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ABSTRACTS



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Presidential welcome – Dr. Zsolt Garami, President of the HMAA

Ladies and Gentlemen, my Friends in the HMAA Hungary Chapter family, Dear Students,

It is a great honor to become president of the HMAA, as I was an exchange student in the society long ago. In the meantime, we must motivate our younger generation and students to follow our founding fathers' and mothers' dreams and vision of educating and sharing medical knowledge without borders.

Welcome back to Vargesztes! With the new location and a more energized team, I hope you will enjoy our annual HC scientific meeting.

We are so excited to learn from each other, not only within the scope of scientific discourse but also about personal and professional milestones in our relaxed atmosphere! Let us learn from each other with fruitful discussions after superb presentations.

Our programs: This year, we are continuing our flagship student exchange program and have reopened the fellowship and observer programs. I am happy to report that 24 students in Buffalo and 12 in Houston have enrolled in our program for this academic year. You will have the opportunity to meet past and future students in person and listen to their lectures. Additionally, we have four research fellows from Hungary working on an annual term at the Houston DeBakey Heart & Vascular Center. We continue to support the HMAA HC student conference and will welcome the best English Lecture Award Winner at our meeting in Sarasota, Florida.

Every year, we are confronted with new global challenges that affect each one of us in some way. Currently, we long for peace and prosperity as we witness unjust and brutal wars. However, we are prepared to confront and discuss these current challenges, just as we have overcome those in the past, such as the recent COVID-19 pandemic. As a proud and supportive community, we come together more vital than ever.

I would also like to thank everyone supporting our organization and programs. Your contribution powers great opportunities and immense innovations. Let us all come together to make our annual meeting another great success. And enjoy listening to the lectures from our next generation of Hungarian doctors and researchers.

My promise is to continue to work hard for our society!

Enjoy your time with each other, make new friends, and stay safe!



Dr. Zsolt Garami
President of the HMAA

Presidential welcome – Dr. Péter László Kanizsai, President of the HMAA Hungary Chapter

Dear Friends!

Time moves incredibly fast. We still remember the last HMAA HC conference in Füred, but we are already preparing for our 2024 annual meeting, putting the finishing touches to the programme, taking care of last minute issues and looking forward to the sixth of September. This year we are organising our conference in a new location, with a slightly different approach to the previous ones in Várgecsztes. Várgecsztes is a wonderful place, a resort village in the Vértes, where we can finally spend two days together with the scientific programmes, accommodation, meals and social activities all at the conference venue. Besides being located in a picturesque setting, the Villapark is easily accessible by public transport from Tatabánya, but it is also only an hour's drive from the capital.

This year 24 presentations and 52 posters were accepted by the scientific committee. I dare to say that the quality of the presentations is rising annually, and this year is no different. As usual, there will be workshops, again an emergency quiz, free activities and a few surprises!

While last year's funding was significantly reduced, we are fortunate to always have sponsors whose generous support makes our annual conference possible. I would like to extend my grateful thanks to them. I owe no less appreciation and thanks to our organisers, especially to our chief organiser, Dr. Dorottya Szabó Steigerwald. The length of this welcome does not allow me to mention the names of all those who have worked so hard to make it possible for us to meet at the new venue, but I would like to express my enormous thanks and gratitude to all those who have actively participated in the organisation.

With unbroken optimism, I am confident that the 18th Annual HMAA HC conference will be a great success! I look forward to September 6-7 with great anticipation and welcome with love and appreciation all the kind participants!



Dr. Péter László Kanizsai
President of the HMAA HC

SS1. Interdisciplinary Oral Session I. (Anatomy-Anesthesiology-Intensive Care-Dermatology-Emergency Care-Immunology-Cell Biology-Pharmacology)

THALAMIC CONTROL OF AGGRESSION

Botond Drahos, Tamás Láng, Árpád Dobolyi (Department of Anatomy, Histology and Embryology, Semmelweis University)

Keywords: aggression, thalamus, MPOA, PIL, vGATE

Aims: In this study we examined the function of the social-tagged neurons in the posterior intralaminar thalamic nucleus (PIL), and their projections to the medial preoptic area (MPOA), in intermale aggression in rats.

Methods: For chemogenetic manipulation of the PIL neurons, we used a viral system called vGATE, which allowed us to selectively express DREADDs in PIL neurons that had previously been c-Fos-activated by social interaction. We performed behavioural tests and examined the effect of DREADD activation by measuring the number of c-Fos-ir cells in the PIL and its target areas. To investigate the PIL-MPOA pathways role in regulating aggressive behaviour, an anterograde spreading virus was injected into the PIL and a cannula implanted in the MPOA, which allowed the manipulation of axon terminals of the PIL neurons.

Results: The chemogenetic stimulation of the social-tagged PIL neurons decreased aggression, while inhibition increased aggressive behaviour. The inhibition of vGATE-tagged PIL neurons during aggressive behaviour decreased c-Fos expression in the PIL and the MPOA. Conversely, the stimulation of the tagged PIL neurons caused the activation of the MPOA even in the absence of social interaction. Stimulation of the PIL-preoptic pathway decreased aggression and increased the duration of positive valence contacts, while inhibition exerted the opposite action.

Conclusions: The activity of PIL neurons reduced aggressive behaviour by their projections to the MPOA. Thus, the pathway does not promote all direct contact interactions but rather elevated behaviours with positive valence.

Support: NAP 3.0, OTKA K1460

CONNECTION OF EXPIRATORY FLOW LIMITATION AND CHRONIC LUNG ALLOGRAFT DYSFUNCTION IN A FOLLOW-UP STUDY

Botond Sipos (Department of Anesthesiology and Intensive Therapy, Semmelweis University)

Keywords: pulmonology, oscillometry, lung transplant, CLAD, airway mechanics

Aims: To investigate the occurrence of tidal expiratory flow limitation (tEFL) during spontaneous breathing in lung transplant patients using intra-breath (IB) oscillometry and its correlation with chronic lung allograft dysfunction (CLAD), which is the most significant cause of morbidity and mortality in lung transplant recipients.

Methods: IB oscillometric measurements were analyzed from 171 lung transplant patients, recorded between 2020 and 2023 at Toronto Lung Transplant Clinic, Canada. Data were processed and visualized in graphs using custom software to identify tEFL patterns, characterized by specific changes in respiratory reactance and resistance. By examining the shape of the loop curves in the graphs, we were able to distinguish the tEFL pattern occurring at the bronchiolar level from that of upper airway obstruction.

Results: Based on ISHLT guideline of CLAD recognition, 66 patients were diagnosed with CLAD, primarily bronchiolitis obliterans syndrome (BOS). The tEFL pattern was identified in 40 patients, of whom 78% were diagnosed with CLAD. Notably, among individuals with a sustained tEFL pattern, the incidence of CLAD was 85%. Key metrics (dXE, XminE, AXV') showed significant differences ($p < 0.001$) between CLAD and no-CLAD groups, with combined thresholds achieving high specificity.

Conclusions: The tEFL oscillometric pattern was significantly more prevalent in CLAD patients. This supports the potential of IB-oscillometry for studying or even predicting CLAD, with ongoing research to further validate these findings.

Support: This research was supported by the Toronto Lung Transplant Clinic, Toronto General Hospital, with special thanks to my supervisors Zoltán Hantos and Chung-Wai Chow.

ROLE OF PIGMENTATION IN THE REGULATION OF FERROPTOSIS IN MELANOMA

Benedek Nagy, Dorottya Pál, Lajos Vince Kemény (Department of Physiology; Department of Dermatology, Venereology and Dermatoooncology, Faculty of Medicine, Semmelweis University)

Keywords: melanoma, ferroptosis, pigmentation, lipid ROS

Aims: We aim to investigate the role of pigmentation in the regulation of ferroptotic cell death in melanoma.

Methods: To modify pigmentation, we performed TYR gene knockout in B16 mouse melanoma cells using CRISPR-Cas9. TYR enzyme was pharmacologically inhibited with a tyrosinase inhibitor. Melanoma cells were treated with ferroptosis-inducing compounds and cell viability was measured using the CellTiter-Glo Assay. Lipid ROS detection was performed by incubation with Bodipy C11 sensor. Quantification was performed using Leica fluorescence microscope. We investigated the correlation of TYR expression in 48 melanoma cell lines from CCLE and CTRv2 databases with the sensitivity of the cell lines to agents inducing ferroptosis. Using a proteomic database of 90 melanoma samples, we investigated the correlation of TYR protein and a marker of ferroptosis (PTGS2).

Results: Inhibition of pigmentation reduced sensitivity to ferroptosis-inducing drugs by 10-20 fold. In pigment-producing cells, 60% ($p=0.0004$) more lipid ROS were generated by ferroptosis-inducing drugs than in non-pigmented cells. In differentiated melanoma cell lines from the CCLE database, sensitivity to ferroptosis-inducing drugs was significantly correlated with TYR expression. In proteomic analysis of patient-derived melanomas, the level of the ferroptosis marker PTGS2 was significantly correlated with the amount of TYR protein.

Conclusions: Our results suggest that pigmentation enhances melanoma susceptibility to ferroptotic cell death, presumably due to increased lipid ROS production.

Support: HCEMM Grant, OTKA KFI Grant, Bolyai Scholarship

TARGETING HARD-TO-ATTACK PROTEIN-PROTEIN INTERACTION SURFACES USING UV-REACTIVE SURFACE FRAGMENTS

Bence Nagymihály, Edit Wéber, Péter Ábrányi-Balogh, Dóra Karancsiné Menyhárd, Nikolett Péczka, Márton Gadanez, Gitta Schlosser, Zoltán Orgován, Ferenc Bogár, Dávid Bajusz, Gábor Kecskeméti, Zoltán Szabó, Éva Bartus, Attila Tököli, Gábor K. Tóth, Tibor V. Szalai, Tamás Takács, 6 Lászl (Department of Medical Chemistry, University of Szeged; HUN-REN-SZTE Biomimetic Systems Research Group; Medicinal Chemistry Research Group, HUN-REN Research Centre for Natural Sciences; Laboratory of Structural Chemistry and Biology, Institute of Chemistry, Eötvös Loránd University; MTA-ELTE Lendület Ion Mobility Mass Spectrometry Research Group, Institute of Chemistry; Eötvös Loránd University; Institute of Molecular Life Sciences, HUN-REN Research Centre for Natural Sciences)

Keywords: KRAS, peptidomimetics, HPLC-MS, NMR, fragment-based drug design

Aims: 80% of the human proteome consists of hard-to-attack proteins without targetable binding pocket. Efficient strategies like fragment-based drug development are not available for these proteins. Our goal was to map the surface of difficult-to-attack targets with peptidomimetic fragments and then increase the affinity with linking the foldamer fragments, thus extending fragment-based drug design to targets without a binding pocket.

Methods: Experiments were performed on one of the most difficult target proteins, KRas G12D, which has a high contribution to many tumors. We tested a 100-membered foldamer library, containing a UV-reactive group, so that the bound foldamers covalently labelled the target that could be identified by HPLC-MS. The binding site of the most effective fragments were determined by proteomic MS-MS analysis and ^{15}N HSQC NMR titration. In dynamic covalent library experiments, foldamer dimers with higher affinity were created.

Results: The surface fragments were able to recognize the protein surface and bind to the target. We found numerous foldamers with a side chain-dependent binding pattern with KRas G12D. The UV-reactive marker made the screening efficient, and we were able to localize the binding site of the fragments. The foldamers found the

known protein-protein interaction surfaces of the target, but also discovered new, potentially attackable regions. In protein-templated dynamic covalent library experiments, dimers with higher affinity were created.

Conclusions: Using the protein surface mimetic foldamer library and connecting the fragments can be a viable general hit generation strategy for challenging protein targets.

HEPATIC STEATOSIS AND CARDIOVASCULAR RISK FACTORS IN CELIAC DISEASE. RESULTS OF A PROSPECTIVE, MULTICENTER, CASE-CONTROL STUDY (ARCTIC STUDY)

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Keywords: celiac disease, hepatic steatosis, cardiovascular risk factors, gluten-free diet, body composition

Aims: Celiac disease, an autoimmune disease triggered by gluten, affects approximately 1% of the population, yet its cardiovascular and metabolic effects remain poorly understood. In the ARCTIC prospective multicenter study, we examined the cardiovascular risk factors of celiac patients on a gluten-free diet.

Methods: We investigated body composition, the prevalence of hepatic steatosis and other cardiovascular risk-related metabolic parameters in celiac patients and healthy controls. Abdominal ultrasound was performed to assess the degree of hepatic steatosis. We compared the data of celiac patients with and without steatosis.

Results: The study included 97 celiac patients and 47 controls. Hepatic steatosis was observed in 11% of controls and 30% of celiac patients ($p=0.012$). Among the celiac patients, 31% with a normal BMI developed steatosis. Hepatic steatosis was more prevalent in celiac patients with higher BMI ($p<0.001$), waist circumference ($p<0.001$), hip circumference ($p<0.001$), percent body fat ($p=0.037$), visceral fat area ($p=0.006$), and triglyceride levels ($p=0.006$). However, no significant differences were observed in waist/hip ratio, skeletal muscle mass, Inbody score, LDL, and total cholesterol level ($p>0.05$). Adherence to a gluten-free diet did not influence the occurrence of hepatic steatosis ($p=0.60$). Notably, 83% of celiac patients with hepatic steatosis met the criteria for Metabolic Dysfunction–Associated Liver Disease (MASLD).

Conclusions: Hepatic steatosis is prevalent in celiac patients following a gluten-free diet, including those with normal BMI. Vigilant examination and monitoring during patient care are crucial, encompassing weight management, dietary adjustments, lifestyle counseling, and proactive identification and prevention of cardiovascular and metabolic disorders.

Support: National Research, Development, and Innovation Office (grant FK 142942 to JB)

SS2. Interdisciplinary Oral Session II. (Pathology-Pathophysiology-Physiology-Oncology)

UNDERSTANDING SMALL CELL LUNG CANCER SUBTYPE HETEROGENITY ACROSS DISTINCT METASTATIC SITES

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Keywords: small cell lung cancer, metastasis, tumor heterogeneity, molecular subtypes

Aims: Although small cell lung cancer (SCLC) is still handled as a homogeneous disease in clinical settings, the underlying molecular profile shows a heterogeneous landscape with four dominant subtypes. The aim of this study was to investigate inter-tumoral heterogeneity and subtype expression across multiple tumor sites in extensive stage small cell lung cancer patients.

Methods: Samples of primary tumors and their corresponding lymph node (LN) metastases from 32 surgically resected metastatic SCLC patients from the National Korányi Institute of Pulmonology, Budapest, Hungary were included for this study. Protein and gene expression differences in tumor sites of select proteins (n=14) were evaluated by immunohistochemistry (IHC) and RNA sequencing (RNAseq). Subtype status was determined in all samples and clustering analysis was performed. Heatmaps were created for visualization and all statistical calculations were performed in R version 4.2.1.

Results: IHC analysis revealed differential protein expression between primary tumors and LN metastases. Specifically, DLL3 expression was statistically significantly downregulated in LNs compared to primary tumors ($p=0.008$) after multiple testing correction, whereas NEUROD1 expression increased in LN metastases ($p<0.001$). IHC and RNAseq datasets moderately correlated between both datasets. Notably, inter-tumoral heterogeneity was observed in selected cases and molecular subtypes tended to differ between primary tumors and their LN metastases.

Conclusions: This study highlights inter-tumoral heterogeneity across SCLC tumor sites reflected in differential protein expression. Since expression differences across metastatic sites might bear relevant therapeutic implications, further investigations are warranted to fully map patterns of heterogeneity in SCLC patients.

CAN WE REPLACE GOMORI'S SILVER IMPREGNATION WITH IN SITU PROTEIN-BASED GRADING OF MYELOFIBROSIS PROGRESSION?

Anna Nagy, László Krenács, Tamás Székely, Botond Timár, Tibor Krenács (Department of Pathology and Experimental Cancer Research Semmelweis University, Faculty of Medicine, Budapest; Laboratory of Tumor Pathology and Molecular Diagnostics, Szeged)

Keywords: myelofibrosis, fibrillin-1, collagen-I, collagen-VI, digital whole slide analysis

Aims: Primary myelofibrosis (MF) is characterized by the accumulation of extracellular matrix (ECM), primarily comprising reticulin, collagen, and fibrillin fibers. Although Gomori's silver impregnation remains the gold standard diagnostic method, its standardization poses challenges and is significantly influenced by pre-analytic conditions. In this research, we aim to validate collagen-I, fibrillin-1, and especially collagen-VI as suitable markers for assessing the grade of MF progression.

Methods: 64 patients' bone marrow Jamshidi biopsies along with tissue microarrays (TMA) were included in the study. TMA and bone marrow biopsy slides were scanned of all grades, including patients without bone marrow fibrosis. We applied automated immunohistochemistry (IHC) and digital whole slide analysis to validate collagen-VI reactions, in addition to the previously validated collagen-I and fibrillin-1.

Results: The study showed that each marker can visualize the ECM scaffolding consistently with the progression of MF. Fibrillin-1 immune signals provided excellent inter-rater agreement during visual assessment. The overall

strongest correlation was determined between the original silver impregnation and the IHC staining of the collagen-VI slides, based on the results of digital whole slide image analysis.

Conclusions: Our findings affirm that the accumulation of all three biomarkers, as detected through in situ IHC, correlates with the progression of bone marrow fibrosis. Consequently, they all – especially collagen-VI – appear to be viable alternative grading methods for primary MF, and could replace it after greater scale validation.

Support: I am grateful for technical support from Éva Balogh Mátrai and Rebeka Bertalan and for the excellent statistical analytical help from Barna Wichmann.

