Sveučilište u Zagrebu, Medicinski fakultet / University of Zagreb, School of Medicine

Dan doktorata 2017 / PhD Day 2017

Knjiga sažetaka / Abstract Book

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Sveučilište u Zagrebu – Medicinski fakultet
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Foreword

PhD Day (Dan doktorata) started in 2012 and last year it became an annual event of PhD students of both PhD programmes (I – Biomedicine and Health Science, and II – Neuroscience) at the University of Zagreb School of Medicine. This year, our institution is celebrating its 100 year anniversary. Thus, we are glad to see that this year's PhD Day consists of presentations of ongoing research of 143 of our PhD students (123 from Biomedicine and Health Science, and 20 from Neuroscience) in a form of published abstracts, posters and selected oral presentations. PhD Day as a one day symposium is mandatory for all the 2nd-year and 3rd-year students. This symposium is a welcome opportunity for our PhD students (for some students this is their first chance to give an oral presentation) and their mentors to exchange ideas among themselves, to present their data to their teachers and experts and get either positive or negative feedback about their scientific work. Thus, this kind of gathering of PhD students, mentors and distinguished internationally recognized scientists provides a great occasion to share experiences and ideas in specific research field as well as in science in general.

We wish that this PhD Day will be fruitful and useful for all participants, and we hope that it will become a traditional day at our institution which celebrates science, research, co-operation and scientific friendship.

Marijan Klarica

PhD Day 2017 Preliminary PROGRAMME

26 May 2017

10.00 – 10.15	PhD Day Opening: Dean, Guest dignitaries, PhD programme Directors
10.15 – 12.30	Guest speakers (Chairs: Zdravko Lacković, Mario Vukšić)
10.15 – 11.00	Prof. Michael Frotscher, Zentrum für Molekulare Neurobiologie Hamburg (ZMNH), Universitätsklinikum Hamburg-Eppendorf: Mossy fiber synapses in the hippocampus have their individual memories
11.00 – 11.45	Prof. Bahman Jabbari, MD, FAAN, Yale University: Botulinum neurotoxin (BoNT) treatment for pain syndromes
11.45 – 12.30	Prof. Fattaneh A. Tavassoli, MD, Yale University: Correlation of molecular and morphologic classification of breast cancer
12.30 – 13.30	Lunch & Coffee Break
13.30 – 14.45	Selected Students' Presentations (Chairs: Ana Borovečki, Marko Jakopović)
14.45 – 15.15	Promotion of the course book: Experimental design in life sciences (Croatian translation)
15.15 – 17.00	Organized Poster Session with Discussion

INVITED LECTURES

MOSSY FIBER SYNAPSES IN THE HIPPOCAMPUS HAVE THEIR INDIVIDUAL MEMORIES

Michael Frotscher, Zentrum für Molekulare Neurobiologie Hamburg (ZMNH),
Universitätsklinikum Hamburg-Eppendorf

The complexity of environmental stimuli is translated into patterns of neuronal signals that change synaptic strength in specific pathways. In this talk, first structural changes at mossy fiber (MF) synapses in response to the induction of chemical long-term potentiation (cLTP) will be reported. However, global induction of LTP at many synapses does not reflect the natural activation of intricate microcircuits involved in the processing of environmental stimuli. It is more likely that nearby synapses are strengthened or weakened depending on the individual input patterns they receive. Therefore, we next analyzed functional differences between individual MF synapses by combining single MF bouton stimulation and recording of Ca2+ transients in the postsynaptic spine. We were surprised to find a great heterogeneity in synaptic strength between individual MF synapses. Moreover, induction of plasticity at these synapses depended on the initially encountered synaptic state, suggesting that MF synapses contribute individually to microcircuits in the hippocampus depending on their individual functional history.

BOTULINUM NEUROTOXIN (BoNT) TREATMENT FOR PAIN SYNDROMES

Bahman Jabbari, M.D. FAAN, Professor Emeritus of Neurology, Yale University

BoNTs in addition the inhibition of acetylcholine release, inhibit the release of pain modulators and transmitters both peripherally and in the central nervous system. In human, randomized and placebo-controlled clinical trials have shown efficacy of BoNT therapy in a variety of pain syndromes. This lecture evaluates the existing level of evidence for efficacy of BoNTs in different pain syndromes using the recommended efficacy criteria from the Assessment and Therapeutic Subcommittee of the American Academy of Neurology (French and Gronseth 2008). There is a level A evidence (effective) for BoNT therapy in chronic migraine, post-herpetic neuralgia, trigeminal neuralgia, posttraumatic neuralgia, pain of chronic lateral epicondylitis and pain associated with cervical dystonia. There is level B evidence (probably effective) for diabetic neuropathy, plantar faciitis, piriformis syndrome, pain associated with total knee arthroplasty, male pelvic pain syndrome and chronic low back pain. BoNTs are possibly effective (level C-one class II study) for female pelvic pain, painful knee osteoarthritis, post-operative pain in children with cerebral palsy after adductor release surgery, anterior knee pain with vastus lateralis imbalance, post-operative pain after mastectomy, anal sphincter spasms and pain after hemorrhoidectomy. There is level B evidence (one class II study) that BoNT treatment is probably ineffective in carpal tunnel syndrome, occipital neuralgia and phantom pain. Great majority of these studies were conducted with onabotulinumtoxinA. More high quality (Class I) studies and studies with different types of BoNTs are needed for better definition of the role of BoNTs in the pain syndromes.

CORRELATION OF MOLECULAR AND MORPHOLOGIC CLASSIFICATION OF BREAST CANCER

Fattaneh Abbas-Zadeh Tavassoli, M.D., Professor Emeritus of Pathology, Yale University

Technological advances over the past 2 – 3 decades have added a new dimension to assessment of breast cancer. In addition to morphologic classification of breast cancers, it is now expected that pathologists at least develop the ability to correlate the traditional classification with molecular based assessments as this could be particularly useful in management of the patients and introduction of novel therapies.

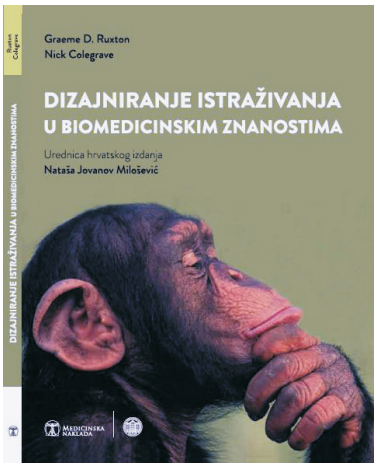
It is important to emphasize that there is continuous evolution of the molecular classification with novel approaches introduced by various investigators. Given the cost of molecular analysis it is also imperative to properly correlate the molecular and morphologic features to help extrapolate the potential molecular pathways that could be utilized as targets for therapy even if such analysis is not immediately available in some centers. It is also noteworthy that as more cancers are analyzed, it is becoming clear that breast cancers will not be divisible simply into four or five subtypes (luminal – A and B; basal; Her2 rich; normal breast-like) as initial studies had suggested. While ER, PR and HER2 status of the tumors, to an extent, correlate with some aspects of the molecular classification, there is no perfect matching with these markers alone. It is becoming clear that additional markers – ie Ki67 and AR- are necessary to improve the correlation. Furthermore, it is becoming apparent that to fully comprehend behavior of carcinomas, understanding the role of tumor associated stromal fibroblasts and tumor infiltrating lymphocytes – tumor microenvironment – is essential.

Finally, it is important for both molecular biologists and pathologists to have at least some understanding of the problems that may be associated with each classification as well as some comprehension of the alternate classification. At present, optimal patient management requires accurate morphologic classification, valid marker assessment and at least some molecular analysis for identification of targets for therapy.

Promotion of the Croatian edition of the course book „Experimental design for the life sciences"

Graeme Ruxton and Nick Colegrave, OXFORD university press
Dizajniranje istraživanja u biomedicinskim znanostima
Nataša Jovanov Milošević, editor of the Croatian edition
MEDICINSKA NAKLADA, ZAGREB

From the back of the book:



"Good experimental design is about clear thinking and biological understanding, not mathematical or statistical complexity. It lies at the core of good research and should be at the heart of any bioscience education. Yet all too often, a successful design comes only after a painful trial-and-error process wasting valuable time and resources. Experimental design in the live sciences equips the students of today with the skills needed to become the researchers of the tomorrow. With refreshingly approachable and articulate style, the book explains the essential elements of experimental design in clear, practical terms enabling you to grasp and apply even the most challenging concepts. Emphasizing throughout the interrelatedness of experimental deign, statistics and ethical considerations the book ensures that you truly understand experimental design in its broader context of biological research, using diverse examples to show how the theory can be applied in active research."

From the preface of the Croatian edition:

"Following the curriculum of postgraduate and doctoral studies, and most of all, following the work of the students, we realized that they lacked systematic education about the process of designing biomedical research. Despite the fact that the designing of the scientific research and experimentation, necessarily precedes the experimentation and greatly determines the quality and the very outcome of the research, the issues of thorough planning and designing of the biomedical research were partially covered through the courses that primarily deal with biostatistics, scientific publishing or scientometry. We conclude that the "*Experimental design in the life sciences*" manual and the *course* of the same contents, that would teach the postgraduate and young scientist systematically and thoroughly all the complexity of designing research in biomedical sciences, were of great importance if not crucial to the quality of their further work and professional development."

RESEARCH RESULTS

Basic Medical Sciences
Preliminary Research Results

THE EFFECT OF BPC 157 ON TRACHEOCUTANEOUS FISTULA HEALING IN RAT

PhD candidate: Goran Madžarac: The effect of BPC 157 on tracheocutaneous fistula healing in rat

PhD thesis: The effect of pentadecapeptide BPC 157 on healing of tracheocutaneous fistula in rat

Mentor/s: Prof. dr. sc. Dinko Stančić-Rokotov, Prof. dr. sc. Predrag Sikirić

Affiliation: University of Zagreb School of Medicine

Introduction: One of the common late complications of tracheotomy is tracheocutaneous fistula. Surgical procedure is needed to close such fistulas. BPC 157, anti-ulcer peptide (GEPPPGKPADDAGLV, M.W. 1419) successful in trials for inflammatory bowel disease, wound treatment, effective alone without carrier. BPC 157 interfere with NO-system in vitro/in vivo on different models and different animal species. The impact of BPC 157 and NO-system on gastrocutaneous, colocutaneous and oesophagocutaneous fistulas healing process indicate potential effect of BPC 157 in tracheocutaneous fistula healing process, which has not yet been investigated.

Materials and methods: Albino Wistar male rats were used in this experiment, 220-280 g. Tracheocutaneous fistula, 4 mm trachea and skin defect, was surgically made under anaesthesia. Animals were treated according to the experiment protocol: a) drinking water p.o., b) BPC 157 (10 μg/kg, 12 ml/rat/day) p.o., c) BPC 157 (10 ng/kg, 12 ml/rat/day) p.o., d) saline 5ml/kg/day i.p., e) BPC 157 (10μg/kg, 5ml/kg/day) i.p., f) BPC 157 (10 ng/kg, 5 ml/kg/day) i.p., g) L-NAME (5 mg/kg/day) i.p., h) L- arginine (100 mg/kg/day) i.p., i) L-NAME L- arginine i.p., j) L- NAME BPC 157 (μg) i.p., k) L- arginine BPC 157 (μg) i.p., l) L-NAME, L- arginine, BPC 157 (μg) i.p., m) L-NAME BPC 157 (ng) i.p., n) L- arginine BPC 157 (ng) i.p., o) L-NAME L- arginine BPC 157 (ng) i.p.. Third, fifth and seventh postoperative day animals were euthanized. Fistula specimens were harvested and macroscopic and histological analysis was made.

Results: A consistent counteracting beneficial effect was shown in all animals treated with BPC 157, alone and with (L-NAME) and/or L-arginine. BPC 157 accelerated healing of tracheocutaneous fistulas and showed macroscopic and histological healing improvements. Tracheocutaneous fistulas healing was improved speedily (BPC 157 completely counteracted L-NAME effects (L-NAME BPC 157 and L-NAME L-arginine BPC 157 groups), or with delay and to less extent (L-arginine) or aggravated, rapidly and prominently (L-NAME). L-arginine reduce aggravation by NOS-blockade (L-NAME) to the control levels. Also, BPC 157 more than nullifies the effect of L-NAME.

Discussion: BPC 157 improved healing of both tracheal and skin defects and mediated fistula closing. This effect was shared by L-arginine, with an opposite effect seen by L-NAME, thereby portraying NO-system involvement in the healing of tracheocutaneous fistula.

Acknowledgments:

MeSH/Keywords: tracheocutaneous fistula, BPC 157, wound healing

Poster code: R-A-4-131

GUT MICROBIOTA COMPOSITION AND INFLAMMATORY MARKERS IN IBD PATIENTS

PhD candidate: Marina Panek, mag.biol.mol.

PhD Thesis: Analysis of gut microbiota composition from colon and faeces samples and quantitative determination of inflammatory factors as relevant biomarkers from newly diagnosed IBD patients.

Mentor/s: 1. Assistant Professor Donatella Verbanac, PhD, 2. Professor Željko Krznarić, M.D, PhD

Affiliation: University of Zagreb School of Medicine, University Hospital Centre Zagreb

Introduction: The healthy intestine represents a remarkable interface where host tissues come in contact with microbiota in a balanced state of homeostasis. The imbalance of gut homeostasis is associated with the inflammatory bowel disease (IBD). IBD is a chronic relapsing process in the gastrointestinal tract which comprises of two clinically and morphologically different entities: ulcerative colitis (UC) and Crohn's disease (CD). CD and UC are the most prevalent forms of IBD, characterized by chronic relapsing inflammation affecting the intestinal mucosa. Although the etiology of both diseases is unknown, there is increasing evidence that intestinal microbial dysbiosis has a role in the pathogenesis.

Materials and methods: Until now the study included 16 IBD patients and 35 non-IBD controls. The composition of gut microbiota from faeces and colon biopsies was determined by amplification and sequencing of bacterial 16S rRNA gene using Illumina MiSeq. Serum samples for 92 different inflammatory biomarkers were collected and tested with proximity extension assay (PEA) method.

Results: Mucosal samples taken along the colon were compared to the faecal bacterial content and the preliminary results suggested there is more Proteobacteria in the mucosa of IBD patient when compared to the IBS control. Results from faecal samples suggested decrease in Firmicutes and Actinobacteria, and increase in Bacteroidetes and Proteobacteria when compared to the healthy control. Preliminary analysis of inflammatory biomarkers from serum sample, showed the existence of differences between IBD and healthy (H) groups (TNFSF14 H vs. IBD, $p < 0, 0001$, ST1A1 H vs. IBD, $p < 0,005$, EN-RAGE H vs. IBD, $p < 0,0005$) and between UC and CD groups (CCL23 UC vs. CD, $p < 0,05$).

Discussion: These studies analyse the microbiota of a newly diagnosed adult IBD patients and found clear differences in bacterial populations and inflammatory biomarkers between IBD and non-IBD patients. Preliminary data also indicate that there is a difference in microbiota composition between colon and faeces samples. We observed that the microbial community associated with the inflamed epithelium had an increased level of Proteobacteria. Serum levels of TNFSF14, ST1A1 and EN-RAGE inflammatory markers were higher in IBD than in healthy individuals, thus allowing the distinction between the two entities, and CCL23 can help to discriminate CD from UC.

Acknowledgments: Marina Panek is supported for her PhD studies by the Croatian Science Foundation Young Investigators Grant (MINUTE FOR IBD: 5467)

MeSH/Keywords: inflammatory bowel disease, gut microbiota, next generation sequencing, proximity extension method

Poster code: R-A-6-96

GENETIC MECHANISMS OF LYSOSOMAL DYSFUNCTION IN PARKINSONS DISEASE

PhD candidate: Antonela Blažeković, MD

PhD Thesis: Genetic mechanisms of lysosomal dysfunction in Parkinsons disease

Mentor/s: Associate Professor Fran Borovečki, MD, PhD. Professor Maja Relja, MD, PhD

Affiliation: Department for Functional Genomics, Centre for Translational and Clinical Research, University of Zagreb School of Medicine, University Hospital Centre – Zagreb

Introduction: Several rare monogenic disorders caused by mutations in lysosomal genes show alpha-synuclein accumulation, a key molecule implicated in pathological processed involved in Parkinson's disease (PD). The exact mechanisms of excessive alpha-synuclein accumulation in the brain have not been fully elucidated, although insufficient protein clearance has been singled out as a possible essential biological mechanism. The aim of this study is to investigate and characterize the underlying genetic mechanisms leading to autophagy-lysosomal pathway dysfunction in PD patients by applying a novel genomic panel consisting of 440 genes associated with lysosomal system, neurodegeneration and alpha-synucleinopathies.

Materials and methods: The study included PD patients and healthy control subjects. We developed the LYSOGENE, a targeted next-generation sequencing panel, which allowed us to obtain a uniform and accurate coding sequence coverage of a comprehensive set of 440 autophagy-lysosomal pathway genes based on the Human Lysosome Gene Database (hLGDB), genes associated with alpha-synucleinopathies and neurodegeneration.

Results: Our results showed 676 variants in 260 genes present exclusively in PD patients. The genetic variants exclusive to PD were involved in over 50 biological processes, with the greatest enrichment observed in categories of catabolic processes, sphingolipid metabolic processes, lysosome organization and organic substance transport. In comparison, variants found in healthy subjects were more diverse, showing less commonality between the different individuals, and were not related to specific biological pathways. Some variants showed extremely frequent occurrence in patients. Three variants of ARSD gene were present in 70% of PD patients, while being completely absent in control subjects. We also observed in PD patients frequent variants in the GALC gene, associated with leukodystrophy, a condition with a growing number of known connections with neurodegeneration.

Discussion: Preliminary data revealed a significant number of gene variants present in autophagy-lysosomal pathway in PD patients. Our analysis shows promise in illuminating the biological pathways that are affected in PD patients. We expect that further analyses and confirmatory experiments utilizing cell-lines will shed novel light on the affected pathways and mechanisms.

Acknowledgments: I would like to thank my mentors, Kristina Gotovac Jerčić and Filip Bingula as well as the Laboratory for Neurodegenerative Disease Research at Institute Ruđer Bošković. This study was funded by Croatian Science Foundation (HRZZ-9386).

MeSH/Keywords: Parkinson disease, Lewy bodies, lysosomes, genomic panel, NGS, alpha-synuclein, ARSD, GALC

Poster code: R-A-6-88

CHEMOKINE RECEPTOR EXPRESSION OF EXPANDED MYELOID LINEAGE CELLS AND OSTEOCLAST PROGENITOR SUBPOPULATION IN MOUSE MODEL OF COLLAGEN INDUCED ARTHRITIS

PhD candidate: Darja Flegar, MD

PhD Thesis: Characterization of osteoclast progenitor responses and increased osteoresorption in mouse model of rheumatoid arthritis

Mentor/s: Professor Danka Grčević, MD, PhD

Affiliation/s: Laboratory for Molecular Immunology, Croatian Institute for Brain Research, Zagreb, Croatia, Department of Physiology and Immunology, University of Zagreb School of Medicine, Zagreb, Croatia

Introduction: Collagen induced arthritis (CIA) is a mouse model of rheumatoid arthritis (RA), characterized by small joint and systemic inflammation. Increased activity of osteoclasts, specialized bone resorbing cells, leads to bone loss and joint destruction. Osteoclast progenitor cells (OCP) arise from myeloid lineage and are present within bone marrow and circulatory monocytes. Our aim was to assess changes in frequencies of distinct OCP subsets and their chemokine receptor expression in circulation and periarticular bone marrow (PBM) related to their increased migration to the sites of osteitis, the inflammatory infiltrate in bone marrow, in CIA.

Materials and methods: C57BL/6 mice were immunized with chicken type II collagen in complete Freund's adjuvant and assessed for CIA development. Hind paw joints were analyzed by micro-CT, histology and histomorphometry. Peripheral blood (PBL), spleen and bone marrow of distal tibia (PBM) were analyzed by flow-cytometry for the expression of hematopoietic markers and chemokine receptors (CD3, B220, NK1.1, CD11b, Ly6c, CD115, CCR2, CCR5, CCR9, CX3CR1). Serum cytokines were measured by ELISA. OCPs were sorted using FACS, cultured with M-CSF and RANKL, stained for TRAP enzyme and counted. For in vitro migration assay, M-CSF and RANKL stimulated PBL and PBM cells were seeded into transwell inserts with chemotactic gradient. Intravascular in vivo staining with hematopoietic markers was used to label PBL cells for migration tracking.

Results: Both hematopoietic lymphoid-negative CD11b+CD115+ and CD11b-/loCD115+ subsets possess osteoclastogenic activity and are enlarged in blood and PBM of affected joints in CIA. OCP subsets substantially express CCR2 and CX3CR1, but express low levels of CCR5, CCR9 and CXCR4. CCL2 serum levels are significantly increased in CIA, whereas CX3CL1 levels are comparable to control. PBL cells from CIA mice demonstrated significantly enhanced migration toward CCL2 chemotactic gradient. Intravascular in vivo staining showed increased recirculation of CD45+CD11b+ cells through arthritis affected PBM.

Discussion: Myeloid lineage and OCP populations are highly induced in CIA, with substantial expression of CCR2 and CX3CR1, possibly responsible for their increased migration and homing to bone surfaces of joints. Therefore therapeutic blocking of chemokine signaling may reduce enhanced osteoresorption in RA.

Acknowledgments: This work was supported by the Croatian Science Foundation under the project 5699.

MeSH/Keywords: arthritis, myeloid progenitor cells, inflammation

Poster code: R-A-7-82

CALRETININ NEURONS IN THE PRIMATE PREFRONTAL CORTEX

PhD candidate: Dora Sedmak, MD 1

PhD Thesis: Calretinin neurons in the primate prefrontal cortex

Mentor/s: Zdravko Petanjek, MD, PhD 1, Moniqe Esclapez, PhD 2

Affiliation: 1 University of Zagreb School of Medicine , Department of Anatomy and Clinical anatomy and Croatian Institute for Brain Research, 2 Aix Marseille University, INSERM

Introduction: During mammalian evolution calretinin neurons expanded from a minor GABAergic subclass in rodents (3%) to one of the most frequent neuron subclass (12%) in primate cerebral cortex. This increase could be the main correlate of neuronal network rearrangement leading to more efficient information processing.

Materials and methods: Three postmortem macaque monkey brains used in this study are a part of a brain collection (Brain Dynamic Institute, Marseille). Serial sections from Brodmann area 24, 32 and 9 were immunohistochemically stained for NeuN (neuronal marker) and calretinin. Estimation of total neuron and calretinin neuron number was done using stereological (optical fractionator) method (Stereo-investigator software, MicroBrightField, Williston, USA). Differences between areas in proportion of calretinin neurons, laminar distribution and density of all neurons and calretinin neurons were statistically analysed using two way ANOVA with Bonferroni correction for multiple comparisons. Double labelling method (immunohistochemistry with RNA scope) was used to affirm GABAergic phenotype of calretinin neurons and determine overlap with other GABA subpopulations (Neurolucida software, MicroBrightField, Williston, USA).

Results: Across analysed areas cortical calretinin neurons are mostly located (80%) in upper cortical layers with highest proportions in layer I (50%), II (30%) and III (20%). Layer I contains around 3% of neurons located mainly densely packed in lower half. Cortical projecting layers (II and III) represent around 50% of total neuron number. Based on double labelling with GAD 65 mRNA most cortical calretinin neurons do not express GAD 65. Co-localization with other major GABAergic subpopulations was less than 1%.

