion: Acute aortic occlusion is a rare complication of pyloric stenosis requiring urgent treatment. Due to its rarity, diagnosis and treatment may be delayed. Despite treatment, the patient developed complications of acute reperfusion syndrome. Immediate and aggressive intervention remains crucial, even in cases with a poor prognosis.

Keywords: Acute aortic occlusion; Gastric dilatation; Pyloric stenosis.

Anatomical Variations of Aortic Arch Branching Pattern on Computed Tomography Angiography

K. Čanak[1]

[1]University of Novi Sad, Faculty of medicine

Cardio vascular

Introduction: The aortic arch, originating from the left side of the heart, serves as the primary conduit for blood flow to the head, neck, and upper limbs. As it traverses the thorax, the branching pattern of the aortic arch can exhibit variations, which may be characterized by the number, type, and order of the arteries emerging from its branches. This study aims to observe, categorize, and investigate the frequency of anatomical variations in the branches of the aortic arch, utilizing computed tomographic angiography.

Methods: This retrospective, descriptive study was conducted at the Radiology Center of the University Clinical Center of Vojvodina, utilizing archived computed tomographic angiographic (CTA) scans of the head and neck, as well as CTA scans of the chest. A total of 300 patient images from 2023 were analyzed. Anatomical variations of the aortic arch branches were classified according to current scientific literature. The prevalence of each variation within the population was assessed and calculated.

Results: Analysis focused on the seven most prevalent variations. The predominant variations observed were Type 1 (76.3%), Type 2 (19.7%), and Type 3 (1.7%). The Chi-square test assessing variance correlation between genders yielded non-significant results (p=0.861).

Conclusion: While the variations identified may not necessarily impact individual quality of life, their significance is underscored by their relevance to invasive radiological and cardiological procedures.

Keywords: Angiography; Aortic arch; Variations; Classification

Cardio vascular

Successful Surgical Management of Traumatic Carotid-Jugular Fistula in an Afghan Patient: A Case Report

N. Ghasemirad[1], M. Kargar[2]

[1]Shahid Sadoughi University of medical sciences, Yazd,Iran. [2]Kerman University of Medical Sciences, Kerman, Iran

Introduction: Carotid-jugular fistulas (CJF) are rare, complex vascular injuries that can be life-threatening if untreated. We report the case of a 23-year-old Afghan man who presented with a traumatic CJF and a left common carotid pseudoaneurysm following a gunshot wound.

Case Presentation: A 23-year-old male patient with a six-month history of throbbing neck pain and pulsation was diagnosed with CJF after a gunshot injury. Imaging revealed aneurysmal dilation of the left common carotid artery and an arteriovenous fistula with the right internal jugular vein. He underwent successful open surgical repair, including resection of the aneurysm and reconstruction of the affected vessels. Under general anesthesia, the surgical team performed a detailed exploration of the carotid artery and jugular vein. After clamping the artery and vein, the aneurysm was resected and repaired using 6-0 Prolene sutures. The fistula was excised, and the jugular vein was also repaired. Hemostasis was achieved, and a Hemovac drain was inserted. Postoperative recovery was uneventful. The patient experienced resolution of symptoms, with normal sensation, movement, and muscle strength. Vascular and neurological examinations showed full distal pulses, and the patient was discharged after two days with significant improvement. CJF requires careful evaluation and treatment. In this case, open surgery was chosen due to the complexity of the injury and the patient's young age. Open repair allowed for direct visualization and complete repair of the damaged vessels. While endovascular treatments may be less invasive, they are not always feasible in complex anatomical cases like this one.

Conclusion: Open surgical repair remains an effective and viable approach for managing traumatic CJFs, particularly in complex cases where endovascular methods may not be suitable. This case highlights the importance of individualized treatment strategies and the potential of open surgery in resource-limited settings.

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Immune Responses in the Nasal Cavity to SARS-CoV-2 Variants and the Effect of Vaccination Status

I.Khan[1], O. Kushnir[1]

[1]Bukovinian State Medical University, Chernivtsi, Ukraine

Introduction: The ongoing evolution of SARS-CoV-2 variants, particularly Delta and Omicron, has raised concerns about their effects on immune responses in the nasal cavity, which serves as the primary site of viral entry. While systemic immune responses have been extensively studied, mucosal immunity, particularly in the nasal epithelium, remains insufficiently understood. Moreover, the influence of vaccination on nasal immune responses in the context of these variants is not fully explored. This study seeks to address these gaps by investigating the impact of SARS-CoV-2 variants on nasal immunity and evaluating how prior vaccination alters these responses.
Aim: To explore immune responses in the nasal cavity triggered by Delta, Omicron, and ancestral SARSCoV-2 variants and to assess the impact of vaccination on these responses.

Methods: Single-cell RNA sequencing (scRNA-seq) was performed on nasopharyngeal samples from vaccinated and unvaccinated individuals infected with Delta, Omicron, and ancestral strains. Immune cell populations, including myeloid cells, T cells, and epithelial subsets, were analyzed. Additionally, the activation of nasal macrophages and the expression of interferon-stimulated genes were evaluated in relation to disease severity.

Results: Analysis revealed that nasal immune responses to Delta and Omicron variants shared similar characteristics, including increased myeloid cells, T cells, and SARS-CoV-2-infected cell subsets. Delta infections exhibited a higher viral RNA load compared to Omicron and ancestral infections. A specific subset of epithelial cells (PER2+EGR1+GDF15+) was enriched in SARS-CoV-2 RNA across all variants. Vaccination was associated with increased nasal macrophage activation and higher expression of interferon-stimulated genes, correlating with reduced disease severity in Delta and ancestral infections, but not in Omicron cases.

Conclusions: Our study highlights the importance of nasal immunity in modulating SARS-CoV-2 infection severity. Vaccination enhances nasal immune responses, potentially mitigating disease progression. Differential immune profiles across variants suggest that tailored vaccine strategies and therapies are essential for managing evolving SARS-CoV-2 strains.

Keywords: SARS-CoV-2, Nasal Cavity, Immunity, Variants, Delta, Omicron, Vaccination, Single-Cell RNA Sequencing, Immune Response, COVID-19e, COVID-19

Subclinical Hypothyroidism and Macro-TSH: Bridging the Gap between Biochemical Data and Clinical Symptoms

E. Sabouri[1], S. K. Habibabadi[1]

[1]Islamic Azad University Najafabad branch

Introduction: Subclinical hypothyroidism (SCH) is a biochemical state, in which serum Thyroid Stimulating Hormone (TSH) levels rise while thyroid hormones free fractions (FT4) stay within the normal range. SCH typically has mild and non-specific symptoms, yet it is noteworthy for its high prevalence (up to 10%) and development into overt hypothyroidism. Occasionally, spuriously elevated readings for TSH levels in laboratories lead to many patients being mistakenly treated for SCH. These false results arise from TSH binding to macromolecules like immunoglobulins (macro-TSH), which lack biological activity.

Methods: In this cross-sectional study on 217 SCH patients, informed written consent was obtained before blood samples were collected. A comprehensive evaluation of each patient's medical history (including demographics, weight, family history of thyroid disorders, and any underlying disease) and existing hypothyroidism symptoms (e.g. fatigue, weakness, weight gain, cold intolerance, constipation, hair loss, dry skin, and depression) was conducted by a trained physician. Serum total TSH and FT4 levels were measured, along with macro-TSH levels, using polyethylene glycol (PEG) to remove macro-TSH complexes before re-assaying the subtracted sera. The cut-off for PEG precipitable TSH ratio was set at 75% using the formula: (Total TSH- Free TSH)/Total TSH*100. All data were analyzed with SPSS software using Fisher's exact test to examine the relationship between hypothyroidism symptoms and serum macro-TSH levels.

Results: In our study population with a mean age of 51.218.2, 71% were female, 41% were asymptomatic, and 22.6% had a ≥75% PEG precipitable TSH ratio. The prevalence of measured variables was: hypertension (13.8%), diabetes (21.2%), thyroid disease family history (41.0%), fatigue (30.9%), weakness (29%), hair loss (26.3%), depression (18%), weight gain (14.7%), cold intolerance (9.2%), dry skin (12.9%), and constipation (6.9%). A significant relationship was found between ≥75% macro-TSH levels and age, thyroid disease family history, and the absence of symptoms (specially fatigue, weakness, and depression).

Conclusions: Considering the challenges in diagnosing and treating SCH and the notable prevalence of macro-TSH more attention should be paid to the presence of symptoms in patients. Moreover, researchers are recommended to conduct further studies on the practical benefits of PEG precipitation TSH test to reduce overtreatment in SCH patients.

Keywords: Subclinical Hypothyroidism, Macro TSH, Macro-TSH, Macro Thyrotropin, PEG-Precipitable TSH, Auto-antibodies

Flow Cytometry and Artificial Intelligence for Immunological Profiling in Female Infertility

G. Didžiokaitė[1], A. Kuznecovaitė[1], V. Pašukonienė[1], A. Darinskas[1], J. Krasko[1]

[1]Vilnius University

Introduction: Immune cells play a crucial role in establishing and maintaining pregnancy, any disruptions in immune homeostasis may contribute to infertility, a condition affecting approximately 17.5% of the global population. While conventional diagnostics focus on hormonal and structural causes, the immunological aspects of infertility remain underexplored. Flow cytometry provides a tool for characterizing immune cell populations, and artificial intelligence (AI) can enhance data interpretation, revealing complex immunological patterns that may be overlooked using standard analytical methods. This study aimed to investigate immune profiles in infertile women using flow cytometry combined with AI-driven analysis to identify potential biomarkers linked to reproductive failure.

Methods: A total of 43 women were included: GR1M (N=20), GR2M (N=6), and GR3M (N=17). Standard statistical methods did not reveal significant differences in immune cell distributions between groups. However, AI analysis identified helper and cytotoxic T-lymphocytes, B-lymphocytes, and NKT cells as potential predictors of infertility. After training on an up-sampled dataset, the model achieved a predictive accuracy of 95%, suggesting that subtle immune variations may play a role in infertility.

Results:
A total of 43 women were included: GR1M (N=20), GR2M (N=6), and GR3M (N=17). Standard statistical methods did not reveal significant differences in immune cell distributions between groups. However, AI analysis identified helper and cytotoxic T-lymphocytes, B-lymphocytes, and NKT cells as potential predictors of infertility. After training on an up-sampled dataset, the model achieved a predictive accuracy of 95%, suggesting that subtle immune variations may play a role in infertility.

Conclusions: This study highlights the potential of flow cytometry combined with AI-driven analysis to identify infertility-related immunological patterns. While standard statistical approaches did not reveal significant differences, machine learning provided valuable insights by detecting complex, non-linear relationships in immune cell profiles. Further studies with larger cohorts are needed to refine predictive models and enhance their clinical applicability in infertility diagnostics.

Keywords: Unexplained infertility; flow cytometry; AI; immunology

Comparison of Immunometabolic Profiles In Whole Blood Versus PBMC

I. Diallo[12], G. Heieis[1]

[1]Center for Infectious Diseases, Leiden University Medical Center, Leiden, The Netherlands. [2]Department of Immunology, Faculty of Medicine, Pharmacy, and Odontology, Cheikh Anta Diop University of Dakar, Dakar, Senegal

Introduction: Immunometabolism has emerged as flourishing field exploring how cellular metabolism regulates immune responses. Peripheral blood mononuclear cells (PBMCs) have so far been the only samples type used for immunometabolic profiling due to their enriched mononuclear cell populations. However, beside excluding neutrophils PBMCs require large blood volume, logistic challenges, and specialized skill for processing, Thus, using whole blood (WB) would provide a full metabolic picture of immune cells with less technical challenges in sample processing. Whole blood (WB) presents an alternative cellular source that may offer a more reliable snapshot of immune cell metabolism as it occurs in vivo.
Objective: Assess the immunometabolic profile in WB compared to PBMCs.

Methods: Paired WB and PBMC samples were collected from six healthy donors. The immune phenotyping and immunometabolic profiles of WB and PBMC immune cells were analyzed using a spectral flow cytometry panel. Our findings show a degree of similarity in immune subset frequencies and metabolic phenotypes between WB and PBMC. However, differences in expression of certain markers were noted in some immune populations. When compared to WB, PBMC GLUT1 levels were higher in PBMC for CD8+ TEMRA, NKT and NK cells, while ATP5a levels were lower in CD4+ naïve T cells. In addition, some discrepancies were seen in certain clusters.

Conclusions: These results suggest that WB can effectively be used for immunometabolic profiling. Nevertheless, caution is advised when interpreting data from immunometabolic studies that involve comparisons between WB and PBMC

Keywords: Metabolism, metabolic markers, immunometabolic profiling, whole blood, PBMC, spectral flow cytometry

Expanding the Clinical and Immunological Spectrum of Cernunnos Deficiency

F.D. Delkhosh[1], H. Abdolhasani[1], N.B Bazgir[1]

[1]Alborz university of Medical Sciences

Introduction: Non-homologous end-joining (NHEJ) is a crucial DNA repair pathway essential for V(D)J recombination, a process necessary for the proper development of T and B cell receptors. Cernunnos deficiency is a rare immunodeficiency caused by biallelic mutations in the XRCC4-like factor (XLF/Cernunnos) gene, leading to defects in DNA repair. While most reported cases present with severe combined immunodeficiency (SCID), neurological abnormalities, and growth retardation, the full clinical and immunological spectrum of this disorder remains poorly understood. In this study, we aimed to expand the current knowledge on Cernunnos deficiency by analyzing genetically confirmed cases from our national registry of inborn errors of immunity.

Methods: We retrospectively reviewed 10 patients (50% female) diagnosed with Cernunnos deficiency. All had biallelic pathogenic variants in XLF/Cernunnos, with a range of clinical manifestations including T-cell lymphopenia, radiosensitivity, and variable neurological symptoms. While most cases fit the classical SCID phenotype, a subset of patients exhibited a milder presentation, retaining normal growth, lacking microcephaly, and showing preserved antibody responses, indicating a broader clinical spectrum than previously described.

Results: A recurrent splicing variant (c.390+1 G>T) was identified in 80% of cases, suggesting a potential founder effect in our cohort. Interestingly, patients carrying this variant displayed a leaky phenotype, with some residual B-cell function, potentially explaining their relatively attenuated clinical course.

Conclusions: Our findings highlight the heterogeneity of Cernunnos deficiency, suggesting that it should be considered in patients with recurrent infections, microcephaly, or growth retardation, even when humoral immunity appears intact. These insights emphasize the need for early genetic diagnosis to improve patient outcomes and tailor therapeutic strategies.

Spider Venom-Derived Peptides as Novel Therapeutic Agents for Cancer Treatment

P. Behnamrad[1]

[1]Shahid Sadoughi University of Medical Sciences

Introduction: Spider venoms are rich in bioactive peptides with diverse pharmacological properties, including cytotoxic, anti-angiogenic, and immune-modulating effects. Recent research has identified venom-derived compounds that selectively target cancer cells while sparing healthy tissues. This study investigates the anti-cancer potential of peptides from spider venoms, focusing on their ability to induce apoptosis, inhibit angiogenesis, and enhance chemotherapy efficacy.

Methods: Venom extracts from Phoneutria nigriventer (Brazilian wandering spider), Latrodectus mactans (black widow), and Atrax robustus (Australian funnel-web spider) were fractionated using high-performance liquid chromatography (HPLC). Cytotoxicity assays were conducted on breast (MCF-7), lung (A549), and pancreatic (PANC-1) cancer cell lines. Apoptosis induction was assessed via flow cytometry (Annexin V/PI staining), while anti-angiogenic effects were evaluated using human umbilical vein endothelial cells (HUVECs) in a tube formation assay. Additionally, venom peptides were tested in combination with cisplatin and doxorubicin to assess synergistic effects.

Results: Selective Cytotoxicity: A peptide from Phoneutria nigriventer (PnTx-1) induced apoptosis in MCF-7 and A549 cells with minimal toxicity to normal fibroblasts, increasing apoptotic cell death by 67% ($p < 0.001$). Anti-Angiogenic Activity: A peptide from Latrodectus mactans significantly inhibited endothelial tube formation by 58% ($p = 0.002$), suggesting potential for blocking tumor vascularization. Chemo-Sensitization: When combined with cisplatin, a venom peptide from Atrax robustus enhanced cancer cell sensitivity, reducing the IC50 dose by 45% ($p < 0.005$), indicating potential for lower chemotherapy dosages and reduced side effects.

Conclusions: Spider venom-derived peptides exhibit potent anti-cancer properties, including induction of apoptosis, inhibition of angiogenesis, and enhancement of chemotherapy response. These findings suggest that venom peptides could serve as promising candidates for novel anti-cancer therapies. Future research should focus on optimizing peptide formulations for clinical application and assessing their in vivo efficacy.

Keywords: Spider venom, cancer therapy, apoptosis, anti-angiogenesis, venom peptides, chemotherapy enhancement, drug discovery

4-1BB agonists as a novel immunotherapeutic approach in Multiple Myeloma

A. Denis[1], H. Satilmis[1], K. De Veirman[1]

[1]Translational Oncology Research Center, Lab of Hematology and Immunology, Vrije Universiteit Brussel, Belgium

Introduction: Multiple myeloma (MM) is an incurable hematological malignancy driven by the uncontrolled proliferation of neoplastic plasma cells in the bone marrow (BM). Therapy resistance in MM is largely influenced by the evolving BM microenvironment, which harbors dysfunctional and exhausted T cells that impair effective anti-tumor immunity. In recent years, 4-1BB agonists have emerged as a promising strategy to reinvigorate exhausted T cells and enhance immune responses. While these agonists have shown encouraging results in solid tumors, their impact on MM and its immune microenvironment remains poorly understood. This study aims to characterize 4-1BB expression in the preclinical 5TMM mouse model and evaluate the therapeutic and immunomodulatory effects of 4-1BB agonists in vivo.

Methods: 4-1BB expression on immune cells and tumor cells was analyzed using single-cell RNA sequencing data and flow cytometry of 5TMM mice. Secondly, we assessed the immunomodulating and therapeutic effects of two different 4-1BB agonists, clone LOB12.3 and clone 3H3, in vivo. Briefly, at day 4 posttumor inoculation, 5TGM1 mice were treated with 100µg of 4-1BB agonists (intraperitoneal, twice a week) until end-stage (n=5-7/group). The impact on tumor cells was assessed by calculating the percentage of plasmacytosis in the BM and spleen (cytospin stainings), and M protein electrophoresis. Immunomodulating effects were investigated using multi-parameter flow cytometry.

Results: 4-1BB was predominantly detected on T cells and natural killer (NK) cells, with its expression further increasing as the disease progressed. Treatment of 5TMM mice with 4-1BB agonists significantly increased the percentage of CD4+ and CD8+ T cells in the BM and spleen. Interestingly, treatment with clone LOB12.3 resulted in a significant reduction in NK cell percentages in both the BM and spleen, while clone 3H3 only reduced splenic NK cells. Therapeutically, we observed a significant reduction in M protein and plasmacytosis ($p<0.01$) in the BM upon treatment with clone 3H3, while no significant effects were observed for clone LOB12.3.

Conclusions: In conclusion, our results suggest that 4-1BB activation can enhance anti-tumor immunity in MM, but the therapeutic effects are agonist-dependent. Further research is needed to unravel the underlying mechanisms and optimize 4-1BB-targeted therapies for clinical application.

Keywords: Multiple myeloma, immunotherapy, 4-1BB

T-cell receptor-engineered T cells targeting hematopoietic-restricted minor histocompatibility antigen LB-IL10RA-1R on acute myeloid leukemia

A. Boeringa[1], M. van de Meent[1], K.J. Fuchs[1], M.W. Honders[1], M.G.D. Kester[1], J.H.F. Falkenburg[1], M. Griffioen[1] and G. Koutsoumpli[1]

[1]Department of Hematology, Leiden University Medical Centre (LUMC), Leiden, The Netherlands

Allogeneic stem cell transplantation (alloSCT) is a potentially curative treatment for acute myeloid leukemia (AML). In alloSCT, the patient's hematopoietic system is replaced with blood-forming stem cells from a healthy donor. After HLA-matched alloSCT, donor-derived T-cells target polymorphic peptides presented by HLA on patient cells, but not on donor cells. These peptides or so-called minor histocompatibility antigens (MiHAs) are caused by genetic differences between patient and donor. Donor T-cells targeting antigens on tumor cells can induce a desired anti-tumor or Graft-versusLeukemia (GvL) effect, while antigens targeted on healthy non-hematopoietic tissues can induce undesired Graft-versus-Host Disease (GvHD). Donor T-cells targeting MiHAs with hematopoieticrestricted expression are relevant for immunotherapy, as these antigens are expressed on patient's malignant cells, but not on healthy non-hematopoietic tissues nor on healthy hematopoietic cells, which are of donor origin after alloSCT. These T-cells are therefore expected to induce GvL without GvHD. We recently identified 11 novel HLA class I hematopoietic-restricted MiHAs that were targeted by T-cells in transplanted patients. These MiHAs include LB-IL10RA-1R, which is presented by HLAB*07:02 and expressed across different AML subtypes by RNA-seq analysis. We isolated LB-IL10RA-1R T-cell clones from three patients, sequenced their T-cell receptors (TCRs) and identified four different TCRs. Here, we introduced the LB-IL10RA-1R-specific TCRs into CD8 T-cells, and investigated their specificity and potential therapeutic relevance to target AML after HLA-matched alloSCT. All TCR-T cells showed specific binding to peptide-HLA tetramers, but with distinct specificity for LB-IL10RA-1R peptide length variants. The TCR-T cells also recognized patient-derived EBV-B-cells, but not donor EBV-B-cells and patient-derived skin fibroblasts, supporting that LB-IL10RA-1R is hematopoieticrestricted. Additionally, upon coculture with peripheral blood samples from LB-IL10RA-1R and HLAB*07:02 positive individuals, the TCR-T cells induced strong lysis of monocytes, whereas no or less killing was observed for B, T and NK cells, demonstrating the potential of the TCR-T cells to specifically target LB-IL10RA-1R on myeloid cells. Currently, we are evaluating whether LB-IL10RA-1R-specific TCRT cells can kill patient-derived AML cells with different maturation phenotypes in a spectral flow cytometry assay. These findings will demonstrate whether LB-IL10RA-1R TCR-T cells can serve as immunotherapy to target AML after HLA-matched alloSCT.

The Achilles heel of the Romanian healthcare system. Nosocomial infections with Stenotrophomonas maltophilia.

A.S. Vizitiu[1], D.A. Toc[1]

[1]Iuliu Hatieganu University of Medicine and Pharmacy Cluj-Napoca, Romania

Introduction: Stenotrophomonas maltophilia is an uncommon Gram-negative bacterium that was shown to be resistant to several antibiotics. Although it was first thought to be a plant pathogen, it has lately been identified as an opportunistic human bacterium. Stenotrophomonas maltophilia is associated with hospital-acquired infections and primarily affects immunocompromised individuals, cystic fibrosis patients, and those undergoing lengthy hospitalizations. The aim of this work is to report the diversity of samples from which Stenotrophomonas maltophilia was isolated, as well as to assess its resistance to trimethoprim/sulfamethoxazole, the sole antibiotic for which the EUCAST recommendation specifies a minimum inhibitory concentration (MIC).

Methods: We conducted an observational, retrospective study at the Emergency County Hospital in Cluj-Napoca, Romania, from January 1, 2020, to August 31, 2023, analyzing all Stenotrophomonas maltophilia strains obtained from clinical samples. In this investigation, we only included strains identified with the Vitek2 Compact System and antimicrobial susceptibility tests done with the same equipment. We analyzed the strains considering the sample type, MIC, and the patient's underlying conditions.

Results: The study included 29 patients. We discovered that 10 of the 29 strains (34.48%) of Stenotrophomonas maltophilia presented a trimethoprim/sulfamethoxazole MIC above 40 mg/L, indicating resistance according to EUCAST regulations. We also found that 5 strains (17.24%) had MICs higher than 160 mg/L. Moreover, the majority of strains have been obtained from wound samples and tracheal aspirates (22/29, 75.86%). Interestingly, five of the ten resistant samples were isolated from wound secretion, three from tracheal secretion, and two from blood culture.

Conclusions: Our findings demonstrated that trimethoprim/sulfamethoxazole resistance among Stenotrophomonas maltophilia strains is widespread in Romania, with some strains having a significantly raised MIC and others being identified even from blood cultures. With few therapeutic options available for eradicating these infections, more research is needed to assess the implications of the antibiotic resistance phenomena in Stenotrophomonas maltophilia, particularly in light of the COVID-19 pandemic.

Keywords: Antibiotic resistance, Nosocomial infections, Immunity

From Skin to Lung: Complex Management in a Case of Diffuse Systemic Sclerosis with Fibrotic Interstitial Lung Disease with Progressive Pattern

C. Stafie[1], A. Şomlea[1], L. Muntean[12]

[1]Faculty of Medicine, "Iuliu Haţieganu" University of Medicine and Pharmacy, ClujNapoca, Romania. [2]Rheumatology Clinic, Cluj County Emergency Clinical Hospital

Introduction: Systemic sclerosis (SSc) is a rare autoimmune disease characterized by inflammation and fibrosis, mainly affecting the skin, internal organs, and vasculopathy. Interstitial lung disease (ILD) represents a leading cause of morbidity and mortality in SSc patients. Although SSc predominantly affects women, the male sex has been identified as an independent risk factor for progressive ILD and poorer outcomes. While SSc remains without a definitive cure, significant therapeutic advancements have emerged for managing its multisystem complications.

Case report: A 51-year-old male presented with Raynaud's phenomenon, sclerodactyly, digital pitting scars, skin thickening extending proximal to the metacarpophalangeal joints, hand arthritis, dysphagia, heartburn, fatigue, and weight loss. The patient exhibited an aggressive disease course with rapidly progressive skin fibrosis, advancing from limited digital involvement to extensive truncal and proximal extremity involvement within 18 months. Laboratory investigations showed elevated C-reactive protein (CRP), high antinuclear antibodies (ANA) titers (1:640) with speckled pattern, and anti-Scl70 antibodies (> 200 UI), confirming the diagnosis of diffuse cutaneous systemic sclerosis (dcSSc). Pulmonary manifestations developed three years post-diagnosis, leading to progressive exertional dyspnea, nonproductive cough, and fine inspiratory crackles ("velcro-type") at the lung bases. High-resolution computed tomography (HRCT) initially showed subtle ground-glass opacities that evolved into a well-established NSIP pattern with predominant ground-glass opacities, reticular abnormalities, and minimal honeycombing in the bilateral lower lungs, indicative of SSc-associated ILD (SSc-ILD) with a progressive fibrotic pattern. Pulmonary function tests showed a restrictive ventilatory dysfunction with reduced forced vital capacity (FVC 58% predicted) and reduced diffusing capacity for carbon monoxide (DLCO 56% predicted). The patient initially received methotrexate, with subsequent escalation to cyclophosphamide pulse therapy when lung involvement became clinically significant. Following the stabilization of respiratory function, maintenance therapy with mycophenolate mofetil was initiated. Due to HRCT evidence of progressive fibrotic disease, nintedanib was added to the regimen, following recent evidence supporting its use in SSc-ILD.

Conclusions: This case exemplifies the aggressive nature of dcSSc in a male patient, characterized by rapid skin fibrosis and early development of progressive fibrotic ILD. It demonstrates a comprehensive approach to immunosuppressive and antifibrotic therapy.

Keywords: Systemic sclerosis; interstitial lung disease; immunosuppressive therapy; antifibrotic drugs.

Vasculitis and spondyloarthritis: where does the inflammation begin? – A case report

A. Șomlea[1], C. Stafie1, L. Muntean[12]

[1]Faculty of Medicine, "Iuliu Hațieganu" University of Medicine and Pharmacy, ClujNapoca, Romania. [2]Rheumatology Clinic, Cluj County Emergency Clinical Hospital

Introduction: Spondyloarthritis (SpA) comprises chronic inflammatory diseases affecting the spine, peripheral joints, entheses, and extra-musculoskeletal structures. Extra-musculoskeletal manifestations include inflammatory bowel disease (IBD), uveitis, and psoriasis. Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitides (AAVs) affect small blood vessels in organs like the respiratory tract, kidneys, skin, and nervous system. The coexistence of AAVs and SpA associated with IBD is very uncommon and can pose diagnostic challenges.

Case report: A 38-year-old male presented with peripheral arthritis, inflammatory back pain, Achilles enthesitis, palmar psoriasis, and abdominal pain with rectorrhagia. Physical examination revealed a painful ulcer on the right calf characterized by raised violaceous edges surrounding a crusted, necrotic, ulcerated center. Histopathological evaluation of a biopsy from this lesion confirmed the diagnosis of pyoderma gangrenosum. After a colonoscopy suggested the presence of ulcerative colitis, the diagnosis of SpA associated with ulcerative colitis was established. One month later, the patient developed multiple concerning symptoms, including severe blistering purpura lesions on the lower limbs that subsequently ulcerated, ulero-necrotic left tonsillitis, scrotal necrosis, and significant weight loss. He also presented severe neuropathic pain in the left hand and lower limbs, accompanied by paresthesia, weakness, and decreased muscle force. Physical examination revealed muscle strength of 4/5 in the first through third digits of the left hand and in both dorsiflexion and plantar flexion of the feet. Electromyography confirmed severe mononeuritis multiplex affecting the left median nerve and bilateral tibial and peroneal nerves. Laboratory studies showed elevated C-reactive protein, proteinuria, hematuria, and positive cANCA. Infection and cancers were ruled out following comprehensive evaluation. Biopsy of the purpuric lesions revealed leukocytoclastic vasculitis. The patient was subsequently diagnosed with ANCA-associated vasculitis. The patient received treatment with high doses corticosteroids and cyclophosphamide, followed by maintenance therapy with azathioprine, which resulted in a favourable clinical outcome.

Conclusions: Patients with IBD who present with purpura and signs of mononeuritis multiplex should be evaluated for small vessel vasculitis. The challenges this case highlights consist in identifying AAV based on the very rare association with IBDassociated SpA

Keywords: Spondyloarthritis; ANCA-associated vasculitis; pyoderma gangrenosum; mononeuritis multiplex.

Unveiling Socioeconomic Status-Linked Immune Signatures by Using a State-of-the-Art Approach to Map Cell Surface Marker Expression across Immune Cell Populations using Spectral Flow Cytometry

M. Cisse[1], M. Yazdanbakhsh[1], S.P. Jochems[1]

[1]Leiden University Center for Infectious Diseases - Research, LUMC, Leiden, the Netherlands

Introduction: The increasing prevalence of inflammatory diseases and discrepancies in vaccine efficacy between high- and low-income countries are associated with lifestyle and environmental factors, which may affect the immune system and influence disease course and vaccine response. Investigating the immunological signature associated with socioeconomic status (SES) is crucial for understanding the underlying mechanisms of immune variations.

Methods and Results: We developed and validated an innovative high-throughput approach for mapping 331 cell surface markers across 33 immune cell subsets with spectral flow cytometry (Cytek Aurora 5 Lasers) using a LEGENDscreen kit and a 28-parameter panel. This enabled the dynamic profiling of Europeans (n = 8) and Senegalese individuals stratified by socioeconomic status (SES: higher SES n = 8, lower SES n = 7). Participants were selected based on geography, lifestyle, environment, diet, and housing. PBMCs were analysed to compare immune marker expression patterns across groups. A limma-based trend test (FDR-adjusted $p < 0.05$) identified an SES gradient (Europeans → high SES → low SES) for most of integrin/chemokine receptors, complement receptors, costimulatory molecules, and immune checkpoints. Validation in an independent cohort (Europeans, n = 10; higher SES, n = 10; lower SES, n = 10) confirmed these SES-associated immune gradients.

Conclusions: Taken together, SES significantly affect immune marker expression, which may influence disease outcome and vaccine efficacy. Moreover, this approach provides the opportunity to profile cell surface markers unbiasedly as an alternative to single-cell RNA-seq.

Keywords: Immune system, socioeconomic status, LEGENDscreen, cell surface markers, Spectral Flow Cytometry

Predicting cerebral involvement in patients with systemic lupus erythematosus using artificial intelligence

M. Barari[1], S. Roudaki[1]

[1]Islamic azad university pharmaceutical sciences branch

Introduction: Systemic Lupus Erythematosus (SLE), or lupus, is a complex autoimmune rheumatic disease that affects multiple organs and cells. It occurs when the immune system malfunctions, leading to potential irreversible damage. Early detection and intervention are crucial in managing lupus, as it can have severe complications. However, identifying the environmental triggers of this autoimmune response remains unclear, and immune dysregulation may occur long before clinical symptoms appear. One major concern is recognizing cerebral involvement, which is a severe complication. The aim of this study is to use artificial intelligence to estimate brain involvement in lupus based on feature selection.

Methods: Medical records of 350 patients were carefully subjected to deep learning techniques, using transformer-based neural networks. These models, equipped with advanced activation functions and self-attention mechanisms, outperformed traditional machine learning approaches by learning directly from raw data. Natural language processing (NLP) was employed to extract textual insights from medical records, enhancing the feature set with semantic information. A deep reinforcement learning framework optimized feature selection, and generative adversarial networks (GANs) were used for data augmentation. The resulting neural networks, characterized by multiple layers, exhibited superior pattern recognition capabilities.

Results: Incorporating cutting-edge artificial intelligence techniques, our research has delivered impressive results in predicting cerebral disease in systemic lupus erythematosus patients. Leveraging advanced neural networks, natural language processing, reinforcement learning, and generative adversarial networks (GANs), our model achieved a remarkable accuracy rate of 96.3%. High blood pressure levels, thrombocytopenia, presence of antinuclear antibodies and low serum levels of C3 and C4 complement components were among the most important features associated with brain involvement in patients suffering from systemic Lupus Erythematosus.

Conclusions: Our study is a significant advancement in the field of medical diagnosis, especially for patients with systemic lupus erythematosus. This approach excelled in early detection, significantly outperforming conventional methods. The exceptional accuracy of our model, backed by advanced neural networks, NLP, reinforcement learning, and GANs, promises to reshape healthcare practices and patient outcomes.

Keywords: Lupus, Prediction, cerebral involvement

Evaluating the Efficacy of Herbacea Immunis in Patients with Low Immune Function: A Randomized Clinical Trial

F. Ranjdoust[1]

[1]Tabriz uinversity of medical sciences

Introduction: Individuals with weakened immune systems face a heightened risk of infections, inflammation, and poor health outcomes, necessitating the development of safe and effective immunomodulatory interventions. Herbacea Immunis, a newly formulated herbal extract, has been proposed to enhance immune function by modulating key immune markers. Despite increasing interest in botanical immunostimulants, clinical evidence supporting their efficacy remains limited. This study evaluates the immunomodulatory effects of Herbacea Immunis in individuals with diagnosed immunodeficiency.

Methods: A randomized, double-blind, placebo-controlled trial was conducted involving 200 immunocompromised participants. Subjects were randomly assigned into two groups: the intervention group received 500 mg of Herbacea Immunis daily for 12 weeks, while the control group received a placebo. Primary outcomes included changes in CD4+ T-cell count, interleukin-6 (IL-6) levels, and immunoglobulin G (IgG) levels. Secondary outcomes included the frequency of reported infections and overall treatment safety. Baseline and post-intervention biomarker levels were assessed using flow cytometry and ELISA assays.

Results: After 12 weeks, participants in the Herbacea Immunis group demonstrated a 23% increase in CD4+ T-cell count compared to baseline ($p = 0.002$), suggesting enhanced immune function. Additionally, IL-6 levels decreased by 18% ($p = 0.008$), indicating reduced systemic inflammation. While IgG levels showed a modest increase (7%), this change was not statistically significant ($p = 0.07$). Participants receiving Herbacea Immunis reported fewer infections compared to the placebo group, with a 27% reduction in self-reported illness episodes over the study period. No severe adverse effects were observed, with mild gastrointestinal discomfort reported in 3% of participants.

Conclusions: These findings suggest that Herbacea Immunis may serve as a natural immunomodulator, enhancing cell-mediated immunity while reducing inflammation. Given the observed benefits and favorable safety profile, this herbal extract holds promise for individuals with compromised immune systems. However, further large-scale, multicenter trials are warranted to confirm its clinical utility and explore its long-term effects.

Keywords: Herbacea Immunis, immunomodulation, interleukin-6, IgG, herbal extract, randomized controlled trial

INFECTION

Advanced Cirrhosis and Liver Dysfunction Predict COVID-19 Mortality: A Prospective Comparative Study

M. M. Alshal[1], T. A. Elshazly[2], A. E. Eldesoky[2], A. S. Hasan[2]

[1]Mansoura Specialized Hospital, Egypt. [2]Mansoura University, Egypt

Introduction: While chronic liver disease (CLD) alone does not worsen COVID-19 severity, advanced cirrhosis (Child-Turcotte-Pugh [CTP] class C) and liver dysfunction markers may drive critical outcomes. This study identifies these underrecognized predictors in a CLD cohort.

Methods: In this prospective study (July 2021–July 2022), 120 COVID-19 patients at Mansoura University Hospitals were stratified into Group A (n=60, no CLD) and Group B (n=60, CLD). Outcomes included disease severity, ICU admission, mechanical ventilation, and mortality. Multivariate regression identified mortality predictors.

Results:
- Advanced cirrhosis (CTP-C) and liver dysfunction markers (hypoalbuminemia, hyperbilirubinemia, elevated INR) independently predicted mortality ($p<0.001$). CTP-C patients faced 75% mortality vs. 18.2% in CTP-A ($p<0.001$).
- ICU admission (100% vs. 50%, $p=0.022$) and mechanical ventilation (100% vs. 31.8%, $p<0.001$) were significantly higher in CTP-C.
- No differences existed between CLD and non-CLD groups in overall mortality (30% vs. 20%, $p=0.206$) or hospital stay ($p=0.799$).

Conclusion: CTP class C and liver dysfunction markers—not CLD itself—are critical predictors of ICU needs and mortality in COVID-19. These findings offer a novel framework for risk stratification in CLD patients.

Keywords: COVID-19, cirrhosis, mortality predictors, liver dysfunction, ICU Ethical Approval: Approved by Mansoura University Institutional Review Board (Code: MS.21.08.1625). Conflicts of Interest: The authors declare no conflicts of interest.