ROLE OF MICROGLIA IN SORL1-RELATED INFLAMMATION AND NEURONAL FATE IN ALZHEIMER'S DISEASE

Sára Vida, Balázs Pósfai, Krisztina Tóth, Nikolett Lénárt, Csaba Cserép, Zoltán Máté, Ferenc Erdélyi, Zsolt Lele, István Katona, Henne Holstege, Olav M. Andersen, Ádám Dénes (Laboratory of Neuroimmunology, HUN-REN Institute of Experimental Medicine, Budapest; Medical Gene Technology Unit, HUN-REN Institute of Experimental Medicine, Budapest; Molecular Neurobiology Research Group, HUN-REN Institute of Experimental Medicine, Budapest; Alzheimer Center Amsterdam, Department of Neurology, Amsterdam Neuroscience, Vrije Universiteit Amsterdam, Amsterdam UMC, Amsterdam; Department of Biomedicine, Aarhus University, Aarhus)

Keywords: microglia, Alzheimer, neurodegeneration

Aims: Alzheimer's disease (AD) is a progressive neurodegenerative disorder. Recently, the contribution of microglia to homeostatic and neuroprotective processes in AD has gained interest. This study delves into the involvement of microglia in the pathogenesis of AD, focusing on microglia-neuron somatic junctions through which microglia monitor and shape neuronal function. Specifically, we study the role of microglia in the context of the sortilin-related receptor SORL1, a key risk gene in hereditary AD.

Methods: In this translational study, we collected fixed tissue, native brains and CSF of triple-transgenic AD-model (PSEN1//App_{swe}//tauP301L) and control mice, from three different age groups. We have also developed a CRISPR/CAS9 targeting strategy combined with in utero electroporation to achieve genetic deletion of Sorl1 in a subpopulation of cortical neurons in transgenic mice. Through the measurement of inflammatory biomarkers and high-resolution immunofluorescent imaging we studied the effects of Sorl1 deletion on cellular- and inflammatory responses. We explore the alterations in microglial morphology and contactology in response to the loss-of-function of Sorl1 in KO mice and in post-mortem brain tissues of patients with pathogenic Sorl1 mutations.

Results: Our results show significant alterations of microglial morphology and function during the aging of mice with chronic neurodegeneration with changes in SORL1 expression. Our data also show marked changes in microglia-neuron interactions in the absence of SORL1 and suggest that inflammatory mechanisms could be important contributors to the pathogenesis of SORL1-related AD.

EFFECTS OF A 12-WEEK TREADMILL TRAINING AND LONG-TERM CALORIC RESTRICTION ON THE LEPTIN RESISTANCE OF MIDDLE-AGED MALE WISTAR RATS

Fanni Dóra Kiss, Márta Balaskó (Institute for Translational Medicine, Medical School, University of Pécs)

Keywords: caloric restriction, exercise, leptin, obesity

Aims: Obesity is a worldwide epidemic. Its rate increases with aging. Age-related obesity is observed also in other mammals, therefore age-related regulatory changes may also contribute to its development.

Adipose tissue-derived leptin shows central anorexigenic and hypermetabolic effects. Both obesity and aging lead to leptin-resistance. Responsiveness to centrally administered leptin decreases significantly in middle-aged obese

male Wistar rats. Earlier studies demonstrated that caloric restriction and training decreased circulating leptin levels indicating improved leptin efficacy.

Methods: We aimed to test the effects of a 12-week treadmill training (TR12) and a life-long 30% caloric restriction (CR12) on the hypermetabolic responsiveness to centrally applied leptin in middle-aged, obese, male Wistar rats (NF12). Training started at age 9-month. Training sessions (45-min) took place 5 days/week. Central thermoregulatory effects of leptin were tested by indirect calorimetry (OxyletPro). Core temperature was detected by colon, heatloss by tail skin thermocouples linked to a Benchtop Thermometer (Cole-Parmer). Permit number: BA/35/66-6/2020.

Results: Hyperthermic responses of TR12 to leptin failed to exceed those of NF12. Leptin-induced hypermetabolism was particularly low in TR12. However, leptin-induced hyperthermia in CR12 strongly exceeded that of NF12.

Conclusions: Long-term CR effectively improved central thermoregulatory responses to leptin, while a 12-week treadmill training failed to increase such responses. Our results emphasize the importance of early prevention of obesity.

THE ROLE OF INTRAAMYGDALOID OXYTOCIN IN NOVEL OBJECT RECOGNITION IN VALPROATE-INDUCED AUTISM RAT MODEL

Bálint Turcsán, Vivien Fodor, Dávid Vörös, Kristóf László (Department of Physiology, Medical School, University of Pécs)

Keywords: autism, amygdala, oxytocin, memory

Aims: Autism spectrum disorder is a neurodevelopmental disorder affecting around 1.5-2% of children, and its incidence shows an increasing tendency. Its treatment is currently not resolved. In autism research, we used the widely accepted valproate-induced rodent model. We have recently shown that intraamygdaloid oxytocin can ameliorate some autism symptoms. In this research, we sought an answer to what effects intraamygdaloid oxytocin has on memory processes in the novel object recognition in valproate-induced autism rat model.

Methods: bilateral guide cannulae were implanted above the central nucleus of the amygdala using the stereotaxic technique in male Wistar rats showing autistic signs and neurotypical control, and examined in novel object recognition test. We investigated the effect of intraamygdaloid oxytocin (10 ng, Sigma–Aldrich Co., O6379) and oxytocin receptor antagonists (20 ng, Sigma–Aldrich Co., L-368-899).

Results: valproate-treated rats that received 10 ng oxytocin performed significantly better on the discrimination index in the novel object recognition paradigm in the test phase, than those valproate-treated rats, who did not receive oxytocin. A pre-administered 20 ng oxytocin receptor antagonist blocked the positive effect of 10 ng oxytocin on memory processes. The 20 ng oxytocin receptor antagonist alone did not affect the discrimination index.

Conclusions: our results show that intraamygdaloid oxytocin improves the memory processes on rats showing autistic signs and that this effect is oxytocin receptor specific.

UNRAVELLING THE ROLE OF HEMOKININ-1 IN AGE-RELATED DETERIORATION OF MOTOR COORDINATION AND MUSCLE STRENGTH

Dávid Vince Simon (Department of Pharmacology and Pharmacotherapy, University of Pécs)

Keywords: Hemokinin-1, motor coordination, muscle strength, tachykinin

Aims: Musculoskeletal problems and consequent fractures significantly reduce the quality of life in old age. Hemokinin-1 (HK-1), the newest member of the tachykinin family, is present in high concentrations in the cerebellum and reproductive organs as well as in bones and muscles. Therefore, we investigated its role in motor coordination, muscle function and sex differences in 3-4-, 12- and 18-month-old C57BL/6 wildtype (WT) and HK-1-deficient (Tac4 KO) male and female mice (n=12-20).

Methods: We assessed motor coordination in the rotarod and the static rod tests, and muscle strength in the grid and the horizontal bar tests.

Results: No difference was found between the WT and gene-deficient groups in rotarod test. In aged animals (12 and 18 months), both males and females, a significant deterioration in locomotor coordination was observed in the static bar test, which was significantly more severe in 12-month-old male Tac4 gene-deficient animals compared to the WTs ($p < 0.01$), but the gene deficiency improved this ability in 18-month-old females ($p < 0.01$). A significant decline in muscle strength was also detected in older WT animals in both tests. In the grid test, the loss of muscle strength was significantly smaller in females compared to males, a phenomenon also observed in the horizontal bar test.

Conclusions: Our results suggest that HK-1 may play a complex regulatory role in motor coordination in old age, also sex differences can be observed. Therefore, elucidating the mechanism of action of HK-1 and its interactions with sex hormones may be important for drug developmental purposes.

Support: Eötvös Loránd Research Network (Chronic Pain Research Group), Pécs, National Brain Research Program 3.0, National Research, Development and Innovation Office - OTKA K138046 and OTKA FK137951, TKP2021-EGA-16, János Bolyai Research Scholarship of the Hungarian Academy of Sciences (BO/00592/19/5), and ÚNKP-21-5 (ÚNKP-22-5-PTE-1447), Project no. RRF-2.3.1-21-2022-00015 (European Union).

SS3. Interdisciplinary Oral Session III. (Dentistry-Neurosurgery-Surgery-Traumatology)

EFFECT OF PERIODONTOGENIC MICROBIOME ON THE OUTCOME OF CEREBROVASCULAR EVENTS

Lídia Molnár, Ágnes Bán, Edit Urbán, Tihamér Molnár (Department of Dentistry, Oral and Maxillofacial Surgery, University of Pécs, Hungary; Department of Microbiology, University of Pécs; Department of Anesthesiology and Intensive Care, University of Pécs)

Keywords: periodontitis, stroke, subarachnoid bleeding, bacteria, outcome

Aims: The prevalence of periodontitis is 11.2% worldwide. It has been associated with many systemic diseases. Its pathogenesis is attributed to oral microbial dysbiosis (OMD), in which *P. gingivalis* plays a critical role by disrupting host immune homeostasis. We aimed to explore the relationship between OMD and cerebrovascular disease.

Methods: In this prospective study, we compared the values of 20 patients suffering from cerebrovascular event (15 subarachnoid hemorrhage, SAH and 5 ischemic stroke) with 8 healthy controls. Clinical probing depth measurement and culture were performed for all participants. Markers of systemic immune response (IL-6, hsCRP) and brain injury (NSE, S100B) were measured between 24-48 hours after the index event. Bad outcome (mRS 3-6, based on the modified Rankin Scale) as the primary endpoint, while development of "delayed cerebral ischemia" (DCI) as the secondary endpoint were chosen.

Results: DCI developed in 8 SAH patients, in all cases pocket depth ≥ 5 mm was measured, and significantly higher hsCRP ($p = 0.001$) and IL-6 ($p = 0.005$) concentrations were found. The co-presence of anaerobic *P. intermedia* or *P. gingivalis* with *F. nucleatum* showed a correlation with deeper pockets and DCI in SAH patients ($p < 0.05$). Higher hsCRP, NSE, S100B (all $p < 0.05$) levels were observed in cases with a worse outcome.

Conclusions: Our results suggest relationship between periodontitis and vascular brain events. The co-presence of certain periodontopathogenic microbes can be assumed to play significant role in disease progression. Since periodontitis is a treatable disease, this link is of public health importance.

THE EFFECT OF BIMODAL PREHABILITATION ON COLON ANASTOMOSIS HEALING IN A RAT MODEL

Hendlein Tímea Helga, Klára Lévy, Szabina Kovács, András Fülöp, Attila Szijártó (Department of Surgery, Transplantation and Gastroenterology, Semmelweis University)

Keywords: prehabilitation, anastomosis healing, colorectal surgery

Aims: We aim to investigate the impact of bimodal prehabilitation on colon anastomosis healing.

Methods: 108 male Wistar rats were divided into 6 groups: ad libitum fed (A), A with exercise therapy (AE), malnourished (M), malnourished with exercise therapy (ME), malnourished with nutritional therapy (MN), MN and exercise therapy (MNE) (PE/EA/00523-6/2023). Preoperatively, we measured bodyweight changes and magnetic resonance imaging was performed (MRI) to characterize body composition, and serum parameters were also determined. After colon anastomosis, welfare was monitored by rat grimace scale (RGS). Animals were exsanguinated 4 and 7 days after surgery, and colon anastomosis healing was characterized by bursting pressure (BP) and adhesion rate (AS). Feces volume of the cecum was also measured.

Results: Bodyweight MRI showed weight loss in M and ME groups compared to the A group, which was caused by a decrease in muscle and not fat ratio. MN, MNE groups reached the values of the A and AE groups in terms of bodyweight and body composition. Serum assays demonstrated improved nutritional status of the A group. In M and ME groups, we observed higher RGS and AS and lower BP. Feces volume of the cecum was higher in M and ME groups in the postoperative period.

Conclusions: Bimodal prehabilitation leads to an effective muscle mass gain and body fat percentage reduction, improves anastomosis healing, reduces passage dysfunction, therefore it could be suitable for preoperative preparation of patients to reduce the rate of surgical complications.

Support: Semmelweis University 250+ PhD Excellence Grant (38898/DIDIT/2024)

BIMODAL PREHABILITATION AFFECTS THE MICROBIOME COMPOSITION OF THE GUT

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Keywords: colon anastomosis, colorectal surgery, bimodal prehabilitation, gut microbiome, animal experiment

Aims: The most common complication after colon anastomosis surgery is anastomotic leakage (AL). Bimodal prehabilitation is a potential approach to decrease the occurrence of AL. Microbiome could be another factor for the appropriate anastomosis healing, therefore our aim was to study the alteration of the gut microbiome after bimodal prehabilitation.

Methods: 108 male Wistar rats were divided into 6 different groups: ad libitum fed (A), A with exercise therapy (AE), malnourished (M), malnourished with exercise therapy (ME), malnourished with nutritional therapy (MN), MN with exercise therapy (MNE). After 7 weeks of bimodal prehabilitation, feces were collected, and microbiome was analyzed by 16S rRNA sequencing. Alpha and beta diversity, Firmicutes/Bacteroides ratio (FMR), and the levels of the most significant bacteria were determined.

Results: Alpha diversity was different between the groups and several bacterial species altered after physical, nutritional or bimodal prehabilitation. The beneficial bacteria: Ruminococcus, Lachnospiraceae_UCG-010, were significantly higher in the A, AE, MN, MNE groups, compared to the M and ME groups. Additionally, the levels of unfavourable bacteria (Alistipes, Akkermansia, Bacteroides, Enterorhabdus.) were increased in the M and ME groups. The FMR was also significantly different in the various groups.

Conclusions: Prehabilitation has an impact on microbiome composition. In case of malnutrition, nutritional or bimodal prehabilitation could be optimal to increase the levels of beneficial bacteria.

Support: Semmelweis University 250+ PhD Excellence Grant (38898/DIDIT/2024)

THE ROLE OF AMPK IN THE EFFECTS OF PHYSICAL PREHABILITATION ON LIVER REGENERATION AFTER PARTIAL HEPATECTOMY IN RAT MODEL

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Keywords: prehabilitation, liver, rat model, hepatectomy, regeneration

Aims: Our aim was to determine the role of Adenosine Monophosphate Kinase (AMPK) in liver regeneration in physically prehabilitated rats.

Methods: 72 male Wistar rats were divided into 3 groups, sedentary (S), physically prehabilitated (PP) and inhibited (I). PP and I groups underwent a 5-week long prehabilitation program. Group I received AMPK inhibitor after each exercise. The animals were exsanguinated 0, 24, 72, and 168 hours after a 70% hepatectomy. We measured the effects of prehabilitation through a multitude of tests, focusing on overall metabolic status, liver morphology, function and regeneration. By a sepsis model, mortality rate was established, and welfare was featured by rat grimace scale (RGS).

Results: Following surgery, liver regeneration and liver function improved significantly in the PP group compared to the S and I groups. Surprisingly volume growth increased in group I compared to the PP group, however liver function did not develop correspondingly. Inhibition harmed the beneficial effect of physical prehabilitation. Physical prehabilitation decreased mortality and lowered RGS compared to the S and I groups.

Conclusions: In conclusion physical prehabilitation has a beneficial effect on functional and morphological regeneration of the liver, through AMPK.

Support: This Study was supported by the New National Excellence Program of the Ministry of Culture and Innovation from the source of the National Research, Development and Innovation Fund (ÚNKP-22-3-I-SE-2) Semmelweis University Scientific Ethical Committee on Animal Experimentation of the National Department of Food Chain Safety (PE/EA/00381-4/2022)

THE PROGNOSTIC ROLE OF MIRNS IN GLIOBLASTOMA

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Keywords: Glioblastoma (GBM), miRNAs, RNA Sequencing, prognostic markers, survival prediction

Aims: Glioblastoma (GBM) is the most common and challenging malignant primary brain tumor to treat. Standard treatment includes surgery, radiotherapy, and temozolomide-based chemotherapy. Despite intensive oncotherapy, the average patient survival is about 15 months, but this can reach 5 years in 4-5% of cases. Researches show that clinical and molecular factors, including miRNAs, impact survival. MiRNAs can regulate mRNAs, and their deregulation can lead to tumor development. We aimed to identify miRNAs that are significantly over- or under-represented in patients with glioblastoma who respond well to treatment compared to those with short survival.

Methods: For this purpose, total RNA was isolated from peritumoral brain tissue samples of 6 low-grade glioma patients as controls and from brain tissue samples of 6 patients with GBM with short and 6 patients with long survival. New Generation RNA Sequencing and bioinformatic analysis were performed on these 18 samples, followed by RT-PCR validation. The miRNeasy Mini Kit was used for RNA isolation, and sequencing was done on an Illumina device in collaboration with UD Genomed. ANOVA evaluated sequencing results, and the miScript II RT Kit was used for cDNA transcription of selected miRNAs. RT-PCR reactions utilized the miScript SYBR Green PCR Kit. Significant miRNA differences were filtered using the Mann-Whitney U test.

Results: Four miRNAs—miR-495-3p, miR-216a-5p, miR-187-3p, and miR-424-5p—showed significant deregulation in GBM samples from patients with good treatment response compared to those with short survival.

Conclusions: In conclusion, miRNA deregulation and detection may serve as prognostic markers, potentially predicting therapy response and survival in glioblastoma patients.

THE IMPACT OF SURGICAL TIMING ON FUNCTIONAL OUTCOME AND SURVIVAL IN PATIENTS WITH SPINAL METASTASES

Adam Kovari, Lukacs Benedek Nemeth (Department of Neurosurgery, Semmelweis University)

Keywords: spine surgery, spinal metastases, functional ability, survival

Introduction: Metastases affecting the spine can cause severe neurological deficits due to the compression of neural elements, significantly impacting patients' life expectancy and functional ability. Currently, there is no evidence-based protocol available regarding the timing of surgical intervention.