Discussion: Absence of differences between the prefrontal areas in macaque monkey confirmed the hypothesis that the principal neocortical input and output cell types are a conserved feature of dorsal telencephalon (Dugas-Ford and Ragsdale 2015). Comparison with orbito-medial cortex (Dzaja, 2015) revealed lower densities in dorso-medial parts suggesting an increase in neuron complexity and connections in dorsal areas of prefrontal cortex during primate evolution. Based on data on calretinin proportion and density it is highly probable that in primate prefrontal layer I, II and IIIa GABAergic neurons are as numerous as projection neurons, thus classification of layer I as non-neuronal layer and layer II as projection neurons layer should be re-evaluated.

Acknowledgments: This work was supported by Croatian Science Foundation project No. 5943

MeSH/Keywords: GABA, interneuron, neocortex, calretinin, human, monkey

Poster code: R-A-9-14

HISTOLOGICAL, IMMUNOCYTOCHEMICAL AND MRI ANALYSIS OF THE DEVELOPMENT OF THE STRUCTURAL BASIS OF THE SOMATOSENSORY THALAMOCORTICAL SYSTEM IN THE FETAL HUMAN BRAIN

PhD candidate: Višnja Majić

PhD Thesis: Histological, immunocytochemical and MRI analysis of the development of the structural basis of the somatosensory thalamocortical system in the fetal human brain

Mentor/s: Željka Krsnik, PhD, Assistant Professor, Ivica Kostović, MD, PhD, Academician Professor

Affiliation: Croatian Institute for Brain Research

Introduction: The neurons of the cerebral cortex begin their migration from the proliferative ventricular zone in the 8 week after conception (PCW) and around 20PCW most neurons arrive at their final destination in the cortical plate. In the mid-fetal period the subplate zone is formed below the cortical plate, where the first synapses and neural circuits in the fetal neocortex appear. During 22PCW thalamocortical fibers "wait" in the subplate zone, and enter the cortical plate between 24-26PCW, thus creating the first synapses in layer 4 of the fetal cortex, followed by elaboration of thalamocortical fibers. Also, thalamus is a key relay station for transmitting sensory information to the cerebral cortex. In recent years great attention was devoted to study the activation of the cortex as a fundamental component of pain perception, mainly because of the increase in the number of intrauterine surgery and the progress in neonatal care. Knowledge of early cortical activity is essential to ensure safe extrauterine environment for premature children and the possibility of treatment of pain.

Materials and methods: Research will be carried out on sections of postmortem human brains, combining histologic, immunohistologic and MR analysis (in vitro MRI) through three developmental stages: early fetal stage (8-13 PCW), middle fetal stage (13-24 PCW), late fetal stage (24-36 PCW). The study involves 15 brains of premature infants aged from 8th to 36th week after conception, which are part of the Zagreb Neuroembryological collection.

Results: Results show early (7.5PCW) outgrowth of thalamocortical fibers through cerebral stalk and late invasion of SP zone of the prospective SSCX around 16.5PCW. The appearance of major thalamic territories occurs between 9-10PCW. Penetration of the CP (around 24PCW) is accompanied with initial lamination of CP as seen on ACh, Nissl and MR images. Structural and chemical differentiation of thalamocortical somatosensory fibers occurs during prolonged period (4 months) with clear centrifugal direction where "waiting" SP period precedes ingrowth in CP for almost 2 months.

Discussion: Since thalamus is a key relay station for transmitting sensory information to the cerebral cortex, it is important to evaluate the development of the somatosensory thalamus (VPL nucleus), thalamocortical projection and the corresponding cortex.The results are important for the interpretation of the early sensations of touch and pain during the fetal period.

Acknowledgments: Supported by HRZZ The Human Subplate Zone – unsolved problems (IK), IBRO RHF (ŽK)

MeSH/Keywords: subplate zone, somatosensory cerebral cortex, thalamus, VPL, fetal pain

Poster code: R-A-9-18

TRANSCRIPTION FACTOR ZBZB20 EXPRESSION DURING PRENATAL DEVELOPMENT OF HUMAN HIPPOCAMPUS

PhD candidate: Vinka Knezović, MD

PhD Thesis: Histological, MRI and transcriptome analysis of the reorganizational processes in the developing human hippocampus

Mentor/s: Associate Professor Mario Vukšić, MD, PhD

Affiliation: Croatian Institute for Brain Research, School of Medicine, University of Zagreb

Introduction: The molecular mechanisms that underlie development and regionalization of human archicortical areas, including hippocampal formation, are not fully understood. These areas express specific molecules whose distinct pattern of expression makes them useful as markers to distinguish a specific area during the development.

Materials and methods: Using publicly available gene expression database (Kang et al., 2011) by means of Partek Genomic Suite 6.6 and R software we analyzed a total of 21757 genes, and created a list of 369 genes with specific expression during prenatal hippocampal development (230 down-regulated and 139 up-regulated). One of these genes has been a transcription factor ZBTB20, which plays a critical role for the specification of CA1 pyramidal neurons identity as well as for postnatal survival of hippocampal neurons in experimental animals. For the selected candidate gene we employed immunohistochemistry on fixed-paraffin-embedded sections of postmortem human brains, ranging from the 12th postconceptional weeks (PCW) to the 13th month of life, to study its spatiotemporal expression pattern.

Results: Expression of ZBTB20 was visible in the hippocampal primordium at 12th PCW, in the future dentate gyrus (DG), revealing nuclear staining in the progenitor cells of the primary dentate neuroepithelium. At 20th PCW this nuclear localization of ZBTB20 immunoreactivity (IR) was pronounced in the immature neurons of the DG cell layer and hilar region as well as in developing pyramidal neurons in the CA1-CA3 fields. During this developmental period, ZBTB20 expression pattern was similar to neuronal nuclear protein (NeuN) expression, a marker characteristic for early differentiated postmitotic neurons. At the border between CA1 and subiculum this ZBTB20 IR diminished and was not visible in the neighboring transitional cortical areas. Between 25th and 40th PCW ZBTB20 IR clearly demarcates a boundary between hippocampus from adjacent transitional cortical areas. In the early and late postnatal period this ZBTB20 expression was not visible anymore.

Discussion: Our results indicate that ZBTB20 represents a part of the regulatory molecular program of archicortical regionalization, and plays an important role for establishment/maintenance of the borders between archicortex, transitional cortices, and neocortex. Since ZBTB20 is linked to several human disorders, such as autism, the obtained data will be used for setting the baseline for studying developmental abnormalities characteristic for these disorders.

Acknowledgments: This PhD thesis has been supported by Croatian Science Foundation (project number: 7379).

MeSH/Keywords: archicortex, areal specification, regionalization

Poster code: R-A-9-38

NEW GC-C INDEPENDENT SIGNALING PATHWAY FOR UROGUANYLIN IN THE BRAIN

PhD candidate: Nikola Habek, MD

PhD thesis proposal: Expression and effects of uroguanylin in the mouse brain

Mentor/s: Prof Aleksandra Dugandžić, MD, PhD

Affiliation/s: Croatian Institute for Brain Research, Department of Physiology and Immunology, University of Zagreb School of Medicine

Introduction: Uroguanylin (UGN) is natriuretic peptide which belongs to guanylin peptide family. UGN activates guanylate cyclase C (GC-C), only know receptor up to date, and leads to an increase in intracellular cGMP concentration. GC-C is present in the midbrain dopamine neurons in substantia nigra and vetral tegmental area where lack of GC-C leads to development of ADHD-like behavior. GC-C is also present in arcuate nucleus of hypothalamus where it regulates energy homeostasis, feeding behavior, and satiety. Here, we report that GC-C is not only existing receptor for UGN in the brain.

Materials and methods: Ca^{2+} imaging was performed on brain slices of wild type (WT) and GC-C knockout (KO) mice, and on primary astrocyte culture isolated from WT newborn animals. 99% pure primary astrocyte culture was isolated by Magnetic Activated Cell Separation (MACS) method. Electrophysiological recordings of primary astrocyte culture were performed by perforated whole-cell patch-clamp configuration. Role of UGN on astrocyte pH was measured by microfluorescent method. GC-C mRNA expression analysis was performed by RT-PCR.

Results: We showed UGN dependent increase in intracellular Ca^{2+} concentration in cerebral and cerebellar cortex of WT and GC-C KO mice, as well as in astrocyte culture which does not express GC-C. The electrophysiological recordings showed the same GC-C independent effect, namely, UGN hyperpolarizes while cGMP depolarizes astrocyte membrane. Via GC-C independent signaling pathway in astrocytes UGN increases recovery slope after acidification by activation of Na^+/H^+ exchanger. Furthermore, after astrocyte exposure to CO_2/HCO_3^- UGN application leads to increase in alkalization slope.

Discussion: We show, for the first time, that GC-C is not only receptor for UGN in the brain. UGN dependent increase in intracellular Ca^{2+} concentration on WT mice and also on GC-C KO mice is GC-C independent. Furthermore, UGN and cGMP change astrocytes membrane potential inversely meaning that cGMP is not second messenger for UGN. These results correspond to previous research showing that cGMP inhibits Ca^{2+} signaling and does not increase intracellular Ca^{2+} concentration. Since astrocytes do not express GC-C we propose them as cell model for research of GC-C independent signaling pathway for guanylin peptides. Astrocytes play major role in extracellular fluid pH regulation that can change neural activity. UGN via this novel signaling pathway can modulate astrocyte intracellular pH by modulation of Na^+/H^+ exchanger and HCO_3^- transport.

Acknowledgments: We would like to thank Dr. Kris A. Steinbrecher (Cincinnati Children's Hospital Medical Center, OH, USA) for donation of GC-C KO animals, Prof Eberhard Schlatter (Uni-Münster, Germany) for donation of set-up for microfluorescent measurements and Prof Michaela Kuhn (Uni-Würzburg, Germany) for donation of MACS astrocyte isolation kit

MeSH/Keywords: UGN, GC-C, cGMP, brain slices, astrocytes, electrophysiology, Ca^{2+} imaging, pH measurements

Poster code: R-A-9-124

COULD MILD ABNORMAL GENERAL MOVEMENTS BE EARLY INDICATOR OF NON-MOTOR NEURODEVELOPMENTAL DISORDERS AND AUTISM IN YOUNG CHILDREN

PhD candidate: Ivana Jandroković

PhD Thesis: Predictive value of mild abnormal general movements assessment in correlation wtih fetal and maternal risk factors for early detection of deviations in communication and social behaviors in toddlers

Mentor/s: Professor Snježana Škrablin Kučić, MD,PhD, Assistant Professor Maja Cepanec, SLP., PhD.

Affiliation: Croatian Institute for Brain Research, Clinic for Gynecology and Obstetrics Petrova Hospital, Clinacal Hospital Centre Zagreb

Introduction: According to data one of six children develops some neurodevelopment disorder in early childhood, furthermore incidence of disorders in social communication and behavioral disorders are on the rise. It is still impossible to predict which of the known risk factors lead to the development of these mild neuronal dysfunctions that are not visible till the age of two or three. What is known is that general movements (GMs) in the neonatal period are an indicator of spontaneous neural activity and have high predictive value for the development of cerebral palsy, and as some retrospective studies suggest one form of GMs (mild abnormal type) could be correlated with mild neural dysfunctions at the age of two including ADHD and social communication disorders. GM assessment has a specificy and sensitivity of 95% each, is quick, noninvasive, and cost-effective compared to other techniques.

Materials and methods: The sample cosistes of two groups: 50 children with no indentified neurorisk factors and 50 at neurorisk. The study is carried in three phases. The GMs assessment by the Prechtl method is during first week from birth.The second is during fourth month of birth. GMs were classified into four classes using a standardized qualitative description: two classes of normal movements (normal-optimal and normal-suboptimal) and two classes of abnormal movements (mildly and definitely abnormal movements).The final assessmet of the child's developmental outcome using Mullen Scales of Early Learning, Vineland Scale and M-CHAT is during first half of second year of life.

Results: Preliminary result of the GMs assessment are based on 30 newborns. For 21 newborns at neurorisk, 19 is assessed with mildly abnormal GMs. Two of them with definitely abnormal GMS are excluded from further research. From 9 newborns with no evident neurorisk factors, three of them are assessed with mildly abnormal GMs and 6 of them with normal-optimal or normal suboptimal GMs. Final assessment of developmental outcome is not yet carried out as children did not reached age of two years.

Discussion: As study is reached only second stage of the research and did not reached full sample of 100 children, it is to early to bring any conclusions. Still it is interesting to notice that contrary to expectations, not all of the children without evident neurorisk factors show normal-optimal or suboptimal GMs. Yet that does not mean that any of these children will develop some delays, but if so, it will be interesting to reassess known screening protocols.

Acknowledgments:

MeSH/Keywords: mild abnormal general movements, Prechtl assessment, neurodevelopmental outcomes

Poster code: R-A-9-71

ALTERED DISTRIBUTION OF RETROMER COMPLEX IN THE BRAINS OF NIEMANN-PICK TYPE C DISEASE MOUSE MODEL

PhD candidate: Kristina Dominko, BSc, MSc in Molecular Biology

PhD Thesis: The effect of intracellular cholesterol and C-terminal fragment of amyloid β precursor protein on retromer function in Alzheimer's disease models

Mentor/s: Associate Professor Nataša Jovanov Milošević, PhD and Senior Research Associate Silva Katušić Hećimović, PhD

Affiliation: Laboratory for Neurodegenerative Disease Research, Division of Molecular Medicine, Ruđer Bošković Institute, Zagreb, Croatia

Introduction: Niemann-Pick type C (NPC) disease is a rare childhood neurodegenerative disorder caused by mutations in cholesterol transport genes NPC1 or NPC2. Interestingly, NPC disease shares several features with Alzheimer's disease (AD), including dementia, neurodegeneration, endosome/lysosome dysfunction, and increased levels of amyloid-β peptides. Previously, we have shown that AD-like phenotype in NPC1-null cells involves sequestration of Alzheimer's amyloid-β precursor protein (APP) and BACE1 within endocytic pathway. We hypothetized that dysfunction of retromer, protein complex involved in recycling of proteins, including APP, from early endosomes to the trans-Golgi network or plasma membrane, is responsible for mistrafficking of APP and BACE1 in NPC1-null cells. Indeed, our previous studies in vitro demonstrated accumulation of retromer proteins within endocytic pathway. The goal of this work is to elucidate whether altered distribution of retromer complex occurs also in vivo in different brain regions of NPC mouse model.

Materials and methods: To determine levels and distribution of retromer proteins in different brain regions, we analyzed hippocampi, cerebella and cortices of NPC1wt/wt (wt) and NPC1-/- (NPC1) mice before onset of the disease (4 weeks old), after behavioral deficits started (7 weeks) and in the terminal stage (10 weeks). The levels of retromer proteins Vps26, Vps35 and retromer receptor sorLA were analyzed by western blotting. Regional distributions of retromer proteins were analyzed on sagittal cryosections by immunohistochemistry.

Results: The levels of retromer components Vps26 and Vps35 and retromer receptor sorLA analyzed by western blotting were not changed between wt and NPC1 mice in different brain regions nor at different disease stage. However, their regional distribution was altered. We observed a decrease of sorLA in all brain regions analyzed in NPC1 vs. wt mice. In addition, Vps35 was shown to accumulate in the cell soma of Purkinje neurons, which are primarily affected in NPC disease.

Discussion: Our results indicate altered regional/subcellular distribution of retromer complex in different brain regions in NPC disease. The changes in retromer distribution seem to recapitulate the spread of the disease, starting in cerebellar Purkinje neurons and spreading to cortex. Altogether, dysfunction of retromer complex in NPC mouse brains may be responsible for the AD-like phenotype previously observed in NPC disease.

Acknowledgments: I would like to thank Lucija Horvat for her technical assistance with confocal microscopy, Dr Mirsada Causevic for brain samples and Facility for laboratory animals RBI for providing us the mice. This work was supported by the Croatian Science Foundation – „Young researchers' career development project – training of new doctoral students" (S.H. and K.D.) and Swiss National Science Foundation – SCOPES: Joint Research Project (S.H.).

MeSH/Keywords: Alzheimer's disease, APP, cholesterol, neurodegeneration, mouse model, Niemann-Pick type C disease, NPC1, retromer

Poster code: R-A-9-95

EXPRESSION OF GABA SIGNALING PATHWAY KEY MOLECULES IN MOUSE AND HUMAN CERVICAL TISSUE

PhD candidate: Marta Skelin, MD

PhD Thesis: Estradiol and signaling pathways in the regulation of human endocervix secretory activity

Mentor/s: Marija Ćurlin, PhD

Affiliation: School of Medicine, University of Zagreb

Introduction: Cervical mucus is a glycoprotein gel produced by secretory epithelium in the endocervical glands. The role of the mucus is protective – it provides a barrier to the infection. Cervical mucus has an important role in fertility, due to the cyclic changes of its properties which are related to the levels of hormones in the blood. It is indicated that, besides the slow processes of transcription and translation of mucus components, the cycling hormones can regulate rapid process of mucus secretion from the endocervical glands. Since the regulation of mucus production in the bronchial goblet cell is mediated by GABA signaling pathway we hypothesized analogous GABA-mediated regulation of the endocervical glands.

Materials and methods: In order to test our hypothesis, the expression of key GABAergic molecules in mouse and human cervical tissue was tested by reverse transcription polymerase chain reaction (RTPCR) and immunohistochemistry.

Results: We have shown that GABA signaling pathway key molecules are present in mouse and human tissue. The examined molecules in mouse tissue were β2 subunit of GABA receptor A (GABAAR β2) and estrogen receptor ERα. The following molecules were shown to be expressed in the human tissue: glutamic acid decarboxylase (GAD), vesicular GABA transporter (VGAT), β2 subunit of GABA receptor A (GABAAR β2) and estrogen receptor ERα.

Discussion: This study is the first step in verifying the novel concept assuming the role of GABA signaling pathway in the regulation of the endocervical mucus secretion. Subsequently, the mechanism of the estrogen driven regulation of mucus secretion remains to be elucidated in the context of GABA mediation.

Acknowledgments: The study was funded by EU FP7 grant GlowBrain (REGPOT–2012–CT2012–316120).

MeSH/Keywords: ENDOCERVICAL GLANDS, MUCUS, GABA, ESTROGEN

Poster code: R-A-9-97

1H-MRS CHANGES, THERAPY AND SEVERITY OF SYMPTOMATOLOGY OF DEPRESSIVE DISORDERS

PhD candidate: Benedict Rak, dr.med

PhD Thesis: Correlation of symptomatology of depression, biological indicators measured by nuclear magnetic resonance spectroscopy at the onset of first depressive episode with regard to presence of external factors

Mentor/s: Prof.dr.sc. Neven Henigsberg

Affiliation: University of Zagreb, School of Medicine

Introduction: Antidepressive therapy is only effective in 60% of patients, taking 3-4 weeks for clinical effect to be demonstrated. Numerous evidence suggests the potential use of magnetic resonance spectroscopy in the assessment of pharmacological intervention, and that the amino acid neurotransmitter systems measurable by 1 H-MRS are associated with the pathophysiology and treatment of mood disorders.

Materials and methods: The research will be conducted on two groups of participants, at the time of the onset of a depressive episode. The first group will consist of patients whose first depressive episode occurred without distinguishing factors from the environment, and in the second the subjects for which it did occur under the influence of external factors that could affect the occurrence of depressive episodes. The study will be monitored through measurable indicators of 1H-MRS in the amygdala and prefrontal dorsolateral cortex, where differences associated with the emergence or during depressive disorder have already been shown, and occipital cortex. The study will include subjects of both genders aged between 18 and 55 years of age, who are not diagnosed with comorbid psychiatric disorder or somatic illnesses directly linked to the onset of etiological depressive episodes. Sample size is determined to be 21 subjects in each group, with the condition $\alpha = 0.05$ and $\beta = 0.8$ for each 1 H-MRS indicator.

Results: It was established in the previous studies of this project that the statistically significant difference of each of 1 H-MRS measured indicators exists between healthy controls and patients diagnosed with depression. Preliminary results show there is also a difference with regard to external stress factors.

Discussion: Biological indicators in defined areas of the brain detectable by 1H-MRS differ in patients with depressive disorder driven by environmental factors to one that occurs without these influences, correlating as well with clinical response to therapy. Therefore, differences in biological parameters measurable by 1H-MRS will contribute to elucidation of the biological basis of the etiology of the emergence of these forms of depressive disorders, prediction of therapeutic response and diferentiation of clinical entities through objectively measurable indicators.

Acknowledgments:

MeSH/Keywords: depression, endogenous, nuclear magnetic spectroscopy, biological indicators

Poster code: R-B-29-100

THE IMPACT OF DIFFERENT WHITE MATTER SEGMENTS DAMAGE ON NEURODEVELOPMENTAL AND ELECTROENCEPHALOGRAPHIC FEATURES IN PREMATURE BORN CHILDREN

PhD candidate: Petra Grđan

PhD Thesis: The impact of different white matter segments damage on neurodevelopmental and electroencephalographic features in premature born children

Mentor/s: Professor Nina Barišić, MD, PhD

Affiliation: The Croatian Institute for Brain Research, University Hospital Centre Zagreb

Introduction: According to the literature, 40 % of prematurely born children have motor development impairment, 10 % cerebral palsy, 26-47 % epilepsy, while 30-60 % cognitive impairment, hyperactivity or visual and hearing disturbances. Periventricular leukomalacia with neuronal-axonal injury and periventricular-intraventricular haemorrhage are two main types of brain injury in premature infants. The imaging studies shown different pathologies after ischemia and haemorrhage based on involvement of different white matter segments. Their impact on the maturation and pathological electroencephalographic features (EEG) in premature born children is unclear.

Materials and methods: The study include 25 prematurely born infants with lesions of different white matter segments on brain MRI and the control group of 15 premature infants with normal MR findings. In all subjects we analyze: gestational age, birth weight, delivery (caesarean section/spontaneous), resuscitation (yes/no), Apgar score, perinatal infection, mechanical ventilation, SNAP II, SNAPPE II. EEG and neurological assessment according to Amiel-Tisson are performed every 4 weeks from birth up to term corrected age, then at the age of 3, 6, 9, 12, 18 and 24 months of life. Brain ultrasound is performed every 1-2 weeks until 3rd months of life, depend on clinical presentation. Brain MRI is performed at the corrected term age and at the age of 2 years.

Results: The study is still in progress, but early results, based on first brain MR and few EEG recordings and neurological examinations, shows motor impairment in 33% of children (10/30), epilepsy and hearing disturbance in 7% (2/30) with pathological MR findings. We also expect that we will define positive correlation between specific maturational/pathological EEG graphoelements and white matter changes.

Discussion: Preterm born children with perinatal brain injury show different neurodevelopmental abnormalities. Understanding the correlation between EEG changes, MRI findings of white matter injuries and neurodevelopmental difficulties will enable us defining positive predictors and early detection of high-risk children, as well as improvement of neuroprotection strategy and rational use of pharmacotherapy.