Antimicrobial Effect of Nigella Sativa Against Antibiotic-Resistant Bacteria: An In Vitro Study

A. W. Alhithlool[1], M. Alghunaim[1], Prof O. M. Zakaria[1]

[1]Saudi Arabia- King Faisal University- College of Medicine

Introduction: Antibiotic resistance is a growing global health crisis, challenging both medical and surgical settings. The emergence of resistant bacterial strains necessitates exploring alternative antimicrobial agents. Natural herbs like Nigella sativa (NS) and plant-based compounds such as Moringa oleifera (MO) have shown promising antibacterial properties. This study aimed to evaluate and compare the antimicrobial eDicacy of N. sativa and M. oleifera against antibiotic-resistant bacterial strains isolated from patients with conjunctivitis.

Methods: Ethanolic extracts of N. sativa seeds and M. oleifera leaves were prepared using the solvent extraction method. N. sativa seeds were washed, dried, and ground into a fine powder before being macerated in ethanol (1000 mL per 160 g of seed powder) at 37°C for 48 hours. The extract was filtered, evaporated using a rotary evaporator at 45°C, and concentrated. Similarly, M. oleifera leaves were collected, dried for 48 hours at room temperature, and ground into a fine powder. A solution (0.13 g/mL) was prepared using 35 g of powder and 262 mL of ethanol, stirred magnetically for 48 hours, centrifuged at 4000 rpm for 4 minutes, and filtered. A portion of the M. oleifera extract was nano-fortified with silver particles for enhanced antimicrobial activity. The antibacterial properties of both extracts were tested against Klebsiella pneumoniae, Staphylococcus aureus, and Escherichia coli, all of which were isolated from patients with conjunctivitis, using standard microbiological assays.

Results: Both M. oleifera and N. sativa demonstrated significant antibacterial activity against antibiotic-resistant bacterial strains. While M. oleifera exhibited potent antimicrobial eDects against Klebsiella pneumoniae and Staphylococcus aureus, N. sativa showed the highest eDicacy against Escherichia coli ($p < 0.001$).

Conclusion: This study highlights the potential of N. sativa and M. oleifera as alternative antimicrobial agents against antibiotic-resistant bacteria. This preliminary result would be verified in the second in vivo part of the study that is currently going on a murine model to estimate their immunological eDect.

Keywords: Nigella sativa, Moringa oleifera, antibiotic resistance

Antimicrobial susceptibility of the most common causative agents of nosocomial infections in patients with COVID-19

J. Amidžić[1]

[1]University of Novi Sad, Faculty of Medicine, Serbia

Introduction: Nosocomial infections occur during hospitalization in health care settings. Such infections may increase morbidity and mortality, therefore the costs and patients' treatment length. Nosocomial infections and growing antimicrobial resistance represent one of the greatest challenges in medicine, escpecially in COVID-19 pandemic. The aim of this study is to determine the most common bacterial causative agents of nosocomial infections in patients hospitalized with COVID-19, as well as to analyze the profile of their antimicrobial resistance.

Methods: The examination was conducted in the period from November 20th, 2020 to July 31st 2021 at the Center for Microbiology in Institute of Pulmonary diseases of Vojvodina. The study included 1038 patients with confirmed COVID-19 infection. A total of 430 nosocomial pathogens were isolated and were identified using the Vitek 2 compact system, and then tested for susceptibility by the disk diffusion method, following the recommendations of EUCAST. Results: Twenty four percent of patients had a confirmed nosocomial infection. A total of 430 bacterial isolates were obtained from blood (33%), secretion from the lower respiratory tract (30%), urine (27%), central venous catheters (5%) and wound swabs (4%). The most frequently isolated pathogens were Acinetobacter baumanii complex (32%), Klebsiella pneumoniae (16%) and Enterococcus faecalis (14%).

Conclusion: Patients with COVID-19 and a confirmed nosocomial infection were mostly male and were in intensive care units. The most common causative agent of nosocomial infections was Acinetobacter baumanii complex. Almost all isolates of the Staphylococcus were resistant to penicillin, and all isolates of the Enterococcus were resistant to the fluoroquinolones. The lowest percentage of enterobacterial resistance was detected with amikacin. All Acinetobacter baumanii complex isolates were resistant to all tested antibiotics except colistin.

Keywords: nosocomial infection; antimicrobial resistance; antibiotics; SARS-CoV-2

Coinfection of Pulmonary Tuberculosis and Mucormycosis in a Patient with Poorly Controlled Diabetes Mellitus: A Case Report

A. Mohammadi[1]*, M. Mohammadi[1]

[1]School of Medicine, Iran University of Medical Sciences, Tehran, Iran

Introduction: Pulmonary mucormycosis and tuberculosis coinfection is rare but poses significant diagnostic and therapeutic challenges, especially in immunocompromised patients. Diabetes mellitus is a major risk factor for both infections due to impaired immune responses. Overlapping clinical and radiological features can delay diagnosis and worsen outcomes. This case highlights the importance of early recognition and tailored management of concomitant pulmonary mucormycosis and tuberculosis in high-risk patients.

Methods: A 60-year-old woman with poorly controlled diabetes mellitus presented with dysphonia, persistent cough, and expectoration. Imaging studies revealed a cavitary lesion and a mass in the left lung, with left main bronchus stenosis. Bronchoscopy identified a bronchomediastinal fistula with pus discharge. Polymerase chain reaction (PCR) testing of bronchial secretions confirmed tuberculosis and mucormycosis coinfection.

Results: The patient was started on appropriate antifungal and anti-tuberculosis therapy. Her symptoms improved, and follow-up imaging showed no disease progression.

Conclusion: Coinfection of pulmonary tuberculosis and mucormycosis is associated with high morbidity and mortality. Early detection through a multidisciplinary approach involving pulmonologists, infectious disease specialists, and radiologists is crucial. Comprehensive screening of high-risk patients can enhance outcomes. Advancements in diagnostic tools may facilitate prompt identification and management of such complex infections.

Keywords: Mucormycosis, Tuberculosis, Coinfection, Diabetes mellitus, Pulmonary infection

Prevalence and distribution of HPV genotypes in women with various cervical abnormalities

A. Zdravković[1], B. Krstić1, M. Ćupić[12]

[1]University of Belgrade, Faculty of Medicine. [2]The Institute of Microbiology and Immunology, University of Belgrade

Introduction: Human papillomavirus (HPV) is one of the most significant carcinogens in both women and men. In men, the predominant site of infection is the genital organ, while in women, the most affected areas are the vulva, cervix, and vagina. Cervical cancer is the second most common cancer among women worldwide. The aim of this study is to determine the prevalence and distribution of different human papillomavirus (HPV) genotypes in women with cervical abnormalities and to examine their association with various grades of cervical lesions.

Methods: The study was designed as a one-year retrospective cross-sectional study, including 780 patients. Samples, collected via endocervical swabs using a cytobrush, were transported in a specialized medium. Nucleic acids were isolated using the QIAamp DNA Mini Kit, and amplification of the L1 and E1 regions was performed using the PCR method. HPV genotyping was conducted through direct DNA sequencing, with identification based on comparison with reference HPV strains using the BLAST tool. The obtained sequences were further analyzed in detail. An isolate was identified as a specific HPV type if the match percentage with the reference HPV genotype was >95%.

Results: Average age of patients in this study was 38.87 ± 10.19. In the HPV testing conducted in the study, 240(30.8%) participants tested positive, while 540(69.2%) tested negative. The distribution of different HPV E and L genotypes is presented in Tables 1 and 2.

Conclusion: The study findings highlight the significant role of high-risk HPV genotypes in the development of cervical abnormalities. The results emphasize the importance of HPV genotyping in screening and early detection of cervical lesions, which can contribute to better prevention and management strategies for cervical cancer.

Keywords: HPV, genotyping, cervical cancer, high-risk HPV types, PCR, epidemiology

Determination of Antibiotic Resistance Patterns and Frequency of the blaCTX-M Antibiotic Resistance Gene in Methicillin-Resistant Staphylococcus aureus by PCR

G. Saremi[1]

[1]Department of Pharmacognosy, Medical Sciences Branch, Islamic Azad University, Tehran, Iran

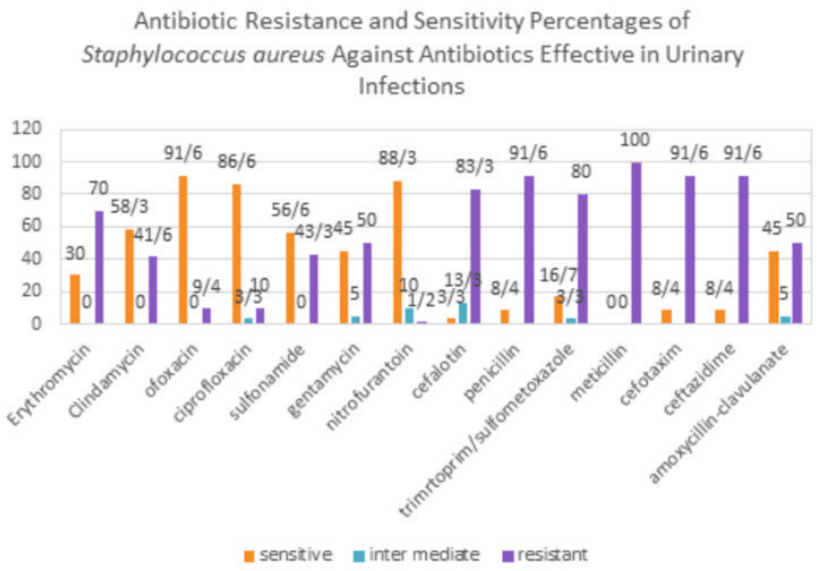
Introduction: Methicillin-resistant Staphylococcus aureus (MRSA) is a major cause of hospital-acquired infections, particularly in pediatric populations. Understanding the resistance patterns and prevalence of key resistance genes, such as blaCTX-M, is essential for improving treatment strategies. This study aimed to determine the antibiotic resistance profile and assess the frequency of the blaCTX-M gene in MRSA strains isolated from children with urinary tract infections (UTIs).

Methods: Urine samples were collected from 700 pediatric outpatients (aged 0–16) at Tehran Medical Center Hospital, all with suspected urinary tract infections. Depending on the child's age, samples were obtained via bag collection, catheterization, or suprapubic aspiration. The samples were cultured within 24 hours, and Staphylococcus aureus was isolated using standard biochemical tests, including the MacFaland test for bacterial identification. The presence of the blaCTX-M gene was determined by PCR.

Results: Among the 60 Staphylococcus aureus strains isolated, all were resistant to methicillin (100%). Resistance was also observed against penicillin (91.6%), cefotaxime (91.6%), and ceftazidime (91.6%). The strains were most susceptible to ofloxacin (91.6%), nitrofurantoin (88.3%), and ciprofloxacin (86.6%). A total of 71.7% of the strains exhibited resistance to at least three different antibiotic classes. None of the isolates tested positive for the blaCTX-M gene.

Conclusion: The high prevalence of methicillin resistance in Staphylococcus aureus strains from pediatric UTIs underscores the need for ongoing surveillance. The absence of the blaCTX-M gene suggests that resistance in these strains may be mediated by alternative mechanisms, highlighting the need for further investigation into MRSA resistance pathways.

Key Words: blaCTX-M, MRSA, Staphylococcus aureus, Pediatric UTI, Antibiotic Resistance, PCR, MacFaland Test


Antibiotic Resistance and Sensitivity Percentages of
Staphylococcus aureus Against Antibiotics Effective in Urinary Infections
120
100
80
60
40
20
0
30
0
70
58/3
0
41/6
91/6
0
9/4
86/6
3/3
10
56/6
0
43/3
45
5
50
88/3
10
1/2
3/3
13/3
83/3
8/4
91/6
16/7
3/3
80
00
100
8/4
91/6
8/4
91/6
45
5
50
Erythromycin
Clindamycin
ofoxacin
ciprofloxacin
sulfonamide
gentamycin
nitrofurantoin
cefalotin
penicillin
trimrtoprim/sulfometoxazole
meticillin
cefotaxim
ceftazidime
amoxycillin-clavulanate
sensitive
inter mediate
resistant

Gastrointestinal Bleeding in COVID-19 patients: Identifying the Predictors of Mortality

E. Sabouri[1], M. Rasapoor[1], H. Mohajer[1]

[1]Islamic Azad University Najafabad branch

Introduction: The high transmission rate of Coronavirus Disease (COVID-19) led to a global pandemic with substantial fatalities, primarily due to acute respiratory distress syndrome. Gastrointestinal bleeding (GIB) with a notable prevalence of 1.5-3% in COVID-19 is another prominent cause of death, resulting from altered hemodynamics, hypovolemic shock, and multiple organ dysfunction. This study was conducted to evaluate GIB prevalence and mortality rate in COVID-19 patients and to assess the role of potential risk factors on patient outcomes.

Methods: This retrospective cross-sectional study, used the records of all confirmed COVID-19 adults, admitted to Isfahan Shariati Hospital between March 2020-2022. Following the ethical guidelines, mentioned records were assessed by two physicians, independently, for overt GIB symptoms (melena, hematochezia, and hematemesis). Patients with prior history of GIB, peptic ulcer disease, diverticulitis, hepatic cirrhosis, inflammatory bowel disease, end-stage renal disease, and gastrointestinal malignancies were excluded. Data on demographics, comorbid conditions (e.g., hypertension, diabetes mellitus, and cardiovascular disease), manifestations of GIB, bleeding onset, and anticoagulants administration was extracted. Patient outcomes in 30 days after discharge were determined through phone interviews. Subjects were divided into two groups of alive and deceased to assess the role of variables on outcomes by Chi-square tests and logistic regression models using IBM SPSS Statistics (Version 26).

Results: Among 7243 COVID-19 patients, 107 (1.5%) individuals experienced GIB symptoms. After exclusion, 63 patients (0.86%) with a mean age of 66.66 ± 13.51 years were enrolled, of which 71.4% were male and 47.6% were reported diseased. The most common manifestations were hematemesis (42.9%) and melena (33.3%), indicating 76.2% of upper GIB source. The prevalence of hypertension, diabetes, and cardiovascular disease was 39.7%, 31.7%, and 19%, respectively. 61.9% of GIBs occurred during hospitalization, while 81.0% of patients received anticoagulants. Other than significant associations between the outcomes and gender (P=0.013, OR=3.70), and the onset of bleeding (P=0.001, OR=5.658), no statistically significant relationship was found among variables. Conclusion: In-hospital bleeding and female gender are crucial prognostic factors of mortality in COVID19 patients experiencing GIB. Considering the fatal consequences of GIB in COVID-19 patients, further studies are recommended to assess the roles of risk factors to prevent adverse outcomes.

Keywords: Gastrointestinal Bleeding, COVID-19, mortality

Infectious keratitis following photorefractive keratectomy: a 13-year study at a tertiary center

M. Mohammadi[1], A. Attar[2]

[1]School of medicine, Shahid Sadoughi University of Medical sciences, Yazd, Iran. [2]Poostchi Ophthalmology Research Center, Department of Ophthalmology, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran

Introduction: Infectious keratitis is a rare but devastating complication following photorefractive keratectomy (PRK) that may lead to visual impairment. This study assessed the clinical features, treatment strategies, and outcomes of post-PRK infectious keratitis.

Methods: This retrospective study was conducted on patients with post-PRK infectious keratitis presenting to Khalili Hospital, Shiraz, Iran, from June 2011 to March 2024. The study was conducted in two stages: the first stage assessed the incidence of post-PRK infectious keratitis among patients who underwent PRK at our center, while the second stage included all patients with post-PRK infectious keratitis, regardless of where their PRK was performed. The following data were collected: demographics, post-surgery presentation time, risk factors, culture results, treatments, follow-up duration, complications, and corrected distance visual acuity (CDVA) at admission and the last follow-up.

Results: Forty-two patients (42 eyes) with a mean age of 28.74 years (male-to-female ratio of 1.2:1) were included. Among 38,938 PRK procedures performed at our center, the incidence of keratitis was estimated to be 0.018% (7/38,938). The odds of keratitis during the COVID-19 pandemic were 7.05 times higher (95% CI: 1.58 to 31.52, p-value = 0.015) than outside this timeframe (February 2020 to August 2023). Gram-positive bacteria were the most commonly isolated pathogens in microbiological studies, accounting for 45.2% (19/42) of cases. Early-onset infections were primarily caused by Staphylococcus aureus (9/26, 34.6%), Staphylococcus epidermidis (4/26, 15.4%), and Pseudomonas aeruginosa (4/26, 15.4%), whereas all of the cases with fungi (4/4, 100%) and Acanthamoeba (3/3, 100%) infections caused late-onset infections. All patients received broad-spectrum antibiotic therapy, followed by adjusted treatment based on microbial results. Cases developing endophthalmitis and those not responding to treatment or having non-resolving corneal scars required further interventions, such as penetrating keratoplasty and deep vitrectomy. The mean follow-up duration was 40.81 months, and 97.6% (41/42) of cases experienced CDVA improvement at follow-up.

Conclusion: This long-term study found a post-PRK keratitis rate of 0.018%, with gram-positive bacteria as the most common pathogens. Prompt management and regular follow-up assessments are essential for achieving satisfactory outcomes.

Kawasaki Disease Presenting as Cervical Lymphadenitis: A Rare Case Report Highlighting Early Diagnosis and Management

M. Hassan Ali[1], E. Emre, E. Gorer[1]

[1]Azerbaijan Medical University, Baku, Azerbaijan

Introduction: Kawasaki disease (KD) is a systemic vasculitis predominantly affecting children under fve years of age. Although common in Asia, the lymph-node-frst presentation (NFKD) is rare, particularly in infants. Early diagnosis is critical to prevent coronary artery complications, which occur in up to 25% of untreated cases. We report a case of NFKD in a nine-month-old boy to highlight the diagnostic challenges and importance of timely intervention. The aim of this study is to report a rare case of Kawasaki disease presenting initially as cervical lymphadenitis in a nine-month-old infant and to emphasize the importance of early diagnosis and treatment to prevent coronary artery complications.

Methods: A previously healthy nine-month-old boy presented with fever, neck tenderness, erythema, and severe edema. Physical examination revealed left-sided cervical lymphadenopathy with restricted neck mobility. Initial diagnosis suggested antibiotic-resistant bacterial lymphadenitis. Additional fndings included bilateral non-exudative conjunctivitis, oral and pharyngeal mucosal erythema, reddened lips and tongue (strawberry tongue), erythema of the hands and feet, and a maculopapular rash. Laboratory tests showed elevated CRP (112 mg/L) and ESR (68 mm/hr). Echocardiography revealed mild dilation of the left coronary artery. The patient met the diagnostic criteria for KD and was diagnosed with NFKD. Treatment included intravenous immune globulin (IVIG) (2 g/kg), high-dose aspirin (80 mg/kg/day), and methylprednisolone (2 mg/kg/day).

Results: Fever resolved within 48 hours of IVIG administration, and symptoms improved signifcantly. Follow-up echocardiography showed no progression of coronary artery dilation. The patient was discharged with a plan for continued aspirin therapy and regular cardiac monitoring.

Conclusions: Kawasaki disease should be considered in febrile infants with cervical lymphadenopathy, especially when accompanied by mucocutaneous fndings. Early diagnosis and treatment with IVIG and aspirin can signifcantly reduce the risk of coronary artery aneurysms, which are the most serious complications of KD. This case underscores the importance of considering KD in differential diagnoses to prevent long-term cardiovascular sequelae.

Keywords: Kawasaki disease, cervical lymphadenitis, infant, coronary artery abnormality, IVIG

Optimization of rabies virus detection in brain tissue

L. Ljubotin[1], M. Avramov[1], P. Banović[1]

[1]University of Novi Sad, Faculty of Medicine, Serbia

Introduction: The gold standard for routine laboratory rabies virus detection in the animal or human brain tissue is the direct fluorescent antibody test (DFAT). The test is based upon the detection of viral antigen aggregates within the cytoplasm of infected neurons by fluorescein isothiocyanate-labeled antibodies after acetone fixation. The aim is to investigate the modified DFAT (rapiDFAT) method efficacy and sensitivity on unfixed histological brain tissue smears versus the standard DFAT method on chemically fixed histological brain tissue smears.

Methods: Brain tissue smears were made from a tissue homogenate (control sample) and it's serial dilutions (10-1 , 10-2 , 10-3 , 10-4 , 10-5 , 10-6 , 10-7 ; test samples). Eight slides (control group) were used for the DFAT as well as for the rapiDFAT (test group). Two brain tissue smears per glass slide were made for each dilution and for the control sample. The specimens were dried at room temperature after which the control group specimens were immersed in cold acetone and dried again. A drop of working dilution conjugate was placed on each histological smear after which they were incubated in a humid chamber and finally observed under a fluorescent microscope.

Results: Out of 8 histological specimens tested by the rapiDFAT method 62.5% were positive for rabies (5/8) as well as for the DFAT method.

Conclusion: RapiDFAT method on unfixed brain tissue smears showed equal efficiency and greater sensitivity compared to the DFAT method.

Keywords: rabies; laboratory diagnosis of rabies; direct fluorescent antybody test (DFAT); monoclonal antibodies; acetone

Potent C5 conversion impairs Membrane Attack Complex-dependent killing of Klebsiella pneumoniae

P. Theofilidis[12], D. Doornduijn[12], B. Bardoel[12]

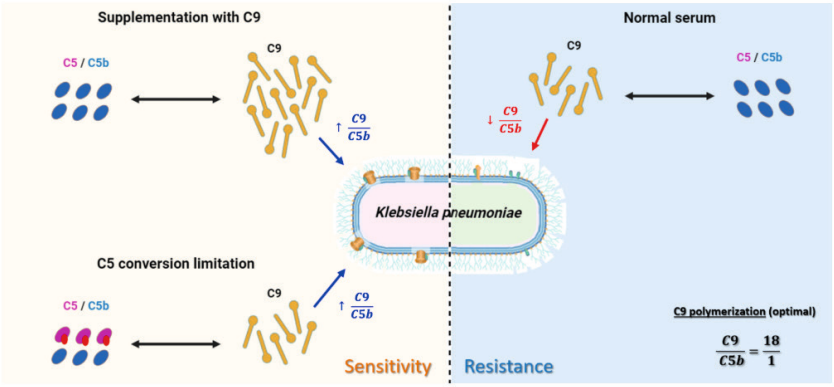
[1]Utrecht University, Department of Medicine, The Netherlands. [2]UMC Utrecht, Department of Medical Microbiology, The Netherlands

Introduction: Klebsiella pneumoniae is a Gram-negative bacterium of global concern, due to the alarming emergence of multidrug-resistance. The complement system is the first line of defence against infections, directly killing Gram-negative bacteria. Its pathogen-triggered activation leads to conversion of the C5 protein into C5b, which associates with more components and up to 18 C9 monomers to generate the Membrane Attack complex (MAC). In Klebsiella and other Gram-negatives, the lipopolysaccharide Oantigen (O-Ag) has been linked with resistance to MAC-dependent killing. Counterintuitively, many highly resistant O-Ag-expressing Gram-negative isolates show more potent C5 conversion than sensitive ones, and hindering of C9 polymerization. Here, we aimed to elucidate the underlying resistance mechanism in K. pneumoniae isolates.

Methods: Five isolates with clinically relevant O-Ags were incubated in serum alone, or either with additional C9 or a titrated C5 conversion inhibitor. Membrane permeabilization was assessed by measuring the fluorescence of the DNA stain SYTOX Green, and killing by colony enumeration after incubation. C5 conversion was assessed with ELISA after every experiment. To assess the effect of C5 inhibition on C9 polymerization, the inhibitor was titrated in C9-depleted serum, repleted with either a fluorescently labelled wt C9 (C9wt-Cy5) or a mutant C9 that cannot polymerize (C9mut-Cy5). For each inhibitor concentration, the fluorescence ratio C9wt-Cy5:C9mut-Cy5 was calculated to determine C9 polymerization.

Results: Despite being barely killed in serum (≤ 2-fold increase in membrane damage over background), all four isolates showed more potent C5 conversion than the sensitive one (> 4-fold membrane damage increase). Partial inhibition of C5b generation enhanced killing of the four isolates compared to serum alone, which was also observed when C9 abundance was increased through C9 supplementation. C9 polymerization peaked at the same C5 inhibitor concentration where killing was maximized. These data indicated that the ratio C9:C5b needs to be optimal for efficient killing and was compromised in serum alone. Conclusions: Potent C5 conversion impairs MAC-dependent killing by decreasing the C9:C5b ratio, thus hindering C9 polymerization and MAC formation. To our knowledge, this is the first time that limiting complement's activity is reported to augment bacterial killing.

Keywords: Klebsiella pneumoniae; complement; resistance; MAC; C5 conversion; C9 polymerization


Supplementation with C9
C5 / C5b
C9
↑ C9/C5b
C5 conversion limitation
C5 / C5b
C9
↑ C9/C5b
Sensitivity
Normal serum
C9
↓ C9/C5b
C5 / C5b
Klebsiella pneumoniae
C9 polymerization (optimal)
C9/C5b = 18/1
Resistance

Primary Ciliary Dyskinesia and Tuberculosis: A Rare Presentation of Kartagener Syndrome

B. V. Roznovan[1], G. Berar1, N. Motoc[12]

[1]Faculty of Medicine, "Iuliu Hatieganu" University of Medicine and Pharmacy ClujNapoca, Romania. [2]"Leon Daniello" Clinical Hospital of Pneumophthisiology, Cluj-Napoca, Romania

Introduction: Primary ciliary dyskinesia is caused by different gene mutations (over 50) that affect the synthesis and activity of the ciliary dynein motor, retrograde intraflagellar transport, and axonemal movement, resulting in cilia with uncoordinated movement or those that are unable to move, leading to recurrent airway infections, degenerative lung diseases, infertility, and defects in sensory and visceral organs. This condition affects approximately 1 in 20,000 people, representing a rare autosomal recessive genetic condition, with a higher frequency in families with consanguinity. In over half of the cases, it can be associated with situs inversus, a condition known as Kartagener's Syndrome.

Case report: This case study reports a 22-year-old man presenting to the pneumology ward with chest pain, fever, chills, dyspnea, productive cough (sometimes with blood stains), and night sweats. The patient's medical history included recurrent cough/respiratory infections from the age of 10, bronchial asthma, and surgical intervention for a deviated nasal septum in 2011. He was born preterm, in the 7th month of pregnancy. Family history suggests possible parental consanguinity. Eye asymmetry, liver dullness on the left side, no murmur in the inferior half on the right, and crackles at the base of the left lung were observed during the physical examination. A chest x-ray was required, which indicated a medium/large pleural collection in the right lung. Thoracentesis revealed high lymphocyte levels and increased ADA (adenosine deaminase), total proteins, and LDH, suggesting a possible infection with Mycobacterium tuberculosis, which was later confirmed by sputum examination. Also, considering the patient's medical history, a spermiogram revealed reduced motility, abnormal morphology, and, in some cases, oligospermia, which directed the diagnosis toward Kartagener syndrome.

Conclusion: Given the high prevalence of Koch's bacillus infections in Romania, a thorough analysis of the patient's history and environmental factors is essential. Although no significant data links Mycobacterium tuberculosis infections with Kartagener's Syndrome, and most bronchiectases are associated with nontuberculous bacilli, it is important to consider it as a possible diagnosis for effective clinical guidance and to identify specific patterns that support optimal treatment, reducing long-term complications and improving quality of life.

Keywords: Kartagener syndrome; situs inversus; Mycobacterium tuberculosis; recurrent respiratory infection; dyspnea

Silent but Deadly: First-Hand Experience of Dealing with Naegleria Fowleri (Brain-eating Amoeba)

M. Ibrahim[1], M. Ahmed Ayaz[1]

[1]Syed Ainan Arshad Aga Khan University, Karachi, Pakistan

Introduction: Naegleria fowleri is a deadly human pathogen recognized as the causative agent of Primary Amoebic Meningitis (PAM). It can be found in warm freshwater environments such as lakes, hot springs, and resort spas. A mortality rate of over 95% has been reported due to its rapid disease progression. In this report, we describe our first-hand experience of dealing with this extremely terrifying pathogen and the lessons we learned along the way.

Case presentation: We describe the case of a 39-year-old male who presented with a two-day history of fever, nausea, and headaches. There were no other signs or symptoms present at the time of admission. There was no prior history of exposure to freshwater lakes or watersports. A spinal tap was performed to rule out meningitis, and empiric antibiotics were started (Ceftriaxone, Vancomycin, and Acyclovir). Within a few hours, the patient's condition started deteriorating rapidly. He started experiencing generalized tonic-clonic seizures that were managed with antiepileptics. The patient was also extremely agitated, and it seemed as if something was literally eating his brain from the inside. CSF analysis studies were unremarkable, and the Biofire meningitis/encephalitis panel was negative for all pathogens. A wet mount for Naegleria sent to look for motile trophozoites came out positive. He was immediately started on Amphotericin B, Rifampin, Fluconazole, and Azithromycin. Unfortunately, the patient soon became unresponsive and was unable to breathe without the assistance of a breathing tube. He was intubated and shifted to the ICU. However, he passed away the next morning.

Conclusion: In this paper, we reported our first-hand experience dealing with a patient suffering from PAM. The result of this case study shows that Naegleria fowleri infections can present very similarly to acute bacterial meningitis and without a history of exposure to freshwater lakes. This should provide clinicians with a better understanding of the frightening nature of N fowleri infections. By sharing our experience, we hope to help budding clinicians identify and treat this deadly pathogen as early as possible.

The controlled human hookworm infection in Africa experience: From Leiden, the Netherlands, to Lambaréné, Gabon (2019-2024)

A. Alabi[1], M. Yazdanbakhsh[1], S. Agnandji[1]

[1]Leiden University Medical Center

Introduction: Hookworm are soil-transmitted helminths estimated to infect 230 million people worldwide, predominantly in the tropics. Candidate vaccines for the prevention of hookworm infection are now in early clinical development. To accelerate development, controlled human hookworm infection (CHHI) for Na was established at Leiden University Medical Center (LUMC). The CHHI involves challenging carefully selected volunteers with well characterised infectious hookworm and closely monitoring to detect infection. To facilitate testing for efficacy in an endemic population who need these interventions the most, we established a CHHI in Centre de Recherches Médicales de Lambaréné (CERMEL), Gabon.

Methods: The LUMC and CERMEL staff completed training and sharing of standard operating procedures despite challenges of the covid-19 pandemic. The preparation of the infectious challenge material involves culture of fecal samples with antimicrobials, followed by preparation of Na larvae. A stakeholder meeting to discuss the CHHI model in Gabon was held, and a CHHI dedicated lab was built by CERMEL. A CERMEL study protocol for a phase 1 trial was approved by CERMEL's Scientific Review and Ethics Committees, and the Gabonese National Ethics Committee.

Results: The local strain of Na, at a dose of 50 larvae, was used for the CHHI. The trial enrolled 15 healthy male individuals (10 infected, 5 placebo), aged 21-45, with minimal exposure to hookworm infection and resident in Gabon. Detection of infection was by Kato-Katz and PCR. Patency of infection was 100% (n=10), peak eosinophilia at week 6, and a mean egg load of 646 eggs/g (range, 192-1932) at week 15. No severe adverse events were observed. Infection was terminated at week 16.

Conclusion: This is the first ever CHHI established in Africa. The transfer of knowledge, expertise and technology empowered researchers in Gabon to conduct the CHHI trial. This creates opportunity to scale-up use of the CHHI to assess vaccines and drugs in endemic settings and populations. Ongoing collaboration between LUMC and CERMEL researchers is a natural continuation of mutual respect for each other's interest and achievement of a common goal: a pivotal role for Africa in the licensure of a vaccine against hookworm disease in the near future.

The Silent Pandemic Caused by the Spread of Multidrugresistant Strains of Bacteria.

N. Khukhunasivhili[1]
Research supervisor: T. Didbaridze, MD, PhD[1]

[1]American MD program of Tbilisi State Medical University, Georgia

Introduction: Humanity is losing leverage (antibiotics) against infections caused by antibioticresistant bacteria. Due to the increasing use of antibiotics, a large number of bacteria have become resistant to antibiotics. Unfortunately, this process is irreversible and progresses quite quickly. By 2050, if urgent measures are not taken, 10 million people will die annually from infections caused by the so-called "Super Bug". That is, humanity will return to the era before antibiotics. The purpose of this project is to study the genome of "Super Bugs" and raise awareness among the population.

Methods: The study includes a laboratory data analysis, and a survey. Bacterial isolates were collected from four clinics in Georgia. Antimicrobial resistance gene content was examined by multiplex PCR, targeting plasmid-mediated AmpC and beta-lactamases, representing fifteen gene families. Among the interviewees were medical students, students from other faculties, doctors, and individuals not involved in medicine.

Results: It was found that the 80% of respondents have taken an antibiotic at least once without doctor's recommendation. 85% of the interviewees, including some medical professionals, is unaware of wide spread of multi resistant strains of bacteria and its implications. As part of the scientific project conducted by the US Walter Reed Army Institute of Research and the First University Clinic of TSMU, titled "Laboratory-Based Monitoring and Genetic Characterization of Antimicrobial-Resistant Bacteria in Georgia,"168 samples laboratory data were analyzed and it became clear that "Superbugs" have plasmid genes (CTX-M-15, CTX-M-14, OXA-48, VIM, IMP). These genes cause their resistance to antibiotics and are activated differently in the human body and on agar plates, making it difficult to start an effective treatment.

Conclusion: Prevalence of multi resistant strains was observed in bacterial isolates found in Georgia. Detection of plasmid-related resistance genes indicates the high potential of horizontal spread of resistance and the danger of emergence of new "superbugs" in Georgia.

Keywords: Superbug, multidrug resistance, plasmid genes

Toxoplasma gondii seroprevalence in traffic accidents victims, is there a link?

H. Ghasemirad[1], Dr. Aalazade[1], Dr. Ghasemirad[1], Ms. Ghasemirad[1], Dr. Owliaey[1], Dr. Kargar[1]

[1]Shahid Sadoughi University of Medical Sciences, Yazd, Iran

Introduction: Traffic accidents are a major cause of injury and death worldwide, with human error often being a key factor. Recent studies suggest that Toxoplasma gondii (T.gondii) infection, known for its neurological and behavioral impacts, may contribute to delayed reaction times in drivers. This parasitic infection forms cysts in the brain, potentially leading to impaired cognitive functions and increased risk-taking behavior, both of which are critical in traffic safety. In this study, we aimed to explore the seroprevalence of T.gondii in individuals involved in traffic accidents in Yazd, central Iran, and to assess the potential link between infection and impaired reaction time.

Methods: Data from 360 individuals, including 180 with positive T.gondii IgG serology and 180 with negative results, all aged 18 years and older, were gathered to investigate the elevated seroprevalence of T. gondii in traffic accident victims. Logistic regression was used to examine the potential link between infection and involvement in accidents, while controlling for confounding factors such as age, sex, and driving experience.

Results: The analysis revealed that the seroprevalence of T.gondii in individuals involved in car accidents was 2.24 times higher than those who tested negative (95% CI: 1.40 to 3.59, $p < 0.01$). Even after adjusting for variables such as age, sex, and driving time, the elevated seroprevalence remained consistently significant, underscoring the widespread occurrence of T. gondii in traffic accident victims.

Conclusions: This study identified a higher rate of car accidents among individuals who tested positive for T.gondii. The findings highlight the need for increased awareness of driving risks in T. gondii-infected individuals. Further research with larger sample sizes is recommended to provide more robust insights into this relationship.

Keywords: Toxoplasma gondii, car accidents, seroprevalence, infectious disease, parasitology

Variable	Coef.	Std.Err.	z	P>|z|	OR	2.5%	97.5%	Model
const	-1.597	0.54	-2.96	0.003	0.202	0.07	0.583	Model 1 (Adjust for Age)
groups	0.79	0.243	3.255	0.001	2.204	1.369	3.547	Model 1 (Adjust for Age)
age	0.007	0.015	0.485	0.628	1.007	0.978	1.037	Model 1 (Adjust for Age)
const	-0.733	0.712	-1.029	0.303	0.48	0.119	1.941	Model 2 (Adjust for Age and Sex)
groups	0.828	0.245	3.38	0.001	2.288	1.416	3.696	Model 2 (Adjust for Age and Sex)
age	-0.005	0.016	-0.296	0.767	0.995	0.964	1.027	Model 2 (Adjust for Age and Sex)
sex	-0.583	0.315	-1.852	0.064	0.558	0.301	1.035	Model 2 (Adjust for Age and Sex)
const	-1.189	0.75	-1.584	0.113	0.305	0.07	1.325	Model 3 (Adjust for Age, Sex, and Time of Driving)
groups	0.854	0.248	3.448	0.001	2.35	1.446	3.819	Model 3 (Adjust for Age, Sex, and Time of Driving)
age	-0.006	0.016	-0.352	0.725	0.994	0.963	1.027	Model 3 (Adjust for Age, Sex, and Time of Driving)
sex	-0.279	0.348	-0.801	0.423	0.757	0.383	1.496	Model 3 (Adjust for Age, Sex, and Time of Driving)
time_r	0.148	0.066	2.237	0.025	1.16	1.019	1.321	Model 3 (Adjust for Age, Sex, and Time of Driving)

Treatment Success Factors for Drug-Resistant Tuberculosis Patients at RSUP Persahabatan (Indonesian National Reference) in 2018-2022

A. F. Mughny Anwar[1], F. Isbaniah[1]

[1]University Indonesia

Introduction: Tuberculosis (TB) is an infectious disease caused by Mycobacterium tuberculosis, with drug resistance (DR-TB) representing a significant challenge in its treatment. Indonesia has the second-highest number of TB cases and the third-highest incidence of multidrug resistance and rifampicin resistance in the world, with numerous factors influencing the success of treatment, including age, gender, comorbidities, and other factors. This study aimed to identify factors that facilitate the successful treatment of DR-TB at RSUP Persahabatan (National Respiratory Center) during 2018-2022 and to provide more effective research and policy recommendations.