Aims: Surgical treatment of spinal metastases is necessary but carries high risk. The aim of our study was to examine the impact of surgical timing on functional ability and survival, particularly in relation to the development of neurological signs.

Methods: In our retrospective clinical study, we processed the 765 operative cases of 665 patients. We performed descriptive statistical analysis, survival analysis (Kaplan-Meier, log-rank test), and Fisher's exact tests using "R" software.

Results: Regarding surgical timing, we defined 3 main groups according to our Kaplan-Meier analysis results (<1 week, >1 week-3 months, >3 months, $p=0.0001$). In cases of acute symptom onset (complaints arising within 1 week before the surgery), no advantage in functional outcome or survival was observed compared to other groups ($p=0.561$).

Conclusions: Based on our results, patients who underwent urgent surgical intervention did not demonstrate better functional ability or survival. This suggests that performing hyperacute on-call surgery requires serious consideration.

SS4. Interdisciplinary Oral Session IV. (Interdisciplinary-Pediatrics-Pulmonology-Radiology)

ASSESSMENT OF TEXTURAL FEATURE IN PET/CT IMAGING: A MULTICENTRIC PHANTOM STUDY

Piroska Kallos-Balogh, Laszlo Balkay (Division of Nuclear Medicine and Translational Imaging, Department of Medical Imaging, Faculty of Medicine, University of Debrecen; Doctoral School of Molecular Medicine, Faculty of Medicine, University of Debrecen)

Keywords: Heterogeneous Phantom, Radiomic Texture Analysis, PET Imaging

Aims: Texture analysis on PET/CT images raises methodological questions that can be answered by phantom measurements, allowing the creation of reproducibly heterogeneous activity distributions. Previously, we created an "activity painting" phantom measurement for this purpose. Our aim was to compare PET/CT images and statistically characterize the reliability of texture indices (TI).

Methods: For our study, we used the "activity painting" phantom technique with three orthogonally placed linear attenuators with a Na-22 point source. To simulate realistic PET imaging, we used a 20-liter water tank, containing a solution of F-18 with an activity concentration of 5kBq/ml. Three lesions of different heterogeneity were simulated in 5 PET/CT cameras. Image segmentation and texture analysis were done using the LifeX software, calculating a total of 46 TIs applying both absolute and relative discretization. Reproducibility and reliability were determined using the coefficient of variation (CV), and the intraclass correlation coefficient (ICC). We also compared the TI values with hypothesis tests.

Results: The visual comparison shows that voxel size influences textural details. Conventional parameters are the most reliable. For higher order TIs, a CV value above 25% is typical. The Wilcoxon test showed significant differences in TIs with absolute discretization. ICC determined that TIs are more reproducible with absolute discretization, and conventional parameters had better statistics and good repeatability.

Conclusions: "Activity painting" made it possible to detect textural differences from different PET/CT camera settings and characteristics. Conventional parameters show high stability. TI reliability depends on the discretization. Reconstructed voxel size fundamentally affects the pattern and radiomics data.

RADIOMIC STUDY OF COLORECTAL CANCERS

Bertalan Tóth, István Szabó, Ádám Domonkos Tárnoki, Dávid László Tárnoki (Faculty of Medicine Semmelweis University; Department of Radiology and Invasive Diagnostic Center and National Tumorbiology Laboratory, National Institute of Oncology)

Keywords: radiomics, colorectal cancer, magnetic resonance imaging, artificial Intelligence

Aims: The study aimed to identify significant radiomic features from four MR sequences taken before therapy for rectal cancer, which can be used in a model to predict KRAS mutation status.

Methods: This retrospective study included patients who had MRI scans before any therapy and undergone histological and genetic examination. The patients were randomized into a training and test cohort, ultimately analyzing 47 patients. The region of interest was contoured on each MR sequence (axial diffusion-weighted, T1, T2FS, and T2HR). Additional information was collected from the patients' history. Radiomic features were calculated for each image and sequence, then with forward selection those that were deemed important predicting markers were selected. Finally, with cross-validation, each feature and sequence was weighted and combined in a model. The predictive performance of the model was measured by ROC analysis.

Results: Out of the 1500 extracted radiomic features, 40 were selected as predictors of KRAS mutation status. The inclusion of the T1 features did not improve the predictive performance of the model. Overall, the area under the curve values on different train/test splits ranged from 0.72 to 0.75.

Conclusions: It is possible to predict the KRAS status of colorectal cancer with adequate significance based on pretherapeutic MR imaging. This method may be used in cases when it is difficult to obtain appropriate histological biopsy.

Support: This work was supported by the Hungarian National Laboratory (under the National Tumorbiology Laboratory project (NLP-17)).

THE PARADOX RELATIONSHIP OF SENSORIMOTOR DEFICIT AND INFARCT SIZE IN ACUTE ISCHEMIC STROKE

Péter Kozák, Ákos Menyhárt, Réka Tóth, Eszter Farkas (Department of Cell Biology and Molecular Medicine, Albert Szent-Györgyi Medical School, University of Szeged)

Keywords: acute ischemic stroke; translational stroke study; infarct size; neurological deficit

Aims: Infarct sizes usually correlate with the degree of neurological deficit in acute ischemic stroke (AIS) patients. We have recently identified select cases in which significant neurological outcome paradoxically showed no correlation with small infarct size.

Methods: Male C57BL/6 (n=13) mice were anesthetized with isoflurane (0.8-1%). AIS was induced by the transient (60 min) intraluminal microfilament occlusion of the middle cerebral artery (MCAO). Total recanalization was achieved by the removal of the microfilament. The AIS-caused sensorimotor deficit of mice was evaluated on the Composite Garcia Neuroscore Scale (GNS, maximum: 21 points) repeated daily during the 72-hour survival period. Infarct size and brain edema was estimated 72 hours after AIS by a small animal MRI system capturing T2, DWI sequences and derived ADC maps.

Results: The infarct sizes showed variations between 7.32-52.35% of the affected hemisphere (hemispheric lesion volume, %HLV T2). In 3/13 mice (atypical cases: infarcts <15%HLV and GNS <11, n=3) the measured small infarcts (14.6±6 vs. 53.1±22 %HLV; atypical vs. typical) were associated with an unexpected profound neurological deficit (9±1 vs. 11±2 GNS points; atypical vs. typical). Consequently, we found no correlation between GNS points and infarct sizes in our AIS model (Pearson: R=0.06). The exclusion of atypical cases strengthened the correlation of infarct size and neurological deficit (Pearson: R=0.629).

Conclusions: The "translational gap" in AIS research means the unsuccessful adaptation of experimentally neuroprotective drugs and therapies into routine stroke care. To bridge the translational gap, we need reproducible animal experiments. Based on our results, we propose the inclusion and analysis of special cases for the future translational stroke studies.

Support: NKFIH (K134377, FK142218, TKP2021-EGA-28), Horizon 2020 (No. 739593), Nemzeti Agykutatási Program 3.0, ÚNKP-23-2 -SZTE-363

STUDY OF CONNECTIVE TISSUE DISEASE-RELATED INTERSTITIAL LUNG DISEASE - BMI AS A PREDICTOR OF FUNCTIONAL CHANGE

Bernadett Mák, Virág Laczkó, Alexandra Nagy, Krisztina Vincze, Noémi Eszes, Anikó Bohács, Veronika Müller (Department of Pulmonology, Semmelweis University)

Keywords: connective tissue disease-related interstitial lung disease, body mass index

Aims: Detailed review and characterization of CTD-ILD cases, which were discussed in the multidisciplinary ILD team at the Department of Pulmonology, Semmelweis University.

Methods: In our retrospective data analysis we detected that 840 cases were presented to the ILD team between 01/01/2017 and 31/12/2021. CTD-ILD was confirmed in 120 patients (14.29%) and 77 cases had a functional follow-up. In all patients symptoms, clinical parameters (including body mass index (BMI)), complex respiratory function testing, 6-min walk test were recorded.

Results: The majority of the patients were female (80.0%). Respiratory function parameters showed a restrictive trend with a decrease in CO diffusion (forced expiratory vital capacity (FVC): 83.19 ± 26.31 , forced expiratory volume in one second (FEV1)/FVC %: 101.44 ± 9.65 , forced expiratory CO diffusion capacity (DLCO): 70.73 ± 22.12). Based on the change in functional parameters, a total of 21 cases (27.27%) showed improvement (group 1, increase in FVC $\geq 5\%$ or increase in DLCO $\geq 10\%$), 22 cases (28.57%) showed progression (group 2, decrease in FVC $\geq 5\%$ or decrease in DLCO $\geq 10\%$). Comparing the two groups at baseline, more patients in group 1 experienced joint complaints (76.19% vs. 45.45%, $p=0.039$), while more patients in group 2 had chest pain (4.76% vs. 31.82%, $p=0.023$). Group 1 showed a significant BMI gain during follow-up (Δ BMI -0.41 vs. 0.87 , $p=0.046$) compared to group 2.

Conclusions: Regular weight monitoring may be an important testing method alongside spirometric controls and may sensitise the treating physician to early detection of possible progression.

PREOPERATIVE PULMONARY REHABILITATION IN THORACIC SURGERY

Jaekyung Lee, Fernanda Büchner Strachman, Janos Tamas Varga (Department of Pulmonology, Semmelweis University, Budapest)

Keywords: pre-operative pulmonology rehabilitation (pre-operative PR), chronic obstructive pulmonary disease (COPD), lung cancer, thoracic surgery, postoperative complication

Aims: Pulmonary rehabilitation (PR) is a comprehensive intervention that can improve physical and mental health, and further prevents postoperative complications in thoracic surgery patients. This study aims to measure changes in functional and quality of life parameters due to pre-operative PR.

Methods: Thirty COPD patients with lung cancer participated in a preoperative PR program, involving multidisciplinary team of respiratory physicians, PR specialists, physiotherapists, social workers, dietitians, and psychologists. The program included chest physiotherapy with breathing training, chest mobilization with shaker deluxe and power breath devices, controlled breathing techniques, patient mobilization, and personalized endurance training for lower extremities. Lung function tests (FEV1, FVC, TLC), chest kinematics (chest wall expansion, CWE), 6-minute walking test (6MWT), and breath holding time (BHT) were measured and quality of life was evaluated using the modified Medical Research Dyspnea Scale (mMRC) and COPD Assessment Test (CAT). The BODE index and an alternative scale score (BMI, FEV1, 6MWT and CAT) were calculated.

Results: Significant improvements ($*p<0.05$) were observed in the following parameters: CWE (4.3 ± 2.1 vs. 5.8 ± 2.2 cm*), BHT (22.3 ± 10.6 vs. 25.6 ± 12.3 s)*, FVC (87.4 ± 17.0 vs. $93.6 \pm 15.3\%$ pred*), FEV1 (66.2 ± 15.7 vs. $72.0 \pm 15.7\%$ pred*), and 6MWD (390.6 ± 110.8 vs. 441.7 ± 96.2 m*). Quality of life improved: mMRC (2.0 ± 0.9 vs. 1.4 ± 0.7 *) and CAT (18.3 ± 8.8 vs. 12.8 ± 7.6 *). The BODE index (3.6 ± 2.4 vs. 2.5 ± 1.6 *) and alternative scale scores (5.0 ± 2.2 vs. 3.9 ± 1.5 *) also showed improvement.

Conclusions: Pre-operative pulmonary rehabilitation allows patients to undergo thoracic surgery with much better pulmonary function and quality of life.

WS. Lecture

MODERN TECHNOLOGICAL ADVANCES IN SUSTAINABLE NUTRITION: PROVIDING BETTER HEALTH TO INDIVIDUALS

Elizabeth Keshchian (Wonder Water, LLC)

Keywords: sustainable nutrition, food safety, biodegradable technology, chronic disease prevention, eco-technological solutions

Aims: This study aims to assess the impact of modern technological advances in sustainable nutrition on individual health outcomes, focusing on innovations that enhance food safety, maintain nutritional quality, and reduce waste.

Methods: A comprehensive review was conducted on recent technological innovations in food preservation, including biodegradable freshness indicators and eco-technological products. Data from case studies in Russia, Asia, and the USA were analyzed to evaluate the public health and economic impacts of these innovations.

Results: The findings demonstrate that biodegradable food freshness stickers significantly reduce risks of contamination and spoilage by maintaining optimal storage conditions. This not only enhances food safety but also results in considerable healthcare cost savings. Additionally, these sustainable technologies help preserve essential nutrients in fresh produce, which is crucial for preventing chronic diseases and promoting overall well-being.

Conclusions: The study underscores the significant public health benefits of modern technological advances in sustainable nutrition, particularly in reducing foodborne illnesses and preserving nutritional value. The economic advantages, especially in reducing global food waste, highlight the need for ongoing innovation and collaboration among scientists, technologists, policymakers, and industry leaders to build a more sustainable and health-supportive food system.

PS1. Poster Session I. (Biochemistry-Biophysics-Cell Biology-Immunology)

SIMULTANEOUS ANTITHROMBOTIC AND ANTIFIBRINOLYTIC EFFECTS OF TRANEXAMIC ACID IN AN IN VIVO THROMBOSIS MODEL

Petra Csikos, Kata Balog Virag, Alexandra Raska, Krisztian Balint, Kraszimir Kolev, Nikolett Wohner (Department of Biochemistry, Semmelweis University; HCEMM-SU Thrombosis and Hemostasis Research Group; Department of Internal Medicine and Hematology, Semmelweis University; National Institute of Hematology and Infectology, South-Pest Central Hospital)

Keywords: fibrinolysis, bleeding, antihemorrhagic, thrombosis, tranexamic acid

Aims: Tranexamic acid (TXA) is a commonly used antifibrinolytic drug, which inhibits plasminogen activation and plasmin. Numerous trials showed that timely administration of TXA reduces bleeding deaths, meanwhile provided no evidence that TXA increases risk of thrombotic side effects, making its use in management of acute bleeding particularly appealing. Therefore, we conducted both in vivo and in vitro studies to investigate mechanisms underlying the favourable therapeutic profile of TXA.

Methods: Thrombus formation was induced using inferior vena cava (IVC) stenosis model in mice, followed by postoperative TXA injection. Blood samples were taken immediately before thrombus retrieval. Plasma was prepared to analyze monocyte chemoattractant protein-1 (MCP-1) levels via ELISA. Thrombin generation (TG) was measured in whole murine blood of IVC-stenotised or control mice. White blood cells (WBCs) were harvested from murine bone marrow and were incubated with plasminogen (+/- TXA, +/- fMLP) to measure plasminogen activation.

Results: Odds showed a 90% decreased risk for thrombus formation in the TXA-treated group. Plasma MCP-1 level was seven times higher in mice after IVC stenosis. In TG test thrombin concentration reached its maximum value twice as fast post-surgery as without surgery, while TXA reversed these effects. In plasma TG inhibitory effect of TXA was not seen. On the surface of activated WBCs plasminogen activation was increased, which was inhibited by TXA.

Conclusions: In vivo, TXA reduces risk of thrombosis in IVC stenotic mice by inhibiting cell-dependent TG at therapeutic TXA plasma concentrations.

Support: HCEMM-SU Thrombosis and Haemostasis Research Group National Academy of Scientist Education

THE METABOLIC CHARACTERISTICS OF ALPHA-KETOGLUTARATE-DEHYDROGENASE E2+/- AND E3+/- DOUBLE HETEROZYGOUS KNOCKOUT MICE

Rebeka Sára Orova, Dániel Gáspár, Márton Kokas, Mozaffaritabar Soroosh, Zsolt Radák Tímea Komlódi, László Tretter (Institute of Biochemistry and Molecular Biology, Semmelweis University, Budapest; Research Center for Molecular Exercise Science, Hungarian University of Sports Science, Budapest)

Keywords: mitochondria, alpha-ketoglutarate-dehydrogenase, ROS production, endurance test

Aims: The alpha-ketoglutarate-dehydrogenase-complex (α KGDHc) catalyses a rate-limiting step in the mitochondrial citric acid cycle producing succinyl-CoA and NADH for energy production. Being in the crossroad of oxidative metabolism, our aim was to test how the heterozygous knockout of the dihydrolipoamide succinyltransferase (E2) and dihydrolipoamide dehydrogenase (E3) subunits of the enzyme impact on the mitochondrial bioenergetic status, the reactive oxygen species (ROS) production, and the whole-body metabolism.

Methods: The experiments were carried out on brain and kidney mitochondria isolated from 100- and 200-day old double heterozygous knockout (DKO) and wild-type mice. We measured in vitro ATP synthesis, oxygen consumption, and hydrogen peroxide synthesis. The endurance of the animals was monitored on a fatigue-treadmill test.

Results: Both the mitochondria isolated from the 100- and 200- day old DKO groups showed decreased ATP synthesis and oxygen consumption compared to the control group. During succinate-induced reverse electron transfer (RET), the hydrogen peroxide production was reduced in DKO mitochondria compared to the controls. On the treadmill test, the 200-day old DKO mice performed significantly worse than their controls.

Conclusions: Our conclusion is that the younger mice can compensate for the metabolic dysfunction, whereas the decreased endurance in the 200-day old DKO mice is in connection with the decreased ATP synthesis and oxygen consumption.

Support: This work was supported by the Hungarian Scientific Research Fund (OTKA grant 143627, to A.A.) and National Research, Development and Innovation Fund (TKP2021-EGA-25 grant, to A.A.)