Acknowledgments: Professor Emeritus Ivica Kostović, MD, Assist. Professor Milan Radoš, MD, Vesna Benjak, MD, PhD, Assist. Professor Ruža Grizelj, MD

MeSH/Keywords: white matter, leukomalacia, brain magnetic resonance imaging, brain ultrasound, EEG, neurological development, premature infant

Poster code: R-A-9-102

NEUROPLASTIN EXPRESSION AND SUBMEMBRANE DISTRIBUTION IS RELATED TO SPECIFIC GANGLIOSIDE COMPOSITION

PhD candidate: Katarina Ilić, MD

PhD Thesis: Association of ganglioside composition and neuroplastin expression with neurodegenerative changes

Mentor/s: Svjetlana Kalanj Bognar, MD, PhD

Affiliation: Croatian Institute for Brain Research, School of Medicine, University of Zagreb

Introduction: Gangliosides are membrane glycosphingolipids particularly abundant and important for modulating various cellular events in mammalian brain. Ganglioside composition influences appropriate positioning and function of specific membrane proteins, such as neuroplastin (Np) – a transmembrane glycoprotein involved in promoting neurite outgrowth, regulation of structure and function of synapses and synaptic plasticity. Our previous results showed changed Np expression in human hippocampi affected by Alzheimer's disease (AD). In addition, we reported altered hippocampal Np expression and distribution in mice lacking complex gangliosides. However, positioning of Np within specific membrane subdomains has not been investigated so far. In this study we aimed to analyze Np expression and submembrane distribution in brain tissue of mice with aberrant ganglioside synthesis and mouse model of AD.

Materials and methods: Cortical tissue was dissected from brains of: APP/PS1 transgenic mice (AD model), B4galnt1 knock-out (KO) and St3gal2/3 double knock-out (DKO) mice with aberrant brain ganglioside composition, and their corresponding wild-type (WT) controls. Membrane proteins were isolated from tissue homogenates and Np expression was analyzed using Western blot followed by ImageJ quantification. Membrane proteins from cortices of KO and DKO mice were additionally segregated in lipid raft and non-raft domains, using procedure for lipid raft isolation modified in our laboratory. Neuroplastin distribution within the specific membrane fractions was analyzed using Western blot and ImageJ quantification.

Results: We report altered expression of two major Np isoforms in cortical tissue derived from all mouse models analyzed as compared to WT mice, most prominently in KO mice. Also, we show differences in Np membrane positioning depending on ganglioside composition. Specifically, there is a shift of Np from lipid raft to non-raft domains in cortical tissue of KO and DKO mice compared to WT animals.

Discussion: The results confirm our hypothesis that Np expression and its membrane distribution depends on different ganglioside milieu. Observed alteration of Np expression and positioning within membrane is clearly related to documented specific changes in ganglioside quantity and composition in brain tissue of APP/PS1 transgenic mice, as well as mice models with interrupted ganglioside biosynthesis.

Acknowledgments: Brain tissue samples from APP/PS1 mice were generously donated by prof. Raquel Marin, La Laguna University, Spain. Brain tissue samples derived from B4galnt1 knock-out and St3gal2/3 double knock-out mice were donated by prof. Ronald L. Schnaar, Johns Hopkins School of Medicine, USA.

MeSH/Keywords: Neuroplastin, Gangliosides, Lipid rafts

Poster code: R-A-9-103

RAT MODEL OF CHRONIC STRESS AND AGING: INFLUENCE ON LIPID RAFTS IN RAT CEREBELLUM AND CORTEX

PhD candidate: Marta Balog, mag. biol.

PhD Thesis: Influence of chronic stress and aging on lipid rafts in rat brain cells

Mentor/s: Prof. Željka Vukelić, PhD, Prof. Marija Heffer, MD, PhD

Affiliation: School of Medicine, University of Zagreb, Faculty of Medicine Osijek, J. J. Strossmayer University of Osijek

Introduction: Stress and aging are risk factors for development of neurodegenerative diseases influencing cell´s energy metabolism. Insulin and leptin signaling have been associated to molecular mechanisms of neurodegeneration. It has been considered that insulin (IR) and leptin (Ob-R) receptors are located within the membrane microdomains – lipid rafts. Chronic stress and aging could cause changes in insulin/leptin signaling, which could lead to a cognitive decline. Changes in glucose/insulin metabolism and body weight as well as loss of memory function are also expected. In this study, selected metabolic and cognitive tests were performed on the improved chronic stress and aging rat model in order to characterize chronic stress- or/and aging-induced changes. The aim was also to define whether or not the IR and Ob-R are located within lipid rafts.

Materials and methods: Male and female Sprague Dawley rats were divided in young and old experimental groups and their matched control groups. Chronic and sham stress protocols were performed during 10 weeks. Glucose and insulin tolerance tests were performed as metabolic tests, while passive avoidance test was used as a cognitive test. Lipid rafts were isolated from cortices and cerebella using a novel method developed by our research group. The presence of IR and Ob-R in both lipid rafts and non-lipid rafts membrane fractions was screened by Western-blotting technique. The Statistica software was used for statistical analysis.

Results: Chronic stress caused statistically significant changes in body weight of animals during the study (as determined in multiple points of measurements) as well as changes in glucose and insulin tolerance. Cognitive decline, determined by passive avoidance test, was detected mostly in old female chronic stress group as compared to control group ($U=0$, $N1=N2=9$, $p=0.00004$). Analysis of lipid rafts from brain cortices and cerebella revealed that both IR and Ob-R are localized outside of the lipid rafts, contrary to literature data.

Discussion: As a part of this study, a reproducible rat model of chronic stress in rats was developed. The most prominent cognitive decline was observed in experimental old female group. Changes in expression of IR and Ob-R in cortex and cerebellum are expected and are yet to be determined. Developed animal model is useful for investigating the induced pathophysiological processes and could contribute to recognition of novel diagnostic biomarkers and of potential therapeutic targets for neurodegenerative diseases.

Acknowledgments: This research has been funded by Croatian Science Foundation project IP-09-2014-2324 and Cedars Sinai Medical Center's International Research and Innovation in Medicine Program and the Association for Regional Cooperation in the Fields of Health, Science and Technology (RECOOP HST Association).

MeSH/Keywords: chronic stress, aging, insulin, leptin, neurodegeneration

Poster code: R-A-9-127

VOLUMETRIC ANALYSIS OF THE CSF IN CERVICAL, THORACIC AND LUMBOSACRAL PART OF THE SPINAL SYSTEM

PhD candidate: Ines Strbačko, MD

PhD Thesis: Effect of body position on cerebrospinal fluid volume in cranial and spinal compartments

Mentor/s: Associate Professor Milan Radoš, MD, PhD

Affiliation: University of Zagreb Croatian Institute for Brain Research

Introduction: According to the classical hypothesis, it is believed that CSF is secreted inside the brain ventricles, has unidirectional flow and finally it is passively absorbed into the dural venous sinuses. Also, according to this hypothesis, changes of intracranial CSF pressure in different body positions are induced by redistribution of CSF between cranial and spinal CSF space. However, our previous experiments on cats and in vitro model showed that intracranial CSF volume is constant in different body positions, so we proposed that intracranial CSF pressure is primarily determined by the biophysical characteristics of the cranial and spinal CSF system. To test this hypothesis on humans we performed volumetric measurement of whole CSF system in different body positions. According to our new hypothesis, changes of body position do not lead to CSF displacement between the cranial and spinal CSF compartment and result with redistribution of CSF exclusively within the spinal compartment.

Materials and methods: We scanned craniospinal CSF system of healthy volunteers aged 18-30 years in magnetic resonance (3T, Magnetom Prisma, Siemens, Germany) in three different body positions (horizontal position, in position with lifted lumbosacral part and in position with elevated head and cervical part). To determine the total CSF volume of the spinal system and separate volumes for cervical, thoracic and lumbosacral part of the spinal system we will use manual segmentation. Due to the time-consuming process of manual segmentation, so far we manually segmented volume of the spinal system in 5 subjects in horizontal position using the program Analyze 8.1 (Mayo Clinic, USA).

Results: The total CSF volume in spinal system in 5 healthy subjects was in range between 79,16ml and 102,85ml (mean: 94,68ml, SD: 9,62). Volume of the CSF measured separately in the cervical segment was in range between 17,50ml and 25,56ml (mean: 20,56ml, SD: 3,75), for the thoracic segment in range between 32,25ml and 53,16ml (mean: 41,70ml, SD:7,51) and for the lumbosacral segment in range between 22,05ml and 37,47ml (mean: 32,41ml, SD: 6,15).

Discussion: These results give valuable information of the volume of the CSF in spinal system in horizontal position. There is a large variability in measured volumes of the CSF in total and separately for each segment in the CSF system between subjects. These results are ground data for further volumetric analysis of cranial and spinal CSF space in different body positions.

Acknowledgments: This study is a part of scientific project entitled The volumetric analysis of craniospinal liquor compartment in humans in different body positions in the magnetic resonance with Marko Radoš, MD, PhD, Full Professor as Head of the project.

MeSH/Keywords: cerebrospinal fluid, CSF volume, magnetic resonance imaging

Poster code: R-A-9-128

Clinical Medical Sciences Research Results

COMPARISON OF THE EFFECT OF BALANCED ANESTHESIA AND ANESTHESIA WITH TARGET CONTROLLED INFUSION IN CHILDREN WITH HYDRONEPHROSIS DUE TO THE SIZE OF OXIDATIVE STRESS

PhD candidate: Sandra Alavuk Kundović

PhD Thesis: Comparison of the effect of balanced anesthesia and anesthesia with Target Controlled Infusion in children with hydronephrosis due to the size of oxidative stress

Mentor/s: Professor Ljiljana Popović, PhD, MD/Maja Peraica, PhD, MD

Affiliation: Children's Hospital Zagreb, Institute for Medical Research and Occupational Health

Introduction: Oxidative stress is defined as the equilibrium shift in the cellular oxidation-reduction reactions in the oxidation direction. This is a condition caused by excessive production of free oxygen radicals. General anesthesia and surgical treatment may change the balance of the immune and antioxidant systems. This research is to determine the magnitude of oxidative stress associated to different anesthetic techniques (balanced anesthesia/TCI/TIVA) using BIS (Bispectral Index) and INVOS (In Vivo Optical Spectroscopy) in children subjected to Anderson – Hynes operation.

Materials and methods: The study includes 60 patients aged 3-16 regardless of gender. It will be carried out in children with hydronephrosis subjected to Anderson-Hynes operation. All patients will be randomized into two groups. Group 1 will countein 30 patients who will be in balanced anesthesia and Group 2 will countein 30 patients in anesthesia with Target Controlled Infusion. Everybody will have the standard monitoring (ECG, SpO2, etCO2, NIBP), INVOS (In Vivo Optical Spectroscopy) and BIS (Bispectral Index). In Group 1 induction of anesthesia will be with Sevoflurane, Fentanyl and Rocuronium, and in Group 2 with Propofol, Fentanyl and Rocuronium. We will measure the oxidative markers, total glutathione (GSH), protein carbonyls, malondialdehyde (MDA), superoxide dismutase (SOD) and total antioxidant capacity of plasma (FRAP). Blood will be taken out in three occasions, before the induction of anesthesia, 30 min from the beginning of anesthesia and 24 hours after onset of anesthesia. By spectrophotometry we will measure GSH, SOD, protein carbonyls and FRAP and with liquid chromatography (HPLC) MDA.

Results: At this time we have examined a few patients, because of randomisation one was with TCI and others were in balanced anesthesia. We have measured GSH (μmol/ml) and MDA (nmol/ml). The results show that GSH is lower in both types of anesthesia 30 minutes after induction, but after 24 hours we didn't get the same results, in some patients was lower and in some was higher than before induction. MDA increase in both types after 24 hours after induction.

Discussion: This research will determine if anesthesia with TCI causes smaller oxsidative stress than balanced anesthesia but to make some relevant conclusions in this moment we can say that both types causes increase of MDA 24 hours after induction and decrease of GSH 30 minute after induction and in some patients after 24 hours which means that other factors also affect on oxidative stress.

Acknowledgments: I offer my sincerest gratitude to my mentors, Professor Ljiljana Popović and Maja Peraica for supporting me throughout my research.

MeSH/Keywords: oxidative stress, balanced anesthesia, anesthesia, intravenous

Poster code: R-B-1-29

COMPARISON OF THE EFFECT OF CONTINUOUS INFUSION AND BOLUS DOSES OF ROCURONIUM DURING ANESTHESIA FOR LUMBAL DISCECTOMY ON MUSCLE STRENGTH OF A HAND GRIP

PhD candidate: Martina Miklić Bublić

PhD Thesis: Comparison of the effect of continuous infusion and bolus doses of rocuronium during anesthesia for lumbal discectomy on muscle strength and quality of patient recovery

Mentor/s: Assistant Professor Ante Sekulić, MD, PhD

Affiliation: University of Zagreb School of Medicine, University Hospital Centre Zagreb

Introduction: Rocuronium is non-depolarising neuromuscular blocking agent,and can be administered in multiple bolus doses or in continuous infusion during general anesthesia. In knee-chest position for lumbal discectomy, striated muscles are in unnatural position, and pressure on chest and abdomen can occur. Therefore good muscle relaxation is needed, as well as satisfactory muscle function recovery at the end of surgery and avoidance of postoperative residual neuromuscular block. Continuous infusion could give more stable neuromuscular block, avoiding periods of unsatisfactory relaxation. A comparison of both mentioned ways of administering rocuronium during lumbal discectomy was made to estimate their influence on a muscle strength of a hand grip and quality of patient recovery.

Materials and methods: After the approval of the Ethics Committee, written consents for participation were obtained from 80 patients ASA 1-2 for lumbal discectomy.They were divided in two groups. Both groups underwent general anesthesia with standard monitoring and bispectral index and train-of-four monitoring. Anesthesia was maintained with propofol, remifentanil and rocuronuim. After intubation dose, rocuronium was administered in the first group in bolus doses when TOF was 5%, and in the second group in continuous infusion to maintain TOF around 5%.Muscle strength of a hand grip was measured with Jamar dinamometer before anesthesia, after anesthesia in the operating room, and 24 hours after anesthesia. The patients also fulfilled standardised questionnare for measurement of the quality of recovery after anesthesia and surgery.

Results: In the first, bolus group, 20 female and 20 male patients were enroled (20% male and 20% female), and in second, continuous infusion group 19 female and 21 male patients (47,5% female and 52,5% male). Median age in first group was 50,88± 11,93 years, and in second group 48,85±12,45 years (p=0,524). Mean body weight in first group was 83,70±15,68 kg, and in second group 82,50±11,41 kg (p=0,962). Mean length of surgical procedure in first group was 128,25±27,26 min and in second group 131,00± 30,11 min (p=0,831). Detailed statystical analysis is in progress.

Discussion: We expect the results of this study to show whether the way of administering rocuronium during general anesthesia has a different impact on recovery of a muscle strength of a hand grip and general recovery that can be assessed with questionnaire.

Acknowledgments:

MeSH/Keywords: rocuronium, continuous infusion, lumbal discectomy, muscle strength, hand grip

Poster code: R-B-1-63

COMPARISON OF PHARMACOLOGICAL PROTECTION USING SEVOFLURAN AND ISOFLURAN IN ISCHEMIC/REPERFUSION GRAFT LIVER INJURY

PhD candidate: Nataša Paklar, MD

PhD Thesis: Comparison of pharmacological protection using sevofluran and isofluran in ischemic/reperfusion graft liver injury

Mentor/s: Assistant Professor Tatjana Filipec Kanižaj, MD, PhD

Affiliation: University Hospital Merkur, Zagreb, Croatia

Introduction: Ischemic/reperfusion injury is the leading cause of graft failure after liver transplantation. After ischemic period refreshed blood in flush through graft leads to massive free radical release. Volatile anaesthetics are used worldwide for conducting anaesthesia. It is considered that protective mechanism of volatile anaesthetics is conducted through ATP mitochondrial sensitive potassium channel (mitoK_{ATP}) on heart and brain models. This study is unique because volatile anaesthetics were studded as a possible method in reducing that injury but till now histological changes related with that effects were not studied.

Materials and methods: In the prospective study we plan to in roll minimal 100 patients who is planned for liver transplantation. In the beginning of study patients will be randomised in 2 groups (anaesthesia with sevoflurane or isoflurane). All other procedures and drugs will be used according to protocol used in our institution. Two biopsy of liver graft would be performed: ´0.´ biopsy – performed immediately after start of cold ischemia of a graft in donor- determining degree of microvesicular and macrovasicular steatosis, degree of activity of chronical hepatitis and the degree of fibrosis, ´1.´ biopsy – performed 2 hours after reperfusion of a graft in recipient- degree of ischemic/reperfusion injury would be semiquantitativly determined: mild, moderate and severe on the base of scoring 8 morphological characteristics: balloon degeneration hepatocytes, microvesicular and macrovesicular steatosis, cholangiolar proliferation, cholestasis, apoptotic bodies, granulocytes infiltration and pericentral confluent necrosis. In case that we need vasoactive drugs more than 30 minutes or to decrease MAC (minimum alveolar concentration) less than 0.5 for period longer than 15 minutes we would exclude patient from the study.

Results: The study started at 1st of January 2017. and so far we enroll 9 patients. One participant had to be excluded from the study due to hemodynamic instability during transplantation, 6 patients were in the sevoflurane group and 2 in the isoflurane group. So far all patient were male (8) with mean age 60.6 years. The study is still in progress, but from this small date collection we might say that results are better on ischemic/reperfusion liver graft injury with use of isoflurane.

Discussion: Conclusions were made on a small sample. The study should be continued and date subjected to more detailed statistical analysis in order to have definitive conclusion.

Acknowledgments: I would like to thank my mentor Assistant Professor Tatjana Filipec Kanižaj, MD, PhD and members of the Transplantation team.

MeSH/Keywords: liver transplantation/adverse effects, ischemic postconditioning/methods , pharmacology, reperfusion injury/prevention

Poster code: R-B-1-105

PREVALENCE OF BRAF MUTATION IN DYSPLASTIC NEVUS AND MELANOMA IN SITU

PhD candidate: Ivana Prkačin, specialist of dermatology and venerology

PhD Thesis: PhD Thesis Proposal: Prevalence of BRAF mutation in dysplastic nevus and in situ

Mentor/s: Prof.D.Sc. Mirna Šitum, Chief of Staff M.D. Co-Mentor: Assistant Prof. Ivan Šamija, D.Sc.

Affiliation: Clinic for Skin and Venereal Diseses and Clinic for Oncology and Nuclear Medicine-the Laboratory for Molecular Diagnostics, Sisters of Charity Clinical Hospital Centre, Zagreb

Introduction: Malignant melanoma represents only 4-5% of all malignant skin tumors, but its mortality is even 71 – 80%. The incidence of melanoma in Croatia in the last 20 years has increased by 140%, whereas the mortality rate caused by melanoma has increased by 50% that corresponds to world trends. Dysplastic nevus placed at skin level are bigger than common nevus, their diameter is from 0.6-1.1 cm, of unclear borders and of unequal pigment. Protein BRAF is a component of the signalling pathway of the MAP kinase and its constituent activation is present in numerous tumours. Disturbance of signalling of the MAP kinase pathway might be a consequence of the constituent activation of the receptors of the factor of growth, of the RAS protein or kinase MEK and ERK in a cascade of kinases resulting in uncontrolled proliferation of the cells.

Materials and methods: The research is carried out by retrospective analysis of the samples of the tumour tissues of the patients with dysplastic nevus and melanoma in situ, in the period from the year 2005 till the year 2016. Analysis was performed on tissue samples fixated with formaline and put into paraffin for safekeeping at Ljudevit Jurak. We made 2-5 incisions of the tissue 7-8 μm thick from which DNA was separated in the Laboratory of the Clinic for Oncology and Nuclear Medicine of the Sisters of Charity Clinical Hospital Centre. DNA was separated by use of the QIAamp DNA FFPE Tissue kit (Qiagene). In the DNA samples from tissue samples of the dysplastic nevus and melanoma in situ the presence of the V600E mutation in the BRAF gene was established and for that mutation specific TaqMan Mutation Detection Assay (Applied Biosystems) was used in combination with the Gene Reference Assay for the BRAF gene (Applied Biosystems). Identification of the V600E mutation of the BRAF gene was carried out on the device for real-time PCR Applied Biosystems 9700.

Results: From the samples processed so far, 10 dysplastic nevus and 10 melanoma in situ, we have established that BRAF mutation exists in 7 dysplastic nevus and 9 melanoma in situ.

Discussion: In view of the obtained preliminary results, we conclude that our hypothesis, that the difference in the prevalence of the BRAF gene mutation between dysplastic nevus and melanoma is not statistically significant, will be confirmed.

Acknowledgments: I would like to express my gratitude to my mentor Prof. D.Sc. Mirna Šitum and co- mentor Assistant Professor Ivan Šamija D.Sc.

MeSH/Keywords: BRAF mutation, atipical nevus, melanoma, MAP kinase, tyrosine kinase inhibitors

Poster code: R-B-2-83

THE VALUE OF TRICHOSCOPY IN THE DIAGNOSIS OF PRIMARY CICATRICIAL ALOPECIA

PhD candidate: Željana Bolanča, MD, dermatovenereologist

PhD Thesis: The value of trichoscopy in the diagnosis of primary cicatricial alopecia

Mentor/s: Prof. Mirna Šitum, PhD, MD

Affiliation: Department of dermatovenereology, University Hospital Centre

Introduction: The hair has a major role in development of a seelfasteam and is one of the major physical atributes for expressing patients own individuality. Therefore, hair diseases and hair shedding have a great impact on quality of life of the patient, psyhological status and social life of the patient. Scarring alopecias are rare but significan hair diseases that cause irreversible follicular destruction with fibrous scar formation and permanent hair loss. Incidence of scarring alopecia is between 2 and 7 %, and prevalence is unknown. Scarring alopecia are classified according to Guidelines of North American Hair Research Society (NAHRS) which is based on clinical status and patohistological analysis of biopsy specimen, respectively according to inflammatory type surrounding hair follicle. A biopsy of the scalp is the gold standard in the diagnosis of scarring alopecia. Histopathological analysis may be insufficient, and the main issue is inadequatelly choosen biopsy site, which is usually taken from the edge of the active lesions and selected by the "naked eye". The aim of this randomized, prospective study is to explore the value of trichoscopy in the selection of optimal biopsy site in the diagnosis of the primary scarring alopecia.

Materials and methods: Patients with scarring alopecia, will be randomized into two groups, of 30 patients each group. In the first group, the biopsy will be done at the edge of the lesion, and the site will be selected by the naked eye. In the second group, the biopsy will be guided by trichoscopy. The criteria for determining the biopsy site will be so far known trichoscopy criteria for scarring alopecia. The two 4 mm punch biopsy will be done

Results: In the first group where the biopsy site was determined by the naked eye, the patohistological analysis confirmed the diagnosis in 17 out of 30 biopsy specimen. In the second group, where the biopsy was guided by the trichoscopy, the diagnosis was confirmed in 28 out of 30 biopsy specimen.

Discussion: The trichoscopy guided biopsy showed superior accuracy in setting the diagnosis of cicatricial alopecia. The trichoscopy sholud be mandatory in choosing the biopsy site. It will decrease the number of repetitive biopsies and increase the accuracy of the diagnosis. Therefore the start and efficacy of the treatment will be improved. In the future, The Classification of cicatricial alopecia will include the trichoscopy criteria which will decrease the number of scalp biopsy.

Acknowledgments:

MeSH/Keywords: primary cicatricial alopecia, trichoscopy, biopsy,

Poster code: R-B-2-90

IMPACT OF BONE MORPHOGENETIC PROTEIN 1-3 ANTIBODY ON DERMAL SCARRING – NOVEL PROMISING THERAPEUTIC APPLICATION

PhD candidate: Anamaria Jović, MD

PhD Thesis: Impact of bone morphogenetic protein 1-3 and its antibody on dermal scarring in rats

Mentor/s: Prof. Zrinka Bukvić Mokos, MD, PhD, Prof. Lovorka Grgurević, MD, PhD

Affiliation: Laboratory for Mineralized Tissues, School of Medicine University of Zagreb, Zagreb, Croatia and University Hospital Centre Zagreb, Department of Dermatology and Venereology

Introduction: Scarring and its accompanying aesthetic, functional and psychological sequelae still pose major challenges. The fact that in the developed countries about 100 million people per year form a dermal scar, puts this problem in the most common in modern medicine. Currently, among commercially available products, there is no efficient treatment option which can successfully overcome impaired skin healing. Bone morphogenetic protein (BMP)1-3 is a key profibrotic protein that plays an important role in all stages of wound healing. In the present study, we utilized our understanding of BMP1-3 monoclonal antibody mechanism of action in procollagen processing and tested it's potential against BMP1-3 to enhance skin scar appearance.