Methods: This cohort retrospective study utilized medical record data of patients with pulmonary DR-TB at RSUP Persahabatan from 2018 to 2022. To be included in the study, patients had to be at least 15 years old and diagnosed with pulmonary DR-TB. Patients who did not meet these criteria were excluded, including those with incomplete medical records, those who were taking medication, and those who had been transferred to other hospitals. A minimum sample size of 87 individuals was utilized for data analysis, which was conducted using the SPSS 27.0 software. This involved the Chi-Square test for categorical groups.

Results: Of the 160 patients, 75 (46.87%) were cured, while 85 (53.12%) were not. No significant correlation was identified between age (p=0.99), gender (p=0.25), BMI (p=0.26), education (p=0.93), type of resistance (p=0.57), comorbid diseases such as type 2 diabetes mellitus (p=0.60), and HIV (p=0.22), smoking habits (p=0.84), bacterial load (p=0.14), and compliance (with or without medication supervision) (p=0.38).

Conclusion: The success rate of DR-TB treatment at RSUP Persahabatan from 2018 to 2022 was 46.87%. No significant effect was observed for any of the following factors: age, gender, education, BMI, comorbidities, smoking, bacterial load, and compliance (with or without PMO) on the likelihood of a cure. These results suggest the importance of exploring additional variables (such as socioeconomic status, patient knowledge, motivation, adverse drug effects, and healthcare access) to identify determinants of positive outcomes.

Keywords: success factors, drug-resistant tuberculosis (DR-TB), cure

LIFE-COURSE

Exploring the Impact of a Multicomponent Frailty Management Plan on HealthRelated Quality of Life in Frail Older Individuals: Insights from the FORTRESS Study

F. Geerlings[1], I.D. Cameron[1]

[1]Department of Hornsby Ku-ring-gai Hospital, Rehabilitation and Aged Care Service (RACS) University of Sydney, Australia

Life- Course

Introduction: Frailty is a critical concern in geriatric research, significantly heightening vulnerability to diseases, falls, hospitalizations, and mortality among older adults. The FORTRESS trial investigated the effects of a tailored frailty management plan integrated into routine care, following the Asia Pacific Clinical Practice Guidelines. The study employed a hybrid stepped-wedge design across multiple hospital sites in Australia, aiming to improve multiple outcome measures, including health-related quality of life (HRQoL).

Methods: Participants, classified as frail according to the FRAIL Scale, received either solely standard care or the added intervention, which included physiotherapy, dietary support, and a medication review. Assessments were conducted at baseline, 3 months, and 12 months, focusing on the EQ-5D-5L HRQoL domains: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression.

Results: Results indicated no significant improvement in HRQoL domains in the intervention group compared to controls. Notably, mobility and anxiety/depression scores were significantly worse in the intervention arm at 12 months compared to the control arm ($p<0.05$). Usual activities scores were found to be significantly worse throughout the whole follow-up period ($p=0.002$), largely driven by results from the hospital wards located in South Australia.

Conclusions: The FORTRESS protocol failed to enhance HRQoL in frail older adults, though it did highlight a previously unknown challenge with the use of the EQ-5D-5L in this population. These findings underscore the need to revisit the intervention strategy, emphasizing intensified exercise programs and improved adherence. The upcoming FORTRESS+ study, now recruiting, aims to address these necessary alterations.

Keywords: Frailty, Older Individuals, Intervention, HRQoL, EQ-5D-5L

Life- Course

A physiotherapist supervised exercise intervention for nursing home residents with dementia: preliminary results of a non-randomized pilot study

D.E. Boer[1], C. Schmidt[1], S. Sterke[1], T.P.M. Vliet Vlieland[1]

[1]Medical University of Leiden, The Netherlands

Introduction: Physiotherapy and exercise are commonly used in the treatment of nursing home residents with dementia. However, no studies have examined an exercise intervention that is adequately dosed according to established guidelines, incorporating sufficient strength, balance, and endurance training in this population. To assess the feasibility of an adequately dosed exercise intervention for nursing home residents with dementia. Feasibility was defined by adherence to the intervention (successful completion of exercise sessions), adverse events, participant satisfaction, and supervisor experiences.

Methods: We conducted a single-arm observational pilot study including twelve nursing home residents with dementia residing in secure dementia wards with no intention of returning to independent living. Eligible participants were able to walk 50 meters independently. Exclusion criteria were the expectation of exacerbation of neuropsychiatric symptoms of dementia, according to the physician in charge. The intervention consisted of twice-weekly group exercises targeting muscle strength and balance, as well as twice-weekly guided individual aerobic exercise using an exergaming stationary bike with virtual routes. The intervention lasted eight weeks.

Results: Preliminary findings from the exergaming sessions indicate a mean adherence rate of 86%, with a mean participant satisfaction score of 4.3 on a 5-point Likert scale. No serious adverse events related to the intervention were reported. Supervisors highlighted the importance of (basic) dementia knowledge, proficiency in using the exergaming software while recognizing its limitations, and the value of fostering a reciprocal connection through exercise.

Exploring the user experiences of healthcare professionals working with the SARA social care robot in long-term care for people with dementia and people with intellectual disabilities: a qualitative study

N.P.A. Zuurbier[1], H.J.A. Smaling[1]

[1]Department of Public Health and Primary Care Medicine, Medical University of Leiden, The Netherlands

Introduction: The Social & Autonomous Robotic Health Assistant (SARA) is a social robot used in long-term care (LTC) for people with dementia and people with intellectual disabilities (ID). SARA can stimulate and calm residents using personalized content, making it a promising intervention to support healthcare professionals in providing person-centered, high-quality care. To explore the user experiences of healthcare professionals working with SARA, a humanoid social robot, in LTC for people with dementia and people with ID. Secondarily, barriers and facilitators for implementation were identified. Lastly, usability was explored.

Methods: A qualitative design using semi-structured interviews. The System Usability Scale (SUS) explored the robot's usability. Setting and Participants Seven healthcare professionals from two Dutch LTC organizations (one for dementia care, one for ID care) participated. Methods Online semi-structured interviews were conducted. The SUS was completed online before the interview. Data were analyzed thematically using inductive and deductive approaches.

Results: Three themes were identified: 1) acceptance of SARA by all involved, 2) impact of SARA on all involved, and 3) user-friendliness. The impact on residents was predominantly positive. Few negative effects occurred when activities didn't match the situation or resident's needs. Acceptance among healthcare professionals grew over time. Its use may enhance job satisfaction and enjoyment while improving efficiency. Although implementation required time investment, SARA later showed potential to save time. Barriers and facilitators for implementation were identified: adequate education, high staff motivation, and supplier support were key facilitators. Usability was deemed marginally acceptable. Participants provided recommendations for improvement.

Conclusions: User experiences with SARA were predominantly positive, making the robot a promising aid for healthcare professionals in delivering high-quality LTC. Recommendations for usability and implementation improvement were mentioned.

Keywords: Robot, dementia, intellectual disability, healthcare professionals, long-term care

Gut Microbiota Dysbiosis as a Predictor of Postoperative Complications in Colorectal Surgery Patients

M.D. Bazamfare[1]

[1]European university of lefke

Introduction: Postoperative complications in colorectal surgery remain a significant challenge, with infections and anastomotic leaks being major concerns. Emerging evidence suggests that gut microbiota composition plays a critical role in postoperative recovery. This study examines whether preoperative microbiota profiling can predict postoperative outcomes.

Methods: A prospective cohort study was conducted on 120 patients undergoing elective colorectal resection. Stool samples were collected preoperatively and analyzed using 16S rRNA sequencing. Patients were monitored for 30 days postoperatively for complications such as surgical site infections (SSI), anastomotic leaks, and prolonged hospital stay. Machine learning algorithms were applied to identify microbial signatures predictive of adverse outcomes.

Results: Patients who developed complications (n=34) exhibited a distinct microbial profile characterized by reduced Faecalibacterium prausnitzii abundance and increased Enterococcus spp. diversity ($p < 0.01$). A predictive model incorporating microbiota data achieved an accuracy of 85% in identifying high-risk patients. Moreover, a decrease in short-chain fatty acid-producing bacteria correlated with prolonged recovery times.

Conclusions: Preoperative gut microbiota composition is a strong predictor of postoperative complications in colorectal surgery. These findings highlight the potential of microbiome-based risk stratification and targeted prehabilitation strategies to improve surgical outcomes.

Keywords: gut microbiota, colorectal surgery, postoperative complications, microbiome, predictive modeling

Barriers and facilitators of family involvement in physiotherapy and exercise for nursing home residents with dementia: a qualitative study

D.E. Boer[1], C. Schmidt[1], L. Van Bodegom - Vos[1], T.P.M. Vliet Vlieland[1]

[1]Medical University of Leiden, The Netherlands

Introduction: An integral delivery of nursing home care in where family caregivers and physiotherapists collaborate may have benefits for all involved. This study aimed to identify barriers and facilitators for involving family members.

Methods: We conducted 28 semi-structured interviews with 19 physiotherapists and 9 nursing home staff members concerned with family participation. Participants were selected from Dutch nursing homes providing care for residents with dementia. Interviews were recorded and transcribed, and subsequently analysed using inductive thematic coding.

Results: The perceived barriers included the burden placed on family caregivers, particularly during the transition to nursing home care, and the need for adequate information and guidance to ensure successful involvement. Additionally, it was found that an unwelcoming environment fostered by physiotherapists and nursing homes hinder family members participation. Facilitators included a proactive approach of physiotherapists regarding the collaboration, and information on practical aspects of exercise, particularly when supported by technology or exergaming. Other facilitators were the family caregivers' prior healthcare experience and cultural factors emphasizing the importance of family support.

Conclusions: In conclusion, this study identified several barriers and facilitators affecting family involvement in physiotherapy and exercise for nursing home residents with dementia. Building on these findings and existing literature, targeted interventions to promote family involvement in physiotherapy and exercise care can be developed.

Keywords: dementia, alzheimer's, nursing home, exercise, family caregivers, physical therapy

What do patients with hip or knee osteoarthritis expect from physiotherapy treatment? Preliminary results of a qualitative study

A.P.M. Konings-Pijnappels[123], M.C. Van der Steen[124], T.P.M. Vliet Vlieland[3], R.P.A. Janssen[125]

[1]Fontys University of Applied Sciences, Eindhoven, The Netherlands. [2]Máxima Medical Center, Eindhoven-Veldhoven, The Netherlands. [3]Leiden University Medical Center (LUMC), Leiden, The Netherlands. 4Catharina Hospital, Eindhoven, The Netherlands. [5]Eindhoven University of Technology, Eindhoven, The Netherlands

Introduction: Physiotherapy has been proven effective in reducing pain and improving physical functioning in patients with hip (HOA) or knee (KOA) osteoarthritis. Whereas the literature shows that patients' expectations of treatment can influence its outcomes, knowledge on patient expectations of physiotherapy for HOA or KOA is scarce. This study therefore aims to explore the expectations of patients with hip or knee OA with regard to physiotherapy treatment and factors influencing these expectations.

Methods: Semi structured interviews with patients with HOA or KOA referred to a physiotherapist by a general practitioner or orthopaedic surgeon, were executed before the start of treatment. Participants were recruited through purposive sampling. The interviews were conducted using a topic guide, including expectations on the outcomes and on the structure and process of the delivery of physiotherapy and on internal and external factors that contributed to these expectations. Data collection continued until saturation was achieved. Thematic analysis was performed by open and axial coding.

Results: The preliminary results were obtained from the first nine participants who were interviewed. Their median age was 72 years, 2 participants were male, 7 had knee OA, and 2 were referred by a general practitioner. Regarding their expectations on outcomes, participants mentioned pain reduction and improved ability to move. With respect to the delivery, participants reported active therapy and supervision of exercises by the physiotherapist. Some participants expected their personal history to be taken into account as well as their current personal situation. Furthermore, the use of equipment such as exercise bikes or other devices were mentioned. Regarding factors that played a role in expectations, general knowledge and significant others with OA or who received physiotherapy for other conditions were reported.

Evolution of muscle mass and strength in patients admitted for a diabetic foot ulcer

J. Terwingen[1], D. Frings[1], Y. Hulshagen[1], P. Lauwers[1], E. Dirinck[1]

[1]University of Antwerp

Introduction: Diabetic foot ulcers (DFU) often cause immobility and extended hospitalizations. Research at Antwerp University Hospital identified high malnutrition rates, low muscle strength and mass in this patient group. However, little is known about how muscle health evolves during longer hospitalization. This study aimed to assess changes in muscle strength and muscle mass in hospitalized DFU patients and to evaluate the impact of malnutrition at admission.

Methods: This prospective observational cohort study included patients from February 12, 2021, to July 9, 2024. Anthropometric measurements, handgrip strength tests (HGS), and impedance analysis were conducted within 48 hours of admission. Nutritional status was assessed using the Mini Nutritional Assessment (MNA). The diagnosis of malnutrition was based on the Global Leadership Initiative on Malnutrition (GLIM) criteria. Data were analyzed using SPSS (p- value < 0,05).

Results: 78 DFU patients (74% men, median age 72 years [44-90], BMI 27,6 kg/m² [16,1–47,0]) were recruited. 50% presented with malnutrition. No statistically significant differences between admission and discharge were observed with regard to muscle mass (18,3±2,1 versus 18,1±2,1 kg/m²) and HGS (26,0±10,3 versus 26,5±11,5 kg). Also in malnourished individuals, no statistically significant differences between admission and discharge were observed in muscle mass (17.3±1.7 versus 17.2±1.9 kg/m²) and HGS (24.8 ± 9.4 versus 25.1±10.6 kg). The change in muscle mass did not differ between malnourished and non-malnourished patients (0.04±1.35 versus –0.56±1.21 respectively). The change in muscle strength did not differ between malnourished and non-malnourished patients (0.4 (–8.3 to 15) and 0 (–2.90 to 2.70) respectively).

Conclusion: DFU patients exhibited no significant changes in muscle mass or muscle strength during hospitalization, regardless of nutritional status. While malnutrition was associated with lower muscle mass upon admission, it did not significantly affect changes in muscle mass or strength during hospitalization under intensive nutritional support and physical therapy.

Keywords: Muscle strength, muscle mass, diabetes mellitus, malnutrition

Life- Course

The mediating effect of mental functioning in the relationship between socioeconomic status and disease activity in patients with rheumatoid arthritis

J.B. Pleij[1], A.H.M. van der Helm-van Mil[1], S.A. Bergstra[1]

[1]Department of Rheumatology, Leiden University Medical Centre, the Netherlands

Introduction: Lower socioeconomic status (SES) has been shown to be related to higher disease activity in patients with rheumatoid arthritis (RA). However, the pathways which explain this association remain underexposed. We hypothesize that worse mental functioning could play a role in the relationship between lower SES and disease activity.

Methods: 650 patients diagnosed with RA and fulfilling the 1987 and/or 2010 classification criteria from the Leiden Early Arthritis Clinic cohort were included. Follow-up was recorded at 3 months, 8 months and yearly thereafter. SES groups (low, intermediate, high) were defined by educational attainment. Mental functioning was examined using the SF-36 Mental Component Scale (MCS) and subsequent domains (SF, RE, MH). Data were analyzed cross-sectionally (linear regressions) and longitudinally over 7 years follow-up (mixed model analyses, bootstrapping). Mediation analyses were performed, followed by percentage mediation calculations. All analyses were adjusted for age and sex.

Results: At baseline, RA-patients with a low or middle SES had worse scores for all domains of mental functioning compared to the high SES group. Moreover, average DAS was significantly higher for the low SES group (low 3.75, ± 0.99 VS. middle 3.46, ± 1.03 VS. high 3.27 ± 1.12). 27% of the total effect between low SES and DAS at baseline was explained through mediation of emotional functioning (RE). During follow-up, DAS remained significantly higher for the middle and low SES group (mean difference middle: 0.24 $p=0.001$, low: 0.56 $p<0.001$). Furthermore, these groups had significantly worse scores for all domains of mental functioning throughout follow-up. Significant mediating effects of MCS as well as all subdomains were observed between SES and DAS (table 1). Mediating effects ranged from 10% to 33% for the different domains during follow-up.

Conclusions: RA-patients with lower SES had significantly higher DAS at diagnosis and during the course of disease, which is partially explained by a worse mental functioning. This increases our understanding of inequities in the course of RA related to patients' socio-economic background.

Keywords: Rheumatoid arthritis, mental health, socioeconomic status

Evaluating the Prognostic Value of Serum Bilirubin and Ammonia Levels in Stage 2 Liver Failure: A Retrospective Study

P. Behnamrad[1]

[1]Shahid Sadoughi University of Medical Sciences

Introduction: Liver failure is a critical condition with significant morbidity and mortality, and its progression is categorized into different stages based on clinical manifestations and liver function. Stage 2 liver failure, characterized by hepatic encephalopathy and impaired synthetic function, requires accurate prognostic tools to guide management. This study investigates the role of serum bilirubin and ammonia levels as predictors of mortality in patients with stage 2 liver failure.

Methods: A retrospective analysis was conducted on 150 patients diagnosed with stage 2 liver failure, admitted to a tertiary hospital over a 5-year period. Patient data, including serum bilirubin, ammonia, international normalized ratio (INR), and lactate levels, were collected at the time of admission. The primary outcome was 90-day mortality. Logistic regression models were used to assess the relationship between serum bilirubin, ammonia, and mortality, adjusting for confounding variables such as age, comorbidities, and liver disease etiology.

Results: Out of the 150 patients, 45 (30%) died within 90 days of admission. Both serum bilirubin and ammonia levels were significantly higher in the deceased group (bilirubin: 8.2 ± 3.4 mg/dL vs 4.1 ± 2.1 mg/dL, $p < 0.001$; ammonia: 103.4 ± 26.7 µmol/L vs 67.8 ± 22.1 µmol/L, $p < 0.001$). Logistic regression revealed that elevated serum bilirubin (OR 2.5, 95% CI 1.6–3.9, $p = 0.002$) and ammonia (OR 1.8, 95% CI 1.2–2.7, $p = 0.004$) were independent predictors of mortality, alongside high INR levels (OR 1.9, 95% CI 1.3–2.7, $p = 0.003$).

Conclusions: Serum bilirubin and ammonia levels are valuable prognostic markers for predicting mortality in stage 2 liver failure. Elevated levels of these biomarkers, alongside traditional indicators like INR, can assist clinicians in identifying patients at higher risk of adverse outcomes. These findings suggest the potential for incorporating these biomarkers into clinical practice to improve early intervention and patient management.

Keywords: Liver failure, stage 2, serum bilirubin, ammonia, prognosis, mortality, hepatic encephalopathy

Fall Risk Screening of Elderly Patients Visiting Internal Medicine Clinic at Hospital X

Rezqita Ramadhani[1], Vera, dr., SpPD-KGer[2]

[1]Maranatha Christian University, Bandung, West Java, Indonesia
[2]Internal Medicine Department, Maranatha Christian University, Bandung, Indonesia

Introduction: Despite potential serious injury due to falls in elderly patients, Hospital X in East Java, Indonesia does not have falls screening for outpatient settings. Aim: To develop a fall prevention program for outpatient elderly in hospitals.

Methods: This descriptive observational study included 113 elderly patients visiting internal medicine clinic of Hospital X in April 2023.

Results: Based on the Timed Up and Go test and 5 Times Chair Stands, the majority of respondents (56.6% and 80.5%, respectively) were at high risk of falling. However, only 13.3% of those reported their falls event. Visual impairments (93.3%), changes in urinary patterns (73.3%), consumption of five or more medications (61%) and having 2 or more chronic diseases (73.3%) were the most common falls risk factors in respondents with a falls history.

Conclusions: Since the percentage of respondents at high falls risk was quite large, healthcare practitioners in Hospital X should evaluate falls risk factors in all elderly patients in the clinic, especially for very old female patients with polypharmacy and multipathology.

Keywords: Elderly Outpatient, Fall, Risk Factors

MEDICAL GENOMICS

Bethlem Myopathy: A Novel Homozygous Variant of c.385C>T (p.Arg129Cys) in the COL6A2 Gene

A. Mohammadi[1], M.Mohammadi[1]

[1]School of Medicine, Iran University of Medical Sciences, Tehran, Iran

Medical genomics

Introduction: Bethlem myopathy (BM) is a rare congenital muscular dystrophy caused by mutations in the COL6A1, COL6A2, or COL6A3 genes. It typically presents with proximal muscle weakness and joint contractures and follows an autosomal dominant inheritance pattern, though autosomal recessive cases have been reported. Diagnosis can be challenging, particularly in resourcelimited settings.This study reports a novel homozygous variant in the COL6A2 gene in an Iranian patient with BM, emphasizing the importance of genetic testing for accurate diagnosis and management.

Methods: We examined an 8-year-old girl from a low socio-economic background, born to third-degree cousins, who presented with progressive muscle weakness and pain since the age of 4. Neurological evaluation and genetic testing were performed to confirm the diagnosis.

Results: Clinical assessment revealed proximal muscle weakness, a waddling gait, and a positive Gowers' maneuver. Genetic analysis identified a novel homozygous COL6A2 variant, c.385C>T (p.Arg129Cys), classified as a variant of uncertain significance (VUS) according to ACMG guidelines. Notably, the patient's 15-year-old half-sister also exhibited BM symptoms.

Conclusion: This case highlights the diagnostic complexities of BM, particularly in consanguineous families. Early genetic testing is crucial for precise diagnosis, guiding management, and providing genetic counseling. Recognizing BM's diverse presentations can enhance early detection and improve patient outcomes.

Keywords: Bethlem myopathy, COL6A2 mutation, congenital muscular dystrophy, genetic testing, rare disease

Medical genomics

The importance of timely diagnosis of familial Mediterranean fever(FMF) with the help of genetic technologies

A.G. Eshagh[1], S.H. Anar[1]

[1]Azerbaijan, Azerbaijan Medical University

Introduction: Familial Mediterranean fever(FMF) is a hereditary inflammatory disorder that mainly affects people living in the Middle East, especially the Mediterranean coast. The incidence rate is higher among Jews and Turks (Turkey, Azerbaijan and northwestern parts of Iran). Transmission occurs as an autosomal recessive trait from both parents. Symptoms of the disease include pain and redness in the abdominal area, periodic fevers, joint pain and frequent headaches. Early diagnosis of this disease is very important because if not diagnosed, it has many effects on the person. Among them, kidney failure can be mentioned, which occurs due to amyloidosis.

Methods: In this study, the diagnosis and treatment process of 11 patients from Iran and Azerbaijan was examined, of which 5 were more accurate and detailed due to voluntary cooperation. Their blood sample was taken and got diagnosed.

Results: In each of the 5 patients, the disease was initially misdiagnosed. The initial diagnosis of 2 patients was appendicitis, 1 patient had arthritis, and 2 patients had a bacterial stomach infection. When the symptoms reappeared after appendicitis surgery in the first case and during the treatment period in the third case (stomach infection), they were diagnosed with Mediterranean fever upon referral to another center. The parents of the patient suspected of arthritis also learned about this disease through social networks and referred for testing, and the main problem was identified. The main method of treating this disease is the use of colchicine, which has a positive result in most patients, but otherwise alternative methods such as Anakinra are recommended. Colchicine was effective in the treatment of all 5 patients.

Conclusion: We recommend that in countries where this disease is common, the necessary genetic tests be performed before marriage and after the birth of the baby so that timely diagnosis causes less harm to the patient and saves the family less time and expense.

Keywords: Familial Mediterranean Fever (FMF), hereditary inflammatory disorder, autosomal recessive trait, amyloidosis, colchicine

Identification of Key Genes Involved in Oxidative Stress in Bronchopulmonary Dysplasia of Prematurity

I. Isgandarov[1], A. Abilbayeva[1], A. Tarabayeva[1]

[1]Asfendiyarov Kazakh National Medical University

Medical genomics

Introduction: Lung injury during mechanical ventilation is a leading factor in the pathogenesis of bronchopulmonary dysplasia (BPD) in preterm infants. Oxidative stress, resulting from the generation of free radicals, damages lung cells, causing inflammation, and etc. The immaturity of the antioxidant system and hyperbaric oxygenation exacerbate oxidative stress in these infants. This study aimed to identify candidate genes encoding proteins crucial to the pathogenesis of oxidative stress in BPD and analyze their functional interactions within molecular networks regulating redox homeostasis.

Methods: The gene expression profiling dataset GSE219156 from the Gene Expression Omnibus (GEO) database was analyzed. Differentially expressed genes (DEGs) were identified using GEO2R with cutoff values $p < 0.05$ and $|\text{Log FC}| \geq 1$. Gene Ontology (GO) and KEGG pathway enrichment analyses were performed using ClusterProfiler and Enrichr tools.

Results: Bioinformatics analysis identified 137 DEGs. There is 90 upregulated and 47 downregulated genes. GO functional enrichment analysis revealed that IGHA1 and IGHA2 genes are involved in the regulation of the respiratory burst process ($p = 0.003$). These genes were also associated with humoral adaptive immunity, phagocytic immune response, and complement activation. Analysis of signaling pathways in the Reactome database showed that these genes play a key role in Binding and Uptake of Ligands by Scavenger Receptors, Hemostasis and Scavenging of Heme From Plasma.

Discussion: IGHA1 and IGHA2 are involved in positive regulation of respiratory burst, a process generating reactive oxygen species (ROS). Activation of scavenger receptors by ligand binding leads to phagocyte activation and subsequent stimulation of NADPH oxidase, a key enzyme in ROS production. Uncontrolled ROS generation can provoke oxidative stress, damaging cellular structures and tissues, contributing to inflammation and chronic diseases. This study also established a connection between these genes and heme metabolism. We found that they may participate in regulating heme clearance from blood plasma. During this process, heme undergoes oxidative modifications, forming free heme. Free heme, possessing catalytic activity, can initiate oxidative damage to lipids, proteins, and nucleic acids, increasing cellular stress and potentially contributing to various pathologies.

Keywords: bronchopulmonary dysplasia, gene expression, oxidative stress

Medical genomics

Impact of Continuous Positive Airway Pressure on the Circadian Clock Signaling Pathwaycin Patients with Obstructive Sleep Apnea

J. Jaromirska[1]

[1]Medical University of Lodz, Poland

Introduction: Obstructive sleep apnea (OSA) has been associated with circadian rhythm disturbances, likely due to alterations in clock gene expression.

Objective: This study aimed to assess the effects of a single night of continuous positive airway pressure (CPAP) therapy on the expression levels of key circadian clock genes — BMAL1, CLOCK, CRY1, and PER1 — at both mRNA and protein levels.

Methods: A total of 30 OSA patients were enrolled in the study. Each patient underwent diagnostic polysomnography (PSG), followed by a single night of CPAP therapy under PSG monitoring. Blood samples were collected in the evening, before, and in the morning after PSG and CPAP treatment. The expression of targeted genes was analyzed at the mRNA level using qRT-PCR and at the protein level using ELISA. This study was funded by the National Science Centre (grant number 2018/31/N/NZ5/03931).

Results: A significant increase in PER1 mRNA expression was observed in the morning after CPAP therapy compared to the evening before treatment ($p=0.005$). In addition, PER1 protein levels were significantly reduced in the morning after CPAP therapy compared to the morning after PSG ($p=0.035$). Significant changes were detected in CLOCK protein levels: an increase in the morning after CPAP compared to the morning after PSG ($p=0.049$), an increase in the morning after CPAP compared to the evening before treatment ($p=0.006$) and a notable difference in morning-evening variation between the CPAP and PSG conditions ($p=0.012$).

Discussion: These findings suggest that even short-term CPAP therapy may contribute to restoring circadian clock signaling pathways in OSA patients, highlighting its potential regulatory effect on clock gene expression.

A SNP chip for DRiP: Designing diagnostic tools to define disease heterogeneity, disease progression and therapeutic intervention

M. Staal[1], R. van Tienhoven[1], B.O. Roep[1]

[1]Department of Internal Medicine, Leiden University Medical Center, Leiden, The Netherlands

Medical genomics

Type 1 diabetes is an autoimmune disease characterized by the destruction of insulinproducing beta-cells in the pancreas by autoreactive T cells. Yet, beta-cells are not just innocent bystanders. Instead, beta-cells are under constant biosynthetic stress which may result in errors that provoke the immune cells. For instance, ER stress in beta-cells can lead to ribosomal misreads, leading to the production of a defective ribosomal product from insulin mRNA (INS-DRiP).

INS-DRiP then can act as a neoantigen triggering an autoimmune response seen in T1D. Insulin gene (INS) variation associates with the risk for development of T1D. A single nucleotide polymorphism (SNP) located in the INS ‘3 UTR correlates strongly with risk for T1D and is expressed in INS-DRiP. The protective variant of this SNP alleviates the biosynthetic burden and ER stress through accelerated mRNA degradation (RIDD), resulting in less neoantigen DRiP, and thus lower beta cell immunogenicity. Furthermore, these beta-cells show better vitality and function.

Building on these discoveries we developed a diagnostic tool that can be used to genotype patients and donors for this INS SNP. Using this assay, it is possible to 1) predict immune response to insulin gene products, 2) define disease progression and prognosis of diabetic complications in T1D patients, 3) select T1D patients for clinical trials or donors for beta cell transplantation to reach superior clinical outcome. Examples of the application of this genotyping tool will be presented to define disease heterogeneity, disease progression and therapeutic intervention.

Medical genomics

The Role of Serum Neurofilament Light Chain (NfL) as a Biomarker for Early Disease Progression in Parkinson's Disease

N. Bolandi[1]

[1]Tabriz University of Medical Sciences, Iran

Introduction: Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by motor and non-motor symptoms. Identifying reliable biomarkers for early disease progression remains a major challenge in PD management. Neurofilament light chain (NfL), a neuronal injury marker, has emerged as a potential indicator of neurodegeneration. This study evaluates the prognostic value of serum NfL levels in predicting disease progression in early-stage PD.

Methods: A prospective cohort study was conducted in 120 patients diagnosed with early-stage PD (Hoehn & Yahr stage 1-2) and 50 healthy age-matched patients. Serum NfL levels were measured at baseline using an ultrasensitive single-molecule array (Simoa) assay. Participants were followed for 24 months, with motor and cognitive assessments performed every 6 months using the Unified Parkinson's Disease Rating Scale (UPDRS) and Montreal Cognitive Assessment (MoCA). The primary outcome was the rate of motor and cognitive decline. Multivariable linear regression was used to determine the relationship between baseline NfL levels and disease progression.

Results: Baseline serum NfL levels were significantly increased in PD patients compared to controls (17.4 ± 6.2 pg/ml vs. 10.1 ± 3.8 pg/ml, $p < 0.001$). Higher baseline NfL levels correlated with faster progression of motor symptoms (UPDRS III annual score increase: 6.8 ± 2.1 in high NfL group vs. 3.4 ± 1.7 in low NfL group, $p < 0.01$) and cognitive decline (MoCA decline: 3.2 ± 1.5 vs. 1.1 ± 1.0, $p < 0.05$). Regression analysis confirmed that serum NfL was an independent predictor of disease progression after adjustment for age, disease duration, and baseline severity ($p = 0.002$).

Conclusion: Serum NfL levels serve as a promising biomarker for predicting disease progression in early PD. Elevated levels are associated with faster motor and cognitive decline, supporting its potential role in personalized disease monitoring and therapeutic trials. Further studies are needed to validate these findings in larger, multicenter cohorts.

Keywords: Parkinson's disease, neurofilament light chain, biomarkers, disease progression, neurodegeneration, motor decline

Advancing Gene Detection: A Novel CRISPR-Based Approach for Rapid and Precise Genetic Screening

M. Hashempour[1]

[1]Ahvaz Jondishapour University of Medical Sciences, Iran

Medical genomics

Introduction: Accurate and rapid gene detection is crucial for diagnosing genetic disorders, guiding personalized medicine, and advancing molecular biology research. Traditional polymerase chain reaction (PCR) and sequencing methods, while effective, are time-consuming and resource-intensive. This study investigates a novel CRISPR-Cas12a-based gene detection platform that offers high sensitivity and specificity for identifying pathogenic mutations.

Methods: A CRISPR-Cas12a detection assay was developed to target specific gene mutations associated with hereditary diseases, including BRCA1 (breast cancer susceptibility) and CFTR (cystic fibrosis). The assay uses guide RNAs designed to recognize target sequences and activate fluorescence-based signal amplification upon successful cleavage. Performance was evaluated on 100 clinical DNA samples and compared with conventional PCR and next-generation sequencing (NGS) in terms of sensitivity, specificity, and turnaround time.

Results: The CRISPR-Cas12a assay demonstrated a detection sensitivity of 98.5% and a specificity of 99.2%, comparable to NGS and significantly higher than standard PCR ($p < 0.01$). The turnaround time for the CRISPR-based assay was approximately 45 minutes, significantly faster than PCR (2–4 hours) and NGS (24–48 hours). The method also detected low-abundance mutations with a detection limit of 10 copies per reaction, making it suitable for early diagnostics.

Conclusion: This study highlights the potential of CRISPR-Cas12a as a rapid, highly sensitive, and cost-effective gene detection tool. Its superior speed and accuracy have the potential to revolutionize genetic screening in clinical and research settings. Future developments may focus on multiplex detection capabilities and point-of-care applications for real-time diagnostics.

Keywords: Gene detection, CRISPR-Cas12a, genetic screening, precision medicine, molecular diagnostics

Medical genomics

Unraveling the Mystery: Identification of Virulence Factors in ExtendedSpectrum Beta-Lactamase E. Coli Strains and Impact on Survival in the Infant Microbiome

M. Ibrahim[1], A. Pasha1, M. Arshad[1]

[1]Aga Khan University, Karachi, Pakistan

Introduction: The increasing spread of infectious diseases is compounded by the antimicrobial resistance crisis, posing a significant public health threat, especially for infants. Drug-resistant sepsis causes up to 214,000 neonatal deaths annually in low- and middle-income countries (LMICs). The development of the neonatal gut microbiome and acquisition of antimicrobial resistance genes in infants are influenced by factors like breastfe ding, delivery type, antimicrobial exposure, and virulence factors such as fimbriae and Phosphotransferase System (PTS). To address this issue, we isolated β-lactamase positive Escherichia coli strains to study the genomes coding for their virulence factors and understand their survival mechanisms in the gut microbiome.

Methods: Stool samples were used to selectively culture strains of E. Coli using MacConkey agar with Ceftriaxone. DNA was extracted using the QIAamp DNA Stool Mini Kit and then sequenced to identify genes coding for virulence factors. This data was then analyzed from the PATRIC, VFDB, and VICTORS databases of sequenced bacterial isolates. Genomes for 16 virulent proteins were compared with that of E. Coli MG 1655, a commensal nonpathogenic control strain. A similarity of less than 80% in the genomes was considered significantly different.

Results and Discussion: The genomes of PTS system IIA and IIB components were different from MG1655 in 93.3% (14/15) samples, while PTS system IIC component and Minor Fimbrial Subunits StfE, stfF and stfG were different in 73.3% (11/15) of samples. The PTS system transports and phosphorylates sugars like glucose, while fimbriae enable mucosal adherence. Mutations may enhance bacteria's survival in the infant microbiome through improved glucose metabolism and adherence, leading to greater diversity and resilience of resistant strains.

Conclusion: Our samples showed significant genomic variations in virulent factorsvcompared to the commensal MG1655 strain of E. coli. This variability in the PTSvsystem and fimbrial proteins likely improves the survival of resistant bacteria throughvbetter glucose metabolism and adherence, leading to ever-increasing disease rates.This is one of the first studies of its kind, and we hope it serves as a foundation for larger multicenter studies worldwide. Our goal is to develop preventative strategies to address this alarming public health crisis before it's too late.

Keywords: Escherichia coli, virulence factors, drug resistance

Genomes of Virulence Factors	Sample Strains (N = 15)														
	ST8131	ST517	ST8130	ST616	ST1201	ST28	ST410	ST10-1	ST641	ST648	ST167	ST10-2	ST38	ST8136	ST10-3
Uncharacterized fimbrial-like protein YadM	57%	99%	34%	99%	100%	99%	100%	100%	99%	63%	100%	55%	56%	100%	100%
Fimbriae usher protein StfC	78%	97%	85%	97%	99%	97%	98%	100%	97%	77%	98%	79%	79%	66%	100%
Uncharacterized fimbrial-like protein YadN	78%	100%	51%	100%	100%	85%	100%	100%	100%	93%	100%	78%	78%	100%	100%
Periplasmic fimbrial chaperone StfD	84%	92%	84%	83%	96%	100%	92%	100%	92%	74%	83%	84%	84%	100%	100%
Major fimbrial subunit StfA	66%	98%	74%	98%	99%	98%	98%	100%	98%	71%	99%	65%	66%	100%	100%
Minor fimbrial subunit StfE	54%	52%	68%	72%	54%	100%	52%	100%	52%	53%	72%	50%	50%	100%	100%
Minor fimbrial subunit StfF	49%	47%	78%	82%	49%	100%	79%	99%	47%	51%	81%	34%	34%	100%	99%
Minor fimbrial subunit StfG	55%	59%	84%	78%	58%	97%	59%	100%	59%	61%	78%	55%	56%	100%	100%
PTS system, IIB component	30%	34%	36%	34%	34%	36%	34%	27%	30%	100%	27%	34%	34%	36%	27%
PTS system, IIC component	46%	45%	45%	45%	46%	46%	46%		46%	100%		45%	46%	46%	
PTS system, IIA component	39%	32%	40%	33%	32%	32%	35%	39%	33%	100%	39%	31%	32%	39%	39%
Uncharacterized fimbrial-like protein YadL	94%	98%	38%	98%	100%	100%	100%	100%	98%	70%	100%	34%	36%	100%	100%
Uncharacterized fimbrial-like protein YadK	55%	83%	41%	83%	100%	100%	100%	100%	83%	68%	100%	51%	55%	100%	100%
Uncharacterized fimbrial-like protein YadC	48%	64%	38%	64%	100%	99%	100%	100%	64%	63%	100%	47%	47%	100%	100%
Fimbria adhesin EcpD	76%	98%	67%	99%	98%	99%	100%	100%	98%	82%	100%	74%	76%	100%	100%
Uncharacterized protein YadU in stf fimbrial cluster	43%	46%	42%	41%	47%	100%	44%	100%	46%	43%	41%	41%	48%	100%	100%

MEDICAL TECHNOLOGY

Predicting the penetration of compounds to placenta based on their structure

E. Gholami[1]

[1]Islamic Azad university, Shahrud branch

Introduction: Placenta is an essential organ that acts as a barrier between the mother, and the fetus, removing waste, and delivering nutrition to the fetus. It also transfers medications from the mother's bloodstream to the fetal environment, exposing possible hazards to the fetus. The aim of this study is to Machine learning algorithms to predict the penetration of molecules to placenta, which could lead to lower dangerous side effects to the fetus.