GENETICALLY MODIFIED MACROPHAGES FOR TUMOR THERAPY

István Révész (University of Debrecen)

Keywords: CAR-M, breast cancer

Aims: Enhancing chimeric antigen receptor macrophage (CAR-M) therapy of breast cancer by genetically engineering macrophages. One in six deaths worldwide is still caused by malignancy. Breast cancer is the second most common cancer in the world. Today's medicine is pinning its hopes on immunotherapy, alongside targeted molecular therapy, to fight the disease. Research in our laboratory is focused on developing genetically modified macrophage-based immunotherapies against solid breast cancer. Adoptive T cell-based attempts have shown less positive results against solid tumors since the microenvironment of solid tumors protects the tumor from immune destruction. We are exploring the possibility of combining the achievements of the other currently viable TAM-related therapeutic approaches with the practices of CAR-M cell manufacturing. We wish to improve the performance of the CAR-M cells by genetically engineering them to express additional factors that boost tumor-killing ability or cooperation with other immune cells.

Methods: We are using lentiviral transduction of CAR-macrophages carrying a CAR against the HER2 tumor antigen to generate IFN- α -overexpressing CAR-M cells and test their ability to engulf and kill JIMT-1 breast cancer cells. In our model system recombinant lentivirus carrying the IFNA, the CXCL9, the sCD40L or the TLR7 cDNA will be generated and used to infect the THP-1-derived CAR-Ms that have demonstrated tumoricidal activity.

Results: The results of our in vitro and animal experiments will hopefully contribute to developing immunotherapeutic procedures for clinical use. The presentation will report the first results obtained with these modified CAR macrophage cells.

INVESTIGATION OF CUTIBACTERIUM ACNES INDUCED INNATE IMMUNE MEMORY (IIM) RESPONSES IN HUMAN KERATINOCYTES

Anett Magyari, Fanni Balog, Lilla Erdei, Bolla Beáta Szilvia, Katalin Burián, Lajos Kemény, Kornélia Szabó (Albert Szent-Györgyi Health Center Department of Dermatology and Allergology; HUN-REN-SZTE Dermatological Research Group; HCEMM-USZ Skin Research Group; Department of Medical Microbiology, Szent-Györgyi Albert Orvostudományi Kar, University of Szeged)

Keywords: keratinocyte, innate immune memory, epigenetics, Cutibacterium acnes

Aims: In response to a pathogen attack, the innate immune system quickly activates and, due to innate immune memory, exhibits an altered response upon repeated activation. Although keratinocytes are not immune cells, microbial agents, such as members of the skin microbiota like Cutibacterium acnes (C. acnes), also induce IIM signaling processes in them, and cells from different body sites show region-specific behaviour. Signs of innate-training were detected in cells originating from the breast region (NHEK-B), and tolerance in the abdominal (NHEK-A) samples. IIM responses are associated with characteristic epigenetic changes in immune cells, and therefore we sought to identify such differences following C. acnes training and specific Toll-like receptor ligand (Pam3Csk4) induction in human keratinocytes.

Methods: The effects of various epigenetic modifications were examined using pharmacological inhibitors applied concurrently with the training. Changes in the whole genome methylation pattern were monitored using an ELISA-based method.

Results: The histone deacetylase inhibitor SAHA further reduced the expression of TNF α and IL-8 mRNA following Pam3Csk4 induction in NHEK-A cells. Pargyline histone demethylase inhibitor, neither alone nor in combination with *C. acnes*, did not modify the expression levels of the genes studied in NHEK-A and NHEK-B cells. The use of 5-Aza-2'-deoxycytidine, a DNA methyltransferase inhibitor, in combination with *C. acnes* treatment, reduced the expression of TNF α and IL-8 in both NHEK-B and NHEK-A cells. Concurrently, the total amounts of 5-mC and 5-hmC in the genome decreased in NHEK-B and increased in NHEK-A cells.

Conclusions: Skin microbiota members are also capable of triggering IIM responses. Keratinocytes from different body regions may react differently to these stimuli, in which epigenetic modifications may be involved.

Support: OTKA K143576, TKP2021EGA28, HUN-REN, HCEMM, Szent-Györgyi A. Kutatási Ösztöndíj 5S444

TESTING OF DOPAMINE-COUPLED, DUAL-TARGETED POLYPEPTIDE NANOCARRIERS ON THE CULTURED MODEL OF THE BLOOD-BRAIN BARRIER

Emese Kincső Páli, Mária Mészáros, Mária A Deli, Szilvia Veszelka (Szent-Györgyi Albert Orvostudományi Kar, University of Szeged)

Keywords: nanoparticle, polipeptide, alanine, glutathione, targeting

Aims: The central problem in the current treatment of brain disorders is to reach suitable drug amount to the brain due to the presence of the blood-brain barrier (BBB). Polypeptide nanoparticles (NPs) are versatile platforms for drug delivery combined high functionality with good biocompatibility. The key to the efficient brain delivery of NPs is the specific targeting of cerebral endothelial cells that form BBB. Aims: The aim of our research was to test dopamine-coupled three-armed polypeptide (3-PLG-dopa) NPs on the cell culture model of the BBB and to investigate whether the combination of glutathione and alanine as BBB targeting ligands can promote the efficient transfer of these NPs across the BBB into midbrain organoids.

Methods: The size and surface charge of NPs were determined by dynamic light scattering. The cellular uptake and BBB penetration of NPs were quantified by spectrofluorometer. The visualization of nanocarrier uptake into endothelial cells and organoids was investigated by confocal laser microscopy.

Results: We demonstrated that physico-chemical properties of NPs was ideal and the tested NPs not decreased the cell viability. Cellular uptake of targeted nanocarriers coupled with dopamine showed significantly better uptake compared to the non-targeted group. In the permeability assays, the presence of ligands promoted significantly higher penetration of NPs across the BBB and increased their internalization into organoids.

Conclusions: The glutathione-alanine ligand combination has been shown to be suitable for BBB targeting of 3-PLG-dopa nanocarriers, and our results may contribute to the development of more efficient drug delivery systems targeting the brain.

Support: This work was funded by the OTKA-PD138930 and the Gedeon Richter Plc. Centennial Foundation. E.K.P. was supported by the ÚNKP-23-2 -SZTE-365 and the National Academy of Scientists Education.

NIMODIPINE IS PROTECTIVE AGAINST SPREADING DEPOLARIZATION AND NEUROINFLAMMATION

Anna Zsigmond, Rita Frank, Eszter Farkas (Szent-Györgyi Albert Orvostudományi Kar, University of Szeged)

Keywords: nimodipine, spreading depolarisation, glial cells

Aims: We aimed to characterize the effects of nimodipine on SD and the SD-related glial reactions to know more about the circulation-independent effect of nimodipine which is primarily known as a cerebral vasodilator by block L-type Ca²⁺ channels.

Methods: We used C57BL/6 mice (n=26) to prepare 350 μ m thick brain slices than incubated them in artificial cerebrospinal fluid. Nimodipine was applied at a concentration of 10 μ M. SDs were induced by hypo-osmotic solution and electrical stimulation. SDs were recorded by local field potential recording and intrinsic optical signal

imaging. Microglial activation was determined by transformational index (TI) on Iba1-stained sections and reactive astrocytes by GFAP immunohistochemistry.

Results: Nimodipine reduced the frequency of spontaneous SDs induced by hypo-osmotic treatment (15/20 vs. 7/21 SDs/slice, control vs. nimodipine), the size of area affected by electrically induced SDs (55.5±17, 1 vs. 34.5±13.8% control vs. nimodipine), the amplitude of SDs (10.2±4.3 vs. 6.1±3 mV control vs. nimodipine) and the latency (201, 9±88.3 vs. 62.1±75.4 s; control vs. nimodipine). Nimodipine moderated microglial activation (5.2±3 vs. 8.6±3.8 TI SD vs. SD+nimodipine) and the number of GFAP positive cells (6±3 vs. 3±1 cells/10 µm² SD vs. SD+nimodipine).

Conclusions: Our results demonstrate that nimodipine is neuroprotective against SD and neuroinflammation which is independent from vascular effects. Thus the use of nimodipine may be extended in the therapy of cerebrovascular pathologies.

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LOCALIZATION OF PEROXIDASIN IN CELL CULTURE SYSTEMS

Lili Hegedüs (Department of Physiology, Semmelweis University)

Keywords: peroxidasin, collagen, glycosylation

Aims: PXDN is a heme-peroxidase, cross-links collagen IV and loses a glycosylated 143-aminoacid C-terminal domain. Its function is unknown. Our aims were to investigate the localization of the PXDN C-terminus in cell culture systems using endogenous and recombinant proteins and examine glycosylation's role in its localization.

Methods: Immunofluorescent labeling and confocal microscopy examined endogenous collagen IV and PXDN, and AU1- and FLAG-epitope tagged recombinant PXDN in human coronary smooth muscle and PFHR9 mouse teratocarcinoma cells. Polyclonal and monoclonal PXDN antibodies were developed, and epitope-tagged PXDN glycosylation mutants were created using PCR-based mutagenesis.

Results: We optimized two antigen retrieval protocols to label endogenous and recombinant PXDN. Using confocal microscopy we found that full-length PXDN showed primarily intracellular localization, whereas the N-terminal region was also in the extracellular matrix where it colocalized with collagen IV. The C-terminal region appeared mainly in the cell medium and was minimally visible in the fixed cells' matrix. Adding epitope tagged PXDN into the cell culture medium resulted in binding of the recombinant protein to the extracellular matrix in a glycosylation dependent manner.

Conclusions: With appropriate fixation and antigen retrieval, we successfully labeled endogenous and recombinant PXDN in cell cultures. Full-length PXDN is mainly intracellular, while the N-terminal is also extracellular. The C-terminal region is also found in the culture medium. Further measurements are needed to quantify glycosylation's effect on localization.

FECAL MICROBIOTA TRANSPLANTATION IN INFLAMMATORY BOWEL DISEASE

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Keywords: fecal microbiota transplantation, inflammatory bowel disease

Aims: Inflammatory Bowel Disease (IBD) is a complex set of diseases that lead to chronic inflammation in the gastrointestinal tract. The relationship between IBD and the gut microbiome is well established, making microbiome manipulation a potential target for therapy. This study aims to investigate fecal microbiota transplantation (FMT) as a treatment for patients with active IBD who have not responded to previous steroid or biological treatments. Our primary focus is on achieving steroid-free clinical remission in Crohn's disease patients following transplantation.

Methods: In the initial phase of our research, after donor recruitment and thorough screening tests, capsules were produced from the stool homogenate of suitable donors. The second phase involved collaborating with gastroenterologists to identify, recruit, and transplant potential recipients. In the third phase, we are monitoring and evaluating the effectiveness of the transplant.

Results: To date, four IBD patients have received transplants, and capsules have been prepared in advance for an additional ten recipients. For further metagenomic analysis, fecal samples have been biobanked.

Conclusions: FMT appears to be a promising alternative treatment for IBD patients with ongoing inflammation or those unresponsive to conventional drug therapies. We hope our investigation will contribute valuable insights into the long-term effectiveness of this treatment.

NLRP3 INFLAMMASOME PROTEIN EXPRESSION IN PANCREATIC NEOPLASMS

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Keywords: IPMN, NLRP3, inflammasome, PDAC

Aims: IPMN is the most common cystic neoplasm of the pancreas. The clinical relevance of the lesion is due to its increased incidence, early detectability by imaging techniques, malignant transformation tendency and better prognosis compared with pancreatic ductal adenocarcinoma (PDAC). IL-1 β and IL-18 production has been extensively investigated in PDAC, but its role in tumor progression in IPMN has not been investigated. The aim of the research is to determine the effect of the effector molecules and their antagonists in inflammasome activation on survival and the pathological properties of IPMN and PDAC.

Methods: In our study, we examined histological specimens from patients diagnosed with IPMN (n=99) and PDAC (n=89). Tissue microarrays (TMA) were prepared from the samples and labeled by multiplex immunohistochemistry using antibodies to NLRP3, Asc, caspase-1, IL-1 β , IL-18, IL-1Ra, IL-18bp and sections were digitized and evaluated using a semi-automated image analysis method.

Results: Asc, IL-1 β and IL-18 proteins showed higher expression in PDAC compared to IPMN (Asc: p<0.0001, IL-1 β : p<0.0001, IL-18: p=0.0097). Compared to the other two subtypes at the intestinal metaplasia of IPMN lower IL-18 and higher IL-18bp expression are observed (gastric vs. intestinal p=0.006, pancreaticobiliary vs. intestinal p=0.0018). Looking at all cases, significantly shorter survival was observed with high Asc, IL-1 β , and IL-18 expression. (Asc: p=0.02, IL-1 β : p=0.05, IL-18: p=0.00024) When only invasive cases were considered, high IL-18 and low IL-18bp expression were significantly associated with shorter survival (IL-18: p=0.003, IL-18bp: p=0.034).

Conclusions: Higher inflammasome activity is observed in PDAC compared to IPMN. Lower IL-18 expression is likely to underlie the improved prognosis in intestinal type IPMN. IL-18 and IL-18bp protein levels are important independent prognostic factors in pancreatic carcinomas.

RARE CASE OF TAMOXIFEN ASSOCIATED DRUG INDUCED LUNG INJURY

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Keywords: drug induced lung injury, tamoxifen

Introduction: More than 350 drugs can cause drug-induced lung injury (DILI). DILI is an interstitial inflammation and fibrosis in the lung that develops as a result of drug exposure.

Aims and Methods: Detailed case report of a 79-year-old patient treated with tamoxifen.

Results: A 79 year old female patient underwent a complex breast examination on 03.2022. UH guided core biopsy of the left breast lesion was recommended. Stereotaxic core biopsy of the left breast confirmed intermediate grade ductal carcinoma in situ (DCIS). She was treated with tamoxifen for left breast DCIS between 2022 and 2024. On 02.2024., chest, abdomen, pelvis CT scan was performed, where radiographic pneumonitis with partial regression in the left lung was seen. On 04.2024. the patient was presented to ILD team, CT scan showed ground-glass opacity (GGO), bronchiectasis, aerobronchogram. In 04. 2024. steroid administration was suggested as a therapy and the tamoxifen treatment was stopped.

Conclusions: The phenotype, imaging and histological patterns differ significantly between drugs. DILI is mostly a diagnosis of exclusion, and this poses many challenges for clinicians. Therefore, close oncological follow-ups and professional reporting of possible drug side effects is exceedingly important.

LONGITUDINAL DETECTION OF GAIT ALTERATIONS ASSOCIATED WITH HYPERTENSION-INDUCED CEREBRAL MICROHEMORRHAGES IN MICE: PREDICTIVE ROLE OF STRIDE LENGTH AND STRIDE TIME ASYMMETRY AND INCREASED GAIT ENTROPY

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Keywords: microhemorrhage, microbleed, gait, preclinical, entropy

Aims: Cerebral microhemorrhages (CMHs) are critical indicators of cerebral small vessel disease (CSVD), significantly impacting cognitive health. They serve as markers for early detection of vascular cognitive impairment. This study explores the effects of hypertension-induced CMHs on gait dynamics in a mouse model, assessing advanced gait metrics as indicators of subclinical neurological impact.

Methods: We used a hypertensive mouse model, inducing CMHs with Ang-II, L-NAME, and phenylephrine. Gait dynamics were analyzed using the CatWalk system, focusing on symmetry indices for Stride Length (SL), Stride Time (ST), paw print area, gait entropy, and regularity. The study spanned 30 days, capturing day-to-day variations in gait parameters to evaluate the impact of CMHs.

Results: Temporary increases in gait asymmetry suggested subclinical neurological signs linked to histologically verified CMHs. Increased gait entropy correlated with periods of heightened gait asymmetry, reflecting the complexity of gait dynamics in response to CMHs. Significant correlations were found between SL and ST symmetry indices and the paw print area symmetry index post-hypertension induction, indicating the interdependence of spatial and temporal gait aspects affected by CMHs.

Conclusions: Advanced gait metrics revealed sensitive, dynamic alterations in gait regulation associated with CMHs, mirroring the temporal characteristics of TIAs. These findings underscore the potential of advanced gait metrics as indicators of CMHs for early diagnosis and monitoring of CSVD.

INVESTIGATION OF TEMPERATURE-DEPENDENT VASOMOTOR RESPONSES TO HYDROGEN SULPHIDE (H₂S) BY USING A NOVEL HEAT-EXCHANGER IN WIRE MYOGRAPHY

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Keywords: hydrogen sulfide, myography, temperature, TRPA1 Cation Channel

Aims: H₂S causes various effects in vessels, but its action mechanism is not yet fully clarified. Previously, we developed a novel heat-exchanging accessory to control the temperature in wire myography. Here, we investigated the temperature-dependent vasomotor responses to H₂S in mice and rats.

Methods: Wire myography was used to record vasomotor responses *ex vivo*. Carotid arteries from TRPA1 wild type (WT) mice and Wistar rats and tail arteries from WT and TRPA1 knockout (KO) mice were tested at two different temperatures; 37 and 17°C and 37 and 20°C respectively against increasing concentrations of Na₂S (10⁻⁶ – 10⁻² M), H₂S donor.

Results: In the carotid arteries, we observed temperature-dependent differences in response to increasing concentrations of Na₂S in WT mice and Wistar rats; there was vasoconstriction at 37°C (with maximum of 0.325±0.114 mN and 0.857±0.277 mN, respectively; p<0.05 for both) while at 17°C, no apparent vasomotor response was present. The tail arteries showed temperature-dependent genotype differences; while there was vasoconstriction in both genotypes with 10⁻² M Na₂S, the KO mice produced more prominent vasoconstriction than the WT mice at 37°C (with maximum of 0.403±0.112 mN and 0.293±0.109 mN respectively; p<0.05).

Conclusions: The arteries' response to H₂S depends on the anatomical location, species and temperature. Our results suggest that TRPA1 channel has an inhibitory effect in H₂S induced vasoconstriction in warm. Furthermore, this study underlines the importance of temperature-dependent mechanisms which should be studied further.