Materials and methods: We established a rat model of primary healing and treated it locally and systemically with different doses of BMP1-3 monoclonal antibody. Two full-thickness, 6 cm linear skin incision were made on the dorsum of each rat at equal distances from the midline. The wounds were closed with 4-0 ethilon sutures. To prove the local efficacy of BMP1-3 antibody, rats were treated with subcutaneous injections. Wounds on the right side of each rat were treated with BMP1-3 antibody, while the left incision was injected with saline. Additionally, two groups were treated systemically, with saline and BMP1-3 monoab. Therapy was administered at days 1, 2, 5, 7 and 14. All wounds and scars were photographed postoperatively and on every second day of the experiment, to enable quantification utilizing the visual scale assessment graded from three independent experts. Histologic analysis was performed on day 21 and scar elevation index (SEI) was calculated.

Results: BMP1-3 antibody significantly improved scar appearance comparing to control group in both locally and systemically treated rats. The average visual score was 1.5 on the control side and 2.2 on the side treated with BMP1-3 antibody administered locally, 2.4 systemically. SEI of the wound treated with saline was 1.57 while was significantly decreased (1.26 and 1.14) after both local and systemic application of BMP1-3 antibody.

Discussion: Targeting BMP1-3 as mediators of fibrosis may throw up new therapeutic approach for reduction and/or prevention of pathological scarring or hypertrophic scars with functionally and cosmetically acceptable outcome.

Acknowledgments:

MeSH/Keywords: Scar, wound healing, collagen, BMP1-3, regeneration

Poster code: R-B-2-120

ASSOCIATION OF THE CLINICAL PRESENTATION AND VIRAL GENOTYPES IN GENITAL INFECTIONS WITH HUMAN PAPILLOMAVIRUS IN MEN

PhD candidate: Ivana Čulav Košćak, MD

PhD Thesis: Association of the clinical presentation and viral genotypes in genital infections with *human papillomavirus* in men

Mentor/s: Professor Mihael Skerlev, MD, PhD

Affiliation: Department of Dermatovenereology and Department of Clinical and Molecular Microbiology, University Hospital Centre Zagreb and School of Medicine Zagreb

Introduction: Genital infection due to Human papillomavirus is the most common viral sexually transmitted disease. Specific HPV genotypes can induce the premalignant lesions as well as invasive cancers in genitoanal region. According to recent investigation oncogenic HPV genotypes can also induce the benign genital lesion. In our study have correlated clinical appearance and localization of genital lesions with certain HPV genotypes.

Materials and methods: The observational cross-sectional study is being conducted in the Department of Dermatovenereology and the Department of Clinical and Molecular Microbiology, University Hospital Centre Zagreb. 80 male patients aged 18-65 years with clinical manifestations of HPV genital infection will be included in the study. The material obtained by curretage from the affected skin and/or mucosa will be analysed by the standard Hybrid Capture II method. Each HC II probe positive for the oncogenic HPV genotypes, as well as negative or inconclusive test sample will be additionally assessed with INNO-LiPA method which allows to selectively determine the specific HPV genotype.

Results: Data collection is still in progress (expected to be finalized in September 2017). At the moment there are not any preliminary results available.

Discussion: Since there is lack of previous comprehensive studies done in male population and the data from existing studies shows conflicting results, this study will give insight into the representation of 18 HPV genotypes in clinically altered skin and/or mucosa of the genitoanal region in men as well as into correlation of the specific HPV genotypes with localization and clinical manifestations of lesions. Consequently, it will contribute to early detection of oncogenic viral types based on the highly specific HPV DNA typing tests and allow persistence in treatment of genitoanal lesions in which oncogenic viral genotypes had been detected regardless their clinically benign appearance. Altogether, it could contribute to prevention of invasive cancer of genitoanal region in male population.

Acknowledgments: I would like to thank my mentor Professor Mihael Skerlev, MD, PhD and Associate Professor Lidija Žele Starčević, MD, PhD for scientific guidance and support.

MeSH/Keywords: HPV, male, sexually transmitted infections, Hybrid Capture, HPV DNA typing

Poster code: R-B-2-134

THE INFLUENCE OF EXERCISE ON REDUCTION OF SACROILIAC DYSFUNCTION IN PREGNANCY – – PRELIMINARY RESULTS

PhD candidate: Manuela Filipec, MPhty

PhD Thesis: The influence of exercise on reduction of sacroiliac dysfunction in pregnancy

Mentor/s: Associate Professor Ratko Matijević, MD, PhD, FRCOG

Affiliation: Department of Physical Medicine and Rehabilitation, University hospital "Sveti Duh", University of Zagreb, School of Medicine, Merkur University Hospital Zagreb, Croatia

Introduction: Sacroiliac dysfunction (SID) is major pain syndrome in pregnancy. It is caused by specific structure and function of the sacroiliac joints and their adjustment during pregnancy. SID incidence in pregnancy is reported up to 76.6%. SID causes limitations in performing routine daily activities, social and sexual life reducing quality of life for pregnant women.

Materials and methods: Randomised controlled trial has been undertaken. This results represents interim analysis of 50% participants included (calculated sample size n=374) by predefined inclusion and exclusion criteria.Study group has conducted four different exercises used in order to stabilize the pelvis performed two times a week for 20 minutes during two weeks period under the supervision of a physiotherapist. The control group was complied with their normal lifestyle without education about exercises used in order to stabilize the sacroiliac joints. Visual Analog Scale (VAS) was used to assess the pain intensity while Quebec scale was used for assessment of the degree of disability in everyday activities.

Results: Preliminary analysis is based on 187 pregnant women included (93 in the study and 94 in control group). There was no statistical significance between both group regarding pain intensity and degree of disability before inclusion in the study ($p=0.06$ $p=0.79$). Statistical significance was found ($p<0.001$) in reduction of pain intensity with significantly reduced disability in study group ($p<0.001$) after intervention. Such difference was not found in control group.

Discussion: Our preliminary results suggest effectiveness of exercise used in order to stabilize the sacroiliac joints during pregnancy, pointing importance of exercise in management of SID during pregnancy.

Acknowledgments:

MeSH/Keywords: sacroiliac dysfunction, pregnancy, exercise

Poster code: R-B-3-25

ASSOCIATION OF VITAMIN D WITH THE RISK FOR RESPIRATORY VIRAL INFECTIONS IN ELDERLY PERSONS

PhD candidate: Ana Godan Hauptman

PhD Thesis: Vitamin D supplementation in elderly persons placed in homes for the care of elderly and disabled persons lowers risk of ARI

Mentor/s: Professor Amarela Lukić Grlić, MD, PhD. Assist Professor Alenka Gagro, MD, PhD

Affiliation: University of Zagreb School of Medicine, University Hospital Centre – Zagreb. Home for the care of elderly and disabled persons „Godan"

Introduction: Vitamin D deficiency is nowadays associated as a risk factor for different human diseases such as viral respiratory infections. Elderly persons placed in homes for the care of elderly and disabled persons are recognized as a risk group for deficiency of this vitamin. Physiological processes of immunosenescence which include reactivation of CMV infection and comorbidities contribute to the fragility of these people and the increased risk of viral respiratory infections. Automated method for simultaneous detection of multiple respiratory viruses allows rapid results and therefore is suited for everyday use. In our research, we plan to examine if vitamin D deficiency in serum and its supplementation in people = 65 years of age placed in homes for the elderly affect the occurrence and severity of viral respiratory infections in relation to the level of serum IgG against CMV. The results of this research may contribute to the expansion of recommendations for vitamin D supplementation in elderly for the prevention of viral respiratory infections.

Materials and methods: In this study we have to include 70 people = 65 years of age placed in homes for the elderly. They are devided in two groups (control and tested). 25(OH)D in serum was tested at the beginig of the study and after 3 months. CMV IgG in serum was also tested at the begining of study. All patient with ARI (acute respiratory infection) symptoms were tested for most common viruses (MariPOC).

Results: So far study is ongoing and we do not have all data to make final conclusion. We tested 75 patients. Twenty of them had ARI symptoms. Nine of them were positive on seasonal influenza A virus. Four of them died during the study due to influenza virus complications. All of patients had lowered level of 25(OH)D in serum.

Discussion: All of patients had lowered level of vitamin D in serum. As study is not finished yet we do not have data about vitamin D supplementation. So far we can conclude that all patients were at risk of ARI. Further investigation and data will show vitamin D correlation with risk of ARI.

Acknowledgments: I would like to thank Professor Amarela Lukić Grlić and Assist Professor Alenka Gagro for guidance with this project.

MeSH/Keywords: vitamin D, elderly, respiratory viruses, infection, cytomegalovirus

Poster code: R-B-4-138

THE RELATIONSHIP BETWEEN THE PREOVULATORY AND POSTOVULATORY PROGESTERONE SERUM CONCETRATION AND THE OUTCOME OF THE IN VITRO FERTILIZATION

PhD candidate: Emina Ejubović, MD[1]

PhD Thesis: The relationship between the preovulatory and postovulatory progesterone serum concetration and the outcome of the in vitro fertilization

Mentor/s: Professor Miro Kasum, MD, PhD[2]

Affiliation: [1] Cantonal Hospital Zenica, Bosnia and Herzegovina, [2] University of Zagreb School of Medicine, University Hospital Center-Zagreb, Department of Obstetrics and Gynaecology

Introduction: The influence of elevated preovulatory and postovulatory progesterone (P4) on the outcome of in vitro fertilization (IVF) has been in the focus of many discussions in contemporary reproductive endocrinology. Numerous studies have found the adverse effect of elevated preovulatory P4 on the outcome of IVF. Other studies, contrary, failed to find the adverse effect of elevated preovulatory P4 on the outcome of IVF. Hence, there are no clearly established strategies in the treatment of patients with elevated preovulatory P4.

Materials and methods: The recruiting of the patients for the study is ongoing. 170 patients of the 300 planned were included in the control group while 42 of the 100 planned were included in the study group so far. Patients are paired according to their age, BMI, stimulation protocol, gonadotropin dosage, the number of retrieved oocytes and transferred embryos. Implantation and clinical pregnancy rate between the study and the control group were analyzed in terms of high preovulatory P4 for the statistical significance.

Results: Both groups were analyzed in terms of their age, number of retrieved oocytes and the IVF pregnancy outcome. No statistical significance (P=0,2662, 95%CI -0.52 to 1.87) was found regarding the age between the groups, with the mean age of 32.71 (min-22, max-37) in the study group and the mean age of 33.39 (min-20, max-37) in the control group. The number of retrieved oocytes between the groups was found to be highly significant (P<0.0001, 95%CI -6.11 to -2.92), with the mean number of oocytes of 12.31 (min-3, max-29) in the study group and the mean number of oocytes of 7.79 (min-1, max-27) in the control group. No statistical significance was found between the groups regarding the IVF pregnancy outcome (P=1.0) with the 26.2% pregnancy rate in the study group and 27.6% in the control group.

Discussion: It has been suggested that elevated P4 accelerates the endometrial maturation, narrows the implantation window and decreases pregnancy rates. However, our preliminary results have failed to establish the relationship between the elevated preovulatory P4 and the adverse IVF outcome. This can be explained by a more appropriate timing of embryo transfer at the blastocyst stage (5th day) with the improved implantation and clinical pregnancy rate. This research will contribute to the implementation of new strategies in the treatment of patients during IVF procedures with no additional cost of cryopreservation and subsequent blastocyst transfer in the natural cycle.

Acknowledgments:

MeSH/Keywords: in vitro fertilization, progesterone, embryo transfer

Poster code: R-B-5-45

EARLY PREGNANCY PREDICTION OF PREECLAMPSIA

PhD candidate: Petrana Beljan

PhD Thesis: Early predictive model for the development of preeclampsia: combination of biomarkers PP13 and copeptin and maternal risk factors

Mentor/s: Vesna Elveđi Gašparović, Assistant professor, MD, PhD, Dept. of Ob/Gyn, School of Medicine, University of Zagreb, Zagreb, Croatia

Affiliation: Dept of Ob/Gyn, School of Medicine, University of Zagreb, Zagreb, Croatia

Introduction: Preeclampsia is a multisystem pregnancy related disorder of unknown etiology with the progressive course and with no established therapy.It complicates 3-5% of all pregnancies and it is the most common cause of fetal and maternal death.The aim of this study is to find an early predictive model for preeclampsia during the first trimester of pregnancy using the combination of biochemical markers PP13 and copeptin with some known maternal risk factors and uterine artery Doppler.

Materials and methods: These are preliminary results of a prospective study which will include 400 pregnant women who will undergo routine first trimester (11-14 weeks) laboratory test in our Department. We used some maternal factors as inclusion criteria for this study: nulliparity, age >35, BMI >25, smoking or some other chronic diseases in personal history.Participants were asked to provide short questionnaire with personal and medical informations.Blood samples were collected and maternal serum PP13 and copeptin levels were measured.Data on pregnancy outcome were collected after the delivery from maternal and pediatric records.

Results: Following the inclusion criteria we analyzed the records of 40 women who gave birth,3 of them (7.5%) developed preeclampsia and 8 of them (20%) had gestational hypertensia(GH).In the PE group compared to unaffected pregnancies was a higher median maternal age and weight as well as a higher prevalence of lowbirth weight and intrauterine growth restriction.In the PE group the values of uterine artery pulsatility index and mean arterial pressure in the first trimester were increased as well as values of serum copeptin.Logistic regression analysis demonstrated that there were significant contributions from maternal factors and biomarkers for prediction of PE.

Discussion: There have been many screening tests evaluated in the literature over the years for predicting preeclampsia using different biomarkers.Nevertheless,if signs of abnormal placental and endothelial dysfunction could be detected prior to the onset of clinical disease,they would represent an extremely attractive target for emerging therapeutic strategies.These are only preliminary results on a small sample.If this model proves to be a reliable early predictor of preeclampsia it could be a great opportunity to integrate this into routine testing already performed as part of prenatal care in the first trimester.

Acknowledgments:

MeSH/Keywords: preeclampsia, PP13, copeptin, perinatal outcome

Poster code: R-B-5-108

CORRELATION BETWEEN SFRP1 PROTEIN EXPRESSION AND GENE DNA METHYLATION STATUS IN SEROUS OVARIAN CARCINOMAS

PhD candidate: Vedran Kardum, MD

PhD Thesis: Expression of Wnt signaling pathway proteins SFRP1, SFRP3, DVL1, DVL2 and DVL3 in serous ovarian cancer

Mentor/s: Associate Professor Ljiljana Šerman, MD, PhD

Affiliation: University of Zagreb School of Medicine, University hospital Merkur

Introduction: Wnt is a highly conserved signaling pathway responsible for tissue regeneration, maintenance regulation and differentiation of stem cells in an adult organism. Aberrant activation of the pathway whilst reduced expression of Wnt signaling pathway inhibitors, such as proteins from the SFRP family, is typical for development of many tumors. In the present study we explored SFRP1 protein expression and gene DNA methylation status in a cohort of serous ovarian carcinomas.

Materials and methods: Ovarian serous carcinoma tissue samples (27 low-grade (LGSC), 26 high-grade serous carcinomas (HGSC) including 5 normal ovarian tissues (controls) were immunohistochemically stained for SFRP1 protein and semi-quantitative analyzed. Randomly chosen, 8 LGSC samples, 13 HGSC and all control samples were analyzed for DNA methylation. DNA was isolated from formalin-fixed, paraffin-embedded 2 x 10 μm tissue sections treated with bisulfite using Methyl Edge Bisulfite Conversion System. Bisulfite-treated DNA was then used for methylation-specific PCR reaction (MSP). All PCRs were done using TaKaRaEpiTaq HS (for bisulfite-treated DNA).

Results: In all healthy ovaries unmethylated SFRP1 genes and strong SFRP1 protein expression were found. SFRP1 protein expression was significantly higher in healthy ovaries compared to LGSC and HGSC. When comparing LGSC and HGSC significantly higher expression was found in LGSC (Mann Whitney test - $p=0.0124$). DNA isolated from LGSC shows almost a complete lack of SFRP1 gene methylation while DNA isolated from HGSC shows SFRP1 gene methylation in 7/13 (54%) of tested samples.

Discussion: Preliminary results indicate good correlation between SFRP1 gene methylation and its protein expression in healthy ovary samples in which the analyzed SFRP1 gene is unmethylated and therefore protein was strongly expressed. LGSCs exhibited low or weak SFRP1 gene methylation in contrast to HGSCs that were characterized by a loss of SFRP1 protein expression and high SFRP1 gene methylation. Our preliminary data indicate loss of SFRP1 protein expression caused by the SFRP1 gene promoter methylation in high-grade serous ovarian carcinomas.

Acknowledgments:

MeSH/Keywords: Wnt, SFRP1, DNA, methylation, ovary, carcinoma

Poster code: R-B-5-86

USEFULNESS OF THORACIC ULTRASOUND IN ASSESSING THE ETIOLOGY OF UNDIAGNOSED PLEURAL EFFUSION

PhD candidate: Nevenka Piskač Živković, MD

PhD Thesis: Diagnostic validity of thoracic ultrasound in distinguishing malignant and non-malignant pleural effusion

Mentor/s: Professor Neven Tudorić, MD, PhD

Affiliation: University Hospital Dubrava, Zagreb.

Introduction: Pleural effusion is a common manifestation of malignancies originating from various primary sites, suggesting progressed disease and a poor prognosis. Thoracic ultrasound (TUS) is an important diagnostic method for the detection of pleural effusion, as well as for the safe performance of invasive procedures to verify the etiology of the effusion. Although the definitive diagnosis of malignant effusion is made by cytological or histological assessment, a thorough analysis of the ultrasound findings can also be of significant diagnostic use.

Materials and methods: Thoracic ultrasound findings of 104 patients with confirmed MPE were analyzed with regard to the ultrasound features of the effusion and pleural thickening or nodularity. The findings were analyzed with regard to the macroscopic features of the pleural effusion.

Results: In 97 patients the pleural effusion was a result of solid tumor metastasis, and 7 patients had disseminated hematologic disease. A comparison of the gross features of the MPEs did not result in a statistically significant correlation ($p=0.159$). Conversely, a comparison of the gross features of septated and non-septated MPEs yielded a significant correlation between effusion septation and the gross finding of blood in the effusion ($p<0.0001$). 56 out of 95 (59%) samples of non-septated and 8 out of 9 (89%) septated pleural effusions were sanguinolent/hemorrhagic. In the only sample of non-hemorrhagic pleural effusion with ultrasound features of complex septated effusion the finding was non-Hodgkin lymphoma, which can be routinely confirmed at the initial cytological analysis of the pleural effusion.

Discussion: Data yielded by this retrospective analysis confirm the significant heterogeneity of the macroscopic findings and ultrasound features of malignant pleural effusions. Nevertheless, they also clearly emphasize the association between MPE septation and their gross appearance (sanguinolent/hemorrhagic). The authors believe that this finding allows for the conclusion that in the case of non-hemorrhagic, complex septated effusions a malignant etiology can be ruled out with high probability. The authors are aware of the study limitations, particularly in view of the fact that it was a retrospective investigation which did not include history data on patients with non-malignant pleural effusion with fibrinous septations. Confirmation of this signal requires a prospective analysis which would include those patients as well.

Acknowledgments:

MeSH/Keywords: thoracic ultrasound, malignant pleural effusion

Poster code: R-B-9-8

SERUM CHITOTRIOSIDASE: A CIRCULATING BIOMARKER OF MACROPHAGE – SUPPORTED PATHOLOGICAL ERYTHROPOIESIS IN POLYCYTHEMIA VERA?

PhD candidate: Ivan Krečak, MD

PhD Thesis: Clinical significance of chitinase-3-like protein 1 and chitotriosidase in Philadelphia negative chronic myeloproliferative neoplasms

Mentor/s: Asst. Prof. Nadira Duraković, MD, PhD

Affiliation: Department of Internal Medicine, General Hospital Šibenik and University Of Zagreb, School Of Medicine

Introduction: Polycythemia vera (PV) and essential thrombocythemia (ET) are clonal hematopoietic stem cell disorders characterised by overproduction of erythroid or megakaryocytic cells due to the activating JAK2 – V617F mutation. It is unknown how a single mutation can cause these two different diseases. Macrophage - supported pathological erythropoiesis in PV was described to be a contributing factor in acquiring PV phenotype. Serum chitotriosidase (CHIT1) activity recently emerged as a nonspecific biomarker of macrophage activation. We hypothesised that serum CHIT1 activity may reflect the increased macrophage activity in PV and serve as a potential disease biomarker.

Materials and methods: Over the period of July 2014 to November 2016 we included 28 PV patients (12 male /16 female, median age 65.5), 27 ET patients (13 male / 14 female, median age 61) and 28 healthy blood donors as controls (16 male / 12 female, median age 59). Serum CHIT1 activity was measured fluorometrically by measuring the enzymatic hydrolysis of product 4 - methylumbeliferone at specified excitation (365 nm) and emission (450 nm) wavelengths on Cary Eclipse Fluorimeter (Agilent Technologies, USA).

Results: Serum CHIT1 activity was significantly higher in PV patients (median 54 μmol/L/h, range 3 – 458) when compared to healthy controls (median 31 μmol/L/h, range 12 – 78) ($p = 0.001$). There was no statistically significant difference between serum CHIT1 activity in ET patients (median 36 μmol/L/h, range 1 – 502) and healthy controls ($p = 0.222$). Serum CHIT1 activity was 1.5 times higher in PV than in ET patients, however, this observation was not statistically significant ($p = 0.074$). Positive correlation was found in PV between the serum CHIT1 activity, hemoglobin ($r = 0.437$, $p = 0.020$) and hematocrit ($r = 0.455$, $p = 0.015$) level. There was no difference between serum CHIT1 activity and absolute leukocyte, granulocyte, erythrocyte and platelet count in both PV and ET.

Discussion: Serum CHIT1 activity in PV may be a novel circulating biomarker of the increased macrophage activity from the "erythroblastic island". These findings provide an additional degree of complexity to this disorder, and further highlight the role of tumor microenvironment in pathogenesis and the clinical presentation of myeloproliferative neoplasms. Additional studies are required to elucidate the role of serum CHIT1 activity in promoting disease progression, bone marrow fibrosis, atherosclerosis and thrombosis in PV.

Acknowledgments: I would like to thank my mentor Asst. Prof. Nadira Durakovic, MD, PhD for all her help and support, members of the expert committee assigned for the appraisal of my doctoral thesis for their valuable and appreciated suggestions and to all my colleagues who helped me in designing this study.

MeSH/Keywords: JAK2V617F, chitotriosidase, biomarker, chronic inflammation, cytokines, myeloproliferative neoplasia.

Poster code: R-B-9-27

ASSOCIATION OF PLATELET SEROTONIN CONCENTRATION WITH ASTHMA SEVERITY – PRELIMINARY RESULTS

PhD candidate: Katherina Bernadette Sreter, MD (1)

PhD Thesis: Association of platelet serotonin, plasma brain-derived neurotrophic factor (BDNF) and Val66Met BDNF gene polymorphism with asthma severity

Mentor/s: Professor Sanja Popović-Grle, MD, PhD (2) and Dr. Dubravka Švob Štrac, BSc, PhD, Senior Research Associate (3)

Affiliation: [1]University Hospital Centre „Sestre Milosrdnice", [2]University Hospital Centre Zagreb, [3]"Ruđer Bošković" Institute, Zagreb, Croatia.