Method: A dataset of 458 molecules with their fetal-maternal blood concentration ratio (F/M ratio), categorizing them into two groups of low penetration (F/M < 0.15), and high penetration (F/M > 0.3) was used in this study. Structural descriptors were calculated by Padel and Volsurf software. Random Forest algorithm, was used to classify molecules to low or high penetration based on structural descriptors. Descriptors with p-value>0.1 were excluded in the final model. Matthews correlation coefficient (MCC), and F1-score were used as evaluation metrics.

Results: Lipophilicity indexes such as LogD7.4, number of rotatable bonds, and acidic oxygen are among the features with the highest importance. The F1-score demonstrates remarkable performance, of 0.94 and 0.91 for validation and test sets respectively. Additionally, the MCC values for validation and test sets were 0.89, and 0.86, respectively.

Discussion: The microvillous, and placental membranes contain fat. Lipid soluble drugs diffuse alongside with fats from plasma to the placenta. Compounds with higher ability to form hydrogen bonds, and higher polar surface area are less permeable to placenta because they are almost insoluble in fats.

Keywords: Placenta, prediction, Lipophilicity

Medical Technology

Predicting Drug Interactions in Chemotherapy Regimens Using a Machine Learning Model in the Oncology Ward of a Referral Hospital

S. Hossein Hajimiri[1], F. Sanieepour[1], A. Abdollahias[1]

[1]Iran, Tehran University of Medical Sciences, Faculty of Pharmacy

Introduction: Drug interactions can result in severe adverse effects, particularly in oncology patients due to the complexity of their treatment regimens and the use of high-risk medications. Traditional identification methods are often labor-intensive and may overlook critical interactions. This study aimed to develop a machine learning model designed to predict drug interactions in the oncology ward of a referral hospital in Iran, utilizing patient demographics, medical history, and detailed medication data.

Materials and Methods: A retrospective observational study was conducted using electronic health records (EHRs) from an oncology ward in a referral hospital in Iran from 2022-24. Data were extracted from 2,568 oncology patients prescribed multiple medications during their hospital stay. Key features included patient age, gender, cancer diagnosis, treatment regimen, and the specific medications administered. A random forest classifier was employed to train and test the model using this dataset. The model's performance was evaluated based on accuracy, precision, recall, and F1-score metrics.

Results: The developed machine learning model achieved an accuracy of 85%, a precision of 82%, a recall of 76%, and an F1-score of 79%. The model demonstrated particularly strong performance in predicting drug interactions associated with commonly prescribed high-risk chemotherapy agents, highlighting its potential clinical relevance.

Discussion: The findings indicate that machine learning can play a significant role in identifying potential drug interactions within an oncology setting. The implemented model can enhance patient safety by providing healthcare providers with alerts about potential drug-related risks, thereby minimizing the likelihood of adverse events. Nonetheless, ongoing research is necessary to validate the model across varied patient populations and clinical environments.

Conclusion: This study successfully developed a machine learning model tailored to predict drug interactions using oncology patient data. The model shows promise for improving patient safety and refining medication management practices in oncology care. Future research should focus on enhancing the model's accuracy and exploring its integration into routine clinical workflows.

Keywords: Drug interaction, Machine learning, Chemotherapy

Patient Opinions of the Adoption of Brain-Computer Interfaces

M. Tahmazov[1], S. Ahmadov[1]

[1]Azerbaijan, Baku, Azerbaijan Medical University

Medical Technology

Introduction: The technology of a brain-computer interface has appeared recently in order to assist people with such an injury type as spinal cord injury (SCI), by at least enabling them to control directly various external devices. While many studies have focused on the technical development and clinical results of BCI systems, few studies have investigated the attitudes of SCI patients toward the acceptance of the technology in everyday life. This article presents an investigation into patient attitudes, perceived benefits, and concerns related to the use of BCIcontrolled assistive devices.

Materials and Methods: In this study, a survey-based research was conducted to understand the attitude of subjects with SCI toward BCI technology used for restoring motor functions and enhancing daily independence. The participants in this study were recruited from the rehabilitation centers and patient support groups, and responses were collected in the form of structured questionnaires. The usability perceived, quality of life improvements expected, probable barriers to adopt, and apprehensions related to device reliability, safety, and affordability were few factors the survey looked into.

Results: Most of the participants were interested in BCI technology, mainly for those applications that would help improve mobility and communication. However, there were also concerns raised regarding the complexity of operating the device, the cost, and possible health risks. Participants emphasized the need for user-friendly interfaces and long-term reliability. Willingness to adopt also varied according to the level of injury and previous experience with assistive technologies.

Conclusion: While patients with SCI consider the potential benefits of BCI devices, broad diffusion will only be achieved by making the devices more accessible, affordable, and easy to use. Future research should be focused on user-centered development, patient training programs, and affordability measures to improve the feasibility of BCIs in daily life.

Keywords: brain-computer interface, spinal cord injury, patients' perspective, assistive technology, usability, barriers to adoption, quality of life, accessibility, neurorehabilitation.

Medical Technology

Minimally Invasive Robotic Surgery for Nipple-Sparing Mastectomy

S. Alam[1]

[1]Ukraine/Bukovinian State Medical University

Introduction: Nipple-sparing mastectomy (NSM) is increasingly used in breast cancer treatment and prevention, preserving the nipple-areola complex (NAC) for better cosmetic outcomes. However, traditional NSM techniques often lead to complications like nipple necrosis and poor aesthetics. Minimally invasive robotic surgery has emerged as a promising solution, offering enhanced precision, fewer complications, and faster recovery. This study evaluates the feasibility and outcomes of robotic-assisted NSM. To assess the safety, efficacy, and cosmetic outcomes of minimally invasive robotic surgery for NSM, comparing it to conventional techniques.

Methods: A prospective study was conducted on 50 patients undergoing robotic-assisted NSM between 2020 and 2023 using the da Vinci Surgical System. Patient demographics, surgical outcomes, complication rates, and cosmetic satisfaction were recorded and compared to a control group of 50 patients who underwent traditional NSM. Follow-up was conducted at 1, 3, 6, and 12 months post-surgery.

Results: Robotic-assisted NSM showed superior outcomes compared to traditional methods. The robotic group had significantly lower rates of nipple necrosis (2% vs. 10%, $p<0.05$) and shorter hospital stays (1.5 days vs. 3 days, $p<0.01$). Cosmetic satisfaction scores were higher in the robotic group (90% vs. 70%, $p<0.05$). Additionally, robotic surgery reduced operative time by 20% and minimized blood loss.

Discussion/Conclusion: Minimally invasive robotic surgery for NSM is a safe and effective alternative to traditional techniques, offering better cosmetic outcomes, fewer complications, and faster recovery. The precision of robotic systems enhances NAC preservation, making it a valuable tool in breast cancer surgery. Further studies with larger cohorts and longer follow-up are recommended to validate these findings.

Keywords: Robotic surgery, nipple-sparing mastectomy, minimally invasive, breast cancer, cosmetic outcomes, da Vinci Surgical System

AI-driven skin cancer screening pipeline with 3D total body photography: A two-step ML validation study

M. Izadloo[12]

[1]Portugal, Universidade Católica Portuguesa, Católica Medical School.
[2]Iran, Azad University of Tehran, Department of Information Technology

Medical Technology

Introduction: Early skin cancer detection remains a significant clinical and public health challenge due to the lack of comprehensive screening modalities. Conventional imaging methods, including 2D photography and dermoscopy, offer limited anatomical coverage and inconsistent lesion tracking. In contrast, 3D Total Body Photography (3D TBP) provides detailed skin mapping, yet its integration into automated diagnostic workflows is underexplored. Existing studies reveal gaps in unified pipelines that combine robust lesion detection with accurate malignancy classification. This study aims to develop and validate an AI-driven, two-step diagnostic system for skin cancer screening using 3D TBP, leveraging its enhanced spatial resolution and incorporating a multi-modal classifier for improved diagnosis.

Methods: We designed a two-step machine learning (ML) workflow system utilizing openaccess public datasets: 1) a YOLO-based model to detect skin lesions in 3D whole-body images. The model was trained on the iToBoS dataset consisting of 16,954 3D TBP images captured by Vectra WB360 and annotated with bounding boxes incorporating metadata [e.g., anatomical location, patient age, sun damage score]. 2) an EfficientNetV2 classification model trained on the SLICE-3D dataset with 400,000 lesion images and diagnostic labels [histopathology-confirmed or clinical assessment] to differentiate malignant vs. benign lesions. Data augmentation and class weighting mitigated class imbalance. Hyperparameters were tuned for high recall (minimizing false negatives). Models were tested using a 90:10 train–test split. Performance metrics included sensitivity, specificity, F1-score, and AUC-ROC.

Results: The lesion classification model reached 93.15% accuracy, 93.64% specificity, 88.14% sensitivity, and a diagnostic odds ratio 109.35. Per-class metrics for class 0 (benign lesion) are 96.86% precision, 94.15% recall, and 95.48% F1-score; class 1 (malignant lesions), 82.17% precision, 89.83% recall, and 85.83% F1-score. The lesion detection model achieved a mean precision of 0.6822, recall of 0.6244, F1-score of 0.6520, and mAP@0.5 of 0.6919, with an inference time of 4.71ms.

Conclusion: The designed ML model for skin cancer screening shows promising lesion classification performance; however, the lesion detection model requires a more complex architecture to be optimal. Future improvements include developing a single custom dataset integrating inputs of 3D TBP to enhance performance for automation of population skin cancer screening.

Keywords: Total body photography; cancer screening; artificial intelligence; skin cancer

Medical Technology

Medical Students' Perceptions of Artificial Intelligence in Gastroesophageal Reflux Disease Management

A. W. Alhithlool[1], Prof O. M. Zakaria[1]

[1]Saudi Arabia- King Faisal University- College of Medicine

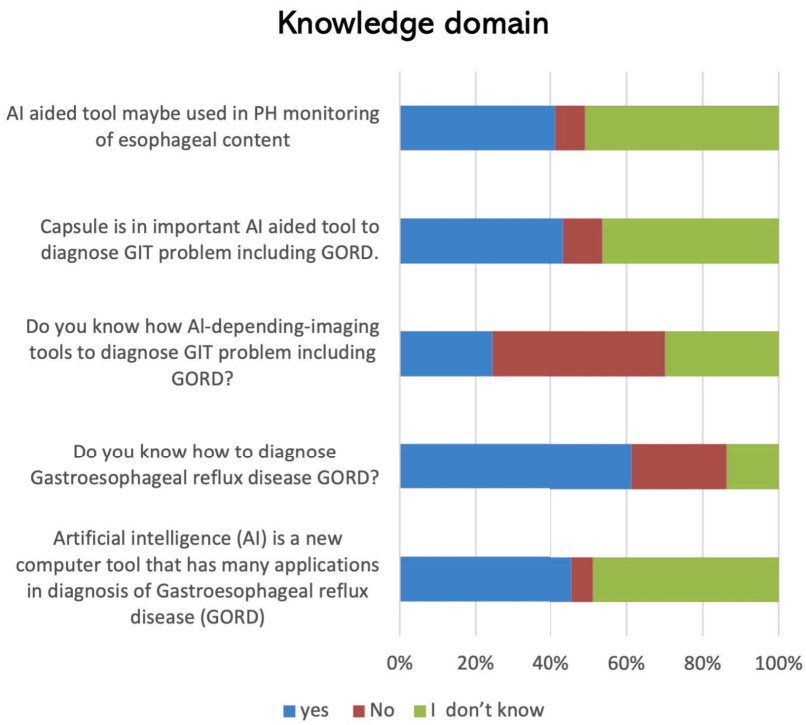
Background: Artificial intelligence (AI) has significantly revolutionized the diagnosis and treatment of various medical and surgical conditions, including gastroesophageal reflux disease (GORD). AI enhances diagnostic accuracy and treatment strategies, offering promising advancements in healthcare. This study aimed to assess medical students' knowledge and attitudes regarding AI applications in GORD management.

Method: A self-administered questionnaire was distributed among undergraduate medical students across multiple national institutions. The survey included sociodemographic data, a validated 5-item knowledge scale (categorized as poor [≤2], moderate [3], and good [≥4]), and a validated 7-item attitude scale (classified as negative [<50%], neutral [50–75%], and positive [>75%]).

Results: A total of 506 medical students participated (233 males [46%] and 273 females [54%]). The majority (85%) were aged 20–26 years, and 76.7% had a GPA >4. The median knowledge score was 2 (range: 0–5), and the median attitude score was 25 (range: 1034). Regarding knowledge, 26.9% demonstrated good understanding, 39.3% had moderate knowledge, and 33.8% had poor knowledge. Senior students had significantly higher knowledge scores than junior students ($p = 0.015$). Most students (65.8%) had a neutral attitude toward AI in GORD management, while 27% were positive and 6.9% were negative. A moderate positive correlation was observed between knowledge and attitude scores ($r_s = 0.33$, $p < 0.001$).

Conclusion: Despite AI's increasing role in GORD management, our findings suggest that medical students have limited awareness and mixed attitudes toward its applications. These results underscore the need for integrating AI education into medical curricula to enhance awareness and engagement with this advancing technology.

Keywords: Artificial intelligence (AI); gastroesophageal reflux disease (GORD); medical students view


Knowledge domain
AI aided tool maybe used in PH monitoring of esophageal content
Capsule is in important AI aided tool to diagnose GIT problem including GORD.
Do you know how AI-depending-imaging tools to diagnose GIT problem including GORD?
Do you know how to diagnose Gastroesophageal reflux disease GORD?
Artificial intelligence (AI) is a new computer tool that has many applications in diagnosis of Gastroesophageal reflux disease (GORD)
0%
20%
40%
60%
80%
100%
yes
No
I don't know

Medical Technology

Operating Room Planning and Utilization Strategies of University Medical Centers: An Observational Study

A. M. Schouten[2], L. Horenberg[1]

[1]Delft University of Technology, [2]Leiden University Medical Center, the Netherlands

Background: Hospitals face increasing pressures due to workforce shortages and rising patient demand, making efficient Operating Room (OR) planning essential. While scheduling research often focuses on short-term operational decisions, long-term planning and resource management receive less attention. Challenges such as late blueprint issuance, staff availability, and a lack of transparency hinder effective OR scheduling. This study examines bottlenecks, current practices, and opportunities for improvement in OR planning.

Methods: Structured interviews were conducted with 54 stakeholders across all eight academic hospitals in the Netherlands to map planning processes, collaborations, and communication methods. Participants also shared their preferred improvements, which were documented as "wish lists".

Results: OR planning varies between hospitals, particularly in decision-making levels and responsibility distribution. Long-term planning remains a bottleneck, with staff shortages and sometimes unrealistic scheduling contributing to inefficiencies. While data-driven tools and capacity centers are emerging, their adoption is slow, as stakeholders prioritize transparency over automation. The absence of clear OR planning policies further complicates decision-making.

Conclusions: Hospitals can strengthen OR planning by addressing key bottlenecks in long-term scheduling, staff shortages, and inconsistent planning frameworks. To improve efficiency, hospitals should focus on three key areas: (1) Leveraging hospital data to enhance transparency and provide stakeholders with a clearer understanding of planning processes; (2) Introducing automation gradually, ensuring it is integrated into well-established systems like Electronic Health Records rather than applied prematurely; and (3) Developing standardized OR planning policies to improve consistency, accountability, and equitable decision-making.

Keywords: Operating Room Planning; Hospital Resource Management; Surgical Scheduling; Healthcare Workforce Optimization; Data-Driven Decision Making.

Characterizing flushing-resistant adherent cells on dialyzer fibers via scanning electron microscopy: a feasability study

G. Ergen[12], F. Janssens[12], P. Laha[3], T. Hauffman[3], K. François[12]

[1]Universitair Ziekenhuis Brussel (UZ Brussel), Brussels, Belgium. [2]Vitality Research Group, Brussels, Belgium. [3]Department of Materials and Chemistry, Vrije Universiteit Brussel (VUB), Brussels, Belgium

Medical Technology

Background: Hemodialysis (HD) is the most commonly used kidney replacement therapy worldwide. During hemodialysis, blood contact with the extracorporeal circuit (ECC) triggers immune cell adhesion to foreign biomaterials and subsequent activation. The spread of pro-thrombo-inflammatory signals from these activated cells to the patient's circulation contributes to systemic thrombo-inflammation, a major driver of cardiovascular (CV) disease, the leading cause of mortality in HD patients. However, the thrombo-inflammatory processes within the ECC, which drive systemic responses, remain poorly understood. Our research group previously developed a protocol to detach ECC-sequestered cells for further analysis. However, to ensure reliable downstream analyses, confirmation of complete cell retrieval is crucial to validate the rinsing procedure's efficacy.

Objective: This study investigates the feasibility of using scanning electron microscopy (SEM) to visualize flushing-resistant adherent cells on dialyzer membrane fibers.

Methods: In this feasibility study, 3 clinically stable patients on maintenance HD using an AVfistula were included. HD sessions were conducted as per routine care. After a 4-hour HD session and blood retransfusion, the ECC was rinsed for 20 minutes with 250mL PBS-3mM EDTA to retrieve sequestered cells, followed by a 20 minute enzymatic rinse with 250mL Accutase® to detach rinsing-resistant cells. SEM of the used dialyzers was used to validate the efficacy of the rinsing procedures. For each patient, SEM analysis of a used non-rinsed and EDTA-only rinsed dialyzer of a consecutive HD session was performed as positive controls.

Results: SEM images confirmed successful and complete detachment of ECC-sequestered cells after EDTA and enzymatic rinsing, validating the efficacy of the rinsing procedures. SEM analysis of a used non-rinsed dialyzer fiber demonstrated feasibility of visualizing ECCsequestered cells. Remaining cell clusters persisted after EDTA rinsing of the ECC, but not after enzymatic rinsing (Fig. 1).

Conclusion: Our developed SEM protocol can be used to validate the efficacy of the rinsing procedures. Our findings demonstrate that rinsing of the ECC using an EDTA rinsing fluid only is insufficient to retrieve ECC-sequestered cells. An additional enzymatic rinse enables full retrieval of ECC-sequestered cells, ensuring reliable downstream analyses.

Keywords: Hemodialysis, extracorporeal circuit, thrombo-inflammation, cell adhesion, scanning electron microscopy

Medical Technology

Development of a Neonatal Cannulation Training Simulator for Artificial Placenta Connection

I. Stapel[1], D. van Galen[1], F. Claybrook[1]

[1]The Netherlands, University of Twente, Engineering Organs Support Technologies (EOST)

Introduction: The ArtPlac project aims to develop a combined lung and kidney support system for critically ill preterm neonates. This device will be connected through umbilical cannulation. A neonatal cannulation simulator is designed to aid in the cannula development and training for this procedure. Previous research determined that more flexible materials are needed for mimicking the umbilical arteries, the umbilical vein, and Wharton's Jelly in the simulator. The aim of this project is to define materials and design properties to develop vasculature models and simulated umbilical cords for use in a realistic neonatal cannulation simulator.

Methods: Shore hardness and puncture force tests were conducted on fresh human and piglet umbilical cords. The umbilical vein, umbilical arteries, and Whartons Jelly were tested using a durometer and a force meter with 3 repetitions per measurement over 7 umbilical cords. Mechanical properties of 3D-printed blood vessels were compared with real umbilical vessels and evaluated for further umbilical cord development.

Results: The 3D-printed vessels showed a relative shore hardness of 81 A compared to 82 A in real umbilical vessels. The puncture force in the printed arteries showed 1.9 N compared to 2.1 N in real umbilical arteries, where the printed veins showed 1.6 N compared to 4.6 N in real umbilical veins.

Conclusion: 3D-printed vascular models successfully mimicked the relative shore hardness required for umbilical vessels and the puncture force required for the umbilical arteries. Nevertheless, a higher puncture resistance is required for the printed vein.

Keywords: Artificial placenta; umbilical cannulation; 3D printing; medical training simulator; preterm neonates; umbilical vessels

Chatbot-Based Artificial Intelligence for Ophthalmology Oral Examinations: A Novel Approach and Performance Analysis

A. E. Kara[1], S. Çakmak[1], I. E. Uluışık[1]

[1]Istanbul University, Istanbul Faculty of Medicine, Department of Ophthalmology

Aim: To evaluate the accuracy, reliability, and readability of responses provided by Artificial Intelligence (AI) applications to questions asked in oral exams for medical students.

Method: A total of 26 English oral exam questions that were asked to 5th-grade students were submitted to three AI applications: ChatGPT-4o, Gemini 2.0 Flash, and Microsoft Copilot (GPT-4-turbo-based) (Bing). The responses were assessed by a team of three ophthalmology specialists and scored on a scale of 0 to 100. Readability was evaluated using the Simple Measure of Gobbledygook (SMOG), Flesch-Kincaid Grade Level (FKGL), and Flesch Reading Ease (FRE) scores. Readability and performance scores were compared across the AI models.

Results: The average scores for the three systems were as follows: performance 95.51±6.86, FKGL 11.22±2.01, FRE 32.58±13.49, SMOG 12.38±1.32. ChatGPT: Performance 98.08±3.76, FKGL 12.03±1.54, FRE 24.60±11.77, SMOG 12.32±1.03. Gemini: Performance 92.31±9.19, FKGL 10.53±1.64, FRE 36.79±11.91, SMOG 11.90±1.34. Bing: Performance 96.15±5.53, FKGL 11.08±2.68, FRE 36.35±14.80, SMOG 12.93±1.58. Normality testing was performed using the Shapiro-Wilk test. FKGL ($p=0.003$) and performance scores ($p=0.000$) did not follow a normal distribution, whereas FRE ($p=0.143$) and SMOG ($p=0.054$) did. Levene's test confirmed the equality of variance for FRE ($p=0.817$) and SMOG ($p=0.162$). The ANOVA test for FRE scores identified a significant difference between the groups ($p=0.001$). Pairwise comparisons using Student's t-test revealed a significant difference between ChatGPT and Bing ($p=0.001$), as well as between ChatGPT and Gemini ($p=0.003$). However, no significant difference was found between Bing and Gemini ($p=0.905$). The ANOVA test for SMOG scores also showed a significant difference between the groups ($p=0.024$). Pairwise comparisons using Student's t-test indicated no significant difference between ChatGPT and Bing ($p=0.212$) or between ChatGPT and Gemini ($p=0.105$). However, a significant difference was observed between Bing and Gemini ($p=0.015$). The Kruskal-Wallis test showed significant differences for FKGL ($p=0.008$) and performance scores ($p=0.023$).

Conclusion: All three AI models demonstrated high accuracy levels, but there were notable differences in readability. ChatGPT achieved the highest accuracy score but used more complex language. In contrast, Gemini, despite having a lower accuracy score, provided more readable responses with higher readability scores.

Keywords: Ophthalmology, Artificial Intelligence Performance Evaluation, Medical Oral Exams

Medical Technology

Reducing Administrative Burden in Cardio-Oncology: An LLMPowered Approach for Automated Summarization of Oncology and Cardiotoxicity Histories in Dutch Medical Records

M. Fatah[1], J.C. Heemelaar[1], C.J.J. Westermann[1], M. Hamer[1], G. Liao[1], M.M. van Buchem[1], J.W. Jukema[1], M.L. Antoni[1]

[1]Leiden University

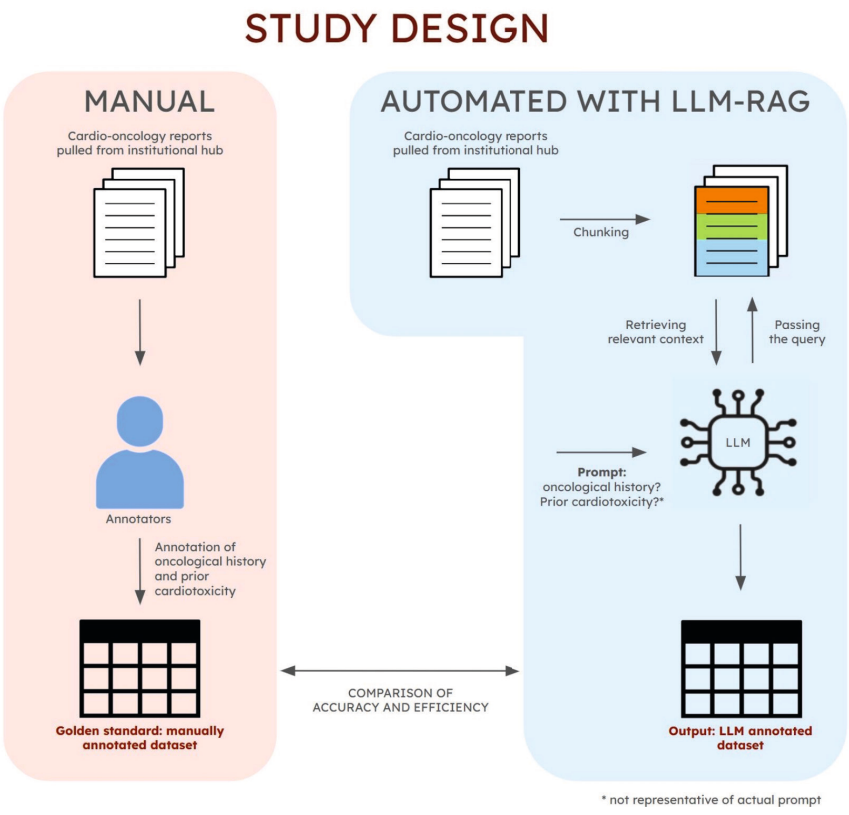
Background: Clinical documentation is a significant administrative burden in cardio-oncology, where comprehensive medical histories are essential for patient care. Large language models (LLMs) using retrieval-augmented generation (RAG) may help automate this task. However, their performance in Dutch medical texts—and most non-English texts—remains unexplored. This study evaluates the feasibility, accuracy, and efficiency of a locally deployed, opensource RAG-LLM infrastructure for automatically summarizing oncology and cardiotoxicity histories in Dutch medical records.

Methods: Patients at the LUMC cardio-oncology outpatient clinic were enrolled in this proof-ofconcept study. In- and outpatient letters were retrieved from the institutional data hub. Two investigators manually annotated prior cancer diagnoses, treatments, and cardiotoxicity history, establishing a gold standard dataset. A RAG pipeline was developed and deployed on the institutional high-performance computing cluster using exclusively open-source components, and incorporated LLaMA3.1 8B, one of the highest-performing smaller-scale LLMs. The system automatically extracted the same key variables from patient records. Three investigators independently compared the generated summaries to the gold standard for accuracy.

Results: A total of 54 patient records were analyzed, containing 412 documents. The most common cancer diagnoses included lymphoma (42.6%) and leukemia (24.1%). Nearly all patients underwent chemotherapy, with 50.0% receiving radiotherapy and 29.6% undergoing stem cell transplantation. The system correctly identified 52/54 prior cancer diagnoses, 53/54 chemotherapy statuses, 49/54 radiotherapy statuses, and 52/54 stem cell transplantations. Systemic antineoplastic agents were fully or mostly identified in 48/54 cases (88.9%). For cardiotoxicity detection, the model correctly identified 9/12 positive cases and 38/41 negative cases, yielding a 75.0% sensitivity and 92.7% specificity. The LLM demonstrated excellent comprehension of Dutch medical jargon, with all errors stemming from retrieval limitations rather than incorrect model reasoning. The model generated summaries in an average of 11 seconds per patient, compared to 3.5 minutes for manual extraction.

Conclusion: A locally deployed RAG-LLM infrastructure can accurately and efficiently summarize medical histories in a Dutch cardio-oncology setting. While accuracy was high for cancer diagnosis and treatment extraction, retrieval inefficiencies limited sensitivity for cardiotoxicity detection and complete treatment identification.

Keywords: Large Language Models (LLMs); Clinical Documentation; Cardio-Oncology; Medical Text Summarization


STUDY DESIGN
MANUAL
Cardio-oncology reports pulled from institutional hub
Annotators
Annotation of oncological history and prior cardiotoxicity
Golden standard: manually annotated dataset
AUTOMATED WITH LLM-RAG
Cardio-oncology reports pulled from institutional hub
Chunking
Retrieving relevant context
Passing the query
LLM
Prompt: oncological history? Prior cardiotoxicity?*
Output: LLM annotated dataset
COMPARISON OF ACCURACY AND EFFICIENCY
* not representative of actual prompt

Medical Technology

Reducing Human Intervention in Rodent Cognition Studies: Automating the Social RatPad

A. Andreasyan[1], R. Bulthuis[1], J. Homberg[1], J. Bos[1]

[1]RadboudUMC

Understanding cognition is crucial for advancing effective treatments for human diseases. Rodent studies are key to uncovering the complex mechanisms underlying cognitive function, yet traditional testing methods often introduce stress and variability that confound results. Hence, high-quality, automated systems that accurately measure cognition while minimizing human interference are urgently needed. This need underpins our study's approach.

The Social Ratpad is a cognitive assessment device consisting of two standalone testing chambers (RatPads) connected via tubes to a shared cage where animals can socialize and access food and water. Previously, the system allowed testing of animals at specific time points. A divider was inserted into the central cage, which enabled one rat to enter a designated testing chamber. This method required daily manual intervention by researchers, often involving animal handling during the divider placement, which could potentially cause stress.

To reduce human intervention, we automated the socialization component of the Social Ratpad by integrating sensor-driven tubes, a modified One-Rat Turnstile (ORT) gate with size-adjusting wings, weight measurement stations, and self-made gates that selectively allow or block access to the testing chambers. Moreover, by modifying the testing protocols so that the touchscreen-based tasks on the RatPads run continuously, the system now empowers the animals to control when they engage in testing.

This study details the design, implementation of components and compares the data obtained from the automated system with human-based observations to assess its accuracy. Preliminary data demonstrate the effectiveness of the automated approach in identification and sorting procedures. The results indicate that, given the appropriate motivation, the animals rapidly adapt to the environment, exercise control over their testing schedule, and participate consistently. The new solution also allows researchers to observe socializing tendencies among different strains by providing the opportunity to precisely measure the time spent in one part of the complex chamber.

The automation procedures may help reduce human interventions, thereby increasing animal welfare and reducing the impact of researchers on testing procedures. The device can serve as an initial point for larger implementations if there is enough space. The solutions may act as plug-and-play components for large-scale applications.

NEUROSCIENCE

Neural Activity and Odor Discrimination: Exploring Familiarity, Novelty, and Regional Encoding

İ. Davutoğlu[1], M.Hassanloo[1], A. Zareh[1], M. Kemal Özdemir[1]

[1]Istanbul Medipol University, Beykoz, Istanbul, Türkiye

Neuroscience

Introduction: Odor perception relies on complex neural mechanisms encoding sensory information across brain regions. While biochemical binding of odorants to receptors is well-studied, the roles of regional neural activity, familiarity-novelty distinctions, and molecular vibrations influencing receptor interactions remain less understood. Understanding these factors can advance sensory science and its applications in diagnostics, robotics, and environmental monitoring. To investigate how neural activity encodes familiarity and novelty in odor discrimination, focusing on the olfactory bulb (OB), anterior olfactory nucleus (AON), and piriform cortex (PCx), while integrating molecular data with AI-based classification models.

Methods: Neural activity was recorded from mitral and tufted cells in the AON, and PCx of C57BL/6 mice using multi-channel electrodes. Mice were exposed to 21 odorants, some familiar and others novel. Neural responses were captured in 0.5-second segments to examine baseline activity and encoding patterns. Data were segmented by region and odor familiarity. Advanced deep learning models were applied for classification, while vibrational spectra from infrared/Raman spectroscopy provided molecular insights.

Results: Preliminary results showed significant regional differences in firing rates, with the AON displaying higher variability and stronger responses to novel odors compared to the PCx. Initial analysis achieved 55% classification accuracy using individual 0.5-second neural data segments but aggregating responses across 10 repeated trials increased accuracy to 77% for classifying familiar versus novel odors.

Conclusion: These findings emphasize the significance of regional and temporal dynamics in odor discrimination, particularly for distinguishing between familiar and novel odors. By combining neural and molecular datasets with AI models, this research offers a novel approach to decoding olfactory processing. Future work will validate findings and broaden applications in sensory technologies, demonstrating the potential for impactful contributions to olfactory science.

Keywords: Odor discrimination, Familiarity, Novelty, Regional encoding, Molecular vibrations, AI-based analysis

Neuroscience

Predictive model of in-hospital seizures after traumatic brain injury: a CENTER-TBI study

E. Viaroli1, S.A. Corper1,2,3, A. Kolias1, P.J.A.Hutchinson1, T.A. Van Essen2

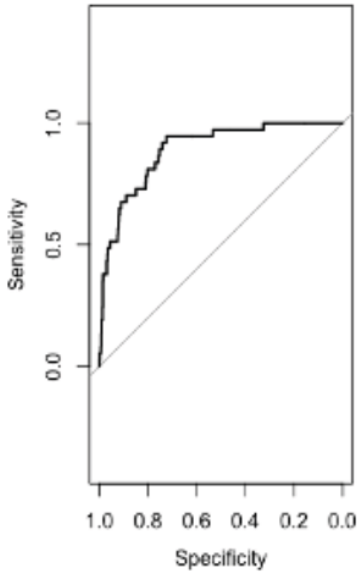
1.Division of Neurosurgery, University Of Cambridge. 2University Neurosurgical Center Holland, Leiden University Medical Center, Haaglanden Medical Center, HAGA, Leiden and The Hague, Netherlands. 3University of Leiden, Leiden and The Hague, Netherlands

Introduction: Posttraumatic seizures (PTS) are a clinically relevant complication of traumatic brain injury (TBI) with an uncertain incidence and risk factors. Our aim is to determine the prevalence and risk factors of ultraearly and early PTS, as well as their association with outcomes in TBI patients, through an analysis of the CENTER-TBI database.

Methods: The CENTER-TBI study was conducted in 65 European trauma centres between 2014 and 2017. We identified patients with PTS after TBI. The prevalence of PTS was stratified into ultra-early (prehospital and ED) and early (in-hospital) phases. The association of baseline variables with early PTS was modelled using multivariable logistic regression to determine risk factors for PTS. The associations of early PTS with patient demographics, past medical history, pre-injury status, pre-injury habits, general and neurological injury assessments, imaging findings, admission laboratory results, ultra-early PTS, surgical and clinical/ICU management, length of stay, functional outcome (Glasgow Outcome Scale Extended [GOSE]), and quality of life (Quality of Life After Brain Injury [QOLIBRI]) were analysed using an appropriate multivariable regression model. Also, adaptive LASSO regression was used to develop a predictive model for PTS risk factors.

Results: The prevalence of post-traumatic seizures (PTS) was 8.7% among ICU patients and 7.2% in the overall population. Early seizures were associated with a history of psychiatric (OR 2.34) and neurological disorders (OR 1.79). Ward admission was protective (OR 0.43) compared to ICU admission.
Lower GCS motor scores (OR 2.62–2.53 for GCS 5–6) and large subdural hematomas (OR 2.57) were also linked to a higher seizure rate. Ultra-Early seizures (OR 4.52–18.60) and neurological deterioration (OR 2.87) were significant predictors of Early seizures. Early seizures significantly increased the odds of poor outcomes (OR 2.54–3.30 for admitted vs. total patients). Adaptive LASSO models demonstrated strong predictive performance for seizures (AUC 0.81–0.87).

Conclusions: To date, this is the first international cohort studying PTS. They appear to be associated with preexisting medical history, pre-hospital insults, lower GCS motor scores, and the presence and size of acute subdural hematomas. The study shows promising results in identifying patients who may benefit from antiepileptic prophylaxis upon admission.


Sensitivity
0.0
0.5
1.0
1.0 0.8 0.6 0.4 0.2 0.0
Specificity

Neuroscience

Assessment of the antineoplastic and antioxidant effects of Lithium and Selenium treatment on LN-229 glioblastoma cells

A. Szklarska[1], D. Luchowska-Kocot, PhD[2]

[1]Student Research Group ISOMERS at the Department of Medical Chemistry, Medical University of Lublin, Lublin, Poland. [2]Department of Medical Chemistry, Medical University of Lublin, Lublin, Poland

Introduction: Lithium is used in treatment of psychiatric diseases, as well as in treatment of neoplasms, however there are limited reports about its effects on the central nervous system (CNS) tumors. Side effects of its usage associated with oxidative stress have been observed and an antioxidant, Selenium, has been proposed to decrease them. This study aims to investigate the impact of Lithium and Selenium treatment on glioblastoma cells, examining the antineoplastic potential of the therapies used in psychiatry against the neoplasms of the CNS and assessing the oxidative stress level of the cells undergoing this treatment.

Methods: Glioblastoma LN-229 cells have been cultured with Dulbecco's modified Eagle's medium containing 10% fetal bovine serum and antibiotics in an incubator with 5% CO2 at 37°C. A control group, hippocampal HT-22 cells, have been cultured in the same conditions. The treatment applied included Lithium and Selenium in variable concentrations and a co-treatment with both of these substances simultaneously. The cellular activity was measured using the MTT assay. After assessing the half-maximal inhibitory (IC50) concentrations of each substance, total antioxidant status was measured using the ferric reducing ability of plasma (FRAP) assay.

Results: The IC50 values were significantly higher for the glioblastoma cells than for the hippocampal cells. In the selenium-treated cells, a shift towards an increased viability of the physiological cells was observed. It was established that lithium has negative effects on the oxidative system, which was considered statistically significant especially in the glioblastoma cells. The addition of Selenium to Lithium treatment not only stopped the decreasing trend of FRAP, but also resulted in its significant improvement in the hippocampal cells whereas in the glioblastoma cells a further decrease of its values was observed.

Conclusions: The inhibitory effects of Lithium treatment on the LN-229 cells were observed, however the higher IC50 values for these cells than for the hippocampal cells indicate a necessity of adding a neuroprotective agent to this treatment. The positive effects of Selenium administration on the antioxidant system indicate that it could become such a substance, however these assumptions require confirmation in further research.