OPTIMISING LASER SPECKLE CONTRAST IMAGING (LSCI) FOR THE SEMMELWEIS STUDY: EFFECTS OF RESISTANCE TRAINING AND HAND DOMINANCE

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Keywords: microcirculation, perfusion, laser speckle contrast imaging, reactive hyperemia

Aims: The Semmelweis Study is a prospective cohort study that utilizes LSCI to assess microvascular function and possibly identify groups with increased risk of age-related cardiovascular disease. Our objectives were (1) to evaluate whether the LSCI methodology is also suitable for us in study that consist of more than one visit and (2) to investigate the effects of short- and long-term resistance training on the microvasculature.

Methods: In this study, 10 healthy volunteers were enrolled, all of whom participated in a one-week training session using a grip-strength ring with their non-dominant hand. Skin and subcutaneous tissue perfusion of both hands were assessed by LSCI before and after training during post-occlusive reactive hyperemia (PORH) stimulation. During PORH, blood flow was restricted with an upper arm cuff for 5 minutes and then released. Perfusion units (PU) were divided by mean arterial pressure to obtain vascular conductance (VC). Paired t-test was used to compare perfusion parameters between dominant and non-dominant arms measured during the two visits.

Results: No significant difference was found in perfusion parameters between dominant and non-dominant hands before exercise. The non-dominant hand showed increased maximal VC on the skin (from 1.9±0.3 PU/Hgmm to 2.2±0.4 PU/Hgmm, p<0.01) and over the nail bed (from 2.5±0.6 PU/Hgmm to 2.9±0.7 PU/Hgmm, p<0.05).

Conclusions: Using PORH testing during LSCI we were able to detect the effects of short-term resistance training on vasculature.

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THE IMPACT OF THE COVID-19 PANDEMIC ON PSYCHOLOGICAL HEALTH IN CANCER PATIENTS

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Keywords: COVID-19, psychological distress, anxiety, mood disorders, screening tests

Aims: Disease caused by a virus named SARS-CoV-2 has been a global health crisis. It has also caused physical and mental effects. Patients may experience a number of symptoms related to brain and psychological health: cognitive and attention deficits (brain fog), seizures, psychological distress, anxiety, mood disorders, posttraumatic stress and suicidal behavior. People with cancer are at increased risk of serious illness if they get COVID-19, because their immune systems have been weakened by the cancer and/or its treatments. Anxiety and depression are the most common psychological symptoms in patients with cancer. In this study the levels of distress, anxiety and depression of oncological patients before and after COVID-19 were compared.

Methods: 30 patients before (group I) and 35 patients after the beginning of COVID-19 pandemic (group II) were involved. Subjects filled Distress Thermometer (DT) with the related problem-list, State-Trait Anxiety Inventory Form (STAI) and Beck's Depression Inventory (BDI).

Results: Significant difference between the means of two groups was in distress ($t(63)=-3,596$, $p=0,001$). The means were tendentially higher in the 2nd group for anxiety and depression. Higher values correlated with more marked difficulties on the problem-list. Means of anxiety and depression were in strong correlation with each other ($r=0,7$).

Conclusions: Screening for emotional distress in oncological patients has increased importance to recognize people who are especially in need of mental (and pharmacotherapeutic) support.

PS3. Poster Session III. (Dermatology-Internal Medicine-Family Medicine-Obstetrics&Gynecology-Rheumatology)

INVESTIGATION OF GUT MICROBIOME COMPOSITION AND THE RELATIONSHIP BETWEEN SERUM AND FECAL CALPROTECTIN IN PATIENTS WITH PSORIASIS

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Keywords: psoriasis, microbiome, calprotectin, gut inflammation

Aims: Psoriasis is a chronic inflammatory skin disease. In its pathogenesis both skin and gut microbiomes significant role has been already proven. Several studies suggest that certain types of bacteria correlate with disease activity. Gut inflammation can influence both gut and skin microbiomes. Calprotectin can serve as a marker for the inflammation's intensity and is produced by neutrophil granulocytes. The aim of this study is to examine and compare the microbiome and calprotectin levels in the blood and stool of patients with psoriasis and healthy controls.

Methods: We evaluated the calprotectin levels in blood and stool samples and analysed the microbiome composition of 20 patients with psoriasis and 20 healthy controls. We studied the following parameters: BMI, PASI (Psoriasis Area Severity Index), gender, age, smoking status and disease duration. We analyzed alpha and beta diversity, compared calprotectin levels and microbiome characteristics in different groups.

Results: In psoriasis patients Bacteroides, Frisingicoccus, Streptococcus, Olsenella, Lachnospira, Lachnospiraceae UCG-008 and Marvinbryantia were more prevalent. Elevated serum calprotectin was associated with more Lachnospiraceae UCG-008, whereas normal level showed higher UCG-002 and UCG-003 count. Elevated fecal calprotectin correlated with higher Family XIII UCG-001 prevalence, while normal levels had more Gemella and Coriobacteriales. Obese patients had higher Bifidobacterium and Eubacterium abundance but lower Marvinbryantia. In psoriasis patients with the disease for less than 5 years, Faecalibacterium and Oscillibacter were more common, while UCG-010 was more frequent in those with the disease for over 5 years. Women had higher Clostridia counts, smokers had more Faecalibacterium, Subdoligranulum and Parabacteroides. There was no significant difference in alpha and beta diversity between psoriasis and control groups.

Conclusion: Several significant differences were identified in the gut microbiome composition between the groups. In the future treating gut inflammation and modifying the gut microbiome could be the part of psoriasis therapy. Calprotectin levels in blood and stool correlating with gut inflammation may serve as therapeutic markers.

DOPAMINE AGONIST-RESISTANT PROLACTINOMA: EARLY RECOGNITION AND TIMELY MULTIMODALITY THERAPY FOR OPTIMAL OUTCOME

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Keywords: prolactinoma, dopamine-agonist resistance, Ki-67 proliferation index, transsphenoidal resection, gamma knife

Aims: Aggressive prolactinoma (APRL) represents a rare subgroup of pituitary tumors, accounting for about 2-10% of prolactinomas. Suggestive features of APRL include dopamine agonist (DA) resistance, male sex, younger age at diagnosis (age < 20), histopathology findings of cellular atypia, polymorphism, tumor transforming gene Ki-67 proliferation index > 3%, rapid growth rate, and early relapse after surgical resection. Delayed APRL recognition results in tumor growth with mass effect and associated neurologic complications, unsuppressed prolactin can lead to hypogonadism, infertility, galactorrhea, and rarely, transformation to carcinoma. Multimodal APRL treatment includes surgical resection, radiotherapy, and occasionally chemotherapy. Our aims are: early APRL recognition with DA-resistance and Ki-67 proliferation index > 3%.

Methods: We present a case of a 21-year-old male referred to the Endocrinology clinic for persistent headache evaluation. Prolactin levels were elevated at 714.20 ng/mL (1.20 - 10.70) and brain MRI revealed

macroprolactinoma of 15x17x15 mm size. Absence of radiologic or biochemical response despite maximum tolerated doses of Bromocriptine and Quinagolide led to surgical referral and transsphenoidal resection of a prolactin-positive tumor with nuclear atypia and Ki-67 index of 10-12%. Close tumor surveillance identified an early recurrence promptly treated with gamma-knife radiosurgery.

Results: On follow-up, the patient has no neurologic complaints, prolactin level remains at the normal range of 9.69 ng/mL and brain MRI reveals tumor regression.

Conclusions: Early recognition of DA-resistant, high Ki-67 proliferation index prolactinoma and implementation of timely multimodality approach with surgical resection and radiotherapy resulted in symptom resolution, biochemical response with normoprolactinemia and tumor regression.

INVESTIGATION OF CARBOHYDRATE METABOLISM DISORDERS IN ADULT WILLIAMS-BEUREN SYNDROME PATIENTS

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Keywords: prediabetes, diabetes mellitus, WBS, OGTT, HbA1c

Aims: We assessed the prevalence of prediabetes and diabetes in Hungarian adult Williams-Beuren syndrome (WBS) patients.

Introduction: WBS is a congenital, genetic disease caused by the deletion of the Williams syndrome critical region (WSCR) on the large arm of chromosome 7. As a result, the function of many genes, which influence the risk of cardiovascular, calcium and carbohydrate metabolism diseases are lost.

Methods: Thirty adult patients, diagnosed with WBS in childhood were included in the study. All patients underwent an oral glucose tolerance test (0-60-120 minutes), HbA1c, and anthropometric data (abdominal circumference and BMI) measurements. During the OGTT, venous blood glucose, C-peptide, and insulin levels were obtained every 60 minutes.

Results: 11 men and 19 women participated in the study, the average age of the population was 34+/-12 years. OGTT confirmed diabetes in 6 (20%) and 14 (46,7%) prediabetes. In the prediabetes group, impaired fasting glucose occurred in two (6.7%), and decreased glucose tolerance occurred in 12 cases (40%).

Conclusions: A large percentage of young adult WBS patients already suffer from some form of carbohydrate metabolism disorder. In the diagnosis, the oGTT seems to be reliable.

Support: Dr. Péter Reismann Department of Internal Medicine and Oncology, Semmelweis University; Dr. Dóra Balogh Department of Internal Medicine and Oncology, Semmelweis University

THE EFFECTS OF SEMAGLUTIDE TREATMENT ON LDL- AND HDL-CHOLESTEROL SUBFRACTIONS IN TYPE 2 DIABETES

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Keywords: Type 2 diabetes, LDL cholesterol, HDL cholesterol, GLP-1 receptor agonist, semaglutide

Aims: There's a close relationship between insulin resistance, obesity, and lipid abnormalities in type 2 diabetes (T2DM). The high cardiovascular risk may be reduced with effective weight reduction, adequate blood sugar and lipid control in T2DM. The once-weekly GLP-1 receptor agonist semaglutide lowers blood sugar in a glucose-dependent manner, stimulates endogenous insulin secretion, and has been proven to have beneficial effects on weight loss and atherosclerosis. Based on the results of previous studies, semaglutide may have a positive effect on lipid abnormalities.

Methods: We included 17 T2DM patients on metformin monotherapy, in whom, after the titration phase, semaglutide 1 mg/week was used in the form of subcutaneous injection. The average HbA1c was 8.2±1.7%, their average body weight was 103.3±28.1 kg, and the average duration of diabetes was 9±5.1 years. After 6 and 12 months, we evaluated the body weight change, the parameters characterizing lipid and carbohydrate metabolism.

Lipid subfractions were determined by polyacrylamide gel electrophoresis (Lipoprint System, Quantimetrix Corp. CA, USA).

Results: After 12 months, the patient's body weight decreased significantly, as well as HbA1c, total cholesterol, non-HDL and LDL-cholesterol levels. We found a significant increase in HDL-cholesterol level. Among the lipid subfractions, the small dense LDL subfraction decreased, the average LDL size and the large HDL subfraction increased and the medium and small HDL subfractions also increased.

Conclusions: Treatment with the GLP-1 receptor agonist semaglutide significantly reduces body weight, improves blood glucose level, and it has a favourable effect on lipid parameters in T2DM, and can thus inhibit the progression of atherosclerosis.

EXAMINATION OF PACAP IN EXOSOMES OF HUMAN MILK SAMPLES OF PRETERM NEWBORNS

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Keywords: exosomes, lactation, infant, Pituitary Adenylate Cyclase-Activating Polypeptide, premature birth

Aims: The pituitary adenylate cyclase-activating polypeptide (PACAP) is an anti-inflammatory, anti-apoptotic and antioxidant neuropeptide that plays an essential role in the regulation of the female reproductive system and neonatal development. In this research we aimed to quantify and compare PACAP-38 levels in the fractionated breast milk phases of preterm (n=12) and term (n=11) neonates by ELISA.

Methods: We used a new fractionation procedure to separate our breast milk samples into aqueous and fatty phases. Intact exosome and exosome-lysate fractions were isolated from the aqueous phase by additional centrifugation and sonication.

Results: We could detect PACAP-38 in all milk fractions by ELISA, although the aqueous and the exosome phases contained significantly more neuropeptide compared to the fatty phase. When comparing different fractions, no significant difference was observed between the preterm and term groups. However, when the preterm group was subdivided into two subgroups, higher PACAP-38 concentrations were measured in the milk fractions of the 30-37 weeks neonates that were significantly higher than that of the total and fatty phase of <30 weeks babies and exosome lysate of term infants.

Conclusions: Our results suggest that the amount of PACAP shows a dynamic variation in breast milk after birth. We suppose that the aqueous and exosome milk fractions containing the highest levels of neuropeptide may play an important role in neonatal development, aid the maturation of the neonatal immune system, and affect the growth and regulation of mammary gland function.

Support: TKP2021-EGA-16, K135457, Natural Brain Research Programme NAP3.0., ELKH-TKI-1401

HEALTH-RELATED QUALITY OF LIFE (HRQOL) IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Keywords: systemic sclerosis, quality of life, impairment, organ involvement

Aims: Systemic sclerosis (SSc) is a chronic autoimmune disease affecting the skin and variable internal organs. Due to proper treatment of the life-threatening complications, survival rates have improved. Therefore, the patient's health-related quality of life (HRQoL) plays an increasingly important role. The aim of this study is to examine the HRQoL and its correlations with clinical factors in SSc patients.

Methods: The clinical and HRQoL parameters were analysed among 160 SSc (138 female, 22 male, average age 55,8±13,1 years, 78 diffuse, 88 limited cutaneous SSc) and 62 healthy controls. To assess HRQoL „Functional

Assessment of Chronic Illness Therapy-Fatigue" (FACIT-F) and „Short Form-36 Mental and Physical Component Summary" (SF-36 MCS and PCS) were used.

Results: SSc patients results in all HRQoL questionnaires were significantly worse compared to healthy controls. The physical condition indicators of late-phase patients (>4 years) were significantly deteriorated than those of early-phase patients, but their mental well-being and FACIT-F scores did not differ. All HRQoL questionnaires results displayed a close negative correlation ($p<0.01$) with the age, the left ventricular mass index (LVMI), the UCLA-Gastrointestinal Test 2.0 value, additionally the pain and fatigue measured on visual analogue scale. There were positive correlations between the test values and the cardiologic result assessing left ventricular diastolic function ($p<0.05$), the manually measured muscle strength (MMT8) and the 6-minute walk test ($p<0.01$).

Conclusions: The most important factors related to the HRQoL are the cardiac diastolic dysfunction, the gastrointestinal symptoms, and the physical condition indicators, which are recommended to consider during rehabilitation of the patients.

HAND FUNCTION TESTING IN PATIENTS INFLICTED WITH SYSTEMIC SCLEROSIS AND RHEUMATOID ARTHRITIS

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Keywords: rheumatoid arthritis, systemic sclerosis, hand function

Aims: Hand function is of paramount importance in both systemic sclerosis (SSc) and rheumatoid arthritis (RA), as it significantly affects patients' health-related quality of life (HRQoL). In the present study, we compared hand function in patients with SSc and RA.

Methods: 160 SSc patients (138 women, mean age 55.8 ± 13.1 years) and 46 RA patients (41 women, average age 60.4 ± 10.5 years) participated in our research. We determined the DAS-28 score of the groups indicating inflammation. To indicate hand-impairment Hand Anatomy Index (HAI), and the rate of 30 joints of the hands with less than 75% range of motion (contractures) were defined. Function abilities were assessed using pinch strength-measure, the Manual Muscle Testing-8, the Cochin Hand Function Scale, the Health Assessment Questionnaire (HAQ); and the 36-Item Short Form Survey Instrument (SF-36) was defined for the HRQoL.

Results: Higher values of inflammation were measured in the RA group than in the SSc group based on DAS-28 ($p<0.001$). However, the number of joint contractures in the hands was higher in the SSc group ($p<0.05$), measuring HAI, no significant difference was shown between the groups. In terms of function, muscle strength of the hands and general health were worse in RA patients (HAQ, MMT8 and SF-36 $p<0.001$).

Conclusions: Although contracture rates were higher in SSc patients, RA patients with more significant inflammation and reduced muscle strength had worse overall health and hand function. This highlights the importance of reducing inflammation and hand exercises in the patients' rehabilitation.

RADIOEMBOLIZATION IN HEPATOCELLULAR CARCINOMA

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Keywords: hepatocellular carcinoma, locoregional treatment, radioembolization, holmium-166 isotope

Aims: Radioembolization is an oncointerventional procedure for the locoregional treatment of liver tumors, which exerts its therapeutic effect through the β -emitting properties of radiolabelled microbeads. Currently two types of isotopes are used in clinical practice: yttrium-90 (Y-90) and holmium-166 (Ho-166). The Ho-166 isotope has the advantage that it is suitable for both SPECT and MR imaging, allowing SPECT-based dosimetric calculations and the assessment of accurate intrahepatic distribution.

We intend to demonstrate the value of Ho-166-radioembolization through a case of a 70-year-old man with liver cirrhosis and hepatocellular carcinoma (HCC), who was candidate for liver transplantation. Using Ho-166-radioembolization our aim was to bridge the waiting time until transplantation.

Methods: First, the arterial blood supply of the tumor was mapped using a diagnostic angiography procedure, and then low-activity Ho-166-microspheres were injected into the selected position. Using SPECT, activity planning was performed, showing that 3 GBq activity was required for treatment. During radioembolization, 3 GBq Ho-166-microbeads were injected in the same position. The treatment was then evaluated by SPECT and MRI.

Results: After radioembolization, an average tumor absorbed dose of 332 Gy was measured. One month after the procedure, contrast-enhanced CT scan showed a non-enhancing necrotic area in the tumor's localization indicating complete tumoral response.

Conclusions: Based on our case report, Ho-166-radioembolization is a promising option as a locoregional treatment for selected patients with HCC.

FEMALE SEX IS AN INDEPENDENT MORTALITY REDUCING FACTOR IN PATIENTS TREATED WITH ENDOVASCULAR STROKE THERAPY FOR CEREBRAL LARGE VESSEL OCCLUSION IN A SINGLE HIGH-VOLUME CENTRE

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Keywords: female sex, mortality, large vessel occlusion (LVO), endovascular stroke therapy (EST), atrial fibrillation

Aims: We aimed to clarify the effect of sex on the 5-year mortality following endovascular stroke therapy (EST).