Introduction: Asthma is a common chronic inflammatory lung disease, with a pathophysiology that is still not fully elucidated. Research has implicated the role of the serotonergic system in asthma. However, most studies to date have investigated the association of asthma with serum/plasma serotonin (5-HT) levels, with few reports focussed on platelet 5-HT concentrations. In addition, previous reports have suggested an association of asthma with BDNF genetic variants and BDNF concentrations in serum and platelets, but few in plasma.

Materials and methods: The objective of this prospective case-control PhD study is to determine the concentrations of platelet 5-HT and plasma BDNF, as well as BDNF gene Val66Met polymorphism, in 120 asthmatic patients (diagnosed according to the Global Initiative for Asthma [GINA] criteria) and 120 healthy controls, and to evaluate their association with asthma. Thus far, the concentrations of platelet 5-HT have been determined for 49 healthy subjects (29 females, 20 males) and 93 asthmatic patients, divided according to severity into 45 cases of intermittent/mild-to-moderate persistent (GINA I-III, 29 females, 16 males) and 48 cases of severe persistent (GINA IV, 27 females, 21 males) asthma. Statistical analysis was conducted using GraphPad Prism program 4.0 with significant p-value < 0.05.

Results: The groups were similar with respect to gender, with females predominating ($p=0.718$, Chi-square test), but they differed significantly in age ($p<0.0001$, ANOVA), with the controls being younger than both groups of asthmatic patients. In all groups, there were more non-smokers (never-smokers and former-smokers) than smokers, but there was a greater percentage ($p<0.0001$, Chi-square test) of smokers in the control group (63%) than in the asthmatic groups (7% in GINA I-III, 12% in GINA IV). There was a significant difference ($p<0.0001$, Kruskal-Wallis test) in platelet 5-HT concentrations between all groups (GINA I-III vs control ($p<0.0001$, Dunn's test), GINA IV vs control ($p=0.004$, Dunn's test), GINA I-III vs GINA IV ($p=0.023$, Dunn's test), demonstrating the lowest concentration of platelet 5-HT in the GINA I-III group.

Discussion: These preliminary results suggest a potential association of the serotonergic system with asthma and its severity. Possible explanations for these differences in platelet 5-HT concentrations will be further explored during the next phase of this PhD research.

Acknowledgments: /

MeSH/Keywords: Asthma, Platelets, Serotonin, Severity

Poster code: R-B-9-39

WNT SIGNALING IN DIFFUSE GASTRIC CANCER

PhD candidate: Maja Sremac, MD

PhD Thesis: The expression of Wnt-signaling pathway components in diffuse gastric cancer

Mentor/s: Professor Nadan Rustemović, MD, PhD, Associate Professor Tamara Nikuševa Martić, PhD

Affiliation: University Hospital Centre Zagreb, University of Zagreb School of Medicine

Introduction: The Wnt genes encode a large family of secreted molecules that play important roles in controlling tissue patterning, cell fate and proliferation. The interactions of Wnt ligands and Fz receptors are modulated by the secreted Wnt antagonists: the soluble frizzled related protein (SFRP) class and the dickkopf class. Members of the SFRP family include Wnt inhibitory factor-1(Wif1), SFRP1, 2, 4 and 5 and frisbee (FrzB, SFRP3). They bind directly to Wnts, altering their ability to bind the Fz receptors. The various secreted Wnt antagonists interact directly and indirectly to affect Wnt signalling and influence a wide variety of biological processes, including developmental cell fate, differentiation and tumorigenesis.

Materials and methods: Samples of 60 diffuse gastric carcinoma and adjacent healthy gastric mucosa tissues were collected from the Department of Pathology, University Hospital Zagreb, Croatia. Immunohistochemistry was performed in order to establish the levels of expression and cellular localization of SFRP1 and SFRP3. The antibodies used for protein detection were rabbit polyclonal anti-human SFRP1 and rabbit polyclonal anti-human SFRP3. Randomly selected paraffin blocks were used for stereological analysis. Statistical analyses were performed using GraphPad Prism 5.01, (GraphPad Software, Inc., San Diego, CA, USA) and also Principal component analysis (PCA) was done using Matlab Software PLS Toolbox. The stereological data were evaluated by descriptive statistics.

Results: SFRP1 expression was found in glandular cells, localised in the cytoplasm. We found statistically significant difference in number of SFRP1 positive cells between normal and tumor tissues ($p < 0, 05$). The amount of SFRP1 protein expression in normal tissues was higher compared to the one observed in tumor tissue. Subcellular localization of SFRP3 protein was observed in cytoplasmic and membranous glandular cells. We found statistically significant difference in number of SFRP3 positive cells between normal and tumor tissues ($p < 0, 05$). The amount of SFRP3 protein expression in normal tissues was higher compared to the one observed in tumor tissue.

Discussion: Preliminary results indicate that the loss of Wnt inhibitors may play an important role in gastric carcinogenesis. The next step will be to evaluate the expression of other components of the Wnt signaling pathway and corelate the results with clinicopathological features to gain a better understanding of biological signaling pathways in diffuse gastric cancer.

Acknowledgments:

MeSH/Keywords: diffuse gastric cancer, Wnt-signaling pathway, Secreted frizzled-related protein (SFRP)

Poster code: R-B-9-50

THE CROATIAN ADAPTATION OF CAMBRIGE PULMONARY HYPERTENSION OUTCOME REVIEW (CAMPHOR)

PhD candidate: Ana Hećimović, MD

PhD Thesis: Correlation of qualitiy of life assesed by CAMPHOR questionnaire with functional and echocardiographic parameters in patients with pulmonary arterial hypertension

Mentor/s: Proffesor Sanja Popović Grle, MD, PhD, Professor Nataša Jokić Begić, Proffesor of Psychology, PhD

Affiliation: University Hospital Centre Zagreb, Clinic for Pulmonary Disease Jordanovac, Faculty of Humanities and Social Science, University of Zagreb

Introduction: Pulmonary arterial hypertension is chronic disease which severely impair quality of life. The Cambridge Pulmonary Hypertension Outcome Review (CAMPHOR) is the first pulmonary hypertension specific tool to assess patient reported symptoms, functioning and quality of life (QoL) in pulmonary arterial hypertension (PAH).

Materials and methods: Translation (employing bilingual and lay panels), cognitive debriefing interviews with patients and validation (assessment of the adaptation's psychometric properties) are the three main adaptation stages. The psychometric evaluation included 50 patients with precapillary pulmonary hypertension from one centre in Croatia.

Results: During translation process there was no major problems and most items were easily rendered into acceptable Croatian translation. Patients thought that questionnaire was relevant and easy to understand and complete during the cognitive debriefing stage. Psychometric analysis showed that adaptation was successful. All three scales of the CAMPHOR questionnaire showed good test-retest reliability correlation (Symptoms = 0.91, Activity limitations = 0.95, QoL = 0.91) and internal consistency (Symptoms = 0.93, Activity limitations = 0.94, QoL = 0.92). Predicted correlations with the SF-36 scales provided evidence of the construct validity of the CAMPHOR scales. The CAMPHOR adaptation also showed known group validity in its ability to distinguish between participants based on perceived general health, perceived disease severity.

Discussion: The results showed that the adaptation of the CAMPHOR for use with Croatian speaking participants was successful. Croatian version showed good internal consistency, convergent validity and known group validity. The Croatian version of the CAMPHOR demonstrated good psychometric properties. All scales in the CAMPHOR had good internal consistency and reproducibility. Croatian CAMPHOR shown its ability to distinguish between groups known to differ by perceived disease severity and general health which is another proof of its validity. The results of the present study indicate that the newly developed Croatian versions of the CAMPHOR represent valid and reliable tool for measuring HRQoL in Croatian patients with PAH.

Acknowledgments: I would like to thank Galen Research from Manchester, United Kingdom, for assigning us user rights to use and validate CAMPHOR questionnaire. I would like to thank Alice Heaney and Jeanette Wilburn from Galen Research for helping us in validation process and statistical analysis of the data and to prof Latinka Basara, psychologist in my institution, who helped me in bilingual and lay panel and cognitive debriefing interviews with patients.

MeSH/Keywords: pulmonary arterial hypertension, quality of life, questionnaire, validation

Poster code: R-B-9-58

THE ROLE OF TRANSRECTAL ULTRASOUND AND REAL-TIME ELASTOGRAPHY IN DIFFERENTIATION BETWEEN CROHN'S DISEASE AND ULCERATIVE COLITIS

PhD candidate: Matea Majerović, MD

PhD Thesis: The role of transrectal elastography in differentiation between Crohn's disease and ulcerative colitis

Mentor/s: Professor Nadan Rustemović, MD, PhD

Affiliation: Department of Internal medicine, Division of Gastroenterology and Hepatology, University Hospital Centre Zagreb

Introduction: Crohn's disease (CD) and ulcerative colitis (UC), two major types of inflammatory bowel diseases, each have distinctive features, but also share many overlapping characteristics, that sometimes poses a difficulty in timely establishment of a definite phenotype.The aim of our study was to evaluate the role of transrectal ultrasound (TRUS) combined with real-time elastography, using two different modalities, Strain Ratio (SR) and Hue Histogram Ratio (HHR), in the differentiation of CD and UC in active rectal disease.

Materials and methods: 51 patients (pts) were included in our study (54% male). They were divided into three groups: control group (29 pts), UC group (13 pts) and CD group (9 pts). Echoendoscope (Pentax EG-3670URK), combined with hardware and software by Hitachi medical systems (HitachiAvius) was used. After obtaining a stable elastographic image and measuring rectal wall thickness (RWT), two regions of interest (ROI) of similar diameter were chosen: ROI-A over the rectal wall and ROI-B over the adjacent perirectal tissue. SR and HHR (ROI-B/ROI-A) were automatically calculated by the software. Each measurement was repeated 5 times and the median value was used for statistical analysis. Descriptive statistics were used for basic characteristics. Variables were compared among different groups using Analysis of Variance (ANOVA), followed by LSD post hoc test for multiple comparisons. A p-value <0.05 was taken as statistically significant for all analyses. We used statistical software ž'IBM SPSS Statistics 24'' for the computations.

Results: We found a statistically significant difference in age across groups, with CD pts being the youngest ($F=8.444$, $p=0.001$). There was no difference in BMI ($F=2.657$, $p=0.080$). We also found a significantly thicker rectal wall in CD group (mean RWT (mm): controls 2.41 ± 0.54, CD 3.71 ± 1.53, UC 2.88 ± 1.02, $F=7.045$, $p=0.002$). Post hoc analysis showed a significant difference between control and CD group ($p=0.001$), as well as between CD and UC group ($p=0.042$). There was no difference in either SR ($F=0.324$, $p=0.725$) or HHR between groups ($F=0.015$, $p=0.985$).

Discussion: We showed that CD patients have significantly thicker rectal wall when compared to UC patients – a feature that may aid in differentiation between the two IBD types. Preliminary results did not show statistical significance in SR and HHR between the two groups, but these results might not be sufficient due to the small cohorts. Further recruitment of patients is warranted.

Acknowledgments: I would like to thank my mentor as well as the staff of the GI Endoscopy Unit for help and support throughout this research

MeSH/Keywords: Inflammatory Bowel Diseases, Endosonography, Elasticity Imaging Techniques

Poster code: R-B-9-78

CAROTID DISEASE IN PATIENTS WITH SYMPTOMATIC PERIPHERAL ARTERY DISEASE

PhD candidate: Ksenija Vučur, MD

PhD Thesis: Prognostic significance of carotid disease in patients with symptomatic peripheral artery disease

Mentor/s: Mislav Vrsalović, MD, PhD, FESC, FSVM

Affiliation: Department of Vascular Medicine, Cardiovascular Center, Sisters of Charity University Hospital Center, Zagreb. Department of Nephrology, University Hospital Merkur, Zagreb, Croatia

Introduction: Peripheral artery disease (PAD) is a multifactorial syndrome and one of the most common manifestations of atherosclerosis. Polyvascular involvement in PAD patients (pts) is associated with an increased risk of all-cause mortality as well as cardiovascular mortality. The aim of the study was to investigate the prevalence of concomitant carotid disease in pts with symptomatic PAD and associated cardiovascular risk factors

Materials and methods: In the retrospective research were included 319 consecutive pts with symptomatic PAD (Rutheford stages 2-6) who were hospitalized and treated in the Department of vascular disease, Clinic of cardiovascular disease in the University hospital Sister of Mercy between January 2010 and January 2016. Patients with malignancy and / or concomitant autoimmune disorders were excluded in the study. Demographic data and baseline clinical characteristics were recorded during the hospital stay and included general information, data about cardiovascular risk factors, biochemical and hematological laboratory data, and data on comorbidities and medications. The diagnosis of PAD was established by clinical examination, ankle brachial index measurement, duplex sonography and/or computed tomography or magnetic resonance, angiography, and confirmed with peripheral angiography using the criteria of the European Society of Cardiology and American College of Cardiology Foundation. The diagnosis of carotid disease was established by duplex sonography and pts with carotid stenosis of 50% or more or carotid occlusion were considered to have carotid disease.

Results: The mean age of the study population was 70±10 years, and 66.5% were men. The mean ankle brachial index was 0.58±0.14. Of 319 symptomatic PAD pts 277 (87%) had hypertension, 242 (76%) had dyslipidemia, 172 (54%) had diabetes mellitus, 138 (43%) had carotid disease, 134 (42%) had critical limb ischemia, 91 (28%) had CAD, 21% had anemia, and 173 (54%) were smokers. Median systolic blood pressure was 140 mmHg (interquartile range, IQR 130-155), and diastolic 80 mmHg (IQR 80-90). The mean eGFR was 63±18.3 mL/min/1.73m2. Compared to pts without carotid disease, pts with carotid disease were older (72±8 vs. 68±10, $p<0.01$). There was no difference in cardiovascular risk factors (hypertension, dyslipidemia, smoking, and diabetes mellitus) or CAD between pts with carotid disease and without carotid disease.

Discussion: Peripheral artery disease represents a major atherosclerotic burden. Pts with symptomatic PAD have a greater probability of having polyvascular disease, indicating an extensive and severe degree of systemic atherosclerosis. As PAD shares the same risk factors as other cardiovascular diseases, the coexistence of carotid disease and PAD is quite common.

Acknowledgments:

MeSH/Keywords: Peripheral artery disease, Carotid disease, Cardiovascular risk factors

Poster code: R-B-9-113

ARTERIAL STIFFNESS AS A MARKER OF VASCULAR AGING IN IBD PATIENTS – A PILOT STUDY

PhD candidate: Radovan Prijić

PhD Thesis: Arterial stiffness as a marker of vascular aging in IBD patients

Mentor/s: Associate Professor Silvija Čuković-Čavka

Affiliation: Division of Gastroenterology and Hepatology, University Hospital Centre Zagreb, Croatia

Introduction: Recent research has demonstrated higher risk of developing atherosclerosis in inflammatory bowel disease (IBD). Noninvasive measurement of aortic pulse wave velocity (PWV) has predictive value for future fatal cardiovascular events and total cardiovascular mortality. The aim of our study was to assess the level of arterial stiffness by measuring aortic PWV as an index of arterial stiffness in IBD patients.

Materials and methods: We conducted a pilot observational study on a cohort of IBD patients during the period from December 2015 to October 2016. We measured PWV with validated, noninvasive oscillometric device in all patients enrolled in this study. Select laboratory data were collected, as well as patients' medical history relevant for the analysis.

Results: A total of 40 patients diagnosed with IBD with median age of 31 years (range: 18-66 yr.) were enrolled: 24 Crohn's disease (CD) patients – median age 28.5 yr. (range: 18-58 yr., 62% males), and 16 ulcerative colitis (UC) patients – median age 41.5 yr. (range: 18-66 yr., 62% males). Mean±SEM PWV value was 8.11±0.35 m/s, 7.83±0.28 m/s, and 8.52±0.78 m/s for IBD, CD and UC groups, respectively.
Significant correlation was found between PWV values and patients' age ($p < 0.0001$, $r=0.71$) and cholesterol levels ($p=0.0206$, $r=0.3649$).

Discussion: CD phenotype and patients' age have a significant impact on arterial stiffness in IBD. There seems to be no difference in aortic PWV between CD and UC patients. However, next step in our research is to measure PWV in a larger cohort of patients.

Acknowledgments:

MeSH/Keywords: inflammatory bowel disease, atherosclerosis, arterial stiffness

Poster code: R-B-9-80

ENDOSCOPIC CHARACTERISATION OF COLORECTAL POLYPS USING NARROW BAND IMAGING (NBI)

PhD candidate: Ivana Tirić

PhD Thesis: Endoscopic characterisation of colorectal polyps using narrow band imaging

Mentor/s: Professor Nadan Rustemović, MD, PhD

Affiliation: Department of Gastroenterology and Hepatology, University Hospital Centre Zagreb. Department of Internal medicine, General Hospital

Introduction: Narrow Band Imaging (NBI) is advanced endoscopic technology allowing for real time characterisation of polyp histology by means of mucosal and capillary patterns at a single push of a button (virtual biopsy). Recently developed NBI International Colorectal Endoscopic (NICE) classification is characterized by simplicity and standardization and is validated. The implementation of this classification in routine clinical practice could potentially lead to changes in present practice towards "resect and discard" strategy for diminutive polyps (=5mm) and "do not resect" strategy for diminutive hyperplastic polyps in the distal colon.

Materials and methods: Since September 2016 until now 47 consecutive patients referred to our clinic for colonoscopy were included in this prospective study. Patients with poor bowel preparation (BBPS = 6) were excluded. Additional exclusion criteria were: findings suggesting inflammatory bowel disease and colorectal cancer, previous colon surgery, optical diagnosis not made, polyp not retrieved and failed colonoscopy. Olympus HD Evis Exera III colonoscopes were used for procedures. Ten colonoscopist with different levels of experience determinated polyp histology by NBI with magnification using NICE classification. The location, shape and size according to Paris classification were recorded for all polyps. Photo documentation of all polyps was performed. All analysed polyps were resected and submitted for pathologic assessment.

Results: A total of 74 polyps were detected in 47 patients. There were 50 (68%) diminutive polyps (=5mm) and 24 (32%) small polyps (6-10mm). Final histology showed that 41 (55%) were adenomas, 28 (38%) were hyperplastic polyps, 3 (4%) were SSP and 2 (3%) were normal mucosa. Colonoscopists correctly diagnosed 52 polyps (70.2%) lesions.

Discussion: These preliminary results suggest that at our clinic colonoscopists do not yet achieve the PIVI threshold developed by ASGE necessary for safe implementation of NBI in routine clinical practice. We plan to refresh training on NICE classiffication hoping for improved results in second part of study.

Acknowledgments: I would like to thank my mentor prof. Rustemović, all the colonoscopists participating in this study and all the patients.

MeSH/Keywords: virtual biopsy, NBI, characterisation of colorectal polyps, NICE classification

Poster code: R-B-9-116

NON-INVASIVE METHOD FOR PARAMETER IDENTIFICATION IN THE FIVE ELEMENT WINDKESSEL MODEL OF PULMONARY CIRCULATION

PhD candidate: Fabijan Lulić

PhD Thesis: Non-invasive method for parameter identification in a mathematical model of pulmonary circulation

Mentor/s: Associate Professor Marko Jakopović*, MD PhD, Professor Zdravko Virag**, PhD

Affiliation: University of Zagreb, *Clinic for Pulmonary Diseases, **Faculty of Mechanical Engineering and Naval Arhitecture

Introduction: The input impedance (Z_{in}) of the pulmonary circulation is the ratio of pulmonary artery (PA) pressure (p_{PA}) and flow (Q_{PA}) in the frequency domain, and it comprehensively characterizes the pulmonary vascular bed (afterload to the right ventricle (RV)). Unfortunately, for the determination of Z_{in} invasive measurements of p_{PA} and Q_{PA} during whole cardiac cycle are needed, and it is a great challenge to find a way of its non-invasive determination.

Materials and methods: Within the proposed research the mathematical model of pulmonary circulation will be used to describe the main features of pulmonary vascular bed (input impedance and the effects of reflection waves of pressure and flow). The model parameters will be identified by using non-invasive method based on echo-Doppler recordings of pulmonary and triscuspid regurgitant flow. Right ventricle pressure is obtained from the tricupid regurgitant flow by using ideal Bernoulli equation, while the pulmonary artrery pressure is defined by the Bernoulli equation containing the inertial and frictional term. The average wedge pressure is estimated based on mitral inflow echo pattern.

Results: The proposed method was applied to a subject with moderate pulmonary hypertension to obtain pulmonary artery proximal and distal compliances, arterial wall viscosity, arterial flow inertance and pulmonary vascular resistance. The sensitivity analysis with respect to the inertial length in the Bernoulli equation, cardiac output and average wedge pressure (that should be estimated) was provided.

Discussion: The proposed method is capable to accurately identify PA model parameters and obtained pulmonary vascular resistance is in good agreement with the results obtained by Swan-Ganz catheterization. The values of PA model parameters are highly sensitive to the accuracy of measured cardiac output, and moderately to the choice of inertial length. It seems that the use of average wedge pressure instead of a time varying one has no crucial impact on the identified values of PA parameters.

Acknowledgments:

MeSH/Keywords: Pulmonary circulation, input impedance, parameter identification, non-invasive method

Poster code: R-B-9-133

ULTRASOUND EVALUATION OF THE ANKLE JOINTS AND TENDONS IN SYSTEMIC LUPUS ERYTHEMATOSUS

PhD candidate: Ljiljana Smiljanić Tomičević

PhD Thesis: Ultrasound evaluation of the ankle joints and tendons in systemic lupus erythematosus

Mentor/s: Miroslav Mayer, MD, PhD

Affiliation: Division of Clinical Immunologyand Rheumatology, Department of Internal Medicine, University Hospital Centre Zagreb, Zagreb, Croatia

Introduction: Musculoskeletal high-resolution ultrasound (MSUS) already proved to be a useful diagnostic tool for the evaluation of pathological changes of the joints and tendons in the majority of inflammatory rheumatic diseases. To date a few studies evaluated joints and tendons in patients with SLE using MSUS, and there are no studies that evaluate frequency of involvement of ankle joints in adult patients with SLE. Contradictory data exist on the correlation between the disease activity in SLE and MSUS findings. The aim of this study was to assess the frequency of ankle joints and tendons involvement in patients with SLE using MSUS and correlate the findings with physical exam and disease activity scores.

Materials and methods: Sixty consecutive SLE patients from our Clinic were enrolled in the study and underwent clinical evaluation, laboratory tests and bilateral high-resolution US of the ankle joints and tendons and hand, wrist and foot joints. Joint effusion, synovial hypertrophy, tenosynovitis, enthesopathy and local pathological vascularization [power Doppler (PD)] were evaluated according to both a dichotomous score and a semi-quantitative (0-3) grading system. In addition, a global US score was calculated by summing the values given to each elementary lesion for every single joint and every joint group. US findings were correlated with physical examination, serological parameters and disease activity indexes (SLEDAI-2K Systemic Lupus Erythematosus Disease Activity Index) and ECLAM (European Consensus Lupus Activity Measurement). Data will be presented using frequency tables and descriptive measures. Student t- test or Mann-Whitney test will be used to compare non-parametric variables and the chi-square and Fisher's exact test will be used to evaluate categorical variables. The findings will be expressed as the mean (S.D). Values of $P < 0.05$ were considered to be statistically significant.