Keywords: psychiatry, oncology, lithium, selenium

Organization of the dorsal root of the spinal nerve – Current state of knowledge and own observations

M. Misiak[1], B. Ciszek[1]

[1]Poland, ZAPiK WUM, WMCM UKSW, Warsaw

Neuroscience

Introduction: Spinal nerves (nn. spinales) connect to the spinal cord bilaterally via ventral and dorsal roots (radices ventrales et dorsales). Current knowledge assumes that each root consists of 5-10 bundles of nerve fibers (radicular fila, fila radicularia). The aim of the study is to determine the anatomical parameters and organization of spinal root bundles in the context of clinical significance.

Methods: Microanatomical dissection of the posterior roots of the lumbar nerves L1-L5 was performed using six cadavers fixed in 10% formalin (ZAPiK WUM). Roots of total 60 spinal nerves from L1 to L5 were examined. Dissection was performed using a Zeiss surgical microscope. Observations were documented using sketches and photographs.

Results: The number of bundles in the root and the occurrence of interradicular fibers were examined. The posterior root of the spinal nerve can be divided into 3 sections: paraspinal section, middle section, and paraganglionic one. In the paraspinal section, 3 to 16 bundles were found. In the middle section, these bundles segregated into 2-4 clusters, which ultimately produced one or two bundles in the paraganglionic section that entered the ganglion. Sometimes a single bundle would split into a dozen or so fibers just before the ganglion. Separate paraganglionic bundles were present conecctd to the biganglia (two seemingly independent ganglial components). The greatest number of interradicular fibers to the segment above were observed at the L4 level on the left. The least anastomoses to the upper segment were found at the L4 level, right. Anastomoses to the segment below were most often found at the L3 level on the left. The fewest interradicular fibers were found between the L1-2 right side and L3-4 right side roots.

Conclusion: The posterior roots of the lumbar spinal nerves show a diverse morphology depending on the root segment, in contrast to previous reports. This information is useful in planning and performing rhizotomy procedures. The presence of interradicular fibers may affect the overlap of segmental innervation ranges.

Keywords: Spinal cord, Roots of the spinal nerve, Dorsal Root Ganglia, DRG, Ganglia spinalia, GS

Neuroscience

Investigating the Link Between Type 2 Diabetes and Parkinson's Disease: A Clinical and Molecular Analysis

F. Ranjdoust[1]

[1]Tabriz uinversity of medical sciences, Iran

Introduction: Emerging evidence suggests a strong relationship between Type 2 Diabetes Mellitus (T2DM) and Parkinson's Disease (PD), with insulin resistance and neuroinflammation playing crucial roles in neurodegeneration. T2DM patients have a higher risk of developing PD, but the exact mechanisms remain unclear. This study investigates the associations between T2DM and PD, focusing on metabolic dysfunction, inflammation, and dopaminergic neuron degeneration.

Methods: A case-control study was conducted on 300 participants:
- 150 PD patients (75 with T2DM, 75 without T2DM)
- 150 age-matched controls (75 with T2DM, 75 without T2DM)
Clinical assessments included Unified Parkinson's Disease Rating Scale (UPDRS), HbA1c levels, insulin resistance index (HOMA-IR), and inflammatory markers (IL-6, TNF-α, CRP). Neuroimaging with dopamine transporter (DaT) SPECT scans assessed dopaminergic neuron loss, while plasma α-synuclein levels were measured as a biomarker of neurodegeneration.

Results: The study revealed a significant association between Type 2 Diabetes Mellitus (T2DM) and Parkinson's Disease (PD), with diabetic patients experiencing more severe motor and cognitive decline. PD patients with T2DM had significantly higher UPDRS scores (38.6 ± 7.2) compared to their non-diabetic counterparts (30.1 ± 6.9, $p < 0.001$), indicating faster disease progression. Metabolic dysfunction played a critical role, as higher insulin resistance (HOMA-IR) showed a strong correlation with dopaminergic neuron loss observed in DaT SPECT scans ($R^2 = 0.62$, $p < 0.01$). Additionally, systemic inflammation was more pronounced in PD patients with T2DM, evidenced by elevated levels of inflammatory markers, including IL-6, TNF-α, and CRP ($p < 0.001$). These findings suggest that chronic inflammation could be a key link between metabolic dysfunction and neurodegeneration.Further, plasma α-synuclein levels were significantly higher in PD patients with T2DM (4.3 ± 1.1 ng/mL) compared to those without diabetes (2.9 ± 0.9 ng/mL, $p = 0.002$). This indicates that T2DM may accelerate the pathological aggregation of α-synuclein, a hallmark of PD.

Conclusions: T2DM contributes to the progression of Parkinson's Disease through insulin resistance, neuroinflammation, and increased α-synuclein accumulation. These findings highlight the need for early metabolic screening and potential neuroprotective strategies targeting insulin signaling in high-risk individuals. Further research should explore whether anti-diabetic drugs, such as GLP-1 receptor agonists, could offer neuroprotection in PD.

Keywords: Type 2 diabetes, Parkinson's disease, Insulin resistance

Bickerstaff Encephalitis in a Pediatric Patient: Diagnostic Challenges and Immunotherapy Success

M.G. Saray[1], M.H. Ali[1], M. Ghods[1]

[1]Azerbaijan Medical University, Baku, Azerbaijan

Introduction: Bickerstaff encephalitis (BE) is a rare autoimmune disorder characterized by acute brainstem dysfunction, often presenting with ophthalmoplegia, ataxia, and altered consciousness. It shares clinical features with Miller Fisher Syndrome (MFS) and Guillain-Barré Syndrome (GBS), making accurate diagnosis challenging. Early recognition and treatment are crucial to prevent long-term neurological deficits. This case report aims to highlight the diagnostic and therapeutic approach to BE in a pediatric patient, emphasizing the importance of timely intervention. The aim of this study is to report a rare case of Bickerstaff encephalitis in a 7-year-old boy, discuss the diagnostic challenges, and underscore the effectiveness of immunotherapy in achieving complete recovery.

Methods: A 7-year-old boy presented with a 5-day history of cough and fever, followed by lethargy, pallor, and neurological symptoms including lower limb paralysis, slurred speech, and ophthalmoplegia. Diagnostic evaluations included brain MRI, cerebrospinal fluid (CSF) analysis, and electromyography (EMG). The patient was treated with intravenous methylprednisolone pulse therapy and intravenous immunoglobulin (IVIG). Follow-up assessments, including a repeat MRI, were conducted at 6 months post-treatment.

Results: Initial brain MRI revealed an abnormal signal in the posterior pons (left side) without diffusion restriction or enhancement. CSF analysis showed mild pleocytosis with elevated protein levels. EMG findings were consistent with peripheral nerve involvement. The patient responded remarkably to immunotherapy, with complete resolution of symptoms. Follow-up MRI at 6 months showed no abnormalities, confirming full recovery.

Conclusion: This case underscores the diagnostic challenges of Bickerstaff encephalitis due to its overlapping features with other neurological disorders. The absence of anti-GQ1b antibody testing was a limitation; however, the clinical presentation and response to immunotherapy strongly supported the diagnosis. Early administration of methylprednisolone and IVIG proved effective, leading to complete neurological recovery. This report highlights the importance of considering BE in pediatric patients with acute brainstem dysfunction and advocates for timely immunotherapy to optimize outcomes.

Keywords: Bickerstaff Encephalitis, Pediatric, Brainstem, Immunotherapy, Anti-GQ1b Antibody

Neuroscience

Optimizing AAV9 and AAV9-PHP.eB viral vector delivery to the retinal pigment epithelium of prenatal mice using intra-amniotic injection

L. Nieuwenhuizen[1]

[1]University of Amsterdam, The Netherlands

Introduction: Oculocutaneous albinism type 1 (OCA1) is an autosomal recessive disorder, characterized by foveal hypoplasia, nystagmus and abnormal projections of the ganglion cells in the temporal retina. The abnormal visual pathway development has been linked to a loss of melanin production in the retinal pigment epithelium (RPE), due to a mutation in the tyrosinase gene. The RPE starts developing around embryonic day 8 and early intervention might reverse or minimize the symptoms and developmental consequences of OCA1. Adeno-associated viral vectors (AAV) could be used for vector-based delivery to the central nervous system (CNS) of mouse pups and the serotypes AAV9 and AAV9-PBP.eB have shown to possess the ability to cross the blood brain barrier and increased CNS-specificity. However, they have yet to be compared to each other when using intra-amniotic injections. In this study, we aim to first test if intra-amniotic sac injections around E8-E10, could enable viral expression in mouse pup RPE and then which viral vector, AAV9 or AAV9-PHP.eB, would be better expressed.

Methods: This was done by injecting individual amniotic sacs of pregnant C57BL/6J mice (N=2) with either the AAV9 or AAV9- PHP.eB viral vector. The viral expression in the RPE and brain of the mouse pups (N=12) was checked through confocal imaging.

Results: Our results showed that the observed viral expression in pup RPE was attributable to autofluorescence for both viral vectors, AAV9 and AAV9-PHP.eB. The brain images revealed that there no viral expression was for both the AAV9 or AAV9-PHP.eB viral vectors.

Conclusion: These findings indicate that the intra-amniotic injections done in this study need protocol optimization for AAV9 and AAV9-PHP.eB vector-based delivery.

Keywords: Oculocutaneous albinism type 1, retinal pigment epithelium, adeno-associated viral vector, intra-amniotic injection, mouse-model

Diagnostic Dilemma: Lyme Neuroborreliosis or Multiple Sclerosis? A Complex Case Report.

V.A.S. Vizitiu[1], V. Vitalie[1]

[1]Iuliu Hatieganu University of Medicine and Pharmacy Cluj-Napoca, Romania

Introduction: Lyme neuroborreliosis (LNB) is an inflammatory condition caused by Borrelia burgdorferi, a spirochete that invades the central nervous system. Multiple Sclerosis (MS) is an autoimmune disease that destroys the myelin sheath. These two neurological conditions can have similar clinical signs in some cases, but nonspecific symptoms in others. As a result, the purpose of this study is to present a rare case with suspicions of both LNB and MS, as well as a clear illustration of the difficulty in determining the final diagnosis and selecting the appropriate treatment.

Case Presentation: We discuss the case of a 51-year-old male forester who presented with paraesthesia in the inferior limbs, dysaesthesia in the abdominal region, and bilateral Babinski sign. The symptoms first occurred 5 years ago as paraesthesia in the inferior limbs, then gradually progressed to the subpopliteal region. The patient had neurotrophic therapy, which resulted in a partial remission of symptoms.

Last year, the patient noticed a tick bite in the left thoracic region, which caused erythema and a worsening of symptoms. The Western Blot analysis revealed positive IgM and IgG anti Borrelia burgdorferi antibodies, and a three-week doxycycline treatment yielded no improvement.

The patient exhibits characteristics of both MS (progressive paraesthesia and MRI demyelinating lesions) and LNB (contact with the vector-the tick bite, anti-Borrelia burgdorferi IgG and IgM, and lymphocytic pleocytosis), as well as abnormal manifestations such as the absence of oligoclonal bands in CSF and no improvement, despite doxycycline treatment.

Conclusions: It is clear that this clinical case raises significant differential diagnosis issues, delaying the initiation of appropriate treatment and resulting in serious complications. This is primarily due to the inaccuracy of the intrathecal/serum antibody levels. There are several approaches for establishing the differential diagnosis, however a CSF marker, CXCL13, which has been demonstrated to be elevated in individuals with LNB, may be beneficial in early diagnosis of LNB.

Keywords: Multiple sclerosis, Lyme Neuroborreliosis, CXCL13, Differential diagnosis

Neuroscience

Significance of macroscopic and microscopic features of meningiomas in surgical treatment and prognosis

M. Wrzesień[1], M.P. Jeżewski[1], B. Jedlak[1], A. Oziębło[1], T. Mandat[1]

[1]Department of Neurosurgery, Maria Sklodowska-Curie National Research Institute of OncologyWarsaw, Poland

Introduction: Meningiomas are the most common primary intracranial tumors arising from the arachnoid mater. Their clinical manifestation may vary from incidental non-symptomatic findings to recurrent and malignant infiltrative tumors. The 5th 2021 World Health Organisation (WHO) classification categorises meningiomas into three grades of their increasing malignant potential and includes histopathological and molecular features. Thus, differences in clinical course require consideration of various parameters beyond sole grading. The aim of this study was to examine the difference in the clinical course of meningiomas depending on their pathologic subtype and brain invasion.

Methods: This is a retrospective analysis of the history of patients with intracranial meningiomas treated surgically in the Department of Neurosurgery in the years 2009-2024. We examined 498 patients whose full medical records were available, including tumor localisation and size, histopathological subtype, brain invasion status combined pre- and postoperative neurological status and history of recurrence. Data was collected, stored in database and analysed statistically.

Results: Analysis was performed on 437 cases of G1, 53 cases of G2 and 8 cases of G3 meningiomas according to their histological subtype. Macroscopic brain invasion was present in 10, 25 and 38% of cases respectively. Statistical significance was observed in higher recurrence rate in cases of higher histological grades and was not influenced by macroscopic brain invasion. On the other hand, brain invasion but not histological grade was associated with postoperative neurological deterioration.

Conclusions: Our material depicts how different parameters of meningiomas influence the clinical course and prognosis. It warrants inclusion of multiple features in their management and neurosurgical practice.

Primary and secondary tinnitus: Is there a difference in the admittance to an ENT clinic versus a specialized private ENT practice?

T. Brkić[1], S. Uščuplić[2], L. Tokić[2]

[1]Friedrich-Alexander-University, Erlangen, Germany. [2]University Clinical Center Tuzla, ENT Clinic Tuzla, Bosnia and Herzegovina

Neuroscience

Introduction: Tinnitus is a symptom that can be associated with multiple causes. It can be classified into primary and secondary tinnitus. Primary tinnitus is idiopathic and may or may not be associated with sensorineural hearing loss (SNHL). Secondary tinnitus, on the other hand, has an identifiable underlying cause (other than SNHL). This study aims to compare the distribution of primary and secondary tinnitus among patients in an ENT clinic versus those in a private ENT practice.

Methods: We analyzed 162 patients admitted to the ENT clinic (Group 1) and 118 patients admitted to a private ENT practice (Group 2) for tinnitus (either primary or secondary). We examined their associated symptoms, sex distribution and age demographics. Primary tinnitus occurs as an independent symptom or alongside SNHL, while secondary tinnitus can be linked to vertigo, hearing loss with vertigo or hyperacusis.

Results:
In Group 1, 77.7% had primary tinnitus and 22.2% had secondary tinnitus.
In Group 2, 64.2% had primary tinnitus and 35.7% had secondary tinnitus.
Male-to-female ratio: Group 1: 35.8%/64.2%, Group 2: 53.4%/46.6%.
Age distribution (18-65 years): Group 1: 61%, Group 2: 83.1%.

Conclusions: Primary tinnitus has no known cure but is associated with multiple comorbidities such as depression, anxiety, and insomnia. Secondary tinnitus is clinically important because it requires a more extensive diagnostic workup, leading to greater involvement of healthcare personnel, resources, and time. Our findings suggest a higher prevalence of secondary tinnitus in private practice settings, which may indicate differences in patient selection, referral pathways or diagnostic approaches.

Keywords: primary tinnitus, secondary tinnitus, sex, age

Neuroscience

Noradrenaline Protects Human Microglial Cells from LPS- and Aβ-Induced Toxicity: Implications for Alzheimer's Disease Therapy

Z. Granek[1], Prof. I. Majsterek[1], Dr habil. W. Rozpędek-Kamińska[1]

[1]Department of Clinical Chemistry and Biochemistry, Medical University of Lodz, Poland

Introduction: Alzheimer's disease (AD) is the most common neurodegenerative disorder, marked by the accumulation of amyloid-beta 1-42 (Aβ) plaques and chronic neuroinflammation. Noradrenaline (NA) has been shown to exert anti-inflammatory effects on activated microglia in AD, although with an unclear mechanism of action. The study aimed to investigate the protective effects of noradrenaline (NA) on human microglial cells (HMC3) exposed to lipopolysaccharides (LPS) and Aβ aggregates, representing an in vitro model of Alzheimer's disease (AD).

Methods: HMC3 cells were exposed to IC50 LPS or IC50 Aβ and treated with 25 and 50 μM NA. The cytotoxicity of the compounds was measured using the XTT colorimetric assay and Pierce LDH Cytotoxicity Assay. The immunocytochemical staining for Aβ was performed to assess the expression of extra- and intracellular Aβ aggregates. The colorimetric caspase-3 assay was used to evaluate the level of apoptosis. The expression of mRNA and proteins associated with ER stress (DDIT3, BAX, BCL2 and HIF-1α) were evaluated by TaqMan Gene Expression Assay and Western blot, respectively.

Results: NA treatment at 25 μM and 50 μM in HMC3 cells exposed to IC50 LPS or IC50 Aβ resulted in a significantly increased proliferation of HMC3 cells, reduced expression of both extracellular and intracellular Aβ deposits, reduced caspase-3 activity, decreased expression of HIF-1α and pro-apoptotic DDIT3 and BAX, and increased expression of anti-apoptotic BCL-2, leading to enhanced cell survival, when compared to that of the HMC3 cells treated only with IC50 LPS or IC50 Aβ.

Conclusion: Our findings suggest that NA may serve as a potential therapeutic target for mitigating microglial dysfunction and slowing AD progression. Its neuroprotective effects, particularly in modulating inflammation and microglial activity, could support the development of new treatment strategies for AD. The project was funded by grant no. SKN\SP\602622\2024 from the state budget allocated by the Minister of Science within the programme 'Student Scientific Circles Create Innovations'.

Keywords: Alzheimer's disease, Noradrenaline, Microglia, Apoptosis, Cytotoxicity

Diagnostic value of anti-glycolipid (complex) antibodies in distinguishing Guillain-Barré Syndrome from its mimics

A.E. van Dommelen[1], R.C.M. Thomma[1], B.C. Jacobs[1]

[1]Erasmus University Medical Centre, Rotterdam, The Netherlands

Neuroscience

Introduction: Guillain-Barré syndrome (GBS) is a neurological condition in which the peripheral nervous system is affected, with a highly variable clinical presentation. Due to its clinical heterogeneity, it is often difficult to distinguish GBS from conditions that mimic GBS early in the disease course. Recent research shows that antibodies to glycolipids and glycolipid complexes (combinations of two glycolipids), which are thought to play an important role in the pathophysiology of GBS, may distinguish GBS from its mimics. In this study, we aimed to develop a predictive model using anti-glycolipid (complex) antibodies to distinguish GBS from its mimics.

Methods: Patients from the GBS mimics and the International Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) outcome study (ICOS) were included. In the GBS mimic study, any patients with GBS or GBS in their differential diagnosis were included. In ICOS, patients with CIDP, a potential GBS mimic, were included. Patient sera from study entry (or week 1, if not available) were screened in glyco-array for IgG, IgA and IgM reactivity against 16 glycolipids and their heteromeric complexes. Models to distinguish GBS (and pure motor GBS) from its mimics were investigated using logistic regression analyses.

Results: Of 435 included patients, 68 had GBS and 317 had a GBS mimic. Univariable logistic regression analysis identified 65 anti-glycolipid (complex) antibodies associated with GBS, with IgM anti-GT1a:Sulph and IgA anti-SGPG:GalNac_GD1a showing the highest discriminative capacity (AUC: 0.78 and 0.78). In multivariable logistic regression analysis, a predictive model based on eight anti-glycolipid complex antibodies performed best (AUC: 0.90). In addition, 16 anti-glycolipid (complex) antibodies were associated with pure motor GBS, with IgG anti-GM1:GD1a and IgG anti-GD1a having the highest discriminative capacity (AUC: 0.85 and 0.83). The model to distinguish pure motor GBS from mimics with best predictive performance created in multivariable logistic regression analyses consisted of four anti-glycolipid (complex) antibodies (AUC: 0.91).

Conclusions: Models based on anti-glycolipid (complex) antibodies may distinguish GBS and pure motor GBS from their mimics. Further research is required to validate these models in larger, more heterogeneous GBS cohorts.

Keywords: Guillain-Barré Syndrome, autoantibody

Neuroscience

Persistent high anti-GM1 antibody titer in relation to clinical outcomes in Guillain-Barré syndrome.

A.E. van Dommelen[1], R.C.M. Thomma[1], B.C. Jacobs[1]

[1]Erasmus University Medical Centre, Rotterdam, The Netherlands

Introduction: Guillain-Barre syndrome (GBS) is a neurological condition in which the peripheral nervous system is affected, leading to progressive bilateral muscle weakness with highly variable disease severity and outcomes. GBS often follows an infection which may induce cross-reactive antibodies against gangliosides in peripheral nerves, such as GM1. Recent research has indicated that persistent high anti-GM1 antibody titers are associated with poor clinical outcome. The aim of this study was to validate these findings in an independent cohort of patients with GBS.

Methods: Patients were included from a previous randomized placebo-controlled trial (SID-GBS trial). Acute-phase sera were screened for IgG and IgM anti-GM1 antibodies in Enzyme-Linked Immunosorbent Assays (ELISA). Positive acute-phase sera and corresponding follow-up sera (weeks 1, 2, 4, and 12) were titrated in ELISA. Clinical outcomes (Medical Research Council (MRC) sum scores and ability to walk unaided) were compared between groups based on the presence of anti-GM1 antibodies and longitudinal titer height.

Results: Of 293 included patients, 47 (16.0%) had anti-GM1 antibodies. Anti-GM1 antibody positivity was associated with lower MRC sum scores at 4, 12 and 26 weeks. Of IgG anti-GM1 positive patients, 12 (66.7% of 18) had a persistent high antibody titer at 12 weeks. A persistent high IgG anti-GM1 titer at 12 weeks was associated with lower MRC sum scores at the same time point. Patients with persistent high IgG antibody titer at 12 weeks required more time to regain the ability to walk unaided and reached this endpoint less frequently.

Conclusions: The presence of high anti-GM1 antibodies and a persistent high IgG antibody titer at 12 weeks are associated with poor outcome in patients with GBS. These findings could be relevant for disease monitoring and personalizing treatment strategies in clinical practice.

Keywords: Guillain-Barré syndrome, autoantibody

Assessing IL-6 receptor antagonist (IL-6Ra) treatment for white matter injury in preterm fetal sheep exposed to progressive systemic inflammation using high-field MRI

K. Aalders[1], Dr. R. Galinsky[2]

[1]Erasmus University, Rotterdam, The Netherlands. [2]The Richie Centre, Hudson Institute of Medical Research, Australia

Neuroscience

Introduction: Intrauterine inflammation/infection is associated with long-term neurological morbidity and neuropsychiatric disorders and currently lacks effective treatment.We aimed to test the hypothesis that IL-6 inhibition started one hour after LPS exposure with novel nonapeptide IL-6 receptor antagonist (Ra) would reduce the severity of MRI signatures of neuroinflammation and brain injury in preterm fetal sheep.

Methods: Chronically instrumented preterm fetal sheep (equivalent age to an extremely preterm infant) were randomly assigned to receive either 2 mL of vehicle (saline; control, n = 8), increasing intravenous (i.v.) doses of LPS (0 h: 100 ng/kg, 24 h: 200 ng/kg, and 48 h: 400 ng/kg, diluted in saline; n = 8), or LPS + IL-6Ra (1 mg/kg i.v. dose, infused 1 hour after each LPS infusion; n = 8). All groups subsequently underwent nine days of recovery before the fetal brain was collected and processed for MRI analysis using a high field (9.4T) Bruker scanner.

Results: Progressive LPS infusions were associated with decreased apparent diffusion coefficient (ADC) in the corpus callosum (CC, $p < 0.05$) periventricular- (PVWM, $p < 0.0005$) and intragyral white matter (IGWM, $p < 0.05$) vs control. Fractional anisotropy (FA) was increased in the CC ($p < 0.05$) and PVWM ($p < 0.005$) for LPS-exposed subjects vs control. Preliminary data suggest there was an intermediate effect of IL-6Ra on ADC and FA, however the data were not adequately powered to detect statistical differences between groups.

Conclusions: Our study showed that progressive fetal inflammation increased markers of neuroinflammation and injury in the preterm brain. Moreover, preliminary analyses suggested a possible benefit of IL-6Ra on MRI markers of inflammation and injury. Future research is essential to explore the broader effect of IL-6Ra treatment on fetal brain inflammation.

Neuroscience

Characterization of spreading depolarization events in cross-bred double transgenic FHM1 and FHM2 mouse models

A.M. Ertienne[12]

[1]University of Amsterdam, Amsterdam, The Netherlands. [2]Leiden University Medical Centre, Leiden, The Netherlands

Introduction: Migraine is a highly debilitating neurovascular disorder characterized by headache attacks. In one third of migraine patients headache attacks are preceded by an aura, the underlying neurophysiological mechanism of which is believed to be a cortical spreading depolarisation (CSD). Familial hemiplegic migraine (FHM) is a rare autosomal dominant subtype of monogenic migraine with aura and transient weakness, and provides the possibility to study mechanisms of migraine attacks via a genetically modified approach. Many FHM migraine mouse models already exist, however all have specific features making them suboptimal for research such as early mortality and no spontaneous attacks.

Methods: Thus we generated a novel double transgenic model that represents both homozygous Cacna1aR192Q FHM1 and heterozygous Atp1a2T345A FHM2 (FHM1*2), and compared this model to homozygous Cacna1aR192Q FHM1 * wildtype Atp1a2T345A FHM2 (FHM1) and wildtype Cacna1aR192Q FHM1 * wildtype Atp1a2T345A FHM2 (WT). Spontaneous SD events features, as well as evoked SD features are researched using direct current (DC) local field potential (LFP) recordings from cortical and hippocampal brain areas in freely behaving FHM1*2, FHM1 and WT mice, and vigilance state analysis was used to determine vigilance state preceding SD.

Results: In the FHM1*2 model, 299 SDs were observed in 10 mice, and in the FHM1 model, 198 SDs were observed in 3 mice, both over the course of 14 recording days. For both models most SDs originated from the hippocampus. Delay between HC and V1, and V1 and HC in FHM1*2 mice proved significantly faster than in FHM1 compared to FHM1*2 mice. Hippocampal threshold to evoke SD proved lower in FHM1*2 mice than in WT mice. Vigilance state analysis showed that most mice were asleep before SD onset, but in some cases woke up right before the attack.

Conclusion: We conclude that the novel FHM1*2 model shows significant promise and holds potential for application in migraine research.

Keywords: migraine, familial hemiplegic migraine, spreading depolarisation, CACNA1A, ATP1A2, EEG, vigilance state

Mechanism of Kisspeptin Neuron Synchronization for Pulsatile GnRH Secretion

I. Bozkurt[1]

[1]Gazi University School of Medicine, Turkey

Neuroscience

Introduction: Fertility in mammals is critically dependent on a hypothalamic central pattern generator that drives the episodic release of GnRH, responsible for pulsatile reproductive hormone secretion. A small population of ARNkiss (kisspeptin neurons) located in the ARN (arcuate nucleus) has been identified as the central pattern generator responsible for this ultradian rhythm. The key unresolved question is how the ARNkiss neurons synchronise their activity to generate repetitive bursts that drive pulsatile hormone release, as well as the relationship between this pulsatility and stress. Our main aim was to expore the impact of dose-dependent insulin-induced hypoglycaemia (IIH) and restraint stress on the GnRH pulse generator by examining the pulsatile LH secretion in ovariectomised (OVX) mice. The observed synchronised events have shown that there are also mini-synchronised events (mSE) as well as synchronised events (SE). The suppression of the calcium peaks, resulting in disappearing GnRH pulsatility under the conditions of stress, may be dependent on the mSEs.

Methods: A microendoscope was implanted into the ARC of the OVX mice, and the frequency of the SEs was observed. A dose-dependent correlation between two different stress models (insulin-induced hypoglycemia and restraint) and the suppressionin LH pulse frequency was observed. Additionally, mSEs were determined on a calcium oscillation graphic after selecting the suitable ARNkiss neurons.

Results: A dose-dependent correlation between IIH (insulin-induced hypoglycemia) and the suppression of LH pulse frequency was observed. The absence of SEs, which is found to be highly dependent on mSEs, during the restraint period indicates disruption of ARC kisspeptin synchronisation, leading to suppressed LH secretion.

Conclusions: The lack of SEs following stress interferes with ARCkiss synchronisation, resulting in reduced LH secretion. The main reason underlying this pulsatility is the dominance of mSEs over SEs. Topics for further research include employing an adequate sample size and performing single-cell analysis. An accurate definition of GnRH pulse generator operation is expected to benefit the treatment of infertility in clinics.

Keywords: Pulsatile GnRh, restraint stress, mini-synchronised events

Neuroscience

HPA axis Functioning and Epigenetic Aging through Childhood and Adolescence

M. Arnau Martinez[1], E. Brinkman[1], C. de Weerth[1]

[1]Donders Institute, Radboud University, The Netherlands

Introduction: Early life is a critical period for development, with early experiences influencing long-term mental and physical health. Research links early life stress to both altered cortisol dynamics and accelerated epigenetic aging, yet longitudinal studies on this relation remain limited. Epigenetic age, estimated through DNA methylation patterns, can diverge from chronological age and this divergence is associated with health risks, including cardiovascular disease and early mortality. Epigenetic aging is also associated with environmental factors like stress and trauma.
Cortisol, a key hormone in the stress response, may mediate this link between early life stress and epigenetic aging. This study examines how cortisol circadian rhythms relate to epigenetic aging in a cohort of healthy children, with circadian cortisol assessed from infancy to adolescence and epigenetic age measured at 6, 10, and 14 years.

Methods / Results: To examine the link between concurrent circadian cortisol area under the curve (AUC) and epigenetic age acceleration at ages 6, 10, and 14, we will conduct three linear regressions. In addition, earlier cortisol measures from infancy and toddlerhood will be incorporated to assess potential cumulative effects on epigenetic aging. We hypothesize a positive association between epigenetic age and circadian cortisol AUC for concurrent and earlier measurements.
To examine the longitudinal relationship between circadian cortisol and epigenetic age acceleration, we will use a linear mixed effects model with random intercepts and slopes. We hypothesize that there will be a positive interaction between chronological age and cortisol suggesting that changes in circadian cortisol predict changes in epigenetic aging across time.

Conclusion: Dysregulation of the hypothalamic-pituitary-adrenal axis, with cortisol as its end product, may serve as a key link between early life stress, epigenetic age acceleration, and long-term health outcomes. This project examines the potential cumulative effects of cortisol on epigenetic aging in a pediatric population. Uncovering this link is essential for identifying potential mechanisms that drive the development of stress-related health risks. Moreover, understanding the developmental dynamics of epigenetic aging in the light of cortisol physiology could inform the prediction of disease risk in adulthood and elucidate possible targets and periods for intervention.

The Role of Physical Activity in Modulating the Gut Microbiota-Brain Connectivity Relationship: A Longitudinal Investigation of Time-Invariant and Time-Variant Effects

L. López Sánchez[1], S. Papalini[1], N. Kohn[1]

[1]Donders Institute, Radboud University, The Netherlands

Neuroscience

Introduction: The gut microbiota and brain communicate through bidirectional pathways, forming the microbiota-gut-brain axis. Emerging evidence suggests that physical activity influences both gut microbiota composition and brain network connectivity, yet its role in shaping their relationship over time remains unclear. This study investigates how physical activity modulates the association between gut microbiota diversity and large-scale brain networks, distinguishing between stable, time-invariant effects and dynamic, time-variant influences.

Methods: This study utilizes data from the Healthy Brain Study, a large-scale longitudinal project on brain health in healthy adults. Participants were assessed at three-time points within one year, with each time point including approximately 700 participants, leading to a total dataset of around 2100 observations across all assessments.
Gut microbiota diversity was characterized through 16S rRNA sequencing, focusing on alpha diversity (e.g., Shannon index, Chao1) and beta diversity (e.g., Bray-Curtis dissimilarity). Resting-state fMRI was used to analyze functional connectivity within three major networks: the Default Mode Network (DMN), the Executive Control Network (ECN), and the Salience Network (SN). Physical activity data was collected via accelerometry, capturing long-term patterns and short-term fluctuations. Statistical analyses will include repeated measures models and random-intercept cross-lagged panel modeling (RI-CLPM) to disentangle stable individual differences from within-person changes over time.

Expected Results: The upcoming analyses will assess the independent effects of physical activity on gut microbiota diversity and brain network connectivity, as well as its potential role in modifying the microbiota-brain relationship. By integrating physical activity into the microbiota-gut-brain framework, this study aims to provide insights into whether and how physical activity influences brain network connectivity in relation to gut microbiota diversity. Understanding these interactions may reveal mechanisms through which lifestyle factors contribute to brain health and cognitive function over time.

Conclusion: This research will contribute to a more comprehensive understanding of the microbiota-gut-brain axis by incorporating physical activity as a potential modulator. The findings could have implications for developing lifestyle-based interventions targeting both brain and gut health.

Keywords: Gut microbiota, brain connectivity, physical activity, resting-state fMRI, longitudinal analysis

Neuroscience

Nocturnal mobility in Parkinson's disease compared to people with sleep-related complaints: An analytical cross-sectional study of wearable sensor data using standard statistics and an artificial neural network

A. van Meer[1], J. Gils[1], L. Pals[1]

[1]University of Antwerp, Belgium

Introduction: Altered nocturnal movements are interesting features of Parkinson's disease (PD) that occur 7-11 years prior to diagnosis. This comprises increased supine body position, lower number of rotations and lower rotation speed. This has rarely been compared to patients with isolated sleep disorders (ISD), despite this being an important group with whom we'll have to be able to differentiate. This study investigates the use of the Activ8 wearable sensor to differentiate nocturnal movements in patients with Parkinson's disease from patients with ISD. The goal is to validate the wearable as a cheaper and more accessible alternative to polysomnography and as a possible future screening for Parkinson's disease.

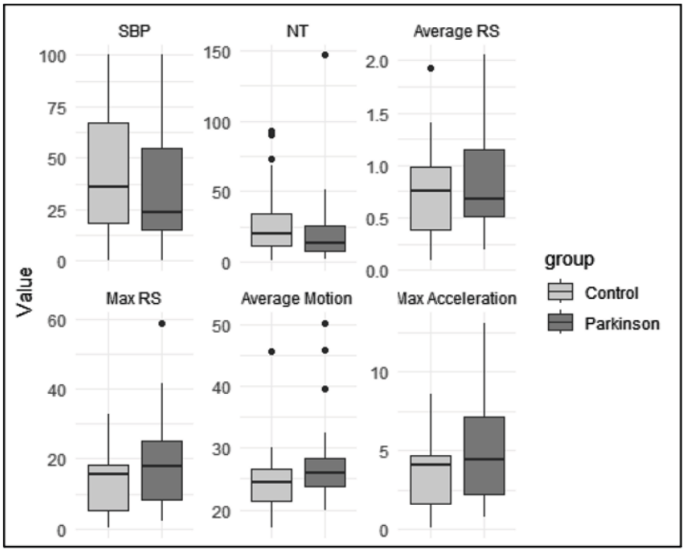
Methods: The following parameters provided by Activ8 were analysed: supine body position, number of turns, motion, rotation speed and rotational acceleration. After validation of the parameters, data from 25 early-stage Parkinson's disease patients and 32 ISD patients was compared. Analysis was performed with inferential statistics and two predictive models, using logistic regression and an artificial neural network (ANN).

Results:
Inferential statistics: PD patients had a significantly higher motion than controls ($p = 0.03937$). No significant differences were found for supine body position (p-value = 0.3346), number of turns (p-value = 0.161), average and maximum rotation speed (p-value = 0.547 and 0.1155) or rotational acceleration (p-value = 0.1547).

Predictive models: The LR model and ANN for differentiation between PD patients and controls resulted in two ROC-curves with, respectively, a sensitivity of 58.3% and 94.1% and a specificity of 80% and 58.3%.

Conclusions: The Activ8 sensor is promising as a more accessible alternative for differenti ating nocturnal movements in Parkinson's disease. A significant difference between PD and controls was observed for motion, but not for other parameters. Predictive models, particularly the ANN, demonstrated potential, though further refinement is needed to improve accuracy.

Keywords: wearable sensor, Parkinson's disease, nighttime movements, early diagnosis, artificial intelligence


SBP
NT
Average RS
Max RS
Average Motion
Max Acceleration
Value
group
Control
Parkinson

Neuroscience

Application of Deep Learning in Early Detection of Alzheimer's Disease from MRI Scans

A. Yousefzadeh[1]

[1]Islamic Azad University, Iran

Introduction: Alzheimer's disease (AD) is a neurodegenerative disorder characterized by progressive cognitive decline, with early detection crucial for effective intervention. Magnetic resonance imaging (MRI) offers valuable insights into brain structure changes associated with AD. This study investigates the application of deep learning techniques for early detection of AD from MRI scans.

Methods: Our methodology involved the acquisition of a comprehensive dataset comprising MRI scans from AD patients, individuals with mild cognitive impairment (MCI), and healthy controls. Preprocessing steps included normalization and registration to ensure data consistency. Deep learning architectures, such as convolutional neural networks (CNNs) and recurrent neural networks (RNNs), were employed for feature extraction and classification. Model training utilized transfer learning and data augmentation strategies to enhance generalizability. Evaluation metrics such as accuracy, sensitivity, specificity, and area under the curve (AUC) were employed to assess model performance.

Results: The deep learning models demonstrated high accuracy in discriminating AD patients from healthy controls and individuals with MCI based on MRI scans. The models effectively captured subtle structural alterations indicative of AD pathology, including hippocampal atrophy and cortical thinning. Furthermore, they exhibited superior performance compared to traditional machine learning approaches and radiological interpretations. Cross-validation analyses confirmed the robustness and generalizability of the models across diverse patient cohorts.

Conclusion: Deep learning techniques offer promising avenues for early detection of Alzheimer's disease from MRI scans. By leveraging complex patterns in brain imaging data, these models can provide timely and accurate identification of individuals at risk of AD, enabling early intervention and personalized treatment strategies. Integration of deep learning-based diagnostic tools into clinical practice holds the potential to revolutionize early AD diagnosis and improve patient outcomes.