Methods: Consecutive patients treated with EST for LVO between 2015-2019 were included in our prospective registry from a single high-volume center. Baseline clinical characteristics and long-term mortality data were compared between women and men. Multivariate cox regression (MCR) analysis was conducted, followed by propensity score matching (PSM) to address confounding. Mortality follow-up data was acquired from National Health Insurance database, with a follow-up rate of over 98%.

Results: The clinical and follow up data of 1246 EST patients were analyzed, 596 (47,8%) were women and 650 (52.2%) patients were men. MCR analysis found that female sex is an independent predictor of decreasing mortality (HR:0.76, p=0.001). Age (HR:1.72, p<0.001), hypertension (HR:1.45, p=0.008), ischaemic heart disease (HR:1.27, p=0.013), and diabetes mellitus (HR:1.34, p=0.02) significantly increased mortality, while atrial fibrillation (HR:1.06, p=0.556) tended to increase mortality, but was not a significant predictor, respectively. PSM

to the mortality predictors of LVO patients showed, that after adjusting for potential confounders, female sex remained an independent mortality decreasing factor ($p=0.017$).

Conclusions: We found that female sex is associated with reduced mortality following EST for LVO. Our results underline the significance of further evaluation of underlying causes of the role of sex in these ischaemic stroke patients to improve prognosis and the use of scoring systems.

OPTIMIZATION OF ULTRA-HIGH-RESOLUTION CORONARY CT ANGIOGRAPHIC RECORDS USING AN EX VIVO MODEL

Dalma Tóth (Department of Medical Imaging, Semmelweis University)

Keywords: Coronary-CT-angiography, Photon-Counting Detector CT, post-mortem, reconstruction, artifacts

Aims: We aimed to investigate the feasibility of the helical and sequential ultra-high resolution (UHR) coronary CT angiography (CCTA) scan modes directly with photon-counting detector CT (PCD-CT) in an ex vivo study. We aimed to optimize image reconstruction.

Methods: Imaging in helical and sequential UHR scan modes was repeated on ex vivo human hearts. Eight vascular kernels were used for reconstruction (Bv40 to Bv89) with matrix sizes of 512 and 1024. Image noise (IN), signal-to-noise ratio (SNR), contrast-to-noise ratio (CNR), vessel sharpness (VS) and blooming artifact were quantified. Subjective image quality (IQ) was assessed.

Results: 5 ex vivo hearts were included. The IN, SNR, CNR, VS and blooming artifacts differed significantly ($p<0,005$). Softer kernels showed the lowest IN, VS and highest SNR and CNR values in both modes (INBv40hel: $30,6\pm 7,3$ HU; SNRBv40hel: $12\pm 6,9$ HU; CNRBv40hel: $16,2\pm 8,4$ HU; VSBv40hel: $421,7\pm 72,4$ Δ HU/mm versus INBv40seq: $26,7\pm 11,8$ HU; SNRBv40seq: $15,5\pm 3,7$ HU; CNRBv40seq: $17,1\pm 6,2$ HU; VSBv40seq: $443,3\pm 22,6$ Δ HU/mm). Sharper kernels showed the opposite results. Comparing quantitative parameters in helical and sequential modes, there was no significant difference for any kernel (all $p>0,05$). Blooming artifacts reduced towards Bv64seq and Bv72hel ($35,2\pm 10,2\%$ versus $33,7\pm 8,4\%$). Subjective IQ, IN and VS were rated excellent for kernels Bv40seq/hel up to Bv64seq/hel.

Conclusions: UHR helical and sequential imaging modes do not differ significantly in IQ and quantitative parameters. Optimal IQ and vessel delineation were achieved using vascular kernel Bv64 with matrix size of 512 in both modes.

DIAGNOSTICS OF HAEMORRHAGIC COMPLICATIONS AFTER RECANALIZATION IN ISCHAEMIC STROKE

András Fekete, Arnold Tóth, Andrea Trajtler (Department of Medical Imaging, Clinical Center, University of Pécs)

Keywords: iodine map, water map single-energy CT, contrast extravasation, haemorrhagic transformation

Aims: Differentiating haemorrhage from contrast staining on post-recanalization follow-up scans in acute ischemic stroke is crucial for appropriate antithrombotic treatment choices, however, it is not possible with routine single energy CT (SECT). The goal was to assess the performance of dual-energy CT (DECT) in distinguishing the two entities.

Methods: SECT and DECT were performed within 24 hours after recanalization to exclude haemorrhage in 103 acute ischemic stroke patients (59 men, 44 women, aged 66.1 ± 13 years) who underwent thrombolysis ($n=52$), thrombectomy ($n=33$), or the combination of both ($n=18$). The prevalence of hyperdensities on SECT and on DECT maps in different treatment groups were assessed.

Results: SECT showed hyperdensity in 17.5% of patients, and its prevalence was higher in thrombectomized patients compared to the other two groups ($p=0.0014$). On DECT, both iodine and blood maps were positive in all patients receiving thrombolysis and combined therapies, while in the post-thrombectomy group, both maps were positive in 46.3%, while the iodine map only was positive in 53.8% of the cases. In all patients showing SECT hyperdensity after thrombolysis, the iodine map was also positive. There was not any case with blood map only hyperdensity.

Conclusions: Since patients receive iodine contrast agent during thrombectomy, the presence of hyperdensity on iodine maps in these patients is not surprising, however, thrombolysis only patients did not receive any contrast agent, therefore, iodine map hyperdensity must be false positive, indicates the limited value of DECT.

COMPARATIVE STUDY OF THE VENTRAL TEGMENTAL AREA IN WILD TYPE AND PITUITARY ADENYLATE CYCLASE-ACTIVATING POLYPEPTIDE (PACAP) KNOCKOUT MICE

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Keywords: PACAP, Parkinson, neurodegeneration, dopamine, microglia

Aims: PACAP is a neuroprotective peptide that attenuates oxidative stress, reduces inflammation, and modulates apoptotic pathways. Numerous earlier studies showed its protective role in Parkinson's disease models. Our prior experiment compared wild-type(WT) and PACAP knockout(KO) mice across different ages, revealing no significant changes in the number of dopaminergic neurons, but an increase in resting microglia in aging PACAP KO mice. Our current study focuses on the ventral tegmental area(VTA), an important dopaminergic region for social behavior regulation.

Methods: We examined WT(n=5-5-5) and PACAP KO(n=5-4-5) mice aged 1.5,4, and 8 months, labeling dopaminergic cells with tyrosine hydroxylase and microglia with Iba1 immunostaining. PACAP-specific PAC1 receptor (PAC1R) expression in neurons was also assessed, and microglia were classified by morphology.

Results: We observed an age-related decline in dopaminergic neurons in both genotypes, more pronounced in KO mice. Colocalization with PAC1R was sporadic. Microglial analysis revealed an age-associated reduction in cell numbers in both groups, with inactive microglia decreasing in aging KO mice and active microglia decreasing in WT mice. 1.5-month-old KO mice had significantly more inactive microglia than age-matched WT mice.

Conclusions: Though dopaminergic cell loss was not evident in the substantia nigra, a significant decline in dopaminergic cells occurred in the VTA with age, particularly in KO animals. This suggests potential earlier behavioral alterations in PACAP KO mice due to age-related loss of dopaminergic VTA neurons. Microglia decreased with age in both genotypes, but active microglia remained unchanged in PACAP KO mice, potentially increasing dopaminergic cell death in the absence of endogenous PACAP's immunosuppressive effect.

OPTIMIZATION OF AN ISCHEMIC RETINOPATHY MOUSE MODEL AND THE CONSEQUENCES OF HYPOXIA IN A TIME-DEPENDENT MANNER

Inez Bosnyak, Nelli Farkas, Dorottya Molitor, Balazs Meresz, Evelin Patko, Tamas Atlasz, Alexandra Vaczy, Dora Reglodi (Department of Anatomy, HUN-REN-PTE PACAP Research Team, Medical School, University of Pécs; Institute of Bioanalysis, Medical School, University of Pécs; Department of Sportbiology; Faculty of Sciences, University of Pécs)

Keywords: retina, ischemia

Aims: The retina has one of the highest metabolic activities and oxygen consumption, so insufficient blood supply leads to visual impairment. The incidence of these conditions is increasing, however, no effective treatment without side-effects is available. Furthermore, the pathomechanism of these diseases is not fully understood. Our aim was to develop an optimal ischemic retinopathy mouse model to investigate the retinal damage in a time-dependent manner.

Methods: Retinal ischemia was induced by bilateral common carotid artery occlusion (BCCAO) for 10,13,15 or 20 minutes, or by right permanent unilateral common carotid artery occlusion (UCCAO). Optical coherence tomography was used to follow the changes in retinal thickness 3,7,14,21 and 28 days after surgery. The number

of ganglion cells was evaluated in the central and peripheral regions on whole-mount retina preparations. Expression of glial fibrillary acidic protein (GFAP) was analyzed with immunohistochemistry and Western blot.

Results and conclusions: Retinal degeneration and ganglion cell loss was observed in multiple groups. Our results suggest that the 20-minute BCCAO is a good model to investigate the consequences of ischemia and reperfusion in the retina in a time-dependent manner, while the UCCAO causes more severe damage in a short time, so it can be used for testing new drugs.

Support: This research work was conducted with the support of the National Academy of Scientist Education Program of the National Biomedical Foundation under the sponsorship of the Hungarian Ministry of Culture and Innovation (FEIF/646-4/2021- ITM_SZERZ).

IMPEDANCE BASED DENTIN THICKNESS MEASUREMENTS

Noémi Bereczki (Department of Oral Diagnostics, Semmelweis University)

Keywords: dentin thickness, impedance measurement, micro-CT, pulp vitality

Aims: The purpose of my work was to determine the remaining dentin thickness (RDT) value of preparational cavities formed on extracted teeth side's using a dentin thickness measuring device developed by Semmelweis University. RDT can be critical in the survival of the tooth.

Methods: I collected 15 extracted wisdom teeth. I drilled a cylindrical cavities with a diameter of approximately 2 mm into the crown dentin, removed the smear layer and measured the impedance of a given area three times. The optical determination of dentin thickness was performed using μ CT in the DataViewer program. This is the measured distance value. I calculated the distance values from the impedance data measured with the dentin thickness measuring device, using an equation. I subtracted the two values from each other. The standard error was defined as 0.61 mm. The statistical analysis was carried out in the SPSS program at $\alpha=0.05$ significance level. After the normality test, we compared the values with a paired sample T test.

Results: There was a significant difference between measured distance values and calculated distance values ($p=0.001$). 64,41% fell inside the error limit of 0.61 mm in absolute value. 30,51% had negative deviation from the error limit, which means we measured the distance smaller with the instrument, compared to μ CT. This is clinically usefull. Only 5,08% had a positive deviation.

Conclusions: Therefore, from a practical point of view, the use of the device is reliable, and with its clinical application, we can avoid unwanted opening of the dental pulp.

LONG-TERM DETECTION OF ELUTED MONOMERS, INITIATORS, AND INHIBITORS FROM VARIOUS TYPES OF DENTAL RESIN COMPOSITES

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Keywords: polymerization, elution, cytotoxic components, bulk-fills, high-performance liquid chromatography

Aims: Cytotoxic components of resin-based dental composites (RBC) are prone to dissolution in the moist environment of the oral cavity. The released molecules can exert their effect both locally and systemically. The purpose of this investigation was to determine the quantity and temporal changes of monomers, inhibitors, photo-, and co-initiators eluted from conventional, bulk-fill, and thermoviscous RBCs.

Methods: Cylindrical 4-mm thick bulk-fill and 2x2 mm thick layered conventional RBC samples were prepared. The thermoviscous bulk-fill RBC was preheated to 65°C before polymerization. Polymerized samples were stored in 75% ethanol for 20 weeks. The solvent was refreshed at the 1st, 2nd, 4th, 8th, and 20th weeks. The quantity of eluted components was determined using high-performance liquid chromatography after identification with standard molecules at the end of each soaking period. One-way ANOVA, Tukey post-hoc tests and generalized linear model statistics were used to analyze the data.

Results: The highest amount of monomer was dissolved at the first week, significantly lower ($p<0.001$) quantities were detected later on. Even in the 20th week, detectable components were released from all the investigated RBCs. Although the dissolution showed a decreasing tendency, the amount of eluted components increased

significantly in the 4th and 20th weeks. Significantly more monomer eluted from conventional, layered samples compared to the bulk-fill RBCs ($p < 0.01$). Both RBC type and soaking time significantly influenced the elution ($\eta^2 = 0.99$; $p < 0.001$).

Conclusions: Depending on the composition and application type of RBCs, molecules dissolved to varying degrees even after 20 weeks.

COMPARISON OF CEREBRAL MICROEMBOLIZATION PATTERNS USING RFA AND PFA ATRIAL FIBRILLATION ABLATION TECHNIQUES WITH ROBOTIC TRANSCRANIAL DOPPLER ASSISTANCE - INITIAL RESULTS

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Keywords: pulmonary vein isolation, radiofrequency ablation, pulsed field ablation, transcranial doppler

Aims: Our objective is to investigate the cerebral microembolization signals (MES) in patients undergoing PF-ablation using r-TCD, and to compare the number of MES between the 90 W radiofrequency ablation (RFA) "very high power short duration (VHPSD)" and "pulsed field ablation (PFA)".

Methods: We compared cerebral microembolization signals (MES) in AF ablation patients using r-TCD between 90 W radiofrequency (RFA) "very high power short duration (VHPSD)" and "pulsed field ablation (PFA)". Sixteen procedures used VHPSD, ten used PFA. MCA flow curves were recorded bilaterally with r-TCD and MES analyzed with AI software. Continuous variables were compared using t-tests and categorical variables with Fisher's exact test. A p-value below 0.05 was considered significant.

Results: Baseline parameters were similar between the two groups (mean age: 63 vs. 58, $p=0.253$; EF: 59% vs. 62.2%, $p=0.33$). Ablations performed with VHPSD were significantly longer compared to PFA (88.7 min vs. 54.7 min, $p<0.001$), with a significantly shorter left atrial time during PFA (52.1 min vs. 29 min, $p<0.001$), however, fluoroscopy duration was significantly longer with PFA (5.4 min vs. 9.3 min, $p=0.009$). No solid emboli, new ischemic lesions on cranial MRI, or neurological deficits were observed. During the ablation part of the procedures, we detected an average of 246 gas MES with PFA and 138 with RFA ($p=0.216$).

Conclusions: More MES were detected during PFA, but the difference was not significant. A larger sample is needed to determine the cerebral safety of PFA compared to RFA.

MAGNETIC RESONANCE IMAGING CHARACTERISTICS OF ISCHEMIC SCAR TISSUE IN PATIENTS WITH MALIGNANT ARRHYTHMIA

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Aims: The infarcted, ischaemic myocardium suffers electrophysiological changes that predispose the patient to the development of malignant arrhythmias. The lack of recognition and timely treatment can result in the deterioration of patient status and even sudden cardiac death (SCD). Seeking correlation between various parameters of the ischemic scar tissue and the later appearance of malignant arrhythmias.

Methods: 62 patients, treated at the Cardiomed heart clinic of Marosvásárhely were included in our study, whose medical history included an ST segment elevation myocardial infarction (STEMI) and a contrast based post-infarction (>1 month) follow-up MRI scan. The group was divided in two: 31 patients (the studied, MA group) suffered a malignant arrhythmic (MA) episode following STEMI; 31 patients (control group) who only suffered a STEMI. On the follow-up MRI images we studied the Late Gadolinium Enhancement of the involved myocardium, obtaining data regarding: total left ventricular (LV) mass; infarcted myocardial mass (IM) and the transmural (HTE) of the ischaemic scar tissue. The acquired data was then displayed and analyzed with the help of the 16 segments heart vortex model.

Results: We found significant differences between the studied and control groups in case of the infarcted myocardial mass (IM g) (30.02 ± 14.89 vs. 15.88 ± 10.18 ; $p<0.0001$); the transmural scar tissue mass (28.51 ± 15.41 vs. 14.61 ± 11.46 ; $p=0.0002$) and the transmural scar tissue volume (27.15 ± 14.68 vs. 10.23 ± 7.086 ; $p<0.0001$), all of them showing larger, more severe values in the studied, MA group. Further dividing

the groups based on culprit arteries (LAD vs. RCS, Cx), we found that in case of the malignant arrhythmia group, the mean infarctised myocardial mass ($p=0.0041$), transmural (HTE g) ($p=0.0046$) and the segmental percentage involvement (HTE %) were all larger in LAD affected patients than in those of the control group with the same affected artery. The segments supplied by the LAD artery (1., 2., 7., 8., 13., 14.) also showed higher values regarding transmurally involved myocardium mass in case of the MA group (30.96 ± 26.85 vs. 19.55 ± 21.78 ; $p=0.0034$).

Conclusions: The extent and degree of transmural involvement are determining factors in the process of arrhythmogenesis. The loss of myocardium and the resulting scar tissue in the LAD perfusion territory correlates significantly with the appearance of malignant arrhythmic events and SCD. The MRI imaging is an exquisite, objective and punctual modality, useful for scar tissue characterization, risk stratification and possibly for SCD prediction.

A DUAL-TASK DEEP LEARNING MODEL TO ACCURATELY ASSESS BIVENTRICULAR EJECTION FRACTIONS FROM SINGLE-VIEW ECHOCARDIOGRAPHIC VIDEOS

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Keywords: deep learning, echocardiography, left ventricular ejection fraction, right ventricular ejection fraction

Aims: We aimed to develop a deep learning (DL) model to predict 3D echocardiography (3DE)-derived left and right ventricular ejection fractions (LVEF and RVEF) from 2D apical 4-chamber (A4C) view echocardiographic videos.