Results: The study is currently in the phase of data collection and preliminary results processing. Preliminary results suggest that there is high prevalence of inflammatory ankle joint abnormalities in SLE using US, however, the number of patient is insufficient for proper statistical analysis.

Discussion: To the best of our knowledge, this is the first study aimed at analysing inflammatory changes in the ankle joints and tendons in SLE patients. The preliminary results show dissociation between clinical and US imaging findings, suggestive of high prevalence of subclinical synovitis.

Acknowledgments:

MeSH/Keywords: systemic lupus erythematosus, ultrasound, ankle,

Poster code: R-B-9-137

SERUM PHOSPHORUS AS A RISK FACTOR FOR CARDIOVASCULAR MORBIDITY IN PATIENTS WITH DIABETES MELLITUS TYPE 2

PhD candidate: Dajana Katičić, MD

PhD Thesis: Serum phosphorus as a risk factor for cardiovascular morbidity in patients with diabetes mellitus type 2

Mentor/s: Assistant professor Draško Pavlović, MD, PhD, Professor Lea Smirčić-Duvnjak

Affiliation: University Hospital Centre Sestre milosrdnice, Zagreb, Croatia

Introduction: Inorganic phosphorus plays an important role in numerous physiological functions. Influence of serum phosphorus level in patients with type 2 diabetes on cardiovascular morbidity will be the subject of this study.

Materials and methods: It is a cross-sectional study on a sample of 280 patients at University Hospital Centre Sestre milosrdnice. Group of 140 patients, male and female, 18 years and older with type 2 diabetes, regardless of duration of disease, on herapy with oral hypogycemic agents and/or insulin who are hospitalized for cardiovascular events. The control group will consist of 140 patients with type 2 diabetes, regardless of duration of disease on therapy with oral hypogycemic agents and/or insulin, without cardiovascular events. In both group there will be determined fasting serum phosphorus level. There will be observed correlation between serum phosphorus and the risk of developing cardiovascular complications. A medical history and physical examination of both group will be done and there will be determined wether there is a correlation between serum phosphorus level and traditional risk factors for cardiovascular disese (age, gender, hypertension, hyperlipidemia, smoking, BMI Framnigham Heart Score). Glomerula filtration rate will be assesed by MDRD formula. Diabetes mellitus will be defined as glucose plasma level =7.0 mmol/L, glucose plasma level random =12.2 mmol/L in two seperate measurements, or the use of hypoglycaemic agents (oral agnets and/or insulin). Hypertension will be defined as blood pressure =140/90 mmHg or taking anthypertensive therapy. Cardiovascular event will be defined as fatal or non-fatal heart attack, angina pectoris (stable or unstable), cardioac arrhythmias, ischemic cardiomyopathy, heart failure, peripheral vascular disease. The level of statistical significance is $P< 0.05$. For analysis will be used Statistica software version 12.0

Results: Preliminary results on a semple of fifty patients, 25 in control group and 25 in the experimental group, male and female, same age and duration of diabetes mellitus type 2 did not show any significant correlation between serum phosphorus level and traditional risk factors for cardiovascular disese (age, gender, hypertension, hyperlipidemia, smoking, BMI).

Discussion: These preliminary results are from a small number of patients so it is necessary to wait for the final results of the research on the estimated number of patients.

Acknowledgments:

MeSH/Keywords: phosphorus, hyperphosphatemia, cardiovascular morbidity, diabetes mellitus type 2

Poster code: R-B-9-144

THE IMPACT OF DEPRESSIVE SYMPTOMS ON THE OPERATING RISK PATIENTS UNDERGOING CORONARY ARTERY BYPASS GRAFT SURGERY

PhD candidate: Stjepan Ivanković, MD

PhD Thesis: Patients who have a higher prevalence of depressive symptoms that undergo coronary artery bypass grafting, have a higher operating risk

Mentor/s: prof. dr. sc. Vedran Ćorić, MD, prof. dr. sc. Alma Mihaljević Peleš, MD

Affiliation: University Hospital Centre Zagreb, Department of Cardiac Surgery

Introduction: Depression as a disorder is present in one out of five patients with ischemic heart disease and one in three patients with congestive heart failure, yet most cases of depression in surgical patients are not recognized. In patients undergoing myocardial revascularization that number is probably higher. The impact of depressive symptoms on operational risk in patients who require myocardial revascularization was studied in several studies, but the results are still deficient and inconsistent. Some studies have linked inflammatory component, depressive symptoms and the length of post-operative hospital stay. Besides the length of stay in the hospital, was examined and quality of life after surgery and post-operative complications. The main objections were that the studies were conducted on a small number of patients and included only one sex. For all these reasons we have decided to conduct a study in order to determine whether and how much the symptoms of depression affect the operating risk in patients undergoing coronary artery bypass grafting. Our intention is to point out this problem, in order to find out whether depressive symptoms could enter as a risk factor in the calculation of the EuroSCORE II.

Materials and methods: The prospective study includes patients (200), who were hospitalized at UHC Zagreb, Department of Cardiac Surgery. Consecutive sample of patients undergoing cabg procedure,after signing an informed consent participated in the study. Severity of depressive symptoms was determined by standardized questionnaire: Primary Care Evaluation of Mental Disorders PRIME MD PHQ 9 test and the Beck Depression Inventory (BDI 2) test. During the operation we measured: time spent with the use of extracorporeal circulation(CBP),length of myocardial ischemia(aortic clamping length).After operation we measured: the length of postoperative mechanical ventilation (LPMV), the levels of inflammatory marker CRP(the first, second and third postop. day), and we determined postoperative mortality (death within 30 days after surgery).As predictors will be taken EuroSCORE 2,the weight of depressive symptoms (PHQ 9 test, BDI test) the characteristics of cardiac surgery duration of CPB, myocardial ischemia and as dependent variable LPMV, days of hospital stay and CRP. Scientific research was approved by the ethics committee of the hospital, PRIM MD PHQ 9 test and calculator EuroSCORE are available online and free of charge, and BDI tests were purchased.

Results: Statistical analysis of data at the time of writing the abstract is not yet complete. But initial results collected in the database show. Mortality was 1.5%, and the patients who died had an average EuroSCORE 2.81%, while the average value of the BDI test was 9, and PRIME MD 3. 25 patients have mildly or moderately expressed depressive symptoms (BDI average 19.3), their average EuroSCORE is 3.54. 2 patients have expressed serious depressive symptoms their average EuroSCORE was 2.2. In 95% of patients CRP grew to the third postoperative day, and only in 5% of patients grew 4th postoperative day. Other data have yet to be analyzed to determine the statistical significance of the same.

Discussion: Hypothesis that patients undergoing coronary artery bypass grafting, with higher incidence of depressive symptoms, have higher preoperative risk from the initial data seems to be true. In 3 patients who died did not express depressive symptoms, but their EuroSCORE was higher than average EuroSCORE. Of course, it is necessary to finish statistical analysis to find out whether there is a correlation with other factors such as characteristics of cardiac surgery, duration of mechanical ventilation after surgery, days of hospital stay and CRP. Interestingly, patients CRP increases in most cases up to the third postoperative day, and in 95% of cases began to fall on the fourth day. This is very useful information because it might determine when to use antibiotics in the absence of clinical signs of inflammation.

MeSH/Keywords: Depressive symptoms, CABG, Operating risk

Poster code: R-B-10-84

LOW IODINE DIET IN PATIENTS WITH DIFFERENTIATED THYROID CANCER

PhD candidate: Margareta Dobrenić, MD

PhD Thesis: Usefulness of low iodine diet performed prior to radioiodine administration and scintigraphy in patients with differentiated thyroid cancer

Mentor/s: Professor Dražen Huić, MD, PhD

Affiliation: University Hospital Center Zagreb, Department of Nuclear Medicine and Radiation Protection and University of Zagreb School of Medicine

Introduction: Low iodine diet, or restricted intake of iodine-rich food is recommended to all patients with differentiated thyroid cancer prior to I-131 administration. The majority of guidelines recommend low iodine diet prior to I-131 application, but its duration and effectiveness, as well as target urinary iodine concentration are not well established. The aim of this study is to evaluate the influence of low iodine diet on total body iodine content and on radioiodine avidity of tumor cells in patients with differentiated thyroid cancer and biochemically persistent disease.

Materials and methods: A total of 77 patients with differentiated thyroid cancer, thyroglobulin > 2 ng/mL, and negative I-131 whole body scan underwent low iodine diet. Each patient underwent a two-week low iodine diet, with the aim to achieve moderate iodine deficiency. Those who accomplished only mild iodine deficiency after a two-week low iodine diet received a recommendation to follow the diet for a further week (three-week diet) before the next I-131 administration. To evaluate the effectiveness of low iodine diet, iodine concentration in morning urine samples was measured in each patient, a day before starting the diet and on the 15th (21st) day after starting it. For the impact assessment of low iodine diet on radioiodine tissue avidity, whole body radioiodine scans before and after low iodine diet were visually compared.

Results: Following self-managed low iodine diet, all patients were able to significantly reduce their total body iodine content by 50% (range 18-64%). A total of 68 patients (88%) accomplished mild iodine deficiency and 9 patients (12%) achieved the targeted moderate iodine deficiency state. There was no significant difference in the reduction of total body iodine content between groups that underwent two and three-week iodine diets. Furthermore, there was no significant impact of reduced total body iodine content on radioiodine avidity of tumor cells in patients who underwent low iodine diet.

Discussion: Low iodine diet is an effective way to reduce total body iodine content in patients with differentiated thyroid cancer prior to I-131 administration. However, in patients with biochemically persistent malignant disease, neither mild nor moderate iodine deficiency had an effect on radioiodine avidity of tumor cells.

Acknowledgments: This study was supported by International Atomic Energy Agency (IAEA) as a part of the project entitled The sentinel lymph node in breast, melanoma, head and neck and pelvis cancer, project number 15413/IAEA

MeSH/Keywords: low iodine diet, differentiated thyroid cancer, radioiodine

Poster code: R-B-17-75

F-18-CHOLINE PET/CT IN PROSTATE CANCER PATIENTS

PhD candidate: Anja Tea Golubić, MD

PhD Thesis: The value of positron emission tomography/computed tomography with fluor-18-choline in follow-up of prostate cancer patients with biochemical relapse

Mentor/s: Professor Dražen Huić, MD, Ph.D.

Affiliation: Department of Nuclear Medicine and Radiation Protection, University Hospital Centre Zagreb

Introduction: Prostate cancer is the second most common malignancy in men and is one of the most common causes of cancer related death. As the treatment of any type of cancer is dependant on establishing early diagnosis and the correct stage, functional imaging methods such as F-18-choline PET/CT, have an increasing role in disease detection. The aim of this study is to explore the value of F-18-choline PET/CT in patients with prostate cancer, with emphasis on the change of patient management.

Materials and methods: Hundred and fifteen prostate cancer patients with biochemical relapse were scanned with F-18-choline PET/CT in the Department of Nuclear Medicine at the University Hospital Centre Zagreb from November 2012 to April 2016. Mean age of our patient population was 70 years (range 52 to 83 years). Mean PSA value was 10,8 ng/ml (range 0,2 to 229 ng/ml) and mean follow-up period was 23 months (range 9 to 44 months). Mean administered activity was 202 MBq of F-18 choline (2-3 MBq/kg, IASOCholine, IASON GmBH).

Results: Eighty-five patients (74%) had a positive finding on the F-18 choline PET/CT. Thirty-three patients (29%) had bone metastases with a mean SUVmax value of 13 (range 3,3-30). Lymph node metastases were found in 50 patients (43%), with a mean SUVmax value of 7,9 (range 1,9-20,1). Other localizations of increased tracer uptake were reported in 10 patients, with F-18-choline uptake in seminal vesicles in 8 patients and lung metastases in 2 patients. A second primary carcinoma was found in several patients – in one chronic lymphocytic leukemia, one mesothelioma, one hepatocellular carcinoma and in two patients a thyroid papillary carcinoma. In 80% of our patients, a change of management was reported in the follow-up period. This includes the start of androgen deprivation therapy, salvage radiotherapy and palliative bone radiotherapy, the beginning of radiotherapy and orchidectomy.

Discussion: Preliminary results of this study show that F-18-choline PET/CT has an important role in the assessment of the volume of metabolically active disease in prostate cancer patients with biochemical relapse. It has an impact on therapeutic strategy, providing physicians with clinical certainty to decide between palliative treatment to treatment with curative intent. As other functional imaging modalities, F-18-choline PET/CT provides more information necessary for the appropriate and individual patient management.

Acknowledgments:

MeSH/Keywords: F-18-choline, PET/CT, prostate cancer, biochemical relapse

Poster code: R-B-17-112

LOCAL CORTICOSTEROID THERAPY IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS ASSOCIATED UVEITIS ON SYSTEMIC IMMUNOMODULATORY THERAPY

PhD candidate: Marija Barišić Kutija

PhD Thesis: Local corticosteroid therapy in patients with juvenile idiopathic arthritis associated uveitis on systemic immunomodulatory therapy

Mentor/s: Nenad Vukojević, MD, PhD

Affiliation: Zagreb University Hospital Centre, Department of Ophthalmology, Zagreb, Croatia

Introduction: Juvenile idiopathic arthritis (JIA) is one of the most common chronic diseases of children. The most common extra-articular manifestation of the disease is anterior uveitis (JIA uveitis), which develops in 12-20% JIA patients. JIA uveitis has insidious, chronic, refractive course, corticosteroid dependent and with severe complications. Therefore, the treatment of JIA uveitis in pediatric ophthalmology is a great challenge. The first line of treatment are local and systemic corticosteroids. Topical corticosteroids (TCS) increase the risk of cataract and glaucoma, and the risk of complications is dose-dependent. JIA uveitis in about 80% cases requires therapy for several years, therefore, the aim in the long-term treatment for chronic, recurrent or refractive cases is to minimize the number of TCS drops and introduce immunomodulatory therapy (IMT). IMT includes methotrexate (MTX) and biological therapy. Despite all the listed therapeutical options, more than 65% patients on IMT need TCS to control the inflammation in the anterior chamber, but so far dynamic of IMT effectiveness on local disease activity and consequently the need for TCS during the whole course of the disease is not known.

Materials and methods: Hypothesis: Systemic biologic IMT in JIA uveitis patients reduces the need for TCS more effective than systemic IMT without biologic therapy. Aims: GENERAL AIM: To evaluate effectiveness of IMT on intraocular inflammation control in JIA uveitis patients. SPECIFIC AIMS: 1. To determine whether the need for TCS in JIA uveitis patients is lower in patients on systemic biologic therapy, than on systemic MTX therapy, whithout biologic therapy. 2. To determine the best corrected visual acuity in JIA uveitis patients on the beginning and the end of the disease course. PhD student (Marija Barišić Kutija, MD) will collect all the data from the clinical medical records from all follow-up examinations in patients, who satisfy criteria from 2011 untill 35 patients (about 80 eyes) are included. Study design: longitudinal observation study. Statistical analysis: repeated measures ANOVA analysis.

Results: The data from 28 patients from 4 to 16 years old were collected, 23 female and 5 male. All of the patients were receiving immunomodulatory therapy, 7 only MTX, and 21 MTX antiTNF.

Discussion: Our study leads to new insights into the dynamics of disease activity changes, depending on the applied combination of systemic and local therapy.

Acknowledgments: Thanks to my mentor, prof. Nenad Vukojević, on the infinitely patience and support.

MeSH/Keywords: Juvenile Idiopathic Arthritis, Anterior Uveitis, Immunomodulatory Therapy, Biologic Therapy, Methotrexate

Poster code: R-B-18-26

EFFECTS OF BEVACIZUMAB AND TRIAMCINOLONE ACETONIDE ON MACULAR EDEMA AFTER THE EXTRACTION OF SILICONE OIL IN PATIENTS WITH DIABETES TYPE 2

PhD candidate: Lucija Vojvodić

PhD Thesis: Effects of bevacizumab and triamcinolone acetonide on macular edema after the extraction of silicone oil in patients with diabetes type 2

Mentor/s: Assoc. Prof. Tomislav Jukić, MD, PhD

Affiliation: Department of Ophthalmology, University hospital Centre Zagreb, Croatia. General hospital Dubrovnik

Introduction: Diabetic macular edema (DME) is the most common cause of vision loss in people with diabetic retinopathy. In the recent past, the standard treatment for DME was focal laser photocoagulation. The current standard of care for DME is intravitreal applications of anti-VEGF (bevacizumab) and anti-inflammatory (triamcinolone acetonide) drugs. Pars plana vitrectomy with instillation of silicone oil takes place in resistant cases of diabetic retinopathy. Since diabetes is a public health problem, this research will try to clarify the role of intravitreal application of bevacizumab and triamcinolone acetonide after removal of silicone oil.

Materials and methods: Patients diagnosed type 2 diabetes that underwent vitrectomy with silicone oil (SO) tamponade were informed about research with a written consent to participate. Patients who had previous cataract/glaucoma surgery or previous intravitreal applications weren´t included. Ophthalmic examinations were performed before SO removal and at months 1, 3, 6 postoperatively including best corrected visual acuity (BCVA) and OCT retinal thickness measurements. Standardised instrument "EQ-5S-5L" was used to measure health outcomes 3 and 6 months after IV application. SO is removed via standardised pars plana approach. Statistical significance $p<0.05$. Confidence intervals: 95% level. Two-tailed tests of significance was used.

Results: Previous studies have confirmed there were major improvements in BCVA and central macular thickness, but these studies included intravitreal applications before SO removal and patients with diabetic retinopathy were mostly excluded from studies. Central retinal thickness, BCVA and quality of life were documented but statistic analysis of the data has not yet been performed.

Discussion: Findings about development of macular edema after PPV and SO removal may contribute to better macular edema pathogenesis understanding. Combined pharmacosurgical treatment may supplement current treatment standards for diabetic retinopathy, changing our treatment protocol which lead to better control of DM eye complications.

Acknowledgments: I would like to thank my mentor Asoc. Prof. T. Jukić for his expertise, guidance and support.

MeSH/Keywords: diabetic macular edema, bevacizumab, triamcinolone acetonide, silicone oil

Poster code: R-B-18-115

VIDEOREHABILITATION IN RECOVERY AFTER TOTAL KNEE ARTHROPLASTY

PhD candidate: Jakov Prenc, MD

PhD Thesis: Videorehabilitation in recovery after total knee arthroplasty

Mentor/s: Professor Esmat Elabjer, MD, PhD, Assistant Professor Damir Hudetz, MD, PhD

Affiliation: Clinic of Traumatology, University Hospital Center "Sestre Milosrdnice"

Introduction: Knee joint replacement, ie. knee arthroplasty is divided into partial, total and revision. Total knee endoprosthesis replaces all three damaged compartment knee joints and can be cemented or cementless. Indication for total knee arthroplasty (TKA) is knee arthritis. The three most common types of knee arthritis are: osteoarthritis or gonarthrosis, rheumatoid arthritis and posttraumatic arthritis. The first line of treatment is conservative therapy such as physical therapy and medications. If the knee stops responding positively to conservative therapy, it is followed by TKA. The main goal of rehabilitation after TKA is establishing a painless functional range of motion of the knee. Over 90% of patients have a successful outcome after TKA.

Materials and methods: The subjects are selected according to inclusion and exclusion criteria. In study we included 60 patients into 2 groups of 30 patients each (experimental and control). All are treated according to the same protocol (preoperative preparation, surgery and post-operative rehabilitation). The information about to which group patient is located will be familiar only to the operator and the patient. The study will thus be a randomized, prospective and blind. Methods: Diagnostics: Gonarthrosis. Procedures: Surgery is being done in the pale track. Rehabilitation: On-line help through the recorded video.

Results: Results will be displayed through evaluation clinical-functional studies: KOOS, Lysholm, IKDC, Tegner, SF-36, the range of motion of the joint, the extent of the thigh muscles.

Discussion: With the help of this method, the patient could be given important messages on a daily basis in the early stages of recovery and the ability to perform kinesiotherapy through the video instructions which could shorten the postoperative period of rehabilitation and improve clinical outcomes.

Acknowledgments: Thanks to both my mentors for their guidance and patience.

MeSH/Keywords: knee, videorehabilitation, total knee arthroplasty, gonarthrosis, rehabilitation

Poster code: R-B-20-140

WIDEBAND TYMPANOMETRY IN OTOSCLEROTIC EARS

PhD candidate: Iva Kelava, MD

PhD Thesis: Diagnostic value of wideband tympanometry in patients with otosclerosis

Mentor/s: Vladimir Bedeković, MD, PhD

Affiliation: University Hospital Center

Introduction: The diagnosis of otosclerosis is confirmed definitively during the surgery but clinical and audiological evaluation is crucial for preoperative diagnosis and indication for surgery. Diagnosis is traditionally made based on combination of characteristic clinical findings and standard audiological evaluation which include pure-tone audiometry, standard single frequency tympanogram and cohleostapedial reflex. Among these tests only pure-tone audiometry provides quantification of hearing loss, upon which the indication for surgery is based. Pure-tone audiometry has its limitation since it depends on patient subjective responses. Wideband tympanometry is a new technique for assessing middle ear transfer function in which probe tone of 226 Hz is replaced by a probe "click" that covers the 226 to 8000 Hz range. Some studies have already shown that wideband tympanometry may be useful in diagnosis of otosclerosis. However, all these studies were done with insufficient number of patients and patterns of wideband tympanogram typical for otosclerosis have not been defined yet. Also it is not clear whether wideband tympanometry can be used to objectively assess the level of hearing impairment.

Materials and methods: Longitudinal prospective study will be conducted. We will include 50 patients with otosclerosis diagnosed according to standard diagnostic procedure with diagnose confirmed during surgery. Control group will contain 50 individuals with normal hearing and normal standard tympanogram. Wideband tympanometry will be performed for all subjects. Wideband tympanogram in otosclerotic ears will be compared to the normal wideband tympanogram. We will also explore the correlation between the degree of wideband tympanogram change and the level of postoperative hearing improvement.

Results: 15 patients with otosclerosis and 15 normal hearing adults were included. Results of WBT were averaged across 1/3 of octave bands for data analysis. Mann Whitney U Test was used to compare absorbances between normal and otosclerotic ears for each frequencies band.Statistically significant lower absorbance was found in otosclerotic group in frequencies lower than 1000 Hz.

Discussion: Our results suggests that wideband tympanometry could be useful in diagnosis of otosclerosis.The main difference was found in lower frequencies that could be explaind with the fact that hearing loss due to otosclerosis mostly affect lower frequencies.

Acknowledgments:

MeSH/Keywords: wideband tympanometry, otosclerosis, cohleostapedial reflex

Poster code: R-B-21-33

HEDGEHOG SIGNALING PATHWAY IN ORAL SQUAMOUS CELL CARCINOMA

PhD candidate: Sandra Baranović, MD

PhD Thesis: Prognostic value of Hedgehog signaling pathway molecules in squamous cell carcinoma of the oral cavity

Mentor/s: Assist. Prof. Ivica Lukšić, MD, MSc, PhD/Prof. Spomenka Manojlović, MD, MSc, PhD

Affiliation: University of Zagreb School of Medicine, Department of Maxillofacial Surgery/Department of Pathology, University Hospital Dubrava/ Department of Head and Neck Surgery, University Hospital for Tumors.

Introduction: Hedgehog (HH) signaling pathway is related with progression of tumor growth,recurrence and resistance to different treatment modalities.Multimodal treatment is often aplied,but patients with oral squamous cell carcinoma (SCC) have poor outcome because of early presence of neck lymph node metastases. Sonic Hedgehog(SHH) activates signalization. Transmembranic proteins Patched (Ptch) and Smoothened (Smo) are the next cascade,activation of transcription factors Gli1 starts. Transcription of genes, involved in cell cycle and migration, angiogenesis and apoptosis, then begins.