Volumetric analysis of gyrus cinguli in people with MMD

M. Jevtić[1]

[1]University of Belgrade, Serbia

Introduction: The gyrus cinguli is part of the limbic system. The centralized position corresponds to its function as a link between the limbic system and the neocortex, building connections and integrating information from both which has made it a target of interest for multifactorial diseases such as depression. Most studies have reported structural changes in the ACC in individuals with depressive disorder. Also, there are hypotheses about the volume change in PCC. Mild to moderate depression (MMD) has a high incidence in clinical practice and shows a high tendency to progress to Major depression disorder (MDD) which can be treatment-resistant. For this reason, early and accurate diagnosis is important. Volumetric analysis of the gyrus cinguli and its parts in persons classified in the group of subjects with MMD and the control group is done to find the structure in which changes first occur.

Methods / Results: The research included 20 subjects, 10 with MMD and 10 controls, age group 30-50 years. The data were taken from the open database Openneuro. MRI images were processed in the software program in T1W and read in NiFTi format. Manual delineation and processing of the values of the examined component was performed. IBM SPSS 21 software (Chicago, IL, 2012) was used for statistical analysis. Statistical analysis was performed with a T-test within types. A statistically significant value was obtained for the entire gyrus cinguli ($p<0.05$). A regression was performed, which found that this difference was not influenced by the factor of gender differences ($p<0.001$). The T-test for other parts of the gyrus cinguli does not show statistical significance ($p>0.05$).

Conclusion: This study found that the gyrus cinguli changes in the early stages of depressive disorders. It has been proven that the volume change is not conditioned by the difference in sexes. A more detailed analysis of the gyrus cinguli and its regions shows no deviation which could indicate that neither of these two regions, in this case, shows changes in the early stages. The suggestion is to further examine changes in neuroplasticity.

Keywords: volumetric analysis; gyrus cinguli; MMD; neuroimaging; MRI; depressive disorder

Neuroscience

How important are the Glasgow Coma Scale and Pupillary reactivity for prognosis in Traumatic Brain Injury: Statistical analysis in the prospective observational cohorts CENTER-TBI and TRACK-TBI

R. J.G. Vreeburg, MD[1], F. D. van Leeuwen, MSc[2], G. T. Manley, MD, PhD[3], J. K. Yue, MD[3], P. M. Brennan, MD, PhD[45], X. Sun, MSc[6], S. Jain, PhD[6], T.A. van Essen, MD, PhD, MSc[17], W. C. Peul, MD, PhD[1], A. I.R. Maas, MD, PhD[89], D. K. Menon, MD, PhD[10], E.W. Steyerberg PhD[2]

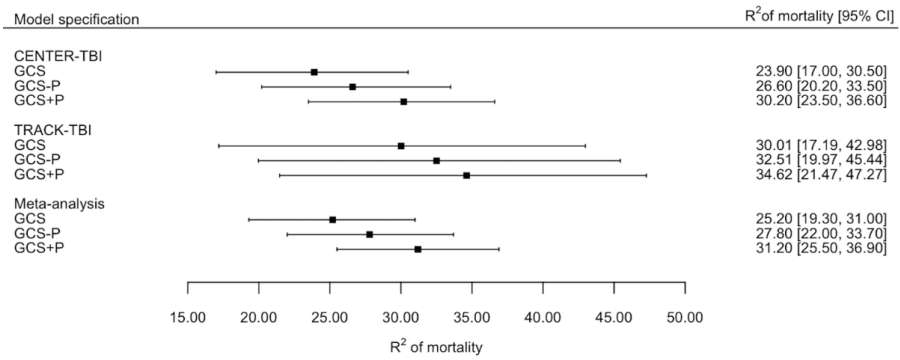
1University Neurosurgical Center Holland, Leiden University Medical Center, Haaglanden Medical Center and Haga Teaching Hospital, Leiden and the Hague. 2Department of Biomedical Data Sciences, Leiden University Medical Center, Leiden. 3University of California, San Francisco, San Francisco, CA, United States. 4Royal Infirmary of Edinburgh, Edinburgh, United Kingdom. 5Centre for Clinical Brain Sciences, University of Edinburgh, United Kingdom. 6Herbert Wertheim School of Public Health and Human Longevity Science University of California, San Diego. 7QEII Health Sciences Center and Dalhousie University, Halifax, Nova Scotia, Canada. 8Antwerp University Hospital, Edegem, Belgium. 9Faculty of Medicine and Health Science, University of Antwerp, Antwerp, Belgium. 10University of Cambridge, United Kingdom

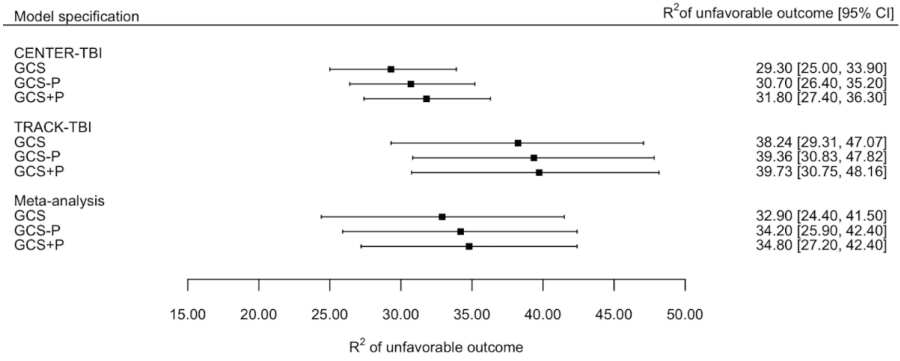
Introduction: The clinical severity of traumatic brain injury (TBI) is commonly reported according to the Glasgow Coma Scale (GCS) but its simplicity but has been challenged as being too crude and may lead to treatment bias. The GCS-P combines GCS and pupil reactivity. It has shown potential to increase information yield compared to using GCS alone and even equaling information yield of GCS and pupil reactivity as separate factors. The aim of this study is to explore the relative value of using the full GCS or the GCS-Pupils score (GCS-P) for classifying the clinical severity of TBI in large contemporaneous datasets including TBI of all severities.

Methods: We analyzed patients enrolled between 2014 and 2018 in the Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury (CENTER-TBI, n=3521) and the Transforming Research and Clinical Knowledge in Traumatic Brain Injury (TRACK-TBI, n=1439) cohorts. Logistic regression was utilized to quantify the prognostic performances of GCS-P and GCS+P versus GCS alone according to Nagelkerke's R2(expressed in percentages). Endpoints were mortality and unfavorable outcome (Glasgow Outcome Scale-Extended score 1-4) at 6-months post-injury. We estimated 95% confidence intervals [CI] with bootstrap resampling to summarize the improvement in prognostic capability.

Results: Among the 4960 eligible participants, 3521 were included in CENTER-TBI and 1439 in TRACK-TBI. In logistic regression, GCS as a linear score explained 24% [95% CI 17-30%] and 30% [17-43%] of the variance in mortality, and 29% [25-34%] and 38% [29-47%] in unfavorable outcome, in CENTER-TBI and TRACK-TBI, respectively. In a meta-analysis, pupillary reactivity as a separate variable improved the explained variance by an absolute value of 6% [4.0-7.7%] and 2% [1.2-3.0%] in mortality and unfavorable outcome respectively, while comparatively half of this improvement was captured by the GCS-P score (3% [2.1-3.3%], 1% [1-1.7%], respectively).

Conclusion: GCS-P showed a stronger association with 6-month outcome after TBI than GCS alone, and provides a single integrated score. However, this comes at a loss of clinical and prognostic information compared to GCS+P. For prognostic models, inclusion of GCS and pupillary reactivity as separate factors may be preferable to using a GCS-P summary score.


Model specification
R^2 of mortality [95% CI]
CENTER-TBI
GCS
GCS-P
GCS+P
23.90 [17.00, 30.50]
26.60 [20.20, 33.50]
30.20 [23.50, 36.60]
TRACK-TBI
GCS
GCS-P
GCS+P
30.01 [17.19, 42.98]
32.51 [19.97, 45.44]
34.62 [21.47, 47.27]
Meta-analysis
GCS
GCS-P
GCS+P
25.20 [19.30, 31.00]
27.80 [22.00, 33.70]
31.20 [25.50, 36.90]
15.00
20.00
25.00
30.00
35.00
40.00
45.00
50.00
R^2 of mortality


Model specification
R^2 of unfavorable outcome [95% CI]
CENTER-TBI
GCS
GCS-P
GCS+P
29.30 [25.00, 33.90]
30.70 [26.40, 35.20]
31.80 [27.40, 36.30]
TRACK-TBI
GCS
GCS-P
GCS+P
38.24 [29.31, 47.07]
39.36 [30.83, 47.82]
39.73 [30.75, 48.16]
Meta-analysis
GCS
GCS-P
GCS+P
32.90 [24.40, 41.50]
34.20 [25.90, 42.40]
34.80 [27.20, 42.40]
15.00
20.00
25.00
30.00
35.00
40.00
45.00
50.00
R^2 of unfavorable outcome

Neuroscience

Neuroprotective Potential of Bacopa monnieri and Donepezil in Alzheimer's Disease: A Comparative Study

A. Yousefzadeh[1]

[1]Islamic Azad University, Iran

Introduction: Alzheimer's disease (AD) is a progressive neurodegenerative disorder marked by cognitive decline and memory impairment. While donepezil, a cholinesterase inhibitor, is commonly used to manage symptoms, herbal neuroprotectants such as Bacopa monnieri have shown potential in cognitive enhancement. This study aims to evaluate the neuroprotective effects of Bacopa monnieri compared to donepezil in an experimentally induced Alzheimer's disease model.

Methods: AD was induced in 40 Wistar rats using β-amyloid (Aβ1-42) injections into the hippocampus. Animals were assigned to four groups: Control, Alzheimer's control, Donepezil (5 mg/kg), and Bacopa monnieri extract (300 mg/kg) for 8 weeks. Behavioral tests (Morris Water Maze and Novel Object Recognition) assessed cognitive function, while oxidative stress markers (MDA, SOD, and GSH) and acetylcholinesterase (AChE) activity were measured in brain tissue.

Results: Bacopa monnieri significantly improved memory and learning ability compared to the Alzheimer's control ($p<0.01$), showing effects comparable to donepezil. MDA levels (oxidative stress marker) were reduced by 41%, while SOD and GSH levels increased by 35% and 29%, respectively. AChE activity decreased by 26%, suggesting improved cholinergic transmission.

Conclusion: The neuroprotective effects of Bacopa monnieri were comparable to donepezil, highlighting its potential as an alternative or adjunct therapy for Alzheimer's disease. Future clinical trials are necessary to explore its efficacy in humans.

Keywords: Neuroprotective, Alzheimer, Extract

Automatic detection of MS lesions in MRI brain images using the Artificial Intelligence techniques

F. Aghajanloo[1]

[1]Zanjan University of Medical Sciences, Iran

Introduction: Multiple sclerosis (MS) is an autoimmune disease in which the body's immune system attacks the axons and destroys the myelin, causing the formation of white spots called plaques on the nerves. Timely diagnosis of the disease and obtaining the size of the plaques are very effective in controlling this disease. Conventional manual segmentation methods are both time-consuming and subject to variations.
The aim of this study is to use Artificial Intelligence (AI) for automating lesion detection. Our study focuses on a practical approach utilizing Support Vector Machine (SVM) classification.

Methods: A dataset of 210 MRI brain images taken from Atieh Hospital, Tehran, Iran, comprising both MS-affected and healthy subjects, was used in this study. A supervised approach utilizing Support Vector Machines (SVM) was employed for lesion segmentation, with manual annotations used for training the SVM model on a 70% training set and 30% testing set. Features characterizing MS lesions and healthy brain tissue were extracted, including intensity, texture, and shape descriptors. Post-processing techniques were applied to enhance lesion maps, and standard evaluation metrics, including sensitivity, specificity, accuracy, and the Dice coefficient, were used for performance assessment.

Results: The AI-based MS lesion detection system demonstrated exceptional diagnostic performance, achieving remarkable sensitivity, specificity, and overall accuracy of 92.4%, 94.7%, and of 93.6%, respectively. The Dice coefficient, a metric of lesion segmentation precision, reached a notable .88, underscoring the system's capacity for accurate lesion localization. The SVM classifier exhibited robust discriminatory abilities, effectively discerning MS lesions from normal brain tissue.

Conclusions: Our AI-driven MS lesion detection system has demonstrated superior diagnostic performance, with high sensitivity, specificity, accuracy, and a notable Dice coefficient, signifying its precision in lesion localization. The integration of advanced AI techniques into medical imaging presents a promising frontier, poised to enhance the accuracy and timeliness of multiple sclerosis diagnosis, ultimately improving patient outcomes.

Neuroscience

Cognitive dysfunction and neurogenesis in a combined mouse model for ischemic stroke and Alzheimer's disease

R. Testaferrata[1], R. Gens[1], D.D. de Bundel[1]

[1]Experimental Pharmacology, Vrije Universiteit Brussel, Belgium

Introduction: Ischemic stroke (IS) and Alzheimer's disease (AD), both common leading causes of disability and death worldwide, are frequently comorbid. Cognitive dysfunction in both disorders has been associated with neurogenesis. IS has been shown to cause aberrant hippocampal neurogenesis, characterized by a transient increase in neuronal proliferation and the formation of mature neurons with abnormal morphology. This can disrupt normal hippocampal function and contribute to cognitive impairment. In contrast, in AD there is a progressive decline in hippocampal neurogenesis, which has been associated with poorer cognitive function. However, it remains unclear how neurogenesis and cognitive function would be affected in comorbid IS and AD. We hypothesize that abnormal post-stroke hippocampal neurogenesis in the pre-symptomatic stage of AD would further disrupt hippocampal function and cognitive outcomes in AD.

Methods: We subjected 4-month-old wild-type (WT) and triple-transgenic AD (3xTg-AD) mice to IS via permanent middle cerebral artery occlusion (pMCAO). Sham controls underwent the same surgical procedures as pMCAO mice, except for ligature sutures. Contextual fear conditioning was conducted 7 days after IS to investigate the formation of new memories. Memory retention was assessed 1 month after IS. We performed Nissl staining to determine infarct size and immunofluorescence co-labeling for bromodeoxyuridine (BrdU) and neuronal nuclei (NeuN) to evaluate neurogenesis.

Results: During the memory retrieval test, we did not observe a significant genotype effect, demonstrating the lack of overt AD-related cognitive dysfunction at this age. However, we observed a significant procedural effect in female mice, with pMCAO mice showing lower memory retention, expressed as freezing, compared to sham mice. In male mice, this trend did not reach statistical significance. We found a significant genotype effect, with less BrdU+ hippocampal neurons in 3xTg-AD mice. Finally, Nissl staining data indicated that infarct size was comparable between WT and 3xTg-AD mice at the studied age.

Conclusion: In pre-symptomatic AD mice, infarct size was similar to that of WT mice. Moreover, pMCAO did not significantly disrupt the studied measures of hippocampal neurogenesis, and while it did affect cognitive function, it did not aggravate cognitive dysfunction in 3xTg-AD mice.

Keywords: Ischemic stroke; Alzheimer's disease; cognitive dysfunction; neurogenesis

Chemogenetic modulation of microglia in the intrahippocampal kainic acid mouse model of drug-resistant temporal lobe epilepsy

E. Gheysens[1], I. Smolders[1], J. Bossuyt[1]

[1]Experimental Pharmacology, Vrije Universiteit Brussel, Belgium

Neuroscience

Introduction: Temporal lobe epilepsy (TLE) is a common form of epilepsy, yet one third of the patients are unresponsive to the currently available anti-seizure medication. Following seizure-induced excitotoxicity and neurodegeneration, microglia initially exhibit neuroprotective functions, but rapidly become overactivated. This stimulates pro-inflammatory cytokine release and aberrant synaptic pruning, collectively exacerbating seizure severity during epileptogenesis. Microglia can be modulated in a cell-specific manner with Gi protein-coupled Designer Receptors Exclusively Activated by Designer Drugs (Gi-DREADDs). Previous studies have shown that microglial Gi-DREADD modulation reduced pro-inflammatory cytokine levels. Therefore, we investigate whether microglial Gi-DREADD modulation can modulate the number of spontaneous recurrent seizures (SRS) and epilepsy-associated hallmarks in a clinically relevant mouse model for TLE.

Methods: We bred CX3CR1CreERT2/+:R26LSL-Gi-DREADD/+ (with Gi-DREADD expression in microglia) and CX3CR1CreERT2/+:R26+/+ (as controls) mice. Kainic acid was injected into the hippocampus to induce status epilepticus. Over a period of 5 weeks, mice developed SRS. Deschloroclozapine (DCZ), a DREADD agonist, was administered as a single injection, or as a repeated regimen (1 injection/day for 4 consecutive days). After the (final) DCZ injection, we assessed neuronal activity (by c-Fos expression) and microglial CD68 expression via immunostainings. A separate group of mice was subjected to continuous EEG monitoring. Changes in the number of SRS, relative to baseline, were examined during the repeated DCZ administration regimen and a three-week washout period.

Results: We observed a significant decrease in CD68 expression in microglia within the ipsilateral hippocampus after repeated Gi-DREADD-based modulation of microglia in epileptic CX3CR1CreERT2/+:R26LSL-Gi-DREADD/+ mice, compared to controls. No changes in neuronal activation were observed. Interestingly, while single Gi-DREADD modulation of microglia did not modify CD68 immunoreactivity, it led to a significant upregulation in neuronal activation. Our EEG results show no difference in seizure number during and immediately after repeated DCZ injections. However, a trend was observed indicating a lower total seizure number 10-12 days and 22-24 days after DCZ injections in CX3CR1CreERT2/+:R26LSL-Gi-DREADD/+ compared to CX3CR1CreERT2/+:R26+/+ mice.

Conclusion: These data suggest that repeated microglial Gi-DREADD modulation attenuated microglial CD68 expression and long-term effects on seizure number, while single Gi-DREADD activation even enhanced neuronal activation.

Keywords: microglia, temporal lobe epilepsy, chemogenetics, DREADDs

Neuroscience

The effects of transcranial Direct Current Stimulation on reward valuation and response inhibition in alcohol and cocaine use disorder

L. Debroux[1], Prof. Dr. C. Crunelle[1], Dr. M. van Kernebeek[1]

[1]Department of Psychiatry, Universitair Ziekenhuis Brussel, Belgium

Introduction: Substance Use Disorder (SUD) is a complex neuroadaptive and neurodevelopmental condition characterized by a recurring cycle of binge/intoxication, withdrawal/negative affect, and preoccupation/anticipation. This cycle leads to dysfunctions in frontal-subcortical brain circuits, affecting cognitive control and decision-making. Traditional symptom-based diagnostic approaches fail to fully capture the overlapping neural mechanisms underlying SUD. To address this, the Research Domain Criteria (RDoC) framework provides a transdiagnostic perspective by focusing on neural circuits and neuropsychological processes. Within this framework, neuromodulation techniques such as transcranial Direct Current Stimulation (tDCS) offer a promising avenue for targeted interventions. By modulating activity in key brain regions involved in executive functioning, such as the dorsolateral prefrontal cortex (DLPFC), tDCS has the potential to enhance cognitive control and reduce addiction-related dysfunctions.

Methods: The study employs a single-blind, randomized design. Participants diagnosed with alcohol or cocaine dependence receive ten sessions of 20-minute 1.5 mA tDCS (active or sham) targeting the DLPFC (anode over left DLPFC, cathode on contralateral supraorbital region). To assess the impact of tDCS on two core RDoC constructs, reward valuation and response inhibition, the study incorporates the delay discounting task and the stop-signal task, respectively. Psychometric data are collected pre-and post-treatment, and at 1-, 3-, and 6-month follow-ups.

Results: No results are available at this stage of the research. Data collection and analysis are ongoing

Conclusion: This study seeks to determine the therapeutic potential of tDCS in targeting neural and cognitive processes linked to SUD. A transdiagnostic approach, as emphasized by the RDoC framework, could enhance personalized treatment strategies. However, further research is needed to refine stimulation parameters, assess long-term effects, and explore potential synergies with other interventions.

Keywords: Substance Use Disorder - neuromodulation - transcranial Direct Current Stimulation - Research Domain Criteria

Diabetic sensorimotor polyneuropathy vs. Mononeuritis multiplex: a Case Report

K. Basant[1], N. Vasylieva[1]

[1]Bukovinian State Medical University, Ukraine

Neuroscience

Introduction: Diabetic polyneuropathy (DPN) is the most common form of peripheral neuropathy in diabetic patients, affecting sensory, motor and autonomic functions. However, focal neuropathies and Mononeuritis Multiplex (MM) can mimic DPN. The aim of this case report is to highlight the diagnostic challenge of differentiating Diabetic Sensorimotor Polyneuropathy from Mononeuritis Multiplex, focusing on clinical examination,neurological findings and ancillary tests.

Methods: A 60-year-old male with type 2 Diabetes Mellitus (since 2020) presented with right foot drop and altered gait, numbness and tingling in both legs (more in the right), numbness in the left 4-th and 5-th fingers of the right and left hands, left-hand weakness,swelling of the feet with redness and pain (especially on the right), unsteadiness in the dark.
Cranial nerve examination revealed no abnormalities, including the absence of nystagmus, ptosis, or ophthalmoplegia. Neurological examination revealed right ankle dorsiflexion and pronation 3/5, leftwrist extension 2/5 with weak hand grip and finger abduction. Deep tendon reflexes such as Achilles, knee, plantar bilaterally were absent. Sensory deficits in a polyneuropathic symmetric distribution including proprioception and vibration in the distal part of both legs just above the ankle, but fine touch, pain, temperature sensations were impaired over the ulnar aspect of both hands, dorsum of the right foot, and left lateral leg. Romberg's test was positive. Also trophic changes in the feet were present . MRI revealed L4-L5 disc herniation. EMG(electromyography) and NCS(nerve conduction study) findings demonstrated diffuse axonal and demyelinated mixed sensorimotor polyneuropathy.

Results: The asymmetry of weakness and superficial sensation raise the suspicion of a Mononeuritis Multiplex superimposed on the Diabetic Polyneuropathy which is manifested in bilateral sensory motor insufficiency, and autonomic dysfunction, possibly due to chronic ischemia and metabolic vulnerability.

Conclusion: This case highlights the complexity of DPN . Differentiating DPN from Mononeuritis Multiplex is challenging due to its overlapping features. However it is of utmost importance as their management and prognosis differ. Multidisciplinary management along with neuropathic pain management is crucial for this patient.

Keywords: Diabetic polyneuropathy, Mononeuritis Multiplex, differential diagnosis

Neuroscience

Is the Clinical Outcome of Lumbar Stenosis Treatment in Achondroplasia Associated with Severity of Stenosis and Sagittal Balance?

H. Cai[1], C. Omara[12], C. L.A. Vleggeert-Lankamp[123]

[1]Department of Neurosurgery, Leiden University Medical Centre, The Netherlands. [2]Brigham and Woman's Hospital, Harvard Medical School, Boston, USA. [3]Spaarne Gasthuis Haarlem/Hoofddorp, The Netherlands

Introduction: Lumbar spinal stenosis (LSS) is common in adults with achondroplasia (Ach) and predisposes individuals to neurogenic claudication. Its impact on clinical outcomes, along with the role of sagittal balance, remains unclear. This study aims to assess the impact of LSS severity, sagittal balance parameters, and their combination on clinical outcomes in achondroplasia.

Methods: Achondroplasia patients who visited the neurosurgical outpatient clinic with neurogenic claudication over the past ten years were evaluated. Surveys were distributed to all patients, including the Oswestry Disability Index (ODI), visual analog scale (VAS), EuroQol-5 Dimensions (EQ-5D), modified Japanese Orthopaedic Association (mJOA) scores, and Hospital Anxiety and Depression Scales (HADS). MRI findings (Schizas scale and dural sac cross-sectional area (DSCA)) and sagittal balance parameters (thoracolumbar kyphosis (TLK), lumbar lordosis (LL), and sagittal vertical axis (SVA)) were evaluated. Linear regression analyzed associations between clinical and radiological parameters.

Results: A total of 45 patients completed the survey and were included. Among them, 32 underwent surgical decompression. The average follow-up time was 4.8 years (range: 0.7-12.4 years). The mean ages of the conservative and surgical groups were 50.7±11.9 years and 53.0±18.4 years, respectively. There were seven male patients (53.8%) in the conservative group and nine (28.1%) in the surgery group. No association could be established between the severity of stenosis and clinical outcome. Regression analyses demonstrated that 'degrees in TLK' was the sole radiological risk factor influencing the clinical outcomes measured by the EQ-5D index scores (B = -0.005, 95% CI [-0.008, -0.002], p = 0.003). Thus, we comprehensively considered TLK and degree of stenosis and found that achondroplasts with severe stenosis (DSCA < 62 mm2) and pathological TLK (> 20°) demonstrated worse functionality quantified by the mJOA scales (12.2±2.7 vs 14.4±3.7, p = 0.046). Furthermore, pathological TLK and smaller DSCA were associated with worse clinical outcomes quantified by mJOA scores (B = -2.559, 95% CI [-4.523, -0.595], p = 0.012).

Conclusion: TLK is associated with worse functional outcomes quantified by EQ-5D and in combination with severe stenosis associated with less favorable mJOA scores in adult achondroplasts with symtomatic LSS. Larger prospective studies are needed to validate these findings.

Beyond the own genes: Maternal tryptophan hydroxylase-1 genotype shapes offspring's brain, cognition, and behavior

R. C. R. Castro[1], J. R. Homberg[1]

[1]Department of Cognitive Neuroscience, Donders Institute for Brain, Cognition and Behavior, Radboud University Medical Centre, Nijmegen, The Netherlands

Introduction: Besides own genotype (1 paternal allele, 1 maternal allele), also maternal genotype influences brain development, cognition, and behavior. However, the latter is often overlooked in gene association studies. Serotonin (5-HT) is crucial for neurodevelopment. Before the embryo can synthesize 5-HT itself, the mother provides the embryo with a 5-HT source via the placenta. Reduced expression of tryptophan hydroxylase-1 (TPH1), responsible for 5-HT synthesis from tryptophan, leads to a drop in 5-HT levels in the peripheral tissues of the mother. This can result in altered transport of 5-HT via the placenta to the embryo. Despite this, it is still unclear what are the consequences of the maternal TPH1 genotype on the postnatal cognition and behavior of the offspring.

Methods: Here, we behaviourally analyzed TPH1+/- rats from postnatal day (P)7 until adulthood, which were produced by crossing TPH1-/- or TPH1+/+ dams with males of opposite genotypes. Motor and sensory function development was repetitively assessed at P7, P9, P11, and P14. At P21, P35, and P70, evaluations of emotionality, recognition memory, and sensory integration were conducted. After P70, tests to evaluate sociability, cognitive flexibility, attention, impulsivity, and motivation were carried out.

Results: Our data revealed that offspring of TPH1-/- mothers presented several developmental and physiological abnormalities, including motor and sensory development retardation and increased body weight. Offspring of TPH1-/- mothers also showed cognitive impairments and increased anxiety-like behavior during adulthood. Interestingly, males, but not females, presented attention deficits and higher levels of aggression and impulsivity.

Conclusion: These results indicate that, beyond the own genes, the maternal TPH1 genotype, and therefore, 5-HT during the embryonic period, has a significant impact on the offspring's brain, cognition, and behavior. Further studies are necessary to elucidate the translational applicability of these findings to human health.

Keywords: anxiety-like behavior; cognition; neurodevelopment; serotonin; tryptophan hydroxylase 1

Maternal serotonin transporter genotype impacts placental and early postnatal environments, shaping offspring's anxiety-like behavior

R. C. R. Castro[1], S. I. Hanswijk1, J.R. Homberg[1]

[1]Department of Cognitive Neuroscience, Donders Institute for Brain, Cognition and Behavior, Radboud University Medical Centre, Nijmegen, The Netherlands

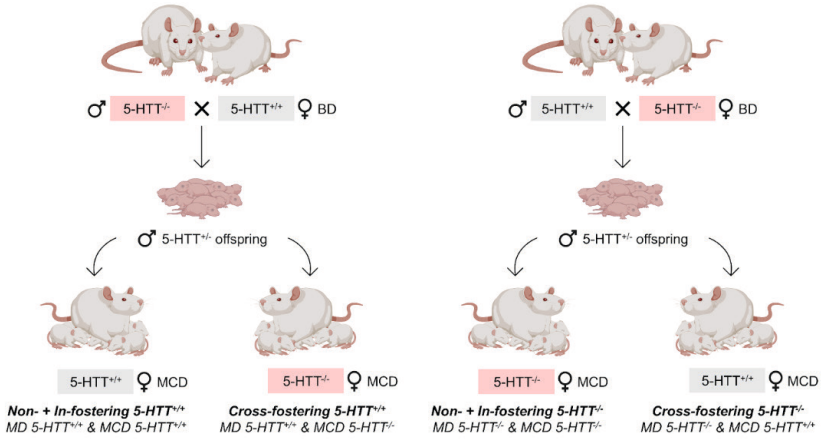
Introduction: Emerging findings implicate the maternal serotonergic system in offspring's susceptibility to neuropsychiatric disorders. Particularly, the maternal serotonin transporter (5-HTT) genotype may affect placental and early postnatal environments, resulting in hard-to-disentangle neurodevelopmental and behavioral implications for the offspring. Here, a 5-HTT knockout rat model and a fostering procedure were employed to control both factors and assess the effects of the maternal 5-HTT genotype in shaping offspring's phenotypes.

Methods: Eighty-four 5-HTT+/- male offspring were produced by crossing 5-HTT-/- or 5-HTT+/+ dams with males of opposite genotypes. A fostering procedure differentiated early postnatal from placental effects. Maternal care quality and offspring's depressive- and anxiety-like behaviors were assessed. Molecular analyses of placental and offspring's embryonic and adult tissues evaluated GABA/glutamate, HPA-axis, serotonin, and neuroplasticity pathways.

Results: 5-HTT-/- dams exhibited reduced maternal care quality, notably licking and grooming. Offspring from and reared by 5-HTT-/- dams showed lower anxiety-, but not depressive-like behavior. Cross-fostering led to reduced body weight and GABA/glutamate- and HPA-axis-related signaling in all animals. Offspring from 5-HTT-/- dams reared by 5-HTT+/+ dams presented the highest serotonin/tryptophan turnover and lowest neuroplasticity marker levels in the medial prefrontal cortex. During pregnancy, 5-HTT-/- dams exhibited smaller embryos and robust alterations in the serotonergic system and BDNF levels of the placenta and offspring's embryonic brains.

Conclusion: This study provides novel evidence that the maternal 5-HTT genotype influences offspring's anxiety-like behavior through alterations in placental and early postnatal environments. These findings underscore the importance of combining maternal genetics and environmental factors to improve neuropsychiatric disorders' pathophysiology understanding.

Keywords: anxiety-like behavior; maternal care; medial prefrontal cortex; serotonin; serotonin transporter; placenta


♂ 5-HTT-/- × 5-HTT+/+ ♀ BD
♂ 5-HTT+/- offspring
5-HTT+/+ ♀ MCD
5-HTT-/- ♀ MCD
Non- + In-fostering 5-HTT+/+
MD 5-HTT+/+ & MCD 5-HTT+/+
Cross-fostering 5-HTT+/+
MD 5-HTT+/+ & MCD 5-HTT-/-
♂ 5-HTT+/+ × 5-HTT-/- ♀ BD
♂ 5-HTT+/- offspring
5-HTT-/- ♀ MCD
5-HTT+/+ ♀ MCD
Non- + In-fostering 5-HTT-/-
MD 5-HTT-/- & MCD 5-HTT-/-
Cross-fostering 5-HTT-/-
MD 5-HTT-/- & MCD 5-HTT+/+

Neuroscience

Neural Networks and Quantum Consciousness: Insights from ASD, Schizophrenia, and Telepathy

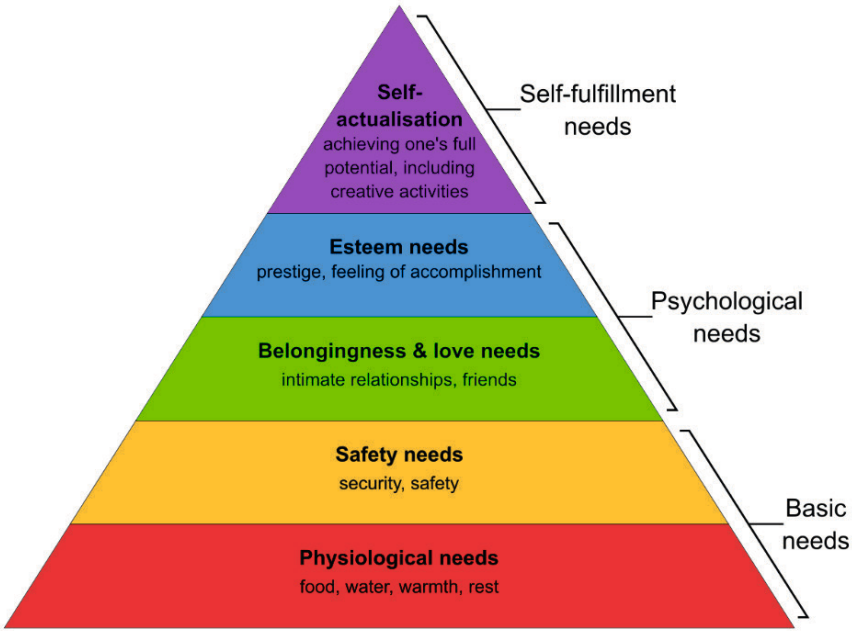
A.S. Kurian[1]

[1]Medical University Varna, Bulgaria

Introduction: Consciousness has traditionally been linked to cortical and subcortical connectivity, yet emerging evidence highlights the significant role of subcortical structures, particularly the caudate nucleus, putamen, and nucleus accumbens, which form part of the basal ganglia. These regions are crucial for cognitive functions, including movement and reward processing. Furthermore, the neural cytoskeleton, particularly within microtubules, incorporates quantum processes that contribute to learning and memory. This case report explores the intersection of neuroscientific findings from MRI studies, particularly in Autism Spectrum Disorder (ASD) and schizophrenia (SZ), with quantum mechanics theories. Additionally, children exhibiting telepathic abilities provide novel insights into consciousness beyond classical neural processing.

Case Presentation: This study investigates subcortical brain volume differences in adults with ASD and SZ. ASD shows volume differences in the left pallidum, thalamus, accumbens, and right amygdala, with a negative correlation between left amygdala volume and social cognition. SZ exhibits reduced volumes in the hippocampus, amygdala, thalamus, and accumbens, with a positive correlation between right caudate volume and full-scale IQ. These structures are critical for memory, emotion, and cognition. Intriguingly, some individuals with ASD exhibit telepathic abilities, suggesting a potential role for the basal ganglia in non-local information transfer. These findings imply a connection between structural brain variations and altered cognitive processing in both conditions, supporting the idea that consciousness may extend beyond the brain.

Conclusion: Consciousness may arise from a complex interplay of classical and quantum processes. Thalamocortical interactions form a “dynamic core” for conscious experience, binding information through coupled oscillators. Within neurons, microtubules may act as quantum processors, influencing consciousness, as seen with anaesthesia and their role in spatial awareness. Some theories suggest microtubules could even enable precognition. Telepathic phenomena and the “universal mind” concept suggest consciousness may extend beyond the brain. Precognition may be an evolutionary advantage through an adaptive advantage for survival through the ability to anticipate dangers and secure resources. Neuropsychiatric conditions like autism and schizophrenia may offer insights into the neurological basis of consciousness, though research findings remain heterogeneous. Further investigation into subcortical structures, quantum mechanisms, and non-local information transfer is essential for a deeper understanding of consciousness.


Self-actualisation
achieving one's full potential, including creative activities
Esteem needs
prestige, feeling of accomplishment
Belongingness & love needs
intimate relationships, friends
Safety needs
security, safety
Physiological needs
food, water, warmth, rest
Self-fulfillment needs
Psychological needs
Basic needs

Neuroscience

Anti-Alzheimer's Potential of Royal Jelly: Antioxidant Properties, Cholinesterase Inhibition, and In Silico Studies

F. Bargharary[1], M. Khanavi[1], Y.A.T. Ahmaditabatabaei[1], M. Saeedi[1], K. Marefat[1], A. Iraji[1]

[1]Tehran University of Medical Sciences, Iran

Introduction: Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterized by memory loss and cognitive decline. Its pathology involves oxidative stress, amyloid-beta plaques, tau protein tangles, and cholinergic dysfunction. Given the limitations of current treatments, natural products such as royal jelly (RJ), recognized for their antioxidant and neuroprotective properties, provide promising therapeutic alternatives. This study evaluates the antioxidant activity, cholinesterase inhibitory effects, and molecular interactions of RJ components with AD-related targets.

Methods: Royal jelly samples were sourced from certified suppliers and lyophilized for uniformity. Antioxidant capacity was assessed using the DPPH radical-scavenging assay, with absorbance measured at 517 nm. Results were expressed as IC50 values (µg/mL). Enzyme inhibition studies targeted acetylcholinesterase (AChE) and butyrylcholinesterase (BuChE) using Ellman's method, wherein hydrolysis of acetylthiocholine iodide and butyrylthiocholine iodide was monitored spectrophotometrically at 412 nm. The inhibitory concentrations were determined in triplicates for accuracy. For in silico analyses, major bioactive components of RJ—10-hydroxy-2-decenoic acid (10-HDA) and major royal jelly proteins (MRJPs)—were identified via published databases. Molecular docking was conducted using AutoDock software against AChE, BuChE, and tau proteins. Ligand-protein interactions, binding affinities, and key residues involved in stabilization were analyzed and visualized with PyMOL.

Results: RJ demonstrated robust antioxidant activity with an IC50 of 45.3 µg/mL. Enzyme inhibition tests revealed dose-dependent suppression, with maximum inhibitory effects of 78% for AChE and 72% for BuChE. Molecular docking indicated high binding affinities for 10-HDA and MRJPs with AChE (−8.6 kcal/mol) and tau proteins (−9.1 kcal/mol), forming stable hydrogen bonds and hydrophobic interactions with critical residues.

Conclusion: These findings emphasize RJ's potential as a multi-target therapeutic agent for AD by mitigating oxidative stress, inhibiting cholinesterase activity, and directly interacting with pathological targets. Further preclinical studies are warranted to translate these effects into clinical benefits.