Methods: After pre-training on 29,424 unlabeled A4C videos from 15,533 echocardiographic studies, the DL model was trained and internally validated on a dual-center database comprising 5,341 labeled A4C videos from 1,408 studies. The model's performance was also assessed on 1,645 labeled A4C videos of 418 healthy adults from the World Alliance of Societies of Echocardiography (WASE) study. Last, we evaluated the model on a low-risk, community-based cohort (1,269 A4C videos of 1,269 individuals) with a 10-year follow-up to investigate the associations between the predictions and all-cause mortality.

Results: During internal validation, the DL model achieved a mean absolute error of 4.62 and 4.58 percentage points and an R^2 of 0.82 and 0.62 in predicting LVEF and RVEF at the study level, respectively. In the WASE study cohort, the model predicted LVEF and RVEF with a study-level mean absolute error of 4.39 and 5.58 percentage points, respectively. In the community-based cohort, both the DL-predicted LVEF (hazard ratio: 0.96 [0.94 – 0.99], $p=0.001$) and RVEF (hazard ratio: 0.95 [0.92 – 0.98], $p<0.001$) were associated with 10-year all-cause mortality.

Conclusions: The proposed DL model enabled the accurate assessment of biventricular systolic function based on a single 2D echocardiographic view. It also exhibited robust performance when validated in a multi-ethnic dataset, and the prognostic value of its predictions was also confirmed in the community.

Support: Project no. RRF-2.3.1-21-2022-00004 (Artificial Intelligence National Laboratory – MILAB) has been implemented with the support provided by the European Union.

IDENTIFICATION OF CARDIOPROTECTIVE MATRIX METALLOPROTEINASE-2 AND BIGLYCAN-ASSOCIATED MICRORNAS BY REVERSE PREDICTION IN A PORCINE ACUTE MYOCARDIAL INFARCTION MODEL

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Keywords: biglycan, ischemic conditioning, matrix metalloproteinase, microRNA, porcine
Aims: We hypothesize that cardiac MMP and BGN signaling involved in the protective effects of ischaemic conditioning (Icon). MicroRNAs (miRNA) targeting MMPs, BGN and their regulation pathways may contribute to their action.

Methods: Reverse mRNA-microRNA target prediction was performed by using the miRNAtarget.com™ software to identify human microRNAs with possible regulatory effect on MMP and BGN-related genes. To validate the identified miRNAs in the predicted network, we compared them to two cardioprotective miRNA omics derived from pig and rat models of MIRI in the presence of ICons. Among the experimentally measured miRNAs, we sought 100% sequence identity.

Results: We identified 1289 miRNAs in the predicted network and among the experimentally measured miRNAs, we found 100% sequence identity to human predicted regulatory miRNAs in case of 37 porcine and 24 rat miRNAs. Upon further analysis, 42 miRNAs were identified as MIRI-associated miRNAs, from which 24 miRNAs were counter-regulated due to Icons. Our findings highlight 24 miRNAs that potentially regulate cardioprotective therapeutic targets associated with MMPs and BGN in a highly translatable porcine model of acute myocardial infarction.

Conclusion: In a clinically relevant porcine AMI model with high translational value, we identified 9 miRNAs as potential therapeutic targets that affect the expression and function of MMP-2 and BGN proteins.

Support: SZTE-SZAOK-SZGYA-2021 proposal, National Research, Development and Innovation Office, OTKA-138223; ÚNKP-23-5-SZTE-704, National Cardiovascular Laboratory (RRF-2.3.1-21-2022-00003).

THE IMPACT OF CORONARY REVASCULARIZATION ON ATRIAL FIBRILLATION

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Keywords: atrial fibrillation, coronary artery disease, catheter ablation, cardiac CT angiography

Aims: Atrial fibrillation (AF) patients undergoing catheter ablation (PVI) have a 8-10% prevalence of obstructive coronary artery disease (OCAD) visualized by cardiac CT angiography (CCTA). There is no clear data on the impact of revascularization of OCAD on the success rate of PVI and cardiovascular (CV) complications. This study aimed to determine whether revascularization of OCAD detected by CCTA before PVI improves ablation success and CV event rates.

Methods: This retrospective study examined patients who were referred for invasive coronary angiography (ICA) based on their CCTA findings between 2013 and 2020 (n=169). We analyzed their ICA findings, the success rate of PVI, and their CV complications down the line. The Fischer test was used for statistical analysis, with a significance level of $p < 0.05$.

Results: 131 patients underwent PVI, and of these, 93 also underwent ICA, with only 52% requiring percutaneous coronary intervention (PCI). Comparing those who underwent PCI and those who underwent PVI alone, we found no significant difference between the rates of AF recurrence (29/51 [57%] vs 42/80 [53%] $p=0.6$), bleeding complications (14/51 [27%] vs 12/80 [15%], $p=0.081$) and acute coronary syndromes (5/51 [9,8%] vs 4/80 [5%], $p=0.3$). PCI was more frequent in the persistent AF group [20/37 (54%) vs 31/94 (33%), $p=0.026$].

Conclusions: CCTA has a lower positive predictive value in patients with atrial fibrillation. PCI did not significantly impact recurrence or CV complications. The need and timing of OCAD revascularization require individual consideration, with particular attention to persistent atrial fibrillation patients.

SAFETY AND FEASIBILITY OF ZERO-FLUOROSCOPY TECHNIQUE IN ABLATION-INDEX GUIDED PULMONARY VEIN ISOLATION: A PROSPECTIVE, SINGLE CENTER TRIAL

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Keywords: atrial fibrillation, catheter ablation, zero-fluoroscopy

Aims: Conventionally, pulmonary vein isolation (PVI) is performed using fluoroscopy, but it can also be conducted using a zero-fluoroscopy (ZF) technique with electroanatomical mapping systems and intracardiac ultrasound. This study aimed to compare procedural data of ablation-index guided point-by-point radiofrequency (RF) PVI performed with non-zero-fluoroscopy (NZF) versus ZF approaches.

Methods: We enrolled 100 consecutive patients undergoing PVI for antiarrhythmic drug-refractory atrial fibrillation (AF) in a prospective observational study. The first 50 cases used the NZF technique, and the remaining 50 used the ZF technique. We compared procedural time, fluoroscopy exposure, ablation parameters, and complication rates between the two groups.

Results: The ZF group had significantly shorter procedural times (59.6±10.7 min vs. 74.6±13.2 min, $p<0.0001$), primarily due to shorter times from puncture to the start of left atrial mapping (17 [16; 20] min vs. 31 [23; 34.5] min, $p<0.001$). No differences were found in the number of RF applications (81 [73; 103] vs. 83 [71; 91], $p=0.67$), total ablation energy (54986 ± 13093 Ws vs. 55500 ± 11907 Ws, $p=0.48$), or left atrial dwelling time (41.5 [36; 52.5] min vs. 40.5 [35; 46], $p=0.14$). The ZF group achieved complete fluoroscopy elimination in all cases, with significant reductions in fluoroscopy time (0 sec vs. 132 sec, $p<0.0001$) and dose (0 mGy vs. 4.8 mGy, $p<0.0001$). The acute success rate was 100%, with no complications in either group.

Conclusions: Ablation-index guided ZF PVI is feasible and safe, offering shorter procedure times and eliminating fluoroscopy exposure while maintaining high success rate without increased complications.

IMPACT OF CANCER CACHEXIA ON CARDIAC HEALTH IN EOSOPHAGEAL CANCER PATIENTS: A PROSPECTIVE PILOT STUDY

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Keywords: Cachexia, Oesophageal Cancer, Cardiac MRI

Aims: Cachexia, marked by muscle wasting and unintended weight loss, is strongly associated with esophageal cancer and has profound impacts on multiple organ systems, including the heart, making it a topic of growing interest in cardiology. Understanding how cachexia influences the heart is vital for providing comprehensive care and improving patient outcomes. This study aims to elucidate the impact of cancer cachexia on heart health, highlighting the importance of addressing this syndrome in the management of esophageal cancer.

Methods: This prospective pilot study gathers the data of patients with oesophageal cancer receiving cardiac MRI examinations starting from 2023. We analyzed their MRI findings in the context of physical parameters such as their weight loss and grade of dysphagia.

Results: Among 32 patients, 2 had surgery, 17 are awaiting surgery or undergoing treatment, and 10 were inoperable due to progression or poor condition. Three patients exited. Initially, 34.4% (n=11) could only consume liquids, and 46.9% (n=15) had over 10% weight loss, both affecting survival. Additionally, 25.0% (n=8) had reduced ejection fractions (EF). 37.8% (n=8) of those with preserved EF had reduced stroke volume index with all 16 of them having decreased left ventricular mass.

Conclusions: The changes in body composition due to cachexia might have a significant impact on the cardiac function and through that on the prognosis as well. However there are many confounding factors regarding this population, so further investigation with a larger sample size and longer follow-up period is needed.

PS6. Poster Session VI. (Anesthesiology-Intensive Care-Emergency Care-Neurosurgery-Surgery-Traumatology)

VISCOELASTOMETRY GUIDED THROMBOLYSIS THERAPY FOR PULMONARY EMBOLISM - NEW PROTOCOL: A SINGLE-CENTER RANDOMISED CONTROLLED TRIAL

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Keywords: pulmonary embolism, viscoelastic tests, systemic thrombolysis therapy, intensive care

Aims: According to the protocol of the ESC, systemic thrombolysis therapy (STT) for treating pulmonary embolism (PE) is recommended only in the high-risk group, following a treatment regimen of 100 mg rt-PA over 2 hours. Our aim was to develop a safer, more effective, time-extended, ClotPro[®] viscoelastic test-guided STT for treating PE.

Methods: Adult patients diagnosed with PE were enrolled in a prospective randomised interventional clinical trial. In the ClotPro[®]-guided group (CPG), the rt-PA dose was adjusted according to the viscoelastometry results. Right ventricular dysfunction (RVD) was monitored every two hours by echocardiography, and thrombolysis was discontinued once RVD was resolved. In the control group (CG), the treatment protocol by the ESC was followed. In both groups, seven viscoelastic tests were performed hourly during thrombolysis.

Results: 33 patients were enrolled in the study, of which 13 were excluded. ClotPro-guided treatment was applied in 13 cases, and the control protocol was followed in 7 cases. In the CPG, the mean length of treatment and the rt-PA dose were 8.38±1.63 hours and 33.00±12.45 mg. Severe bleeding complications occurred in 2 cases in the CG and 1 case in the CPG. In the CPG, RVD resolved in all cases except for one patient with chronic pulmonary hypertension, while persistently occurred in 2 patients in the CG. Severe coagulopathy was observed multiple times in the CG.

Conclusions: The extended, ClotPro[®]-guided STT for PE that we have developed seems to be more effective and safe.

Support: DiaCare Solution Kft.

TIME DEPENDENT CHANGES OF SERUM (NEURO)BIOMARKERS DURING NON-SUSTAINED PULSELESS VENTRICULAR TACHYCARDIA CAUSED CEREBRAL HYPOPERFUSION

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Keywords: neurobiomarkers, NSE, S100B, arrest, TAVI

Aims: According to the European Resuscitation Council guideline, the neuron injury marker Neuron-Specific Enolase (NSE) indicates potential irreversible central nervous system (CNS) involvement after circulatory arrest (CA). An increase in serum S100B also signals CNS injury. However, the changes of neurobiomarkers following short CA remain not clearly understood. **HYPOTHESIS** During CA-induced cerebral hypoperfusion, serum concentrations of NSE and S100B exhibit time-dependent kinetics.

Methods: Patients without neurological involvement who undergo transcatheter aortic valve implantation were selected for self-controlled study. CA was performed by temporary VVI pacemaker (150-250 beats/min). Blood samples were taken 20 minutes before CA (Pre), then 1-(R), 20-(P1), 65-(P2) and 110 minutes (P3) after the return of spontaneous circulation. Statistical significance: RM-ANOVA ($p < 0,05$).

Results: S100B serum concentration increase from the prearrest until the P2, then decrease to the P3 (0: $51 \pm 3,92$ ng/L, R: $117 \pm 22,03$ ng/L, P1: $174 \pm 26,51$ ng/L, P2: $220 \pm 43,51$ ng/L, P3: $143 \pm 25,39$ ng/L, $n=27$, $p < 0,05$). NSE serum concentration increase from the prearrest until the P3 (0: $10,65 \pm 0,39$ ug/L, R: $12,7 \pm 0,62$ ug/L, P1: $14,80 \pm 1,72$ ug/L, P2: $15,32 \pm 1,23$ ug/L, P3: $17,28 \pm 1,15$ ug/L $n=27$, $p < 0,05$).

Conclusions: According to our results, serum concentration of NSE exhibits a linearly increasing, while serum S100B concentration shows an inverse “U-shape” tendency. S100B demonstrates higher sensitivity compared to NSE in short-term cerebral hypoperfusion. The changes of serum neurobiomarkers exhibit a time-dependent distribution.

TIME-DEPENDENT CHANGES OF S100B AND NSE NEUROBIOMARKER SERUM KINETICS AFTER SEVERE BRAIN INJURY IN EMERGENCY DEPARTMENT

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Keywords: sTBI, neurobiomarker, NSE, S100B

Aims: Severe traumatic brain injury (sTBI) is a common cause of death and disability worldwide. sTBI is defined by both the initial primary injury and the subsequent secondary injuries. To determine the severity, the everyday diagnostic aspect were supplemented with a so-called neurobiomarker kinetics. The most commonly used neurobiomarker is S100B. The serum kinetics of S100B increases with minor to moderate TBIs, but the way it changes in the first hour is lesser known. We hypothesized that after sTBI, the serum concentrations of Neuron Specific Enolase and S100B neurobiomarkers shows time-dependent changes in the emergency department.

Methods: Patients with sTBI in the T1 triage category were selected in the study. Samples were taken immediately after ED admission (I.), and at the 20. (II.) and 40. (III.) minutes. Serum NSE, S100B and Troponin concentration were determined by conventional laboratory testing. Significance ($p < 0,05$): RM-ANOVA.

Results: NSE decreased from the I. to the III. timepoint (I: 62.37 ± 7.05 ng/l vs. II: 45.83 ± 5.79 ng/l vs. III: 41.83 ± 5.13 ng/l; n=4). S100B decreased from from the I. to the III. timepoint (I.: 5530 ± 560 ng/l vs. II: 2322.5 ± 386.1 ng/l vs. III: 1937.5 ± 253.33 ng/l; n=4). Troponin increased from the I. to the III. timepoint (I: 16.06 ± 1.34 ng/l vs. II: 17.93 ± 4.59 ng/l vs. III: 22.79 ± 7.58 ng/l; n=4).

Conclusions: Our preliminary results show that serum concentrations of NSE and S100B after TBI exhibit time-dependent serum kinetics different from troponin kinetics. This raises the importance of more precise determination of sampling times.

EXPLORING THE PREDICTIVE VALUE OF NLR FOR SEPTIC COMPLICATIONS IN PANCREATIC CANCER: A NON-CONVENTIONAL APPROACH

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Keywords: pancreatic cancer, Neutrophil-to-lymphocyte ratio (NLR), sepsis

Aims: Pancreatic cancer is one of the leading causes of tumour-related mortality in developed countries. Currently, surgical removal remains the only significant chance for recovery. However, complications arising after surgical care continue to exhibit high morbidity. Timely recognition of these complications is crucial, and markers that can be conventionally applied in everyday clinical practice play a key role in their early detection, such as C-reactive protein (CRP) or procalcitonin (PCT). The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR), calculated from parameters of the routine complete blood count, may also serve as potential markers for the occurrence of postoperative complications. The primary aim was to assess the predictive capability of traditional and non-conventionally used markers in predicting postoperative septic complications of pancreatic cancer surgeries.

Methods: We followed 47 patients who underwent pancreatoduodenectomy for five days after postoperative admission to the Intensive Care Unit of the University of Pécs Medical School. During this time, we measured CRP, PCT, NLR, and PLR levels and compared the changes in these markers between patients who developed sepsis and those who remained complication-free.

Results: Among the patients, 31 remained complication-free, while 16 developed sepsis. Significant differences were observed between the two groups regarding PCT and NLR. During the postoperative period, both septic and complication-free patient groups exceeded the upper limit of the laboratory-defined reference range (5 mg/L) for CRP levels. However, no significant differences or significant differences in lymphocyte count or PLR values were observed.

Conclusions: We conclude that PCT and NLR levels could be useful prognostic tools for predicting septic complications in patients undergoing pancreatic cancer surgery.

Support: "Thematic excellence program- NVA- 06" Establishment of the Center of Excellence in Defense Health at the University of Pécs

MONITORING APIXABAN SERUM LEVELS AND EFFICACY IN PATIENTS AFTER PULMONARY EMBOLISM

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Keywords: Viscoelastic Coagulation Monitoring, anticoagulation

Aims: Apixaban is a reversible inhibitor of activated Factor X. Several methods are available for measuring the drug level, but its correlation with efficacy has not yet been determined. Our aim is to compare serum drug levels with mass spectrometry (MS) and chromogenic-based (Chr) measurements and to monitor the effects observed at different drug levels.

Methods: Twenty patients were included in the study who had previously been enrolled in the clinical trial of viscoelastometry-guided thrombolysis in case of pulmonary embolism (PE) and subsequently received 2x5mg apixaban. Follow-up examinations were conducted 1, 3, and 12 months after PE diagnosis. MS and Chr-based drug level determinations and viscoelastic clotting monitoring with ClotPro were performed before drug intake

and 2 hours afterwards. To evaluate the results, we conducted various statistical analyses using GraphPad Prism software.