Materials and methods: Tissue specimens were obtained from 120 patients with histologically confirmed oral SCC (T1-T3N0M0), treated primary surgically between 1st of January 2006 and 31st of December 2010. Expression of HH molecules will be semiquntified using immunohistochemistry.Starting point is the date of surgical resection and the outcome is time until death-OS (overall survival), recurrence-DFS (disease free survival) or 5 years after surgery. A generalized linear model will be used for correlation between protein expression and clinical/pathological factors,and Cox's regression model for correlation of protein expression and OS/DFS.

Results: Median age of patients was 74 years. Male to female ratio was 4:1.The tumor was most often localized in the tongue, in 41 cases.Other locations were as follows: 32 floor of the mouth, 16 mandibular gingiva,10 maxillary gingiva,14 retromolar trigone,3 buccal mucosa,4 hard palate.Thirty nine patients had T1 stage tumors, 46 had T2, 35 had T3 stage. Neck dissection was performed in 44 patients and intraoral excision was performed in 76 patients. Fifty four (45%) patients had recurrence. Forty eight patients died due to disease. The 5-year overall survival rate was 42.2%.

Discussion: The aim of this study is to investigate the correlation between expression of Shh, Ptch, Smo and Gli1 and recurrence of the oral squamous carcinoma and overall survival. Results of previous studies are not unanimously and our advantage is a large sample size. We will correlate the expression of HH signaling molecules with clinical (age, gender, tumor location, TNM stage) and pathological factors (pTNM, grade, tumor size, perineural and perivascular infiltration, extracapsular lymph node metastases). Recurrence rate of 45% is 8-13% higher and OS of 42.2% is 9-12% lower than in some reports, therefore the prognostic value of Hedgehog signaling pathway molecules is of great interest in treatment modality planning.

Acknowledgments:

MeSH/Keywords: oral squamous cell carcinoma, Hedgehog pathway, recurrence, immunohistochemistry, prognostic factor

Poster code: R-B-21-89

POLYSOMNOGRAPHIC EVALUATION OF SLEEP ARCHITECTURE AND RESPIRATION IN CHILDREN WITH INTRACTABLE EPILEPTIC ENCEPHALOPATHIES

PhD candidate: Nataša Nenadić Baranašić MD (1)

PhD Thesis: The structure and organization of sleep and assessment of sleep-disordered breathing in children with epileptic encephalopathies using overnight video-polysomnography

Mentor/s: Prof. Nina Barišić, MD PhD (2), Romana Gjergja Juraški, MD PhD (1)

Affiliation: (1) Unit for Sleep Disorders in Children, Srebrnjak Children's Hospital, Zagreb, Croatia, (2) Division of Pediatric Neurology, Department of Pediatrics, University Hospital Centre Zagreb

Introduction: Polysomnographic studies on sleep architecture and sleep-disordered breathing in children with epileptic encephalopathies (EE) are deficient and results inconsistant. The aim of this study was to determine clinical characteristics of children with intractable EE and to assess their sleep architecture and respiration in sleep using the overnight video-polysomnography (V-PSG).

Materials and methods: Since 2015 we have recorded overnight V-PSG for 13 children with intractable EE (9 boys, aged 7.25±3.48 years, BMI 16.83±2.62 kg/m2) and 13 healthy sex-, age- and BMI- matched children in the control group.

Results: Genetic etiology was proved in 5/13 (38%) children with EE, 2/13 (15%) children had structural cause of disease and others have unconfirmed but presumable genetic origin. Motor deficiency was found in 10/13 (77%) children with EE. Intelectual disability, learning or behaviour problems were present in all of the children with EE. Results on sleep architecture showed that children with EE, relative to controls, had increased total wake time 61.00 min IQR (36.50-73.25) vs. 30.00 min IQR (21.50-42.50) (p=0.04), reduced sleep efficiency 80.73% IQR (77.42-85.86) vs. 88.15% IQR (82.87-89.29) (p=0.02), lower number 10.00 IQR (9.00-13.75) vs. 21.00 IQR (12.75-22.75) (p=0.02), but longer duration of arousals 3.81 min IQR (2.51-7.36) vs. 1.81 min IQR (0.83-2.47) (p=0.005), higher percentage of N1 sleep 2.10% IQR (1.20-3.05) vs. 1.20% IQR (0.65-1.90) (p=0.03) and lower percentage of REM sleep 13.80% IQR (9.70-14.90) vs. 17.60% IQR (14.15-19.10) (p=0.007). We haven't found significant difference in the number of respiratory events between the two groups 0.00 IQR (0.00-1.75) vs. 1.00 (1.00-1.00) (p=0.19). Only one child (7.7%) with adenotonsillar hypertrophy had increased pediatric AHI 1.34 due to central apneas.

Discussion: Children with intractable EE should be referred for sleep evaluation that can reveal potentially treatable comorbidities, unrecognised seizures and/or interictal night discharges. Improving the knowledge on sleep phenotypes in children with intractable EE could lead to better management and sleep quality in those children.

Acknowledgments:

MeSH/Keywords: overnight video-polysomnography, children, sleep architecture, sleep disordered breathing, epileptic encephalopathy

Poster code: R-B-24-15

CARDIOPULMONARY EXERCISE PERFORMANCE IS REDUCED IN CONGENITAL DIAPHRAGMATIC HERNIA SURVIVORS

PhD candidate: Katarina Bojanić, MD

PhD Thesis: Congenital diaphragmatic hernia: the impact of short-term outcome predictors on long-term health and quality of life

Mentor/s: Ruža Grizelj, MD, PhD

Affiliation: University of Zagreb School of Medicine, University Hospital Centre Zagreb, Depatment of Pediatrics, University Hospital Merkur, Zagreb, Croatia.

Introduction: Congenital diaphragmatic hernia (CDH) is a rare anomaly with high perinatal mortality attributed to lung hypoplasia and pulmonary hypertension. In some CDH survivors, respiratory problems gradually dissipate with lung maturation, whereas in others pulmonary morbidity persists. CDH survivors may have pulmonary morbidity that can decrease cardiopulmonary exercise. We aimed to examine whether cardiopulmonary exercise testing (CPET) rezults differ in CDH survivors versus healthy age and sex matched controls and whether CPET results among CDH survivors differ according to self-reported daily activity.

Materials and methods: In one medical center in Croatia, University Hospital Centre Zagreb, CDH survivors, patients with surgically corrected CDH who were alive at age 5 years, were invited to participate in spirometry and CPET. Values were compared with those of controls matched 2:1 by age and sex for each CDH survivor aged 7 years or older.

Results: Among 27 CDH survivors aged 5–20 years, 13 (48%) had continued symptoms or spirometric evidence of pulmonary disease. Compared with controls (n =44), survivors (n = 22) had lower peak oxygen consumption (V_{O2} mean ŠSDĆ, 35.7 Š6.9Ć vs. 45.3 Š8.2Ć ml/kg per min, P< 0.001). At peak exercise, V_{O2} /heart rate (P< 0.001), tidal volume (P = 0.005), and minute ventilation (P< 0.001) were lower in survivors, but the maximal respiratory rate was not different (P = 0.72). Among survivors, mean (SD) V_{O2} peak (ml/kg per min) differed by self-reported activity level: athletic, 40.3 (5.0), normal 35.8 (6.5), and sedentary 32.1 (6.8) (by ANOVA, P = 0.10 across three groups and P = 0.04 athletic vs. sedentary).

Discussion: More than half of CDH survivors continue to have chronic pulmonary disease. CDH survivors had lower aerobic exercise capacity than controls. Self-reporting information on daily activities may identify CDH patients with low V_{O2max} who may benefit from physical training.

Acknowledgments: I would like to thank my mentor Ruža Grizelj for her unconditional support. I would also like to thank Danijel Dilber for performing the CPET testing as well as acknowledge all patients who agreed to participate in this project.

MeSH/Keywords: cardiopulmonary exercise performance, cardiopulmonary exercise testing, congenital diaphragmatic hernia, pulmonary function, maximal exercise capacity

Poster code: R-B-24-48

THE EFFECT OF ADJUVANT PROBIOTIC THERAPY ON DISEASE ACTIVITY INDICES AND FECAL CALPROTECTIN IN JUVENILE SPONDYLOARTHRITIS

PhD candidate: Mandica Vidović

PhD Thesis: The influence of inflammasome on development of juvenile spondyloarthritis

Mentor/s: Professor Miroslav Harjaček, MD, PhD

Affiliation: Clinical Hospital Center Sestre Milosrdnice, Department of Pediatrics, Division of Clinical Immunology and Rheumatology, Zagreb

Introduction: Juvenile idiopathic arthritis (JIA) with its subtype juvenile spondiloarthritis (jSpA) is a heterogenic, multifactorial and multigenetic disease affecting children under 16 years of age. Calprotectin is a neutrophil derived protein that belongs to the S100 family. It can be quantified in feces (fCAL) and is established as a marker of gut inflammation which is present in inflammatory bowel disease IBD but also in jSpA. There are some evidences supporting the role of the VSL-3 probiotic in decreasing fCAL in patients with IBD. This study monitored the effect of probiotic on both fCAL and disease activity in patients with jSpA.

Materials and methods: Sixteen patients diagnosed with ERA, according to the ILAR criteria, were treated with VSL-3, in addition to standard therapy (NSAIDs and DMARDs). All patients were negative for gastrointestinal (GI) symptoms. Four patients received biologics- two adalimumab and two infliximab respectively. In addition to general clinical and laboratory data, patients completed the BASFI and BASDAI questioners and fCAL was measured by the Calprest ELISA method (Eurospital Spa, Italy). After VSL-3 was introduced, two follow up visits were scheduled- the first after one month and the second after three months. BASFI and BASDAI were reevaluated on both visits and fCAL value was obtained on second visit.

Results: The baseline mean fCAL level was 52,3 mg/kg (normal < 50 mg/kg). Fifteen patients have completed all scheduled visits to date, and twelve had markedly decreased fCAL levels (mean value 15,6 mg/kg). The BASFI index was decreased in twelve patients and the BASDAI index in ten patients. At the follow-up visit, none of the patients were found to have developed GI symptoms or other signs and symptoms suggestive of IBD.

Discussion: There is a strong need for biomarkers as help in diagnosing and monitoring rheumatic diseases in children. S100 protein family with its member fCAL are a possible choice both in IBD and jSpA. This study also showed potential effect of adjuvant probiotic therapy in patients with jspA and elevated fCAL. Preliminary data suggest that the use of VSL-3 can decrease fCAL levels, and together with standard therapy improve clinical symptoms and decrease disease activity in patients with jSpA. A larger patient cohort is needed to confirm VSL-3 efficacy in jSpA.

Acknowledgments:

MeSH/Keywords: juvenile spondyloarthritis, fecal calprotectin, probiotic, disease activity

Poster code: R-B-24-98

ACCELERATION OF WEIGHT GAIN IS FOLLOWED BY EMERGENCE OF RETINOPATHY OF PREMATURITY PHASE 2

PhD candidate: Ana Čolić, MD

PhD thesis proposal: Acceleration of weight gain is followed by emergence of retinopathy of prematurity phase 2

Mentor/s: Professor Nenad Vukojević, MD, PhD

Affiliation/s: Division of neonatology, University hospital for obstetrics and gynecology, University hospital center Zagreb

Introduction: Premature birth delays normal vascularization that continues with abnormal blood vessels growth in retinopathy of prematurity (ROP) phase 2. ROP mostly affects very premature infants and can be mild or progress to blindness. Ophthalmic examinations are performed to detect severe cases requiring treatment. Stress and pain of necessary procedures, including ophthalmic examinations, have immediate and long-term consequences so efforts to reduce them are of essence. In very premature infants weight loss is unavoidable, followed by slow, then accelerated catch-up growth. Weight gain trend correlates with levels of insulin-like growth factor 1 which is necessary for normal retinal vascularization and neovascularization in ROP. Aim is to prove that weight gain acceleration is followed by emergence of ROP phase 2.

Materials and methods: In this retrospective study at least 42 premature infants of gestational age ≤28 weeks and birth weight ≤1250 grams will be included. Findings of ophthalmic examinations and their relations to weight gain acceleration are analyzed. ROP is graded according to the Early Treatment of Retinopathy of Prematurity (ETROP) study. Acceleration of weight gain is calculated. Possible confounding factors for the onset of ROP phase 2, cessation of mechanical ventilation support and ambiental oxygen therapy, are analyzed as well.

Results: Data were collected for 19 infants. In all infants at the time of weight gain acceleration and one week later immature avascularized retina was detected. Two weeks after weight gain acceleration ROP phase 2 emerged in most infants and by the time of three weeks after acceleration it was detected in all cases. There were no cases of severe ROP requiring treatment in the analyzed period. There were no cessation of respiratory support a week prior to the onset of ROP phase 2 in analyzed cases.

Discussion: Data obtained so far indicate that weight gain acceleration is followed by emergence of ROP phase 2. Such association contributes to knowledge on pathogenesis of ROP with applicability in clinical practice. Weight gain acceleration might serve as an indicator to monitor the disease, with possible reduction of required ophthalmic examinations and exposure of newborn to stress, with timely diagnosis.

Acknowledgments: I would like to thank my mentor, family and friends for their support.

MeSH/Keywords: premature infants, newborn, retinopathy of prematurity, growth, insulin-like growth factor I

Poster code: R-B-24-145

MULTIPARAMETRIC MR ANALYSIS OF FEMALE BREAST CARCINOMA AS RESPONSE TO NEOADJUVANT THERAPY

PhD candidate: Marko Petrovečki

PhD Thesis: Multiparametric MR analysis of female breast carcinoma as response to neoadjuvant therapy

Mentor/s: doc. dr. sc. Maja Prutki

Affiliation: University of Zagreb School of Medicine

Introduction: Breast cancer is the most common malignancy in Croatian women and a leading cause of death due to malignant disease. In locally advanced and inoperable breast cancers neoadjuvant therapy is given according to guidelines of Croatian Society of Oncology from 2010. Breast MRI made early after first or second cycle may detect breast cancers that are resistant to applied therapy and will not respond to it after all the cycles.

Materials and methods: Patients with inoperable breast cancer that have no prior history of breast malignancy and are planed for neoadjuvant therapy are included in study. All patients have had a core needle biopsy and a baseline breast MRI prior to treatment. A second breast MRI is done between second and third cycle of therapy. Surgical treatment after therapy with final PHD used as golden standard for residual disease - residual cancer burden (RCB). Patients with RCB score 0, I and II are considered as responders and patients with RCB score III are considered as nonresponders to therapy. Data from both breast MRI exams will be recorded, including lesion morphology and kinetics with diffusion coefficients and when possible a MR spectroscopy. Univariate logistic regression was used to associate binary responder status with other variables in the study.

Results: Median patient age was 58 years with range from 29 to 73 years. From eighteen analyzed tumors ten were categorized as luminal B, three were Her2 positive luminal B, two were basal like and two Her2 positive and one was luminal A. Median tumor size before therapy was 29 mm (range 21-105) and median size after second cycle was 25 mm (range 12-93). Göttingen score median before therapy was 6 (range 5-8) and after second cycle the median was 5 (3-8). Apparent diffusion coefficient (ADC) median was 609 mm^2/s (range 482-827) before therapy and the median after second cycle was 782 mm^2/s (range 531-1214). Using univariate logistic regression none of variables showed significant prediction model, tumor size (p=0,064), Göttingen score (p=0,372) and ADC value (p=0,840).

Discussion: Preliminary results show that there might be correlation between tumor size reduction and response to neoadjuvant therapy. It does not seem possible to determine whether a patient will or will not have a response to neoadjuvant therapy by observing change in Göttingen score or ADC value. When data from more patients is collected and analyzed more appropriate results might be given.

Acknowledgments:

MeSH/Keywords: breast cancer, neoadjuvant therapy, breast MRI

Poster code: R-B-25-10

CORRELATION OF FMD AND WALKING DISTANCE IN PERIPHERAL ARTERIAL DISEASE

PhD candidate: Stipe Radoš,MD

PhD Thesis: Association of sonographically estimated endothelial function with claudications and ankle brachial indices in PAD

Mentor/s: Professor Boris Brkljačić, MD, PhD

Affiliation: University of Zagreb School of Medicine, University Hospital Dubrava

Introduction: Peripheral artery disease(PAD)has prevalence of 25% in general population over 70 y,and with accelerated aging of population number of patient with PAD is increasing rapidly. An advanced stage of disease is characterized by more or less impaired ambulation, rest pain, non-healing wounds and limb loss, increased mortality and morbidity. As for the CAD(coronary artery disease),diabetes is one of main risk factors for development of PAD. Physicians who deal with PAD can relay on clinical exam but it is important to have noninvasive diagnostic tool for early detection of the disease, like ABI test.Based on previous research we can conclude that ABI test have limited value in some PAD patients and especially in those with diabetes. In development of PAD main role plays atherosclerosis and endothelial dysfunction. The assessment of endothelial function can be performed indirectly by measuring FMD on ultrasound machine.The lower value of FMD should indicate endothelial dysfunction.

Materials and methods: The research will be conducted prospectively at two test groups with 60 patients within each group. The key difference to form group will be presence of diabetes. Including criteria for both groups will be symptomatic PAD, and in diabetic group that the duration of the disease is more than five years. Exclusion criteria for both groups will be renal insufficiency with a GFR less than 45 ml/min calculated by MDRD formula, acute infectious disease, great surgery within 30 days.The control group will include 20 patients without symptoms of PAD and without diabetes.In all patients will be performed measuring of flow mediated dilatation(FMD)in the upper arm artery using standard protocol, and ABI. For FMD measuring will be used ultrasound device Aloka Alpha 10. The FMD measuring will be carried out according to the guidelines of the American College of Cardiology.

Results: Data collection are still in progress. Just few patients were examined in each group, insufficient for adequate statistical analysis.

Discussion: Patients who complain on their walking disability can have significant PAD but also many other conditions that may reflect on walking distance.AB indices are standard in practice but in some diabetic patients may produce false negative finding. And this particular group of patients can have benefit from FMD measuring.It is known from earlier research that FMD is in correlation with PAD severity and Rutherford category. I want to show relationship of FMD and ABI in diabetic sub group.

Acknowledgments:

MeSH/Keywords: PAD, CAD, diabetes, FMD, ABI

Poster code: R-B-25-12

DIFFUSION WEIGHTED IMAGING (DWI) OF SMALL LYMPH NODES IN PATIENTS WITH HEAD AND NECK SQUAMOUS CELL CARCINOMA (HNSCC)

PhD candidate: Andrijana Jović

PhD Thesis: Prognostic value of diffusion weighted magnetic resonance imaging in lymph node staging of head and neck carcinoma

Mentor/s: Assist. Prof. David Ozretić, Assoc. Prof. Mirko Ivkić

Affiliation: UHC Sisters of Mercy, Zagreb, Croatia

Introduction: The lymph node status is one of the most important prognostic factor in (HNSCC). Aim of our study is to establish whether subcentimeter metastatic and metastatic-free lymph nodes of the neck from the HNSCC can be distinguished with diffusion weighted imaging (DWI).

Materials and methods: From January 2016, 15 patients with biopsy proven HNSCC have been admitted at UHC Sisters of mercy for operative treatment. MRI exam was performed on MRI Espree 1.5 T, Siemens. DWI of the head and neck was performed using Spin echo prepared EPI sequence.3 b values were used. ADC value of neck lymph nodes was automatically calculated by positing ROI on lymph node. All patients underwent neck dissection. Lymph nodes intraoperatively were mapped and sent to pathology. Measurement results from the MRI images were compared with the results of the pathological examination

Results: We analysed 26 lymph nodes. The mean minimum axial diameter was greater in metastatic lymph nodes (mean ± SD, 8.4 ± 1.3 mm, range, 5.2–10.7 mm) than in benign lymph nodes (mean ± SD, 5.5 ± 2.4 mm, range, 5.2–10.0 mm) ($p = 0.018$). For malignant lymph nodes mean ADC value was 0.903 × 10-3 mm2/sec (range: 0.400–0.996mm2/sec). In benign lymph nodes, ADC maps showed an average value of 1.650 × 10-3 mm2/sec (range: 0.945–2.370 ×10-3 mm2/sec).

Discussion: DWI has potential to be included in preoperative imaging in the evaluation of head and neck malignancies. ADC is non invasive method for differentiate benign from malignant lymph nodes.

Acknowledgments:

MeSH/Keywords: Diffusion magnetic resonance imaging, Head and neck cancer

Poster code: R-B-25-54

BIOMARKERS FOR VIOLENCE IN YOUTHS WITH CONDUCT DISTURBANCES

PhD candidate: Josip Podobnik, MD, psychiatrist, certified forensic psychiatrist, subspecialist in child and adolescent psychiatry

PhD Thesis: Association between gene polymorphism of the catechol-O-methyl-transpherase and gene polymorphism of the monoaminooxidase type B and platelet monoamine oxidase activity with aggressive behaviour and psychopathological characteristics in adolescents in cor

Mentor/s: Assistant Professor Nela Pivac, DVM, PhD, senior scientist, Division of Molecular Medicine, Laboratory of Molecular Neuropsychiatry, Rudjer Boskovic Institute

Affiliation: Psychiatric Hospital for Children and Youth Zagreb, Kukuljeviceva 11, 10000 Zagreb, Croatia

Introduction: Neurobiology of violence and aggression can be associated with deranged dopaminergic neurotransmission and certain components of dopaminergic system (e.g. activity of monoaminooxidase type B /MAO-B/ and catechol-O-methyltransferase /COMT/). The aim of this study was to determine the relationship between genotype/allele frequencies of COMT Val108/158Met (rs4680 polymorphism), A/G 13. intron variants of MAO-B gene (rs1799836 polymorphism, activity of platelets MAO-B and the severity of conduct disorder according to DSM-IV criteria, the presence or absence of major criminal offence (homicide attempts, larger damage) and antisocial behaviour features.

Materials and methods: 182 male adolescents were included and devided into categories depending on the form of conduct disorder (DSM-IV) – partial, mild to moderate and severe forms, on the presence of court imposed measures, on the homicide attempt, on the larger damage infliction, on the presence of aggitation (agitated v. non-agitated) and on the severity of symptoms assessed by psychometric scales.

Results: Participants with conduct disorder, as well as those with the severe form of conduct disorder scored more points on scales measuring depression, psychopathy, aggressive behaviour and overt aggression in relation to participants with partial diagnosis and those with mild form of conduct disorder. Statistically significant correlation was found for polymorphism rs4680 (Val108/158Met) COMT and the score of just one subscale from the domain of aggression OAS-M (Overt Aggression Scale-Modified) – ´aggression against objects´. Participants without court imposed measure, with symptoms of agitation, pronounced verbal aggression and inner irritability had significantly higher platelet MAO-B activity than participants without these symptoms, signs or with court measure. There were no significant differences in platelet MAO-B activity between allele A or G rs1799836 polymorphism MAO-B gene carriers.

Discussion: These findings could offer easily available biomarkers for aggression and associated psychopatological characteristics of youths with conduct disturbances with the purpose of improving treatment strategies. Polymorphism rs1799836 MAO-B gene does not play a significant role in the development of conduct disorder and the intensity of deliquent behaviour. This research confirmed the assumption that certain biological/cognitive parametres are associated in significant degree with psychosocial phenotypes that have aggressive behaviour in common.

Acknowledgments:

MeSH/Keywords: conduct disorder, violence, monoaminooxidase type B, catechol-O-methyltransferase

Poster code: R-B-29-40

SCHIZOPHRENIA SYMPTOMS AND THALAMO-CORTICAL CONNECTIVITY CHANGES

PhD candidate: Aleksandar Savić, MD

PhD Thesis: Identifying charcteristics of thalamo-cortical changes and their relationship with symptoms in schizophrenia

Mentor/s: Neven Henigsberg, MD, PhD, Alan Anticevic, PhD

Affiliation: University of Zagreb School of Medicine, University Psychiatric Hospital Vrapce, Yale University

Introduction: Schizophrenia (SCZ) is a debilitating disorder with clinical presentation that can vary significantly, but includes changes in thinking, cognition, perception, and emotions, resulting in different behavioral disturbances. Current leading conceptualizations recognize SCZ as a heterogeneous syndrome rather than a single disease with one underlying etiological factor. Newer neuroimaging methods have recently been used to explain processes and changes underlying the disorder and its symptoms. Previous functional magnetic resonance imaging research has showed changes in thalamo-cortical connectivity and scaling of those changes with overall disease severity.

Materials and methods: Participants: 500 individuals diagnosed with SCZ and 500 demographically matched healthy controls will be included and the gathered data pooled under already approved protocols of Yale University. Clinical assessment: Clinician administered Positive and Negative Syndrome Scale (PANSS) is used to assess severity of the illness, positive and negative symptoms, and general psychopathology. Neuroimaging Data Acquisition and Analyses: Magnetic resonance imaging data will be acquired using 3T scanners. Subcortical anatomically-defined thalamic nuclei will be used as seeds in seed-based functional connectivity analysis and relationship between the thalamus and all voxels in the brain will be evaluated by computing a seed-based thalamus correlation map. Correlation will be calculated psychopathology scores of participants, and signal in regions showing changes in connectivity with thalamic seed.

Results: Given the phase of the research and the complexity of pooling and preprocessing neuroimaging data, no preliminary results are available at this stage.

Discussion: Analysis of a large schizophrenia patients sample allows for a more detailed characterization of thalamocortical changes in SCZ, and of their possible connection to specific symptoms, opening the road to identifying underlying biology of different symptoms and the disorder itself. Identification of possible biological markers of the disorder or specific symptoms allows the possibility of developing diagnostic instruments, as well as creating more focused research of therapeutic interventions aimed at specific symptoms.

Acknowledgments:

MeSH/Keywords: schizophrenia, thalamus, magnetic resonance imaging

Poster code: R-B-29-49

THE CONNECTION OF PSYCHOLOGICAL FACTORS WITH THE OUTCOME OF EXTRACORPOREAL CONCEPTION – IN VITRO FERTILIZATION (IVF) IN PRIMARY INFERTILE WOMEN

PhD candidate: Andrea Ražić Pavičić

PhD Thesis: The connection of psychological factors with the outcome of extracorporeal conception – in vitro fertilization (IVF) in primary infertile women

Mentor/s: Professor Rudolf Gregurek, MD, Phd

Affiliation: Department of Psychological Medicine, University Hospital Centre Zagreb

Introduction: Numerous studies examine psychological constructs in the context of infertility and medical assisted reproductive procedure, but constructs such as attachment, personality dimensions and their role in the way of coping with stress are scarcely studied and the scientific evidence supporting this view is limited.

Materials and methods: The research includes a total of 150 women divided into three groups. Clinical group consists of women diagnosed with primary infertility who are for the first time entering into the IVF treatment. There are two points of investigation:The first (T1), before the start of treatment, and the second (T2), at 6-8 weeks' gestation when the fetal heart rate is detected. Regarding the outcome, the group will be divided to primary infertile women with positive IVF outcome (N=50) and primary infertile women with negative IVF outcome (N=50).Control group (N = 50) consists of women with natural conception. Instruments: General data questionnaire, Experiences in close relationships inventory, Parenthood motivation scale, Cope Inventory, Brief cope

Results: At present, the study is in the phase of data collection. The questionnaires were applied to 8 women diagnosed with primary infertility (without previous pregnancy) who are for the first time entering into the IVF treatment. Their samples are being analysed. Five had positive outcome, three negative. At present no controls has been collected.

Discussion: The collected sample is at present very small and the collection of data for control group has not yet started. Due to these reasons it is not possible to make any more detailed analyses or conclusions until a larger sample is collected.

Acknowledgments: I would like to thank my mentor prof. Gregureg for guidance and support

MeSH/Keywords: attachment, personality, character, temperament, coping, infertility, in vitro fertilization

Poster code: R-B-29-92

COMPARISON OF THE PROBLEMS IN IDENTITY DEVELOPMENT IN ADOLESCENTS WITH NON SUICIDAL SELF INJURY BEHAVIOR AND SUICIDE ATTEMPT

PhD candidate: Nela Ercegović, MD

PhD Thesis: Comparison of the problems in identity development in adolescents with non suicidal self injury behavior and suicide attempt

Mentor/s: Darko Marčinko, Associate Professor, MD, PhD, Vlatka Boričević Maršanić, MD, PhD

Affiliation: Psychiatric Hospital for Children and Adolescents, Zagreb

Introduction: Identity is a fundamental organizing principal which allows one to function autonomously from others. Establishing a stable identity is important developmental task in adolescence. Identity diffusion is a pathological concept which represent pathological identity development, leading to a broad spectrum of maladaptive behaviors, like non-suicidal self injury and suicidal behavior. The aim of this study is to investigate differences in identity development between adolescents with non-suicidal self injury (NSSI) behavior and suicide attempts (SA).

Materials and methods: It is planned to examine 150 adolescent psychiatric inpatients of both gender, aged 12 to 18. Inclusion criteria are presence of NNSI or SA in the past six months. According to these criteria participants are assigned to two groups: adolescents with non suicidal self injury behavior and with suicidal attempt. Differences between groups are analyzed by the test set including: Assessment of Identity Development in Adolescence (AIDA), Youth Self-Report for ages 11-18 (YSR,11-18), Childhood Trauma Questionnaire (CTQ), Family Adaptability and Cohesion Evaluating Scale (FACES-III), Deliberate Self Harm Inventory (DSHI), and sociodemographic questionnaire.

Results: The research is still in progress, and currently is in the phase of data collecting. Up to now we completed the data for 50 adolescents, 28 (56%) with NNSI, and 22 (44%) with SA. Data collected from study participants are still not sufficient for statistical analysis, but for now indicate that the impairment of identity development is present in adolescents with non-suicidal self injury behavior and suicidal attempt.

Discussion: We believe that results of this research will show differences in identity development between adolescents with NNSI and SA, and that impairments of identity development make independent contributions to NNSI and SA even after controlling for psychopathology and experience of childhood abuse. For more detailed analysis and conclusion a larger number of patients is required. We hope that results of this study will help to unravel the factors that hinder the development of identity in adolescence, and their influence in predicting and distinguishing NSSI and SA, which may help to improve assessment of adolescents with self harming behavior.

Acknowledgments:

MeSH/Keywords: Identity, Adolescence, Non suicidal self injury, Suicidal attempt

Poster code: R-B-29-94

BRAIN DERIVED NEUROTROPHIC FACTOR CONCENTRATION AND DIFFERENCES IN DEPRESSION RATING SCALES SCORES BETWEEN FIRST AND RECURRENT DEPRESSIVE EPISODES PRIOR TO ANTIDEPRESSANT TREATMENT

PhD candidate: Anja Maravić, MD

PhD Thesis: Effects of vortioxetine and escitalopram on plasma brain derived neurotrophic factor level and platelet monoamine oxidase B activity in subjects with depressive disorder

Mentor/s: Assistant professor Marina Šagud, MD, PhD, Associate Professor Nela Pivac, PhD, senior scientist

Affiliation: University of Zagreb School of Medicine, University Hospital Centre Zagreb, University Psychiatric Hospital Vrapče, Ruđer Bošković Institute, Zagreb

Introduction: While lower peripheral brain derived neurotrophic factor (BDNF) concentration is found in depression, it is usually normalized with antidepressant treatment in majority of studies. Effects of two antidepressants, vortioxetine and escitalopram, on plasma BDNF concentration, platelet serotonin concentration and platelet MAO-B activity haven't been compared so far. The differences in clinical and biochemical parameters between first and recurrent depressive episodes are poorly investigated.

Materials and methods: We will include 120 medication-naive patients with first or recurrent depressive episode randomized to treatment with vortioxetine or escitalopram. Severity of depressive symptoms and cognitive functioning will be evaluated using psychiatric and psychological scales. BDNF will be measured with enzyme linked immunosorbent assay. Platelet serotonin concentration and MAO-B activity will be measured spectrofotofluorimetrically. Biochemical and clinical parameters will be determined at baseline and after 4 weeks of treatment.

Results: Preliminary results of the baseline data are reported for 74 patients enrolled so far. In the entire sample, women had significantly ($p=0.001$) higher severity of symptoms, as measured by the Hamilton Depression Rating Scale (HDRS) and Montgomery–Åsberg Depression Rating Scale (MADRS) scores than men. Significant differences were detected in the HDRS ($p=0.016$) and MADRS ($p=0.005$) total scores between patients with first and recurrent episodes, since subjects with multiple episodes had more severe symptoms. First-episode compared to recurrent episodes patients had marginally higher BDNF concentration ($p=0.056$). Positive correlation was found between the MADRS ($p=0.017$) and HDRS ($p=0.031$) total scores and BDNF concentration in first-episode but not in recurrent episode patients.

Discussion: Those preliminary findings confirm that patients with recurrent depression have more severe clinical presentation compared to first-episode patients. Higher BDNF concentration in first-episode patients did not reach the level of significance, presumably due to the small sample-size. If the difference arises in a larger sample, lower BDNF concentration would agree with the neurodegenerative theory of recurrent depression. Taken together, those data highlight the need for both early intervention and relapse prevention in patients with depressive disorder.

Acknowledgments: The study is supported by the University of Zagreb, Project Code: BM126

MeSH/Keywords: depression, BDNF, depression rating scales

Poster code: R-B-29-111

THE EFFECTIVENESS OF THE PSYCHOTHERAPEUTIC PROGRAM ON THE TREATMENT OUTCOMES OF PATIENTS WITH RHEUMATOID ARTHRITIS

PhD candidate: Aldenita Matić MD

PhD Thesis: The effectiveness of the psychotherapeutic program on the treatment outcomes of patients with rheumatoid arthritis

Mentor/s: Prof. Jadranka Morović Vergles MD, PhD and Assoc Prof. Lana Mužinić MD, PhD

Affiliation: University Hospital Dubrava

Introduction: Rheumatoid Arthritis is a chronic disease that results in pain, reduction of functionality and disability which reduce quality of life for the patient. Patients with RA have often psychiatric comorbidity, most often depression. Psychotherapeutic approach has proven effective as an adjunctive method with improvement of quality of life, coping with stress and accepting a disease as a result.

Materials and methods: Patients with RA will be randomized into two groups. Psychotherapeutic approach will be applied in the first group (30 patients), and the second group (30 patients) will be a control. Both groups will receive the same rheumatologic treatment. Psychotherapeutic treatment will last 12 weeks and comprise education, relaxation techniques and dynamic group psychotherapy.

Results: The research is in the eary stage, there aren't preliminary results available.

Discussion: The aim of this study is reduction of depressive and anxiety symptoms, education about rheumatoid arthritis and improvement in quality of life, and functional status.

Acknowledgments:

MeSH/Keywords: Rheumatoid arthritis, Psychotherapeutic programe

Poster code: R-B-29-136

DIFFERENCES OF BLINK REFLEX IN CLINICAL DEFINITIVE MULTIPLE SCLEROSIS AND CLINICAL ISOLATED SYNDROME

PhD candidate: Lidija Dežmalj Grbelja

PhD Thesis: Differences of blink reflex in clinical definitive multiple sclerosis and clinical isolated syndrome

Mentor/s: Vida Demarin

Affiliation: Department of Neurology, University Hospital Centre Sestre milosrdnice

Introduction: BR is very sensitive and useful diagnostic tool in assesment of brainstem function.We aimed to determine differences in electrophysiological characteristics of blink reflex (BR) in clinical definitive multiple sclerosis (CDMS) and clinical isolated syndrome (CIS).

Materials and methods: The study included 20 patients, diagnosed as CDMS, 20 with CIS, and 15 health controls. Median age was 41 years in the group of CDMS patients, 36 in CIS group and 37 in control group. Both sex were included. We stimulated opthalmic branch of trigeminal nerve and registered response on orbicular oculi muscle bilaterally. We recordered latencies of early (R1), late component ipsilaterally (R2) and contralaterally (R2′) and occurrence of irritative component (R3). R1 latency >13 ms, R2 >41 ms and R2′ >44 ms considered abnormal.

Results: In CDMS group median value of R1 component was 15,6 ms, R2 39,2 ms, R2′ 37,4 ms. R3 component was recorded in 3 patients. In the group of CIS patents median value of R1 was 15,2 ms, R2 37,6 ms and R2′ 35,2 ms. In the control group median value of R1 was 12,4 ms, R2 34,6 ms, R2′ 32,4 ms. R3 component was not recorded in CIS and control group.

Discussion: This study found out that latencies of early component of BR are prolonged not only in CDMS but in CIS, as the first clinical manifestation of disease. Slowing of R1 component as a result of disfunction of afferent part of reflex arc is although not very specific but highly sensitive finding. BR could be a predictive paraclinical criteria for diagnosis of CDMS.

Acknowledgments: I thank to Mrs Katarina Sruk, for technical assistance in my study.

MeSH/Keywords: blink reflex, multiple sclerosis, clinical isolated syndrome

Poster code: R-B-30-70

TONGUE SOMATOSENSORY EVOKED POTENTIALS REFLECT MIDBRAIN INVOLVEMENT IN PATIENTS WITH CLINICALLY ISOLATED SYNDROME

PhD candidate: Luka Crnošija, MD

PhD Thesis: The modified evoked potentials score in the follow-up of clinically isolated syndrome

Mentor/s: Mario Habek

Affiliation: University Hospital Centre Zagreb, Department of Neurology

Introduction: To test the hypothesis that tSSEP findings reflect clinical and MRI MS lesions, the aim of this study was to investigate tSSEP changes in patients with clinically isolated syndrome (CIS) in relation to clinical and brainstem MRI findings. The second aim was to investigate whether the interpretation of the tSSEP results in the form of the tSSEP score enables better evaluation of the afferent trigeminal pathway involvement than analysing each tSSEP parameter separately.

Materials and methods: One hundred fifteen consecutive CIS patients were enrolled from August 1, 2014 until March 1, 2016. Facial sensory symptoms and brainstem MRI (1.5 T) lesions were analysed. tSSEP testing was performed for each patient. The tSSEP score was calculated from the raw tSSEP data separately for the left and right side (according to the cut-off values for absent response and prolonged latency of the main component, P1 (0=normal response, 1=prolonged latency, 3=absent response) and the two values were summed.

Results: There was no difference in the absolute values of the tSSEP variables regarding the presence of clinical symptoms. No association was found between tSSEP abnormalities and clinical symptoms (P=0.544). Brainstem lesions (midbrain and pons) were associated with the absent tSSEP responses (P=0.002 and P=0.005, respectively). tSSEP score was significantly higher in patients with brainstem lesions (P=0.01), especially midbrain (P=0.004) and pontine (P=0.008) lesions. Binary logistic regression showed that tSSEP score had a significant effect on the likelihood that patients have midbrain MR lesions, $\chi^2(1)=6.804$, P=0.009, and the model correctly classified 87% of cases.

Discussion: The consistent finding of this study was the association between tSSEP and midbrain lesions on MRI, indicating that tSSEP evaluates proprioception of the face. This study establishes the value of tSSEP in assessing brainstem function in early multiple sclerosis.

Acknowledgments: This study was funded by the Installation Research project HRZZ UIP-11-2013-2622 of the Croatian Science Foundation.

MeSH/Keywords: afferent trigeminal pathway, tongue somatosensory evoked potentials, brainstem, clinically isolated syndrome

Poster code: R-B-30-139

ANALGESIC EFFECT COMPARISON OF PARACETAMOL ADMINISTERED INTERMITTENTLY AND THROUGH PATIENT CONTROLLED ANALGESIA PUMP AFTER LUMBAR DISCECTOMY: A PROSPECTIVE CLINICAL STUDY

PhD candidate: Biljana Kurtović

PhD Thesis: Opioid derivates analgesia and nonopioid analgesia assessment through intermittent application and patient controlled analgesia pump after lumbar discectomy

Mentor/s: Professor Krešimir Rotim, MD, PhD

Affiliation: Department of Neurosurgery, University Hospital Centre Sestre milosrdnice, Zagreb, Croatia

Introduction: Pain after spine surgery comes from the skin, muscle, intervertebral discs and joint capsules, and depends on the vertebrae number involved in surgery and type of surgery. Effective control of postoperative pain have critical importance in early rehabilitation promoting with reduced morbidity. Sharma, Balireddy, et al. state that there are several strategies which are used for pain relief after lumbar discectomy, but there is a lack of sistematic analgesic treatment documentation in that patients population. Aim of this study is to compare postoperative analgesic efficacy of paracetamol administered intermittently and through patient controlled analgesia pump (PCA) after neurosurgical procedure of intervertebral extrusion level L4-L5.

Materials and methods: Research participants were patients who underwent elective lumbar discectomy of intervertebral disc extrusion level L4-L5, established by lumbosacral spine MRI. Group I (intermittent application group) was given the first paracetamol dose of 1500 mg after the neurosurgical procedure finished in the operating room, and 1500 mg every 6 hours through 48 hours. Group P (PCA pump group) was given the first bolus dose of paracetamol 166 mg after the neurosurgical procedure finished in the operating room with lockout time bolus administration of 120 minutes and a basal flow rate of 16.6 ml/h. Pain was assessed at regular intervals for 48 hours through a shortened version of McGill pain questionnaire in the Croatian language.

Results: There were no significant difference in investigated groups regarding sociodemographic variables, exept in terms of physical activity, participants from intermittent group were significantly more active (100.0% vs. 83.3%, $P=0.017$). When pain is monitored as summarised variable for each measurment, PCA group significantly stands up after 36 hours with better perception of pain compared to intermittent group (X2 test, $P<0.05$).

Discussion: Postoperative pain is a clinical condition that should be treated accurately and completely. Adequate pain relief is important facet of spinal surgery patients postoperative care. Our statement is that paracetamol use even through intermitent use or PCA pump can relieve postoperative pain in patients undergo¬ing lumbar discectomy.

Acknowledgments:

MeSH/Keywords: paracetamol, postoperative analgesia, lumbar discectomy

Poster code: R-B-31-107

ANALYSIS OF PROFESSIONAL VALUE SYSTEM AMONG INTENSIVE CARE NURSES IN CROATIA

PhD candidate: Hrvoje Premuž MSN, RN

PhD Thesis: Analysis of professional value system among intensive care nurses in Croatia

Mentor/s: MENTHOR: Doc.dr.sc.Ana Borovečki, Prof.dr.sc. Chris Gastmans

Affiliation: General Hospital, Slavonski Brod, Croatia, Department for anaesthesia, reanimation and intensive care

Introduction: Professional value system (of physicians and nurses) has an immediate impact on all processes of healthcare delivery and their numerous outcomes. Professional values are standards of behavior for performance that provide a framework for appraising beliefs and attitudes that influence behavior. Development of professional values has been a continuous and long process and it is influenced by different factors. Professional value ethics is a new concept in nursing and provides an Quality guidance for nursing clinical practice. However, little is known about how professional values has been defined and studied in nursing science also used in clinical reality.

Materials and methods: Design and data sources: Systematic literature searches from 2010-2017, using the CINAHL, PubMed and Scopus electronic databases to look at previously published peer-reviewed studies. Review method: a modified version of Cooper's five-stage integrative review was used to review and analyze current knowledge.

Results: 21 papers were included in this research. According to our analysis, professional value ethics is an intra -professional approach to clinical care ethics. Professional ethics consist of values, duties, rights and responsibilities, regulated by national legislation and international agreements and detailed in professional codes. Professional ethics is well established in nursing, but is constantly changing due to internal and external factors affecting the profession.

Discussion: Despite the obvious importance of professional value ethics, it has not been studied much in nursing science. Greater knowledge of professional value ethics is needed to understand and support nurses' moral decision-making and to respond to the challenges of current changes in health care and society. Considering the effect of educational, cultural and individual factors in developing nurses' professional values it is recommended to the educational and health providers to consider value-based care in clinical environments for the patients in addition to considering the content of educational programs based on ethical values in the students' curriculum.

Acknowledgments:

MeSH/Keywords: ethics, integrative review, nursing values, nursing, professional values

Poster code: R-B-31-119

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TRANSLATION AND VALIDATION OF THE HARDSHIP (HEADACHE-ATTRIBUTED RESTRICTION, DISABILITY, SOCIAL HANDICAP AND IMPAIRED PARTICIPATION) QUESTIONNAIRE INTO CROATIAN LANGUAGE

PhD candidate: Lukrecija Jakuš

PhD Thesis: Epidemiological characteristics of primary headaches among University of Applied Health Sciences students in Zagreb

Mentor/s: Prof. dr. sc. Darija Mahović Lakušić

Affiliation: University of Applied Health Sciences

Introduction: Primary headache disorders, principally migraine and tension-type headache have public-health importance by virtue of being common, ubiquitous, disabling and treatable. The epidemiology of headache disorders in Croatia is only partly documented. The studies have used variable methodology, which has influenced findings and made comparisons difficult. In addition, data on headache-related disease burden, which implies some level of disability, are insufficient. Lifting the Burden and its collaborators developed both a standardized protocol and a survey instrument: Headache-Attributed Restriction, Disability, Social Handicap and Impaired Participation (HARDSHIP) questionnaire.

Materials and methods: As a prerequisite for a cross-sectional study of the prevalence and burden of primary headache disorders among University of Applied Health Sciences students in Zagreb we undertook translation and adaptation of the HARDSHIP questionnaire, and validation headache screening and diagnose headache type question set. It was translated from English into Croatian, in accordance with the Lifting the Burden translation protocol for hybrid documents. Sensitivity, specificity and positive and negative predictive values were calculated for migraine and tension-type headache to compare questionnaire-derived diagnoses with "gold-standard": diagnoses made by headache experts.

Results: For the validation sub-sample, 143 students with and 47 without headache, according to the diagnose headache type question set based on the criteria of the International Classification of Headache Disorders, 3rd edition beta version, were interviewed and examined by headache expert neurologist. The questionnaire had sensitivities and specificities of 67% and 94% for migraine (j = 0.58) and of 58% and 91% for tension-type headache (j = 0.54). The overall kappa was 0.59 [95% CI: 0.49–0.68].

Discussion: The validation demonstrated sensitivities, specificities, positive and negative predictive values that were acceptably high for migraine and tension-type headache. The overall agreement between questionnaire diagnoses and neurologist diagnoses was 0.59, very close to be a strong agreement. The performance of the questionnaire is good, and its quality is in line with reported validation studies in other languages.

Acknowledgments:

MeSH/Keywords: Epidemiology, primary headache disorder, questionnaire, validity

Poster code: R-C-1-22

PREVALENCE OF HEPATITIS E INFECTION IN CONTINENTAL CROATIA

PhD candidate: Pavle Jeličić, MD, MHM

PhD Thesis: Epidemiological and epizootiological characteristics of hepatitis E infection in continental Croatia

Mentor/s: Assist. Prof. Tatjana Vilibić Čavlek, MD / Assist. Prof. Lorena Jemeršić, DVM

Affiliation: Croatian Institute of Public Health

Introduction: Hepatitis E virus (