Keywords: Royal jelly, Alzheimer's disease, acetylcholinesterase, antioxidant activity, in silico docking, 10-HDA, MRJPs

Multifaceted impact of Ω3-polyunsaturated fatty acids on Kv1.2 channels

M. A. Isacov[123], L. Wang[3]

[1]Sant'Anna School of Advanced Studies, Health Science Interdisciplinary Center, Pisa, Italy. [2]University of Pisa, Department of Translational Medicine, Pisa, Italy. [3]Hospital for Sick Children, Department of Brain and Mental Health, Toronto, Canada

Neuroscience

Introduction: Kv1.2 is a voltage-gated potassium channel of the Shaker family, and plays a critical role in neuronal physiology by regulating membrane potential, action potential firing, and neurotransmitter release. Mutations in the KCNA2 gene encoding Kv1.2 are linked to several neurological disorders, including epilepsy, ataxia, and autism spectrum disorders. Docosahexaenoic acid (DHA), an omega-3 polyunsaturated fatty acid, has demonstrated therapeutic potential in managing conditions such as autism, ADHD, and refractory epilepsy, likely through its influence on microglia, barin innate immune system, and neuronal plasticity. At physiological concentrations (50 nM), DHA acts as a positive allosteric modulator of Kv1.2, facilitating channel activation and slowing down deactivation kinetics, but its effects at pharmacological levels (50 mM) remain less well-characterized.

Methods: Here, using a stable CHO cell line expressing wild-type Kv1.2 channels, we performed patch-clamp experiments in calcium-free conditions to investigate the dose-dependent effects of DHA on Kv1.2 currents.

Results: At 50 µM, DHA significantly reduced Kv1.2 current amplitude following prolonged depolarizing pulses (+90 mV, 500 ms). This reduction was characterized by two distinct phenomena: a reduction in the initial peak current amplitude, suggesting closed-channel block, and a diminished inactivation time constant, potentially linked to incomplete recovery rather than open-channel block.

Conclusion: Our findings reveal that DHA exerts dual and opposing effects on Kv1.2 at physiological and pharmacological concentrations. This highlights the nuanced role of omega-3 fatty acids in modulating neuronal excitability and may explain variable responses to ketogenic diets in refractory epilepsy. Understanding these concentration-specific effects on Kv1.2 could inform the development of targeted therapies for neurodevelopmental and neurological disorders.

Keywords: mega 3, epilepsy, ketogenic diet

Neuroscience

Recurrent Cage Migration and Pseudoarthrosis Development Following Lumbar Stabilization: Lessons from Triple Surgical Revision – A Case Report

P. Penchev[1], P. P. Petrov[2], D. Haritonov[3]

[1]Faculty of Medicine, Medical University of Plovdiv, Bulgaria. [2]Department of Anatomy, Histology and Embryology, Medical University of Plovdiv, Bulgaria. [3]Neurosurgery clinic, MHAT „Heart and Brain“, Pleven, Bulgaria

Introduction: Posterior lumbar interbody fusion (PLIF) and transforaminal lumbar interbody fusion (TLIF) are widely used in the surgical treatment of lumbar degenerative diseases. Common complications of these procedures include nerve injury, screw or nut loosening, cage migration, and adjacent segment disease. While interbody cage migration and pseudoarthrosis are rare, they are serious complications that require revision surgery. We aim to present a complex case of recurrent cage migration at L5-S1, leading to pseudoarthrosis and multiple revision surgeries.

Methods / Results: A 51-year-old female underwent L4-L5-S1 screw stabilization with an interbody cage for spondylolisthesis. Postoperatively, she experienced low back pain radiating to both legs. After undergoing physiotherapy, her symptoms initially improved, and she was discharged. However, six months later, she developed recurrent low back and leg pain. MRI revealed cage migration into the spinal canal, requiring surgical repositioning. Despite initial symptom relief, the patient experienced a relapse of pain three months postoperatively. Follow-up MRI confirmed recurrent cage migration and pseudoarthrosis at L5-S1. The imaging findings suggested that the cage had been undersized, leading to instability and repeated migration. A third surgery was performed at another hospital, where the previous stabilization was removed via a posterior approach. A new cage was then implanted using anterior lumbar interbody fusion (ALIF) with a microsurgical technique. Following the final revision, the patient underwent physiotherapy, achieved significant pain relief, and was discharged on the 5th day.

Conclusion: Proper implant selection, particularly cage sizing, prevents migration and pseudoarthrosis. Undersized cages may lead to instability, risking patients to implant failure and revision surgery. This case highlights the importance of cautious preoperative planning and the role of anterior approaches like ALIF in revision surgery for failed posterior fusion. A multidisciplinary team, including physiotherapy, is crucial in optimizing patient outcomes.

Keywords: cage migration, pseudoarthrosis, lumbar fusion, ALIF, spondylolisthesis

Complete blood count (CBC) inflammatory ratios as prognostic predictors in elderly acute ischemic stroke

A. Rezaei[1]

[1]Tehran University of Medical Sciences, Iran

Introduction: Acute ischemic stroke (AIS) is a leading cause of long-term disability among elderly patients. Identifying reliable biomarkers to predict functional outcomes is critical for optimizing treatment strategies. The neutrophil-to-lymphocyte ratio (NLR) and lymphocyte-to-monocyte ratio (LMR), as markers of systemic inflammation, have shown potential prognostic value in various conditions. However, their utility in elderly AIS patients remains underexplored. This study aimed to evaluate the prognostic significance of NLR and LMR in predicting unfavorable outcomes in elderly AIS patients.

Methods: We conducted a retrospective cohort study involving 318 elderly AIS patients admitted to a tertiary care center. Baseline demographic, clinical, and laboratory data were collected at admission. NLR and LMR were calculated from complete blood count results. The primary outcome was functional status at three months, categorized as favorable (modified Rankin Scale [mRS]<3) or unfavorable (mRS≥3). Multivariate logistic regression models were used to assess associations. Predictive performance was evaluated using receiver operating characteristic (ROC) curve analysis, with area under the curve (AUC) values reported.

Results: Of the 318 patients, 58.5% experienced unfavorable outcomes (mRS≥3) at three months. The mean NLR was significantly higher in patients with unfavorable outcomes compared to those with favorable outcomes (4.5±1.8 vs. 3.1±1.3, $p<0.001$). The mean LMR was significantly lower in patients with unfavorable outcomes (2.9±0.6 vs. 3.8±0.8, $p<0.001$). Multivariate logistic regression revealed that elevated NLR was associated with a 42% increase in the odds of an unfavorable outcome (adjusted odds ratio [aOR] 1.42; 95%CI: 1.18–1.70; $p<0.001$), while lower LMR reduced the odds by 22% (aOR 0.78; 95%CI: 0.65–0.93; $p=0.007$). ROC curve analysis demonstrated that NLR alone had a predictive AUC of 0.79, while LMR alone yielded an AUC of 0.74. Combining NLR and LMR improved predictive accuracy to an AUC of 0.82, demonstrating excellent discrimination between favorable and unfavorable outcomes.

Conclusion: NLR and LMR are valuable independent predictors of unfavorable outcomes in elderly AIS patients. Their combination enhances predictive accuracy, offering a simple, cost-effective tool for early risk stratification. These findings support the integration of inflammatory biomarkers into routine AIS management and highlight the need for further studies exploring anti-inflammatory interventions.

Neuroscience

Predicting rebleeding in subarachnoid hemorrhage: a multi-center machine learning study

A. Rezaei[1]

[1]Tehran University of Medical Sciences, Iran

Introduction: Subarachnoid hemorrhage (SAH) is a life-threatening condition with high morbidity and mortality, often complicated by rebleeding within the first 48 hours. Early prediction of rebleeding is critical for timely intervention, but current methods lack precision. This study aims to develop and validate a multimodal machine learning (ML) model to predict rebleeding within 48 hours in 500 cases of SAH using clinical, radiological, and laboratory data.

Methods: This prospective multicenter study enrolled 500 patients with confirmed SAH. Data included: (1) clinical variables (age, Glasgow Coma Scale [GCS], blood pressure, comorbidities), (2) radiological features from CT scans (Fisher grade, intraventricular hemorrhage, hemorrhage location), and (3) laboratory data (coagulation profiles, inflammatory markers such as C-reactive protein [CRP]). A multimodal ML model was developed using convolutional neural networks (CNNs) for CT image analysis and ensemble methods (Random Forest, XGBoost) for integrating clinical and laboratory data. The primary outcome was rebleeding, defined as a new hemorrhage on follow-up CT scans within 48 hours. Model performance was evaluated using the area under the curve (AUC), sensitivity, and specificity. Feature importance was assessed using permutation importance and logistic regression analysis, with odds ratios (OR) and 95% confidence intervals (CI) reported.

Results: The ML model achieved an AUC of 0.90 (95%CI: 0.87–0.93), with sensitivity of 84% (95%CI: 80–88%) and specificity of 86% (95%CI: 82–90%). Key predictors of rebleeding included Fisher grade (OR= 1.95, 95%CI: 1.60–2.38, p=0.002), intraventricular hemorrhage (OR= 1.75, 95%CI: 1.40–2.18, p=0.003), and elevated CRP levels (>10 mg/L, OR= 1.82, 95%CI: 1.45–2.28, p=0.003). Permutation importance analysis confirmed the significance of radiological features, with Fisher grade and intraventricular hemorrhage contributing 35% and 28% to the model's predictive power, respectively.

Conclusion: This study demonstrates the feasibility of a multimodal ML model for predicting rebleeding within 48 hours in SAH patients using CT scans, clinical data, and laboratory markers. By leveraging readily available data, the model provides a robust tool for risk stratification, enabling timely interventions and improving patient outcomes. This approach has the potential to enhance SAH care by providing clinicians with a reliable, data-driven tool for early decision-making.

Keywords: Subarachnoid hemorrhage, Machine learning, Rebleeding prediction, Artificial intelligence

PREVENTION & LIFESTYLE

The incidence of chronic kidney disease between nonalcoholic fatty liver and without nonalcoholic fatty liver patients with type 2 diabetes mellitus in Kyrgyz population

M. Uzair[1], A. Moldobaeva Z.[1]

[1]International Higher School of Medicine, Bishkek, Kyrgyzstan

Prevention & Lifestyle

Introduction: The number of people with diabetes mellitus (DM), is expected to reach 783 million by 2045, making it one of the 21st century's fastest-growing global health catastrophes. Among people with type 2 diabetes mellitus (T2DM), nonalcoholic fatty liver (NAFLD) is extremely common. Diabetes and obesity are significant risk factors for NAFLD development. The prevalence of chronic kidney disease (CKD), is higher in people with NAFLD.

Methods: Study design: cross-sectional retrospective. The data was obtained between 2023 and 2025 from Vedanta University Hospital in Bishkek, Kyrgyzstan. Our study included 100 patients over 50 with T2DM. Glycated hemoglobin (HbA1C), lipid profile and creatinine were determined in the blood tests, and the body mass index (BMI) was calculated using anthropometric data. The estimated glomerular filtration rate (eGFR) level was utilized to quantify renal impairment. The eGFR was computed using the CKD-EPI. The Mann-Whitney U test was used to determine whether there was statistical difference between the two groups in these parameters. The Mindray DC 70 2021 model year of the equipment was used for liver ultrasounds as one of the instrumental research approaches. Patients are divided into 2 groups with non- alcoholic fatty liver disease and without non-alcoholic fatty liver disease.

Results: Our study did not reveal statistically significant differences in the following parameters: HbA1c, eGFR and lipid profile. There were statistically significant variations in BMI; the group with NAFLD had a considerably higher BMI (P<0,005).

Conclusions: We come to concluded that additional databases are needed to observe the relationship between NAFLD and CKD in patient with T2DM. Nonetheless, we discover a correlation between obesity and NAFLD in individuals with T2DM.

Keywords: Type 2 diabetes mellitus, Non-alcoholic fatty liver, Chronic kidney

Prevention & Lifestyle

Preparation and evaluation of kojic acid nanofibers for skin patch development in Acne treatment.

M. Hassanpour Amnieh[1], A. Falahati Marvast[1]

[1]Department of Pharmacy, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.

Introduction: Acne is a common dermatologic condition with an estimated prevalence of 70 to 87%. Acne has been shown to have a significant impact on patient quality of life and mental health, especially as inflammatory lesions typically occur on cosmetically sensitive areas with the potential for permanent scarring. Kojic acid with antimicrobial and anti pigmentation effects can be useful in treatment of acne .Electrospinning is a technique for creating continuous nanofibers networks that can architecturally be similar to the structure of extracellular matrix (ECM)

Methods: To preparation the efficient delivery of kojic acid we formulated kojic acid in chitosan and polyvinyl alcohol(PVA) nanofiber. Then we made chitosan/PVA/PEO nanofiber with electrospinning method. Nanofiber size, drug loading and pattern of release were evaluated by dynamic light scattering, and release test respectively.

Results: The results indicated Co-formulation of kojic acid and chitosan resulted in formation of the nanofiber with the range size of70-250nm. These nanofibers were suitable to release of kojic acid as long as 1400 min after in-vitro test with artificial membrane. The higuchi order release helps to make the constant medical effect on the acne during time.

Conclusions: According to the results, nanofibers containing chitosan ,polyethylene oxide, polyvinyl alcohol have bioadhesive properties ,due to the presence of polar group in their chemical structure. Also, the drug release of nanofiber follows the Fick's rule. So, kojic acid traces on acne.

Keywords: Kojic acid, Nanofiber, acne, Electrospinning, Polyvinyl alcohol, Polyethylene oxide

Evaluation of Medical Students' Lifestyle Problems and Their Impacts on Education and Future Careers in Medicine

S. Hasanzadea[1], A. Ghorbaniazara[1]

[1]Department of General Medicine, Azerbaijan Medical University, Azerbeidzjan

Prevention & Lifestyle

Introduction: Since medicine has always been one of the most challenging majors, studying this field has always been accompanied by challenges. By studying and examining the lifestyles of students, problems that have become a crisis in some nations today can be prevented.

Methods: In this research, a survey and in-person and group interviews were conducted with students, professors, and university administration staff to obtain information about the lifestyle of students. We also learned about some of the challenges faced by students in cooperation with the University Psychology Center. Before collecting data, the necessary permissions were obtained from university officials, and personal information was not collected during the research. Everyone cooperated with us voluntarily.Issues such as sleep hours, nutrition, membership in voluntary organizations, use of social networks, academic obstacles, feelings of discomfort, and consumption of harmful products were examined.

Conclusions: The results showed that second- and fifth-year students feel the most discomfort because the volume of courses in these years is very high, and there are serious concerns about their future careers.The most common problems cited by respondents were financial problems, lack of experience, time management difficulties, long distance between their home and university, and lack of motivation. Unfortunately, most people who feel unwell avoid seeing a psychologist or psychiatrist because they don't want to jeopardize their future employment status. The study was not funded, and the researchers had no conflicts of interest.

Keywords: Medical student lifestyle, Academic challenges, Survey research, Academic obstacles, Time management, Student well-being, Psychological discomfort, Sleep hours, Motivation

Prevention & Lifestyle

Enhancing Chemotherapy Adherence through an mHealth Intervention: A Pilot Trial

D. Soltani[1], M. Saadatirad[1]

[1]Cancer Institute, Tehran University of Medical Sciences, Iran

Introduction: Medication adherence is crucial for optimal outcomes in cancer patients undergoing chemotherapy. However, challenges such as side effects, complex treatment regimens, and psychosocial distress can significantly hinder adherence. Electronic interventions have shown promise in improving adherence, but further investigation is needed in diverse populations. This study aims to evaluate the preliminary impact of a mobile health solution designed to enhance medication adherence through electronic notifications on chemotherapy outcomes in Iranian cancer patients.

Results: Preliminary analysis indicated that patients using the mobile health intervention demonstrated a 31% improvement in adherence to chemotherapy regimens, with adherence rates increasing from 65% to 89% ($P < 0.01$). Additionally, reported anxiety levels related to medication management decreased significantly, from a mean score of 6.5 to 3.2 on a 10-point scale ($P < 0.05$). Enhancements in quality of life were noted, with overall scores improving from 58 to 75 ($P < 0.01$). These findings suggest a positive impact of the mobile health intervention on both adherence and the overall patient experience.

Conclusions: The pilot study provides encouraging evidence that a mobile health intervention can enhance adherence to chemotherapy among cancer patients. Future research should explore the long-term effects of such interventions and their applicability across various cancer types and demographic groups to optimize patient outcomes.

Healthcare experiences of Afghan immigrant families: assessing satisfaction in a pediatric outpatient clinic

M.M. Mohammadi[1]

[1]School of Medicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

Prevention & Lifestyle

Introduction: Patient satisfaction is a critical indicator of healthcare quality, influencing treatment outcomes and resource utilization. Immigrant populations, particularly in countries hosting large numbers of refugees, often face healthcare access barriers, impacting satisfaction and health outcomes. Iran, one of the top 10 refugee-hosting countries, has a significant Afghan immigrant population. This study aimed to assess the satisfaction of Afghan immigrants with pediatric outpatient services at Firoozabadi Hospital in Tehran, Iran, and identify factors influencing their satisfaction.

Methods: A cross-sectional study was conducted from January to July 2023, involving 251 Afghan immigrant caregivers of children aged 0-18 years attending the pediatric outpatient clinic. Data were collected using the Patient Satisfaction Questionnaire (PSQ-18) and a personal information checklist through oral interviews. The PSQ-18 assessed satisfaction across seven subscales: general satisfaction, technical quality, interpersonal manner, financial issues, time spent with the doctor, communication, and accessibility/convenience. Statistical analyses were performed using SPSS version 26, with non-parametric tests applied due to non-normal data distribution.

Results: The overall satisfaction score was 72.95±12.57 out of 90. Financial issues received the lowest satisfaction scores (6.19±3.00), while interpersonal manners scored the highest (9.26±1.90). Among respondents, 48.6% (n=122) were completely satisfied, 32.7% (n=82) were satisfied, 10.6% (n=27) had no opinion, and 8.8% (n=22) expressed dissatisfaction. Notably, 92% (n=231) of participants lacked health insurance, and 30.7% (n=77) lacked identification documents. Statistical analysis revealed no significant correlations between satisfaction levels and income (p=0.94), education (p=0.288), possession of identification documents (p=0.395), or length of stay in Iran (p=0.98). However, caregivers other than the child's parents reported significantly higher satisfaction levels (p=0.01). Subgroup analysis showed that 29.9% of participants without health insurance expressed dissatisfaction, compared to only 5% of those with insurance.

Conclusions: The study highlights high overall satisfaction among Afghan immigrants with pediatric outpatient services, particularly regarding interpersonal interactions. However, financial issues remain a significant concern, exacerbated by the lack of health insurance. Policymakers and healthcare administrators should prioritize improving access to health insurance for immigrants to address financial barriers and enhance satisfaction. These findings underscore the importance of culturally sensitive healthcare delivery and targeted interventions to improve immigrant healthcare experiences.

Prevention & Lifestyle

What factors influence student engagement and perceived effectiveness in peer-led medical teaching sessions

A. Bose-Mandal[1], A. Sharma[1]

[1]University of Buckingham Medical School, United Kingdom

Introduction: Student engagement and perceived effectiveness are critical factors in the success of peer teaching, a well-established practice in undergraduate education. Widely employed across professional degrees, peer teaching is a key component of medical education, integrated into all UK medical schools through formal programs, informal networks, or medical societies [1]. Understanding the elements that influence engagement and effectiveness not only enhances the learning experience for students but also supports peer educators in refining their teaching skills, which are invaluable in their future careers [2].

Methods: Eighteen modules were delivered by second- and third-year medical students to 282 attendees during an October 2023 revision series. A post-session Google Forms survey was conducted to identify key factors that enhanced student engagement with the taught content, providing insights into the effectiveness of peer-led teaching ahead of the UBMS end-of-year examinations.

Results: The study, which involved 282 respondents, identified key factors influencing student engagement and perceived effectiveness in peer-led medical teaching. Confidence levels significantly increased, with scores rising from an average of 6.09/10 before the session to 7.97/10 afterward. Clear communication was crucial, as 58.5% strongly agreed that the teacher communicated effectively. Additionally, 93.1% of respondents found the session engaging and felt comfortable asking questions, underscoring the importance of teacher clarity and interaction in enhancing engagement and the overall effectiveness of peer-led teaching sessions.

Conclusions: Overall, this revision series appeared to aid the preparation of UBMS students for their end of year exams. Results showed that peer teaching increased respondents' confidence in their learning of modules by 31% and students feedbacked that they were 86.2% more likely to return for future teaching sessions which in turn reflected the increased level of student engagement. The factors that appeared to influence student engagement included the relative informality of the sessions, the experience of the teaches and the relatability of vignettes and content.

Perspectives of Medical Students on Methylphenidate: Academic Doping or a Harmless Focus Enhancer?

Y.B.Topkarci[1], B.Onal[2]

[1]Gazi University, Faculty of Medicine, Turkey. [2]Biruni University, Faculty of Medicine, Medical Pharmacology Department, Turkey

Prevention & Lifestyle

Introduction: Over the past decade, the use of psycho-stimulants typically prescribed for Attention Deficit Hyperactivity Disorder (ADHD), such as methylphenidate (MP) has become popular among undergraduate students to enhance academic performance. Despite potential health and legal repercussions, the misuse of these medications has become a significant public health issue not only within the general population but particularly within medical schools across Turkey. The purpose of this study was to determine the frequency of MP misuse among medical students in Turkey and the associated triggers that drove them to appeal to such prescription drugs.

Methods: A survey of 418 medical students (257 female, 161 male), covered addiction history, physician-recommended ADHD medication, sharing and recommending MP among peers, initial exposure to MP misuse information, reasons for non-prescription MP use, duration of misuse, perceptions of MP's addictive potential, and ethical views on MP use for exams.

Results: The findings revealed that senior students showed higher awareness and earlier initiation of MP misuse compared to younger students ($p < 0.05$). Residing in student housing emerged as a significant trigger for exposure to and subsequent misuse of nonmedical prescription MP ($p < 0.05$). Both MP misusers and non-users acknowledged the MP's addictive nature. Peer influence was the primary factor for initial recommendations of MP misuse ($p < 0.05$).

Conclusions: While academic achievement appears to be the primary motivator for MP misuse, effectiveness of this practice in non-ADHD students is uncertain. Proactive measures are crucial to curb such misuse, particularly among medical students, to prevent a future global health crisis.

Keywords: Attention Deficit Hyperactivity Disorder, Methylphenidate, Misuse, Medical School Students, Addiction

Prevention & Lifestyle

Stress and Self-Care: Unraveling the Impact on Sexual Desire in Men with Type 2 Diabetes

A. Sharifi[1], N. Rahimizadeh[1]

[1]Shiraz University of Medical Sciences, Iran

Introduction: Type 2 diabetes mellitus (T2D) accounts for about 90% of diabetes cases, with studies indicating that around 50% of men with diabetes experience sexual dysfunction. While the impact of T2D on organic sexual dysfunction is well-documented, the relationship between perceived stress and sexual desire—a precursor to organic dysfunction—remains underexplored. Sexual well-being is crucial for both mental and physical health; however, cultural issues often hinder open discussions about sexual problems. Moreover, the high prevalence of perceived stress among diabetic patients may negatively influence psychological well-being and glycemic control, further impacting sexual health. This study evaluates the effect of perceived stress and self-care behaviors on sexual desire in patients with T2D, highlighting its significance for overall sexual health.

Methods: This cross-sectional study involved 303 male patients with T2D. Participants completed three validated questionnaires: the Diabetes Self-Care Behaviors Questionnaire, Halbert's Sexual Desire Level Questionnaire, and Cohen's Perceived Stress Questionnaire.

Results: Demographic data indicated a mean age of 53.9 ± 10 years and a mean HbA1c of 8.7%. Our analysis revealed that lower sexual desire was significantly associated with poorer self-care behaviors($p \leq 0.001$) and higher perceived stress ($p \leq 0.001$). Additionally, a significant negative relationship was identified between self-care and perceived stress ($p \leq 0.001$, CC:-0.21). Notably, each one-unit increase in perceived stress resulted in a decrease in sexual desire of -0.51 (95% CI -0.64, -0.36), while each one-unit increase in HbA1c led to a decrease of -1.28 (95% CI -1.91, -0.66).

Conclusions: Self-care behaviors are essential for managing T2D and mitigating complications, including sexual dysfunction. Our findings suggest that poor self-care and elevated perceived stress levels adversely affect sexual desire in men with T2D. Poor self-care contributes to lower glycemic control, impairs blood supply to sexual organs, and disrupts hormone transmission. Increased perceived stress not only diminishes sexual desire but also undermines self-care behaviors, creating a detrimental cycle. Therefore, promoting self-care and stress management may enhance both psychological and physical well-being in men with T2D, specifically regarding sexual desire.

Keywords: Type 2 Diabetes Mellitus, Sexual Dysfunction, Sexual Desire, Perceived Stress, Self-Care Behaviors, Sexual Health

Sleep to Succeed: The Power of Sleep in Academic Performance and Emotional Well-being of Medical Students

S.H. Abraham[1], A.George[1], S.Agouzzal[1], et.al.

[1]West China School of Medicine, Sichuan University, China

Prevention & Lifestyle

Introduction: Adequate sleep is essential for cognitive functions such as memory, attention, and decision-making. Inadequate sleep often leads to drowsiness, poor concentration, and low mood, which negatively affects grades and overall well-being. Medical students face intense schedules and rigorous study demands, making them particularly vulnerable to sleep deprivation. This study aimed to investigate the relationship between sleep patterns and academic performance among medical students, exploring how sleep deficits correlate with mental breakdowns and mood stability.

Methods: A cross-sectional study utilizing a questionnaire that models the Pittsburgh Sleep Quality Index (PSQI) was conducted with the participation of 98 undergraduate medical students. The survey comprised of 18 questions relating to
sleep patterns, academics, and emotional well-being; which was distributed to students of West China School of Medicine through WeChat social media platform. Data collected was analysed using SPSS ver. 29.0 (IBM); the Pearson chi-square
test was used to establish significance.

Results: 43.3% sleep 5-6 hours per night, below the National Sleep Foundation (NSF) recommended amount for optimal cognitive functioning, while only 8.3% achieve >7 hours. Students sleeping 3-5 hours have more mental breakdowns compared to those sleeping 7-8 hours. Shorter sleep (<6 hours) leads to negative moods, while 7-8 hours promotes positive moods. Academic achievement is highest (66.7%) among students sleeping 7-8 hours, compared to those that sleep (16.7%) for 3-5 hours ($P<0.001$, 95% CI=0.72-0.86). About 67.0% of students take naps; naps may compensate for insufficient nighttime sleep. 67.2% identify 6-8 hours of sleep as optimal for personal improvement.

Conclusions: The findings highlight the profound impact of sleep duration, patterns, and consistency on medical students' mental well-being and academic success.Many students suffer from suboptimal sleep, leading to impaired mood, reduced concentration, and heightened stress levels. This underscores the importance of integrating sleep education into the medical curriculum to empower future healthcare providers with tools to prioritize their own well-being. Investment in sleep awareness can ripple into better patient care and healthier lives. Moreover, further research into targeted, evidence-based interventions is imperative to combat stress, improve sleep hygiene, and prevent mental burnout.

Keywords: Sleep Deprivation, Medical Students, Academic Performance, Emotional Well-Being, Sleep Patterns

Prevention & Lifestyle

The impact of stress on medical students' transfer exam results

P. Kyiko[1], Y. Volkova[1]

[1]Kharkiv National Medical University, Kharkiv, Ukraine

Introduction: The transfer exams causes to the maximum psychological and emotional stress in the students before their conduct. The aim of our study was to determine the most informative prognostic factor of exam results.

Methods: 60 students with an average score of 187.4±2.6 ECTS were divided into 2 groups, randomized according to the level of personal anxiety (PAI): Group I, 30 students, average PAI level 27.1±2.2 points, who completed the preparation an 36 hours before the exam, Group II, 30 students, average PAI level 26.4±1.9 points, who completed the preparation an 12 hours before the exam. In each group, an hour before the examination, the reactive anxiety (RAI)level was determined by the questionnaire STAI and the number of micronuclei in buccal epithelial (BE) cells. To prepare the preparation, BE cells were collected from the inner side of each student's cheek with a sterile spatula and applied to a glass slide. Micronuclei were counted using microscopy.

Results: According to the results of the study, significant differences ($p<0.05$) were found between the average RAI level one hour before the exam in groups I (52.1±4.4 points - high) and II (38.6±2.1 points - moderate). A direct strong correlation was established between the RAI level in points and the number of BE micronuclei in students of group I $r = 0.87$ and a direct weak correlation in students of group II $r = 0.32$. A strong negative correlation was found between the level of RAI and the number of points obtained on the exam in students of group I (average score 169.4±6.1 points), $r = – 0.84$, in group II this relationship was identical, $r = – 0.86$ with a significantly ($p<0.05$) better average score on the exam, 192.2±4.1.

Conclusions: Completing exam preparation 36 hours before the exam significantly improves exam results, reduces reactive anxiety, and reduces stress levels in students. Completing preparation 12 hours before the exam increases stress levels and negatively affects exam results.

Keywords: Reactive Anxiety, Buccal Epithelial Cells, Exam Results

Emphysematous Pyelonephritis in a Child with Diabetes: A Case Report Emphasizing Timely Intervention and Prevention of Complications

M. Ghanbari Saray[1], M. Ghods[1], M. Hassan Ali[1]

[1]Azerbaidjan Medical University, Azerbaidjan

Prevention & Lifestyle

Introduction: Emphysematous pyelonephritis (EPN) is a rare, life-threatening condition characterized by gas accumulation within the renal parenchyma and surrounding tissues. While predominantly reported in adults, EPN is exceptionally rare in children, with only a few documented cases. We present a case of EPN in a diabetic child initially misdiagnosed with diabetic ketoacidosis (DKA). The aim of this study is to report a rare case of emphysematous pyelonephritis in a diabetic child, highlight the diagnostic challenges, and emphasize the importance of early recognition and treatment to prevent severe complications.

Methods: A 10-year-old boy with poorly controlled type 1 diabetes presented with abdominal and flank pain, fever, and fatigue. Initial assessment suggested DKA, but further evaluation revealed no evidence of DKA. Urinalysis indicated active infection, and imaging (CT scan) confirmed gas within the pyelocaliceal system, consistent with EPN. The patient was treated with intravenous meropenemand vancomycin for seven days.

Results: The patient showed significant clinical improvement following antibiotic therapy. Repeat imaging revealed resolution of gas within the renal system. He was discharged with normal kidney function and no residual complications.

Conclusions: This case underscores the importance of considering emphysematous pyelonephritis in diabetic children, even when initial symptoms mimic DKA. Early diagnosis and prompt treatment with broad-spectrum antibiotics are crucial to prevent morbidity and mortality. Strict glycemic control and regular monitoring of urinary tract infections in diabetic children are essential for prevention.Clinicians should maintain a high index of suspicion for EPN in diabetic children presenting with atypical abdominal or flank pain, as delayed diagnosis can lead to severe complications such as sepsis or renal failure.

Keywords: Emphysematous Pyelonephritis, Diabetes Mellitus, Child, Antibiotic Therapy, Diabetic Ketoacidosis

Prevention & Lifestyle

Using School Absenteeism to Predict Acute Respiratory Infection Rates in Primary School-Aged Children

A. Rus[1], C. de Korne[1]

[1]Julius Center for Health Sciences and Primary Care, UMC Utrecht, The Netherlands

Introduction: School-aged children play a key role in the transmission of respiratory pathogens due to their frequent interactions in educational settings and beyond. Consequently, monitoring acute respiratory illness (ARI) rates in this group could be a valuable component of syndromic community surveillance. School absenteeism has emerged as a promising proxy to monitor ARI rates in school-aged children. This study assessed the relationship between primary school absenteeism and ARI rates in both school-aged children and the broader community and explored how absenteeism data can enhance ARI rate forecasting through predictive modelling.

Methods: Weekly general practitioner (GP) visit rates for ARI in children aged 5–9 years from 2017-2023 were obtained from Nivel. Daily absenteeism records from 69 Dutch primary schools over 2017-2018, 2018-2019, and 2022-2023 school-years were obtained from TIG. Parents of absent students completed surveys from November to December 2023, and reported on absence duration and associated symptoms, allowing classification of absence as due to ARI or gastrointestinal (GE) infections. We analysed weekly time patterns of ARI and school absenteeism rates and used cross-correlation analysis to measure the strength and timing of their correlation. Predictive modelling of the ARI rates was performed using Autoregressive Integrated Moving Average (ARIMA) models, and ARIMA with eXogenous input (ARIMAX) models, which included school absenteeism as external regressor.

Results: Absenteeism data exhibited seasonal peaks corresponding to ARI trends. Cross-correlation analysis revealed a strong relationship between absenteeism and ARI rates ($r = 0.6$-0.7), with absenteeism matching or leading ARI trends by one week. Extending the ARIMA model to an ARIMAX model, by including current or lagged absenteeism rates, significantly improved ARI trend predictions. This demonstrated the added value of incorporating absenteeism for accurate forecasting of ARI rates.

Conclusions: School absenteeism data has potential to serve as a real-time, cost-effective tool for ARI surveillance. Integrating school absenteeism into predictive models for ARI rates may facilitate early public health interventions, enhancing outbreak mitigation and reducing healthcare burdens.

Keywords: School Absenteeism, Acute Respiratory Infections, Predictive Modelling, Syndromic Surveillance

The Influence of Social Determinants on Fatigue, Health-Related Quality of Life, and Flares in Patients with Inflammatory Bowel Disease: IBD-SocioScope

N. Al Kuhaili[1], H. Schaefers[1], Dr. P.J.W. Maljaars[1]

[1]Leiden University Medical Center, The Netherlands

Prevention & Lifestyle

Introduction: Fatigue is a prevalent and challenging symptom experienced by individuals with inflammatory bowel disease, which significantly impairs their health-related quality of life and daily functioning. Emerging evidence suggests that social determinants of health (SDoH), such as socioeconomic status, food security, and social support, may play a role in the progression of chronic conditions, yet their specific influence on fatigue and health-related quality of life in IBD remains poorly understood. This study aims to investigate the association between SDoH and the severity of fatigue in IBD patients, and to evaluate the impact on health-related quality of life and disease activity.

Methods: This cross-sectional, multicenter study was conducted at the Leiden University Medical Centre and Haaglanden Medical Centre, with a sample of 135 adult patients diagnosed with Crohn's disease, ulcerative colitis, or IBD-unclassified. Data were collected through patient-reported surveys and a review of electronic medical records. Fatigue was assessed using the FACIT-F, and health-related quality of life was measured using the EQ-5D-3L questionnaire. The study evaluated SDoH, including perceived socioeconomic status and food security, using validated screening tools. Clinical and biochemical disease activity were assessed using the HBI, SCCAI, and fecal calprotectin levels. Statistical analyses included multivariable regression models that accounted for key confounding variables.

Results: Higher SDoH total scores were significantly associated with increased fatigue severity ($\beta = 3.672$, 95% CI [0.816–6.528], P=0.016), independent of clinical disease activity. Patients with lower socioeconomic status and food insecurity exhibited higher fatigue levels and worse HRQoL ($P<0.05$). Older patients with stable socioeconomic conditions reported lower fatigue levels, whereas those with financial strain and limited social networks exhibited comparable fatigue severity to younger patients. Biochemical disease activity was not significantly associated with fatigue ($P>0.05$), reinforcing the influence of social determinants over inflammatory markers.

Conclusions: This study highlights the critical role of SDoH in shaping fatigue and HRQoL in IBD patients. Addressing socioeconomic challenges, may have a more significant impact on fatigue reduction and HRQoL improvement than clinical interventions alone. Future research is also needed to focus on longitudinal assessments and targeted interventions integrating social support and multidisciplinary care to enhance IBD management and patient outcomes.

Prevention & Lifestyle

A population-based preventive initiative for early identification of type 1 diabetes among asymptomatic children in northeastern Poland

F. Bossowski[1], M. Skorupska[1]

[1]Endocrinology and Diabetes with a Cardiology Unit, Department of Pediatrics, Medical University of Bialystok, Poland

Introduction: A population-based investigation focused on early detection of type 1 diabetes (T1D) was conducted in asymptomatic children from the Podlaskie region of Poland. This work extended the Pre-d1abetes Study, carried out between 2019 and 2023, in collaboration with 14 Polish diabetes centres. A total of 1,288 children aged 7 months to 18 years and with a positive family history of T1D were initially enrolled. Of those, 112 (8.69%) had positive 3-Screen ELISA results, and further analysis identified 76 children with multiple (two or more) autoantibodies, representing a pre-diabetes subgroup (5.9%). Recognizing high-risk groups is essential to implement preventive measures and minimize severe clinical manifestations of T1D.

Methods: Blood samples were collected and stored at -20°C. The 3-Screen ELISA (RSR Ltd, Cardiff, UK) was employed to detect T1D-related autoantibodies for screening. Whenever a sample tested positive, additional assessments were performed for anti-GAD, anti-ZnT8, anti-IA2, and anti-insulin (IAA) autoantibodies using both ELISA and RIA methods. This approach confirmed positivity and classified participants according to their risk level. In the pilot study phase, eight counties in the Podlaskie voivodeship were selected, and 3,000 children aged 1 to 9 years were screened.

Results: Out of the 3,000 children tested in the pilot study, 85 (3.46%) had positive 3-Screen ELISA results. In total, 0.44% showed two autoantibodies, and 0.65% had two or more, placing them at the highest risk for T1D. All children with positive findings will be followed up with a protocol, clinical visits, education on the early signs of diabetes, advice on low glycemic diet and exercise recommendations. This initiative is the first of its kind in Poland and represents significant progress in T1D prevention research across Europe.

Conclusions: The 3-Screen ELISA test identifies pre-clinical T1D before major metabolic issues arise. Early intervention, including education and preventive measures, lowers the risk of complications and supports the development of novel therapeutic strategies.