Results: Significant differences were found between MS and Chr-based drug levels (Wilcoxon; difference of medians: 21 ng/ml; $p < 0.0001$), Bland Altman test indicating tendentially higher values measured by MS. The determination of viscoelastic clotting time (CT) values depending on MS levels showed strong correlation (Spearman-correlation; $r = 0.72$ in case of RVV-test).

Conclusions: When comparing the results of MS and Chr measurements, significant differences were observed in favour of MS, showing higher serum levels. During effect monitoring, significant CT time prolongation was observed at high drug levels across all three ClotPro tests. However, in IN tests, CT values falling within the normal range suggest that 2x5 mg apixaban therapy only resulted in prophylactic-level anticoagulation.

Support: DiaCare Solution Kft.

POSSIBILITIES OF OMITTING SENTINEL LYMPH NODE BIOPSY IN PATIENTS OPERATED FOR MALIGNANT BREAST CANCER

Anna Erdodi, Zoltan Horvath (Department of Surgery, University of Szeged)

Keywords: breast cancer, axillary surgery, sentinel lymph node biopsy

Aims: Our study aims to identify which preoperative factors, when present together, predict a negative lymph node status.

Methods: We retrospectively analyzed the data of 974 patients who underwent surgery for malignant breast tumors at the SZTE SZAKK Surgical Clinic between January 1, 2019, and December 31, 2022. We examined which combination of preoperative factors (ultrasound examination, BMI, age, histological results, etc.) best predicts non-metastatic axillary lymph node status, thereby potentially avoiding the need for the currently recommended sentinel lymph node biopsy.

Results: Out of the 974 patients who underwent surgery for malignant breast tumors, 716 underwent SLNB. The final histological results showed positivity in 227 cases and no metastatic sentinel lymph nodes in 489 cases. Our statistical analysis, based on logistic regression, indicated that patients with negative lymph node status as assessed by preoperative ultrasound, Grade 2 tumor stage, age under 40, and a BMI under 30, had a higher probability of not having metastasis in the sentinel lymph node upon final histological examination (Nagelkerke $R^2 = 52.6$, $X^2(2) = 13.05$, $p = 0.001$).

Conclusions: As breast cancer treatment evolves, the focus on personalized therapy is increasing. Our results suggest that omitting SLNB in the appropriate patient group could minimize unnecessary surgical interventions and their associated complications, without affecting mortality.

EFFECT OF BGP-15 ON THE REGENERATION OF ARTERIAL MICROVASCULAR ANASTOMOSES IN RATS

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Keywords: microvascular anastomosis, BGP-15, tensile strength, hematology, hemorheology

Aims: Systemic sclerosis (SSc) is a chronic autoimmune disease affecting the skin and variable internal organs. Due to proper treatment of the life-threatening complications, survival rates have improved. Therefore, the patient's health-related quality of life (HRQoL) plays an increasingly important role. The aim of this study is to examine the HRQoL and its correlations with clinical factors in SSc patients.

Methods: The clinical and HRQoL parameters were analysed among 160 SSc (138 female, 22 male, average age 55.8 ± 13.1 years, 78 diffuse, 88 limited cutaneous SSc) and 62 healthy controls. To assess HRQoL „Functional

Assessment of Chronic Illness Therapy-Fatigue" (FACIT-F) and „Short Form-36 Mental and Physical Component Summary" (SF-36 MCS and PCS) were used.

Results: SSC patients results in all HRQoL questionnaires were significantly worse compared to healthy controls. The physical condition indicators of late-phase patients (>4 years) were significantly deteriorated than those of early-phase patients, but their mental well-being and FACIT-F scores did not differ. All HRQoL questionnaires results displayed a close negative correlation ($p<0.01$) with the age, the left ventricular mass index (LVMI), the UCLA-Gastrointestinal Test 2.0 value, additionally the pain and fatigue measured on visual analogue scale. There were positive correlations between the test values and the cardiologic result assessing left ventricular diastolic function ($p<0.05$), the manually measured muscle strength (MMT8) and the 6-minute walk test ($p<0.01$).

Conclusions: The most important factors related to the HRQoL are the cardiac diastolic dysfunction, the gastrointestinal symptoms, and the physical condition indicators, which are recommended to consider during rehabilitation of the patients.

STEM CELL THERAPY FOR COMPLEX PERIANAL FISTULAS IN CROHN'S DISEASE

Elisabeth Garcia (Department of Surgery, University of Pécs)

Keywords: stemcell, Crohn's, perianal fistulas, darvadstrocel

Aims: The incidence and prevalence of Crohn's disease (CD) is rapidly increasing year by year. Despite the development of more effective treatments, it is still incurable. The main goal is to achieve remission, maintain it and prevent flares. Perianal fistulas are among the most frequent complications and have significant impact on patients' quality of life. Their treatment options are limited, and the results are modest. Darvadstrocel is an expanded allogeneic adipose-derived mesenchymal stem cell therapy which may become an effective treatment for perianal fistulas.

Methods: We demonstrate a case of a woman diagnosed with CD at the age of 51. Despite medical treatment combined with seton placement, the fistulas did not heal. Darvadstrocel injection was applied as a second-line treatment. Before the surgery, the patient underwent MRI to confirm the expansion of fistula tracts. The surgery consisted of two stages with 3 weeks in-between.

Results: She had regular medical check-ups and 6 months after the stem cell therapy, perianal fistulas were not detectable anymore on MRI. Until now 4 patients have underwent stem cell therapy in Pécs with 75% effectiveness.

Conclusions: Our results are encouraging, but further investigations and long-term follow-ups are necessary to confirm its therapeutic potential.

MOBILITY OF THE SACROILIACAL JOINT IN HEALTHY YOUNG ADULTS.

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Keywords: sacroiliacal joint, pelvic incidence, EOS 2D/3D, SI mobility

Aims: Pelvic incidence is the most important geometrical parameter of the pelvis which can be measured on EOS radiographs. This is a position independent parameter which defines the shape of the pelvis. It used to be considered as a permanent value, but this assumes that the sacroiliacal joint has only micro movements. Any change of the pelvic incidence means the sacroiliacal joint has a bigger range of motion as we known. The aim of our study was to examine the mobility of the sacroiliacal joint in healthy young adults.

Methods: 50 healthy volunteers (age: 19-25; 29 male, 21 female) were recruited who had no pelvic or lumbal pathology. Using the 3D reconstruction modality of the EOS system we measured pelvic parameters in three different (normal, forward and reclining) positions. We focused on the pelvic incidence looking for measurable deviation in the different positions. We examined if there is significant movement in the sacroiliacal joint against the assumptions.

Results: The average difference of the pelvic incidence between normal, forward and reclining positions was 5,5°. This difference was higher than 6° in 38%, and it was higher than 10° in 12% of the volunteers. The average difference in male patient (6,1°) was higher than in women (4,6°).

Conclusions: We found a significant difference between the pelvic incidence in normal, forward and reclining positions, thus the sacroiliacal joint has more range of motion as it widely accepted. Contrary to our expectations sacroiliacal joint has bigger mobility in man than in women.

FINDINGS ABOUT MANAGEMENT OF SEPTIC PROCESSES AFFECTING NATIVE SHOULDER JOINTS AND PERIARTICULAR REGIONS

Anna Hunkár, Imre Sallai, Viktor Weninger, Eszter Tulassay, Imre Antal, Gyula Prinz, Gábor Skaliczki (Septic Unit, Department of Orthopaedics, Semmelweis University)

Keywords: septic arthritis, shoulder, pathogens, follow-up care, life quality

Aims: We conducted the retrospective analysis of patients admitted due to glenohumeral joint septic arthritis or septic arthritis originating from and affecting the periarticular region between 2019 and 2023 at the Department of Orthopaedics, Semmelweis University. Main aim was to review the clinical history of the patients, analyze their results, follow up care and estimate the life quality.

Methods: During the study period, we treated 10 patients. Through telephone follow-up, we were able to reach 8 patients whose quality of life was measured using the WORC questionnaire. Two patients were able to attend in-person examinations; our elderly patients could only be followed up by phone. We estimated the function and QoL with NPRS, Constant-Murley score and ASES score.

Results: Common comorbidity was diabetes mellitus (3 patients; 30%). Hematogenous spread of infection was confirmed in all cases. Methycillin sensitive Staphylococcus aureus (MSSA) was the most common pathogen identified (5 patients), followed by streptococcal species (4 patients). Every patient underwent surgery. The complex treatment included a 14 days long specific, parenteral antibiotic treatment which was followed by a 4 weeks long oral antibiotic medication. 3 patients were able to participate on physical examination, their numeric pain rating score was 2. The mean Constant Score value was 47,6.

Conclusions: Native septic arthritis of the glenohumeral joint is a rare occurrence, but is life-threatening condition. Despite timely surgery, a significant deterioration in shoulder function must be anticipated, complex postoperative care is necessary.

INVESTIGATION OF INFLAMMASOME ACTIVITY IN RODENT MODELS OF DUCHENNE MUSCULAR DYSTROPHY

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Keywords: inflammasomes, cardiomyopathy, muscular dystrophy, inflammation

Aims: Duchenne muscular dystrophy (DMD) is an inherited, X-linked disease characterized by severe muscle loss. Affected young boys die prematurely due to respiratory and heart failure. Given that the inflammation of the muscle is a therapeutic target, our aim was to elucidate whether inflammasomes, multiprotein complexes of the innate immune response, play roles in the pathomechanism.

Methods: We investigated skeletal and heart muscle samples from dystrophin-deficient rodent models: mdx mice and DMD(mdx) rats, at early (3 month old) and late (10 month old) stages. The expression of inflammasome proteins was assessed by immunoblotting. The control groups consisted of time- and age-matched wild-type animals.

Results: The inflammasome adaptor protein (ASC) showed significant expression in the skeletal muscle ($p=0.003$; and 0.017 , respectively) of mdx mice at early and late time points. Meanwhile, the effector cytokines of the inflammasomes (IL- 1β) were more augmented in rat skeletal muscle ($p=0.049$; and 0.03 , respectively). Only tendentious changes were detected in heart muscle.

Conclusions: The different phenotypes of the models can cause the altered inflammasome activation patterns. The skeletal muscle was more prone to inflammation than the heart muscle in both species, highlighting the potential limitations of the anti-inflammatory therapies regarding heart failure.

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THE EFFECTIVENESS OF PHENOBARBITAL IN NEONATAL SEIZURES CAUSED BY HYPOXIC-ISCHEMIC ENCEPHALOPATHY

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Keywords: neonatal seizure, hypoxic-ischemic encephalopathy, phenobarbital, amplitude-integrated EEG

Aims: Neonatal seizures are the most common neurological emergencies in the Neonatal Intensive Care Unit. Hypoxic-ischemic encephalopathy (HIE) is the leading cause, but stroke, intraventricular haemorrhage, sepsis, metabolic disorders and developmental brain malformations are also known risk factors. Electrographic seizures without clinical symptoms can only be detected by EEG or an amplitude-integrated EEG (aEEG). Current guidelines recommend phenobarbital (PHB) as first line treatment regardless of the aetiology, however significant differences in effectiveness have been reported due to heterogenous sample groups or lack of EEG. We aimed to evaluate the 24-hour effectiveness of PHB in neonates with moderate or severe HIE by using amplitude-integrated EEG.

Methods: Our single center retrospective observational study included neonates born between 2013-2018 with moderate or severe HIE treated with therapeutic hypothermia at the Pediatric Center, Semmelweis University. aEEG background pattern and seizure activity was evaluated for 84 hours. The primary outcome was the 24-hour electrographic seizure cessation rate of PHB treatment.

Results: We enrolled 267 neonates, 54 of whom received phenobarbital based on clinical symptoms. 32 patients had electrophysiological convulsions at a median of 7,2 (5,1-14,2) hours of life and received phenobarbital treatment (median 20 mg/kg) at a median 10,8 (6,8-28,2) hours. 26 (81%) of the treated patients had seizures during the following 24 hours. 16 (50%) neonates received a second dose phenobarbital while 13 (41%) patients required second line treatment.

Conclusions: Phenobarbital provided 24-hour electrographic seizure cessation in only 6 (19%) neonates with moderate or severe HIE treated with therapeutic hypothermia.

THE ASSESSMENT OF INCIDENCE AND RISK FACTORS OF RETINOPATHY OF PREMATURITY

Aliz Pándi (The George Emil Palade University of Medicine, Pharmacy, Science, and Technology of Târgu Mureş)

Aims: Retinopathy of Prematurity (ROP) is a multifactorial ophthalmic disorder, which can lead to potentially severe and permanent childhood visual impairment and blindness. Its incidence is directly proportional to the number of very low birth weight and gestational age preterm infants. It is characterized by abnormal neovascularization of the retina, vitreous haemorrhages, and eventually tractional retinal detachment. The aim of our study was to investigate and compare with the literature data the prevalence, severity, and perinatal risk factors of ROP in the patient population of the Neonatology Department of Mureş County Clinical Hospital over a two-year period.

Methods: We conducted a retrospective study between January 2022 and December 2023, in which the data of 149 admitted patients were analysed. The examined variables were gestational age, birth weight, invasive or non-invasive oxygen therapy, ophthalmic examinations results and type of treatment administered. Excel and GraphPad programs were used for statistical analysis.

Results: Throughout the examined timeframe, there were 149 admissions. We studied preterm infants (n=125). Ophthalmic examinations were conducted in 96 patients (76.8%) based on professional guidelines and perinatal risk factors. Out of the screened children, 20 (20.83%) were diagnosed with ROP, including 13 boys (65%) and 7 girls (35%). All 20 preterm infants diagnosed with ROP required prolonged respiratory support, and 11 (55%) needed blood transfusion due to severe anemia. The average birth weight of the patients with retinopathy was 1030.5 grams [550;1700], with an average gestational age of 28.3 weeks [25;34]. In 76 cases (79.17%), retinopathy was not diagnosed. In those found to have stage 2 and 3 ROP in zone II with plus disease (n=6), intravitreal anti-VEGF injections and/or retinal laser treatments were performed. No ROP-related blindness developed in any of the cases.

Conclusions: In the studied patient group, ROP screening and management was carried out effectively according to national guidelines. Identified perinatal risk factors for retinopathy of prematurity included respiratory distress syndrome requiring mechanical ventilation or non-invasive oxygen therapy, blood transfusion, intraventricular haemorrhage, and severe anaemia. Our results are consistent with the literature data.

PRENATAL DIAGNOSTICS OF CONGENITAL HEART FAILURES IN HUNGARY

Letícia Anna Bagó, Alexandra Turi (Gottsegen National Cardiovascular Center)

Keywords: prenatal diagnosis, congenital heart disease, foetal echocardiography

Aims: Analysis of the effectiveness of fetal echocardiography in Hungary over a two-year period.

Methods: We retrospectively searched the Gottsegen National Cardiovascular Center database for patients born with CHD diagnosed by fetal echocardiography in 2021 and in 2022, and for infants who underwent surgery or catheterisation during the same period. The cardiac malformations were analysed individually and grouped together.

Results: We determined whether a prenatal diagnosis was made, at which gestational week, what was the indication for fetal echocardiography and we recorded the outcome. 419 infants and fetuses were diagnosed with cardiac malformations during this period, of which 251 cases were fetal diagnosis. The most common indications for these fetal echocardiography examinations were abnormalities seen on previous obstetric ultrasound (176 cases), maternal age (15 cases) and higher nuchal translucency (13 cases). The mean gestational age at prenatal diagnosis was 24 weeks. It was found that the most frequent abnormalities were those affecting the left ventricle, its outflow tract and the aortic arch. Termination of pregnancy occurred in 55 cases and 24 cases died postnatal. In 182 cases, after surgery or catheter intervention, the children were alive until the follow-up.

Conclusions: A diagnosis of CHD in fetal age provides the opportunity to fully educate the parents, and in the case of a diagnosis before the 24th week of gestation, to terminate the pregnancy. It also helps to prepare for acute postnatal care, which can improve the outlook for life.

Support: This work was supported by Gottsegen National Cardiovascular Center.

ROMA ETHNICITY AND CHILDHOOD DEFICIENCIES: PUBLIC HEALTH INSIGHTS FROM HUNGARY

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Keywords: optimal breathing, respiratory frequency, COVID-19, cardiorespiratory function, athletes

Aims: This study aims to investigate the prevalence and types of deficiencies among Roma and non-Roma children, identify if Roma ethnicity is a unique risk factor, assess the public health impact of Roma-specific deficiencies, and suggest preventive strategies for Roma children.

Methods: Utilizing 2011 Hungarian census data on under-18 participants, the study analyzed housing conditions, personal traits, and ethnicity through self-declaration. The primary outcome was the occurrence of at least one deficiency, categorized into 12 sub-categories per United Nations recommendations. Secondary outcomes included age at deficiency onset and activity limitations. Descriptive statistics, χ^2 -tests, standardization, and logistic regression were employed for analysis.

Results: Among 1,410,911 records, 28,249 children had deficiencies. Roma children had higher prevalence (3.07%) than non-Roma (1.91%). Roma ethnicity was a significant risk factor for having at least one deficiency in the multivariate logistic model that controlled for deprivation indices (OR=1.40), affecting movement, mental, speech, vision, hearing, and internal organs; autism was lower among Roma. Congenital deficiencies were higher in Roma children, while before school-age deficiencies were lower. Roma children faced more learning, working, family life limitations but fewer in self-sufficiency, communication.

Conclusions: Higher deficiency rates in Roma children, with differences in type and age of onset, confirm Roma ethnicity as a distinct risk factor. Furthermore, the high prevalence of deficiencies and associated activity limitations among Roma children underscores a significant public health concern. Preventive strategies should include targeted healthcare interventions, improved housing conditions, and educational support to mitigate the higher risk of deficiencies in Roma children in Hungary.

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With questions or suggestions, please contact beyco27@gmail.com

*Thank you,
HMAA HC*

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