Keywords: Prevention, Type 1 Diabetes, Early Detection

Clinical profile of alcohol dependent patients according to Lesch typology one year after Covid- 19 pandemic-comparative study

J. Amidžić[1], L. Ljubotin[1], D. Kuljančić[1]

[1]Faculty of Medicine, University of Novi Sad, Serbia

Prevention & Lifestyle

Introduction: In addition to physical health, COVID-19 pandemic also affects people's mental health. It has contributed to the increase in general social tension. There was an increased use of alcoholic beverages as a form of self-help. Lesch typology classifies alcoholics into allergic, anxious, depressive and compulsive type. The aim of the study is to determine the sociodemographic and clinical characteristics of alcoholics one year after the COVID-19 pandemic.

Methods: The research was conducted as a retrospective cross-sectional study at the Department of the Addictions, Psychiatry Clinic of the Clinical Center of Vojvodina in Novi Sad. It included 218 patients who were admitted for treatment in the period from October 2022. to October 2023. In order to classify patients according to Lesh typology, MS Windows software available in the public domain was used.

Results: Of the 218 patients treated for alcohol addiction, 83% were male with an average age of 51 (SD±11). According to Lesch typology, 51% of patients belong to type III, 21% to type I, 17% to type II and 11% to type IV.

Conclusions: The majority of patients treated for alcohol addiction are male aged 35 to 65. According to Lesch typology, the most represented type was depressive, followed by allergic, anxious and the least compulsive type. The most prevalent psychiatric comorbidities are depression and suicidal tendencies.

Keywords: Alcoholism, COVID-19 Pandemic, Lesch Typology

Prevention & Lifestyle

Surfing on experiences: A qualitative evaluation of adolescents' experiences of skills training "Surfen op emoties" in the context of dialectical behavioral therapy

B. van Hulst[1]

[1]Leiden University Medical Center, The Netherlands

Introduction: Borderline personality disorder (BPD) profoundly impacts individuals' daily lives, manifesting in interpersonal challenges, impulsivity, and difficulties in emotion regulation. Additionally, it places a significant burden on the already overburdened (mental) health care system. Early and effective intervention during adolescence is crucial to prevent long-term adverse outcomes and reduce societal and health costs. A frequently used treatment approach is dialectical behavior therapy for adolescents (DBT-A), which includes a structured skills training program, in the Netherlands called "Surfen op emoties". While DBT-A skills training has shown beneficial impact, substantial interindividual differences exist in (long-term) outcomes and the underlying factors driving these differences remain unclear. To address this knowledge gap and to provide practical recommendations to enhance the efficacy of DBT-A, this qualitative study aimed to elucidate the experiences of adolescents with skills training "Surfen op emoties" to identify both helpful and non-helpful factors of the skills training program.

Methods: Audio-recorded semi-structured interviews were conducted with 5 of the 7 adolescents who were in the DBT-A program at LUMC Curium in October 2024. A thematic analysis was conducted to identify key themes.

Results: The results revealed helpful and non-helpful factors in three categories: (1) recognition in a group setting, (2) application of skills, and (3) the role of the skills trainer.

Conclusions: The research highlighted the indispensable role of the skills trainer in supporting participants both emotionally and practically, identified difficulties in transferring learned skills to daily life, and reveals that while group recognition could be beneficial, its impact is diminished by a reluctance to share personal experiences. The findings of this study highlight key areas and practical recommendations for improving DBT-A skills training, suggesting that optimizing the group setting and aligning exercises with real-life contexts can enhance the impact of skills training, ultimately contributing to more effective treatment for adolescents with (characteristics of) BPD, preventing long term adverse outcomes.

Keywords: Borderline Personality Disorder (BPD), Dialectical Behavior Therapy (DBT), Qualitative Research, Adolescence

Vestibular Recruitment Patterns in Ménière's Disease: A Comparative Analysis of the Post-Caloric Recruitment Inde x with Vestibular Neuritis Patients

T. Hemedi[1]

[1]Vrije Universiteit Amsterdam/Leiden University Medical Center, The Netherlands

Prevention & Lifestyle

Introduction: Ménière's disease (MD) is a chronic inner ear disorder, accompanied by vertigo attacks, tinnitus and aural fullness. The aim was to investigate vestibular recruitment in MD patients, a potential compensatory mechanism, through the Post-Caloric Recruitment Index.

Methods: The study included 177 subjects, 133 healthy controls from a previous study, 30 MD patients and 14 Vestibular Neuritis (VN) patients from the Apeldoorn Dizziness Center. Using PCRI calculations, differences in PCRI across MD patients, VN patients and healthy controls were compared. Additionally, relationships between PCRI and age, post-diagnosis time, and gender were analysed.

Results: Statistical analysis reveal significantly higher PCRI values in MD patients compared to VN patients ($p = 0.012$). No significant differences were found between controls and either patient group. Furthermore, no significant correlations were observed between the PCRI and age or post-diagnosis time, and no gender-based differences were detected in MD patients.

Conclusions: The PCRI reveals distinct patterns between MD and VN patients. Further prospective studies with larger cohorts and longitudinal measurements are required to fully explore the potential of the PCRI as a vestibular recruitment marker in MD patients.

Keywords: Ménière's disease (MD), Vestibular Recruitment, Post-Caloric Recruitment Index (PCRI), Vestibular Neuritis (VN)

Prevention & Lifestyle

Optimizing management of children with acute abdominal pain in primary care: design of a randomized trial evaluating the impact of a diagnostic strategy for appendicitis

E. Hogervorst[1], R. Venekamp[2], G. Knol-de Vries[1], T. Platteel[2], R. Watjer[3], N. Koning[3], D. Hurkmans[3], M. Numans[3], G. Blok, E. Naber[1], M. de Boer[1], K. Vermeulen, M. Hogenes, E. Hiddink, C. Tromp, R. Gorter[4], B. Holvast, J. Hulscher, C. Everts-Panman, C. van der Pal, G. Welker, A. van der Bilt, E. Deuring, M. Berger[1], E. Doganer, H. Burger[1], G. Holtman[1]

[1]Department of Primary and Long-term care, University Medical Center Groningen, the Netherlands
[2]Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, the Netherlands
[3]Department of Public Health and Primary care, Leiden University Medical Center, the Netherlands
[4]Department of Pediatric Surgery, Amsterdam University Medical Center, the Netherlands

Introduction: General practitioners often face difficulties in distinguishing acute appendicitis (AA) from common self-limiting conditions in children with acute abdominal pain. As a result, 19% of AA cases are not recognized during the first GP consultation, increasing the risk of perforation and potentially fatal peritonitis. Additionally, about 70% of children referred for acute abdominal pain will not have AA, leading to a burden on patients, families, and the healthcare system. To evaluate the impact of using a diagnostic strategy, consisting of a clinical prediction rule (cPR) including C-reactive protein point of care testing (CRP-POCT) for AA, among children presenting with acute abdominal pain in primary care, as compared with usual care.

Methods: This is a cluster randomized controlled trial performed in primary care. Children aged 4 to 18 years presenting at the GP with acute abdominal pain (≤ 7 days) will be included. GPs in the intervention group will use an externally validated cPR based on 7 symptoms and signs, implemented within the GP information system, followed by CRP-POCT in the medium risk group. GPs in the control group will provide care as usual, i.e. following recommendations of the Dutch College of GPs guideline 'abdominal pain in children', in which no specific referral criteria for AA are included and CRP-POCT is not recommended. The primary outcome is referral efficiency (proportion of non-referrals amongst patients with no evidence of AA during 30 days follow-up). Secondary outcomes are safety (proportion of referrals amongst AA patients during first consultation), proportion of children with CRP-POCT, proportion of children with planned reassessment, child anxiety, parent or child satisfaction, quality of life, and costs. We plan to include 566 children from 150 GP practices to determine an improvement in efficiency of 88% to 95%.

Conclusions: We hypothesize that the use of this diagnostic strategy will decrease the number of non-AA referrals, without delaying a diagnosis of AA.

Keywords: Appendicitis, Primary Care, Children, Clinical Prediction Rule, C-Reactive Protein

The complex relationship between substance use and schizophrenia: A case-based perspective

R. Bieś[1], M. Kalicka[2], M. Krzystanek[3]

[1]Doctoral School, Department and Clinic of Psychiatric Rehabilitation, Medical University of Katowice, Poland. [2]Student Scientific Association, Faculty of Medical Sciences in Katowice, Medical University of Katowice, Poland. [3]Department and Clinic of Psychiatric Rehabilitation, Department of Psychiatry and Psychotherapy, Medical University of Katowice, Poland

Prevention & Lifestyle

Introduction: The potential link between psychoactive substance use and the onset of psychotic disorders is widely studied, particularly in young adults. Research suggests that substances such as cannabis, MDMA, and hallucinogens may trigger transient psychotic episodes or contribute to the development of chronic psychiatric conditions like schizophrenia, especially in vulnerable individuals.

Case report: A 24-year-old man, previously mentally healthy and studying in the Netherlands, developed a psychotic episode. Since the age of 16, he had occasionally used marijuana, increasing to regular use in 2020. He had also experimented with amphetamines and hallucinogenic mushrooms. In December 2021, a few days after taking his first single dose of MDMA, he experienced first psychotic episode, characterized by grandiosity, reduced need for sleep, referential thinking and suicidal thoughts. His parents brought him back to Poland, where he was hospitalized in Chorzów in January 2022. He was diagnosed with paranoid schizophrenia and substance-induced mental disorders. Treatment with haloperidol, aripiprazole, and diazepam was discontinued due to side effects, and he discharged himself. In February 2022, he was re-hospitalized at a private clinic and treated with olanzapine and aripiprazole, leading to partial remission. However, affective flattening and motivational deficits persisted. A day therapy program followed, during which fluoxetine was introduced. In February 2023, after discontinuing medication and resuming substance use, he experienced a severe relapse requiring urgent hospitalization. Symptoms included hallucinations, persecutory delusions, and disorganized behavior. His aggressive behavior necessitated direct restraint. Treatment included olanzapine, risperidone, and ultimately clozapine (150 mg/day), leading to gradual improvement. He continues treatment with clozapine and amisulpride, aims to remain abstinent, and plans to resume his studies. Ongoing monitoring is necessary due to the risk of relapse.

Conclusions: This case highlights the association between psychoactive substance use and the onset of schizophrenia in a previously healthy individual. Relapses following substance use emphasize the need for long-term treatment adherence and substance avoidance in preventing psychotic episodes.

Keywords: Schizophrenia, Substance-Related Disorders, Psychotic Disorders

Prevention & Lifestyle

Knowledge and Attitude Regarding Electronic Cigarette Use Among Parents of High School Children: A Cross-Sectional Study

M. Mohammadi[1], M. Pashmchi[1], M. Mirzaei[1]

[1]School of medicine, Shahid Sadoughi University of Medical sciences, Yazd, Iran

Introduction: Electronic cigarette use has increased among adolescents and young adults globally. Parental knowledge and attitudes play an important role in shaping adolescent behavior and preventing social harms. This study aimed to assess the knowledge and attitudes of parents of high school students regarding electronic cigarettes.

Methods: This cross-sectional study was conducted on parents of 12th-year students from randomly selected high schools in Yazd, Iran, between December 2024 and January 2025. Data were collected using a self-reported questionnaire covering socio-demographic factors, tobacco use behaviors, knowledge, attitudes, and policy support. Descriptive analyses were performed to assess knowledge, attitudes, and policy support. Additionally, the association between different socio-demographic factors and knowledge was assessed using SPSS version 22.

Results: A total of 160 parents (125 mothers, 34 fathers) with a mean age of 42.70 ± 8.13 years participated in the study. Notably, only 19.38% (n=31) of parents had sufficient knowledge about electronic cigarettes, while 80.62% (n=129) had poor knowledge. Lower family income was significantly associated with lower knowledge levels (p-value < 0.05). Only 21.25% (n=34) of parents knew where to find appropriate resources regarding the effects of electronic cigarettes on the body, and 33.75% (n=54) knew how to talk to their children about the harms of electronic cigarettes. However, 81.87% (n=131) supported educating adolescents about the harms of electronic cigarettes, and 73.25% (n=117) supported adding nicotine-related education to school curricula. Moreover, more than 70% supported educating parents, and 68% supported adopting policies such as restricting advertising and online sales, increasing taxes, banning use in public places, and promoting educational campaigns.

Conclusions: This study showed that parental knowledge about electronic cigarettes and their risks was low. However, parents supported preventive policies. These results highlight the need for educational strategies to raise awareness and promote preventive measures. Such strategies may effectively protect adolescents from the harms of electronic cigarettes and pave the way for building a healthier society.

Patient and Public Involvement and Engagement in Research of Acute Health Conditions

I. Pósta[1], Prof. A. Janssens[1] , Prof. L. Bont[1]

[1]UMC Utrecht, The Netherlands

Prevention & Lifestyle

Introduction: Patient and Public Involvement and Engagement (PPIE) refers to conducting research 'with' or 'by' patients, relatives and members of the public. PPIE focuses on working towards meaningful researcher-patient partnerships; this collaborative research practice can enhance the quality, rigour and relevance of research. The World Medical Association, in the revised Declaration of Helsinki (2024), and the World Health Organization, in its 2024 convention, stimulate and support this practice of social participation. While PPIE is increasingly incorporated in health research on chronic conditions, there is limited or no information available about PPIE in studies focusing on acute conditions. The present study seeks to address this gap. This study aims to gain insight into PPIE in research on acute conditions, specifically respiratory diseases. It seeks to establish the extent researchers of acute health conditions involve patients and relatives in the research process, and to understand researchers' perspectives on collaborating with patients and relatives during the research process.

Methods: A short online survey is designed to gather insights from researchers and medical professionals specialising in acute health conditions regarding their current practices, experiences and perspectives about involving patients and relatives in their research. The survey is distributed at the 13th International Society for Influenza and other Respiratory Virus Diseases in Brazil, between 12-15th March 2025. Data will be analysed using descriptive statistics to illustrate uptake of PPIE practice and content analysis to identify patterns regarding their perspectives.

Conclusions: The study aims to advance the current understanding of PPIE in research on acute conditions and use this knowledge to support patient-researcher partnerships in this field of research.

Keywords: Patient and Public Involvement and Engagement; Acute Health Conditions; Patient-Researcher Partnership

Prevention & Lifestyle

Examining the relationship between oral and dental health-related quality of life and dental caries severity prevention

T. Karimi[1], S. Hashempour[2], A. Akbari[3]

[1]Azerbaidjan Medical University, Azerbaidjan

Introduction: Environment, habit, and knowledge can affect oral health, which is related to general health. The oral cavity has been described as "the window to general health" It is also the intersection of dentistry and medicine, semi-independent professions that share the common goal of improving patients' health and quality of life. Whatever your age, taking care of your mouth is crucial for your general health and well-being. Conditions such as dental caries (tooth decay), periodontal disease (gum disease), tooth loss, dry mouth, or oral cancer can affect your chewing function and nutritional intake. They can also impact your ability to interact socially and enjoy a good quality of life.

Methods: The study was conducted on 20 individuals (male and female) aged 20-50 years living in Baku. The sampling method was available and was selected from among those who were referred to a specialized dental clinic, and the samples were included in the study based on the inclusion and exclusion criteria.

Results: The results of this study underline the significant relationship between oral health-related quality of life (OHRQoL) and the severity of dental caries. The findings suggest that individuals with more severe dental caries experience a lower quality of life, particularly in areas related to pain, discomfort, and difficulty in eating or speaking. This reinforces the importance of early detection and effective prevention strategies in improving overall well-being.

Conclusions: This study highlights Early Childhood Caries (ECC) as a major health concern influenced by oral hygiene, diet, socioeconomic factors, and parental awareness. Preventive measures like fluoride, early dental visits, and education are crucial. ECC affects children's well-being, stressing the need for public health interventions

Keywords: Tooth Decay, Oral Hygiene, Quality of Life, Child, Prevention

Factors Influencing Length of Stay After Total Knee Replacement: Insights from Secondary Care Hospital

A. Almutlaq[1], A. Alsharari[2], A. Kamal[3]

[1]College of Medicine, King Faisal University, Saudi Arabia. [2]College of Medicine, Al-Jouf University, Saudi Arabia. [3]Department of Surgery, King Faisal University, Saudi Arabia

Prevention & Lifestyle

Introduction: Total knee Replacement (TKR) is an effective treatment for knee osteoarthritis (OA), offering pain relief and improved quality of life. Research shows that many elective TKR patients can safely have reduced lengths of stay (LOS) without affecting post-discharge outcomes, making LOS a key factor in care quality and costs. This study aims to evaluate LOS after primary TKR procedures, analyze readmission rates, and identify factors contributing to these readmissions.

Methods: This observational-analytical retrospective study evaluated patients undergoing total knee replacement at Prince Metaab Bin Abdulaziz Hospital from January 2019 to June 2024, excluding those under 15 and revision surgeries. A total coverage sampling technique was employed. Data were collected from electronic medical records, covering demographics, clinical metrics, and postoperative outcomes. Statistical analysis using normality tests, descriptive statistics, and a negative binomial regression to assess length of stay associations.

Results: This study examined 194 patients undergoing total knee replacement, with a median age of 63 years and predominantly female (77%). Most were obese (72%) or overweight (26%), and 15% were smokers. Common comorbidities included hypertension (49%) and diabetes (37%). Readmission occurred in 6.7% of cases, the most common reasons being infection, joint pain, and knee stiffness. ASA grade classification showed 6.7% grade 1, 65% grade 2, and 28% grade 3 patients. Postoperative complications occurred in 10% of patients.

Conclusions: This study showed that patients referred for total knee replacement experienced favorable outcomes, with a median postoperative hospital stay of four days and a low readmission rate. Key factors influencing the length of stay (LOS) included postoperative mobility, which was associated with a shorter stay, while dyslipidemia and smoking history were linked to longer stays. To improve outcomes, early mobility and shorter hospital stays can reduce the risk of infections and enhance recovery for total knee replacement patients.

REGENERATIVE MEDICINE

Immune-related cellular niches in the regenerating zebrafish heart

E. Razaghi Siahroudi[1], T. Gungoosingh[1], S. Tüzüner[1], K. Çil[1], C. King[1] and F. C. Simões[1]

[1]Institute of Developmental & Regenerative Medicine, Department of Physiology, Anatomy and Genetics, University of Oxford

Regenerative Medicine

Zebrafish have the remarkable ability to regenerate their heart after injury. Macrophages are critical in this process: they clear up dead cells and debris, participate in fibrosis but also contribute to regeneration through interactions with their tissue microenvironment. However, little is known about the precise regulation shaping macrophage identity and function in response to cardiac injury. By combining single-cell and spatial transcriptomics, we discovered the composition and activation states of various immune cell populations found in distinct spatial territories of the regenerating and homeostatic heart. We uncovered information about macrophage, dendritic, B and NK cell transcriptomes and their corresponding location within the cardiac tissue, including the epicardium, the outflow tract, as well as the injury-zone cardiomyocyte microenvironment. By reconstructing immune-related cellular niches across the regenerating and the homeostatic heart, we were able to discover the molecular signatures mediating such specific cell-cell communication, therefore contributing towards dissecting the regulatory programmes driving macrophage pro-fibrotic and pro regenerative phenotypes. Further analysis is underway to understand how specific microenvironmental signalling interactions may be enhanced or disrupted to support tissue regeneration. Our findings reveal how knowledge of cardiac niche-specific immune interactions could guide more effective pro-regenerative and anti-fibrotic therapies.

Keywords: Macrophage, Regulation, Cardiac, Regeneration

Differentiation of endocrine cells as a mechanism for beta cell loss in T1D – a lentiviral transduction approach to examine cell plasticity

L. Rusznyak[1]

[1]LMU Munich

Regenerative Medicine

Introduction: Diabetes mellitus is an incurable chronic disease characterized by short-term complications such as hypoglycemia and ketoacidosis and long-term micro- and macrovascular complications. In type 1 diabetes (T1D), the gradual loss of beta cells leads to impaired endogenous insulin (INS) production. However, the mechanisms behind beta cell destruction have not been fully deciphered. Immune-mediated destruction by cytotoxic T lymphocytes (CTL) represents a widely postulated but extensively discussed trigger. The lack of beta cells might partly be caused by a less investigated mechanism of endocrine cell plasticity, namely the processes of de and transdifferentiation. These embody the transformation of one endocrine cell type into another, e.g., beta cell into alpha cell.

Methods and Results: A lentiviral lineage tracing approach is used in this work to investigate the occurrence of transdifferentiation in human islets of Langerhans. Islets were dissociated into single cells and transduced with lentiviral vector pairs designed for Cre-dependent gene expression in alpha and beta cells separately. After that, cells were cultured in microwell-containing agarose molds to form physiological-like pseudo isletsin distinct glucose concentrations. Stable viral vector expression was examined 24-48 h after induction with tamoxifen, and islets were cultured for five until up to 10 days. Potential transdifferentiation was determined by inspecting the colocalization of INS and glucagon (GCG) with the viral vectors using immunohistochemistry (IHC). Islet architecture and cell composition were analyzed using image-analysis software. Moreover, the expression of islet cellspecific genes was studied using real-time quantitative PCR (qPCR). Beta cells were successfully transduced, and pseudo islets could be cultured and structurally maintained for up to 7 days. Although the colocalization of the beta cell lineage tracing vector with INS was observed in most of the transduced beta cells, some of these cells showed co-expression with GCG or no expression of the two islet cell hormones.

Conclusion: These findings suggest that beta cells undergo conversion into alpha cells or other cell types, but further quantification and evaluation are necessary for a conclusive interpretation of these preliminary results. Differentiation of endocrine cells is a little explored, but promising mechanism to explain beta cell loss in T1D.

Keywords: type 1 diabetes; beta cells; dedifferentiation; pseudo islets

A rare case of medial radiocarpal arthrosis treated through proximal row carpectomy for mobility regainment and pain relief

D. C. Vişan[1], C. G. Ceian-Şerban[2], D. Oltean-Dan [31]

[1]"Iuliu Haţieganu" University of Medicine and Pharmacy Cluj-Napoca, Romania. [2]Rehabilitation Hospital Cluj-Napoca, Romania. [3]"Alexandru Rădulescu" Orthopedics-Traumatology Clinic Cluj-Napoca, Romania

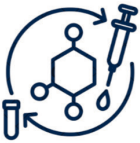
Regenerative Medicine

Introduction: Proximal row carpectomy (PRC) is a procedure which involves the resection of triquetrum, lunate and scaphoid bones, allowing the capitate to articulate with the lunate facet of the distal radius. It isindicated primarily in patients with scapholunate advanced collapse wrist or advanced Kienböck disease, with the aim of regaining mobility of the wrist and reducing the pain. The following case report presents such an intervention, performed on a patient with medial radiocarpal arthrosis.

Case Report: A 50-year-old male suffered a road accident resulting in a vertebral fracture at C2 level, which led to spastic tetraparesis. He was admitted to the ICU, then to the neurology department for treatment. After 1,5 years, he presented to the orthopedic clinic complaining of chronic pain and stiffness in the right radiocarpal joint, with very reduced flexion and extension. Following objective examination and radiography, volar displacement of the lunate bone of the right wrist was found, with secondary necrosis and spasticity. The establi hed diagnosis was medial radiocarpal arthrosis. It was decided that PRC is needed. An 8 cm approach was made dorsally on the radiocarpal joint, followed by 0,5 cm neurectomy of the dorsal branch of the ulnar nerve. An "U"-shaped capsulotomy, followed by ostectomy of the scaphoid, lunate and triquetrum bones was performed, with good intraoperative radioscopic control. The limb was immobilized in a volar short arm splint for 2 weeks and an orthosis for the following 4 weeks. Wrist pain improved soon after the intervention, with no complications reported. Physio- kinesiotherapy commenced after removing the immobilization. Improved range of motion was achieved 6 months after surgery, with 40 degrees of wrist flexion and 30 degrees of extension, our result being comparable to similar studies. The intervention was chosen among other motion-preserving procedures, like 4-corner arthrodesis, being less strenuous, not dependent on bony union and having lower risk of infections.

Conclusion: This case emphasizes the importance of PRC in relieving pain and improving wrist range of motion in patients with medial radiocarpal arthrosis and spasticity. Due to PRC leading to less possible complications and its fast rehabilitation period, it is preferred to other treatment methods.

Key words: Proximal Row Carpectomy, Medial Radiocarpal Arthrosis, Spasticity, Arthrodesis



Risk Prediction of Incisional Hernia in Liver Transplant Recipients: Logistic Regression vs. Machine Learning

S. Dhaene[1], A. Ghazinoer[1], F. Berrevoet[1]

[1]Department of General and HPB Surgery and Liver Transplantation, Ghent University Hospital, Ghent, Belgium

Regenerative Medicine

Introduction: This analysis evaluates predictive models for incisional hernia (IH) development in liver transplant (LT) patients, aiming to optimize risk prediction and facilitate possible prevention strategies.

Methods: A retrospective analysis was conducted on 308 LT recipients at Ghent University Hospital (2010–2019). Demographic, clinical, and surgical variables were analyzed to predict IH risk. The Penn Hernia Risk Calculator's General and Transplant-Specific models, recognized as the leading tools for IH risk assessment, were externally validated in this cohort. Subsequently, a revised logistic regression (LR) model incorporating seven LT-specific predictors was developed and compared with nine other machine learning (ML) models, using 10-fold crossvalidation to reduce the risk of overfitting and provide a more reliable estimate of its predictive performance.

Results: IH occurred in 17.9% of patients, with a median onset of 17.3 months post LT. Both the General and Transplant-Specific Penn models demonstrated suboptimal predictive performance (AUC: 0.612 and 0.649, respectively). The revised LR model identified seven key predictors (hypertension, history of abdominal surgery, age ≥ 60, reduced preoperative functional status, history of herniation, re-transplantation and polycystic liver disease) and achieved superior performance (AUC: 0.808). ML models showed variable sensitivity, specificity, and calibration, with support vector machines and XGBoost achieving the highest AUCs (0.782 and 0.781, respectively). The revised LR model exhibited the most balanced predictive performance.

Conclusions: Tailoring general predictive models to LT patients significantly enhances IH risk prediction. Rather than relying solely on AUC, the choice of model should balance the clinical implications of false negatives (missed IH cases) and false positives (incorrectly predicted IH). The revised LR model demonstrates balanced sensitivity and specificity, offering robust clinical utility that could support targeted prevention strategies such as prophylactic mesh augmentation. Emphasizing specificity is critical to minimizing unnecessary morbidity in this high-risk cohort.

Keywords: Incisional Hernia (IH), Liver Transplantation (LT), Risk Prediction, Logistic Regression (LR), Machine Learning (ML)

An investigation of vitamin D levels in patients who have undergone bariatric surgery and liver stiffness

M. Parchianloo[1]

[1]Zanjan university of medical sciences

Regenerative Medicine

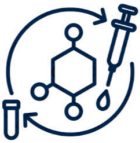
Introduction: Obesity is a growing problem in various communities. Several complications are associated with this condition, especially in the cardiovascular system. Moreover, obesity can result in heterogeneous body system involvement, termed metabolic syndrome. Obesity poses a problem not confined to a few body systems. Our study aimed to evaluate the relationship of different vitamin D levels with liver stiffness laboratory indices and elastography findings in obese patients who were candidates for bariatric surgery.

Methods: This cross-sectional study was conducted on bariatric surgery candidates aged 18 and 60 between 2020 and 2022. Patients with contraindications for bariatric surgery were excluded. A pre-designed questionnaire was used to extract the needed data. These included demographic and anthropometric data such as age, gender, height, weight, and body mass index. Different laboratory indices and elastography were employed for liver stiffness measurements. These included the AST to ALT ratio and AST to platelet ratio index.

Results: This study contained 851 patients who met the criteria. The median age of the cases was 37.00 years old, and 655 cases (77.05%) were female. Among the included cases, 451 (53.05%) had vitamin D deficiency, 190 (22.35%) had insufficiency, and 210 (24.70%) had sufficiency. Total bilirubin ($p=0.012$), ALP ($p<0.001$), FIB-4 ($p<0.001$), and NFS ($p=0.025$) showed significant differences between the three study groups.

Conclusion: In conclusion, our study revealed a notable prevalence of vitamin D deficiency. It also revealed a significant association with liver health parameters. The findings emphasize the complex interconnections between obesity, vitamin D status, and liver complications. Recognizing these relationships is crucial for informed clinical management and highlights the need for further research to refine therapeutic strategies in this population.

Keywords: Obesity, Vitamin D Deficiency, Liver Stiffness



The Role of Platelet-Rich Plasma Bioscaffolds in Sciatic Nerve Regeneration

N. Gjorgioski[1], L. Momiroski[1], A. Angelova1, V. Belevska[1], T. Lozanovska[1], T. Georgieva[1]

[1]Faculty of Natural Sciences and Mathematics, Ss. Cyril and Methodius University, Skopje, North Macedonia

Regenerative Medicine

Introduction: Peripheral nerve injuries often result in long-term functional impairments despite surgical interventions. Recent research has emphasized the role of the microenvironment in axonal regeneration. Platelet-rich plasma (PRP), an autologous blood-derived product rich in growth factors, has emerged as a promising bioscaffold for nerve repair due to its regenerative properties. This study aimed to evaluate the effects of PRP bioscaffolds on sciatic nerve regeneration using a rat model, focusing on functional recovery and histopathological changes.

Methods: A sciatic nerve transection model was established in eight female Wistar rats (n = 8), with both hindlimbs repaired using end-to-end neurorrhaphy. PRP was extracted from a healthy Wistar rat and applied to one hindlimb, while the other served as a control. Functional recovery was assessed using sciatic functional indices (SFI) derived from walking track analysis, video based assessments, and static sciatic index calculations. After 20 weeks, histological evaluations were performed to assess inflammation, fibrosis, and macrophage presence. Statistical comparisons between PRP-treated and control limbs were conducted using three distinct calculation methods.

Results: Walking track-based SFI showed significant improvements of 66.0%, 47.8%, and 71.6% ($p < 0.05$). Video analysis-based SFI indicated enhancements of 36.7% and 27.3% ($p < 0.05$). Static sciatic index calculations revealed a 19.4%improvement in vertical standing and a 26.7% improvement in four-limb stance ($p < 0.001$). Histopathological analysis showed reduced inflammation, decreased fibrosis, and absence of macrophages in PRP-treated sciatic nerves, with muscle tissue also displaying significantly lower fibrosis levels ($p < 0.05$).

Conclusion: These findings suggest that PRP bioscaffolds significantly enhance peripheral nerve regeneration by improving functional recovery and reducing tissue damage. PRP holds promise as a potential therapeutic strategy for nerve repair, with implications for both fundamental research and clinical applications.

Keywords: Platelet-rich plasma, bioscaffold, sciatic nerve regeneration, peripheral nerve injury, nerve

Thermo-Responsive Hydrogel Loaded with Ascorbic Acid and Green-Synthesized Selenium Nanoparticles for Enhanced Diabetic Wound Healing

P. Shahbazpour[12], N. Arbabi[12], K. Zandsalimi[2]

[1]Islamic Azad University Central Tehran Branch, Tehran, Iran. [2]Wound and Tissue Engineering Innovation Center, ACECR, Yara Institute, Tehran, Iran. [3]Medical Laser Research Center, ACECR, Tehran, Iran

Regenerative Medicine

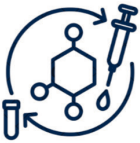
Introduction: Diabetic foot ulcers (DFUs) are a major challenge in chronic wound management, affecting 40–60% of diabetic patients. DFUs are associated with a mortality rate of nearly 50% within five years. This study investigates the incorporation of green-synthesized selenium nanoparticles (Se NPs), prepared using Origanum majorana extract, into a poloxamer-based hydrogel enriched with ascorbic acid. The formulation aims to enhance wound healing by controlling inflammation, infection, and promoting collagen synthesis. Green synthesis of Se NPs offers advantages such as simplicity, cost-effectiveness, and the use of non-toxic chemicals. Additionally, the poloxamer hydrogel exhibits in situ gelation, making it suitable for cavity wounds.

Methods: Se NPs were green-synthesized using Origanum majorana extract as both reducing and stabilizing agents. Characterization of nanoparticles was performed using XRD, SEM, and UV-visible spectroscopy. The nanoparticles were incorporated into a poloxamer hydrogel (25% w/v P407 and P188) along with ascorbic acid to promote collagen synthesis and reduce oxidative stress. Biocompatibility was assessed via MTT assay on human dermal fibroblasts. Antimicrobial efficacy was tested against Staphylococcus aureus and Escherichia coli. Wound healing potential was evaluated through in vitro scratch assays and in vivo studies using streptozotocin-induced diabetic rat models. Statistical analysis was conducted using one-way ANOVA followed by Tukey's post-hoc test (p-value < 0.05).

Results: UV-visible spectroscopy confirmed the successful synthesis of Se NPs with a characteristic peak at 265 nm. MTT assays showed >95% cell viability, indicating excellent biocompatibility. Antimicrobial testing revealed inhibition zones of 16–20 mm. In vitro scratch assays demonstrated 80% wound closure in treated samples versus 55% in controls within 72 hours. In vivo studies showed complete wound closure by day 15 in treated groups compared to 65% wound closure in controls. Histological analysis confirmed enhanced collagen deposition, reduced inflammation, and improved tissue regeneration.

Conclusion: This study developed a novel wound dressing combining ascorbic acid, green synthesized selenium nanoparticles, and a thermo-responsive poloxamer hydrogel. The formulation exhibited excellent biocompatibility, potent antimicrobial activity, and accelerated wound healing. The hydrogel's in situ gelation property further expands its applicability for complex wound geometries. These findings highlight its potential for clinical translation in managing DFUs.

Keywords: Diabetic foot ulcer, Selenium nanoparticles, Infection, Inflammation, In situ gelation



Regenerative Medicine

When Less is Better: An Effective Solution to Primarily Close a Tracheostomy Wound in a Young Patient

D. Şerbănescu[1], I.M. Rusu[1], A. Paşcu[2]

[1]Faculty of Medicine, "Iuliu Haţieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania. [2]Department of Plastic and Reconstructive Surgery, "Prof. Dr. Ion Chiricuţă" Institute of Oncology, Cluj-Napoca, Romania

Introduction: Following tracheostomy decannulation, wounds are usually closed by secondary intention. This often leads to the formation of depressed scars, adherent to the subjacent trachea, with further scar elongation in pediatric patients. A layer by-layer restoration of the anterior cervical region using the sternocleidomastoid (SCM) and platysma muscles, thus eliminating the tracheocutaneous tethering and restoring both the functionality and esthetics of the affected region, can prove to be a simple yet effective approach of managing extensive tracheostomy wounds.

Case Report: A 19-year-old patient presented with a deeply depressed scar, two years after a short-term tracheostomy was performed, following a vehicular trauma causing neurocranial injury. On examination, the presence of tracheal tug, dysphagia and exaggerated elongation of the scar, worsened by the patient's young age, supported the decision of scar revision surgery. While a more complex free flap transfer was discussed, layer-by-layer reconstruction of the affected area was the elected approach for the condition, regarded in this particular case a more suitable approach, especially considering the patient's age. All the preoperative measures were taken, then the patient was submitted to the OR. Hydrodissection was performed, ensuring the detachment of the scar without damaging the trachea, followed by complete scar excision. The sternocleidomastoid muscles were exposed bilaterally, dissected, approximated medially and sutured. Then, the SCMs were layered by the platysma muscles, that were sutured to one another, along the median line. Finally, primary closure of the wound was achieved by subcutaneous and dermal suturing. The patient spent the night in the ICU, then negative pressure wound therapy was administered for five days, promoting the formation of granulation tissue, while also reducing the risk of vicious scarring. One-month follow-up showed correction of tracheal tug and substantial appearance improvement of the cervical region, with no complications noted.

Conclusions: While there are numerous possibilities when managing tracheostomy scars, considering a simple yet effective approach to the condition can ensure a better quality of life for the patient, even when dealing with complex scarring. A layer-by layer restoration of the anterior cervical region can restore the functionality and aesthetics of the affected region, with highly positive results.

Keywords: Tracheostomy scar; Tracheocutaneous tethering; Reconstructive surgery

The isolation of Dental Pulp Stem Cell-derived Exosomes and their NTA (Nanoparticle Tracking Analysis) Characterization

J. Milašin[1], M. Lazarević[1], R. Hossein Pour[1]

[1]Republic of Serbia/ University of Belgrade/ Faculty of Dental Medicine, Department of Genetics

Regenerative Medicine

Introduction: Dental pulp stem cells (DPSCs) are known for their self-renewal and multi-lineage differentiation abilities.Despite their promising role in regenerative medicine, stem cell-based therapies face significant hurdles. In response, a cell-free approach utilizing exosomes has emerged as a potential alternative, offering therapeutic benefits similar to stem cells. Exosomes sourced from DPSCs may exhibit distinct functionalities compared to other MSC-derived exosomes. The aim of the study was exosomes isolation from DPSCs and their characterization in terms of their size and concentration.

Methods: Exosomes were isolated from DPSCs using Magnetic-Activated Cell Sorting (MACS) technique. Initially, 2×106 DPSCs were grown, and 2 mL of serum-free growth medium was collected and processed to obtain a cell-free supernatant. The supernatant was then subjected to centrifugation to remove cellular debris and large vesicles. Subsequently, exosomes were isolated from the supernatant using MACS-based protocols, following the manufacturer's instructions. The isolated exosomes were characterized using Nanoparticle Tracking Analysis (NTA). Briefly, the concentration and size distribution of exosomes were determined using a Nanosight instrument equipped with a laser-based system. The samples were diluted in particle-free buffer to ensure optimal measurement conditions.

Results: The MACS technique effectively isolated exosomes, resulting in a pure exosome population. NTA analysis revealed the size distribution of DPSC-derived exosomes, with an average size of 92.6 nanometers. The concentration of exosomes in the samples was 1.5×1012 particles per milliliter. The size distribution profile demonstrated the presence of homogeneous populations of exosomes, indicative of successful isolation and purification. The size and concentration of DPSC-derived exosomes were consistent with previously reported values for exosomes derived from different mesenchymal stem cells.

Conclusion: This combined approach of MACS-based isolation and NTA-based analysis facilitated the characterization of DPSC-derived exosomes, providing valuable insights into their physic-chemical properties, which is the starting point for future application of these extracellular vesicles in regenerative medicine.

Keywords: Exosomes ; Dental Pulp Stem Cells ; " NTA" Analysis ; " MACS" technique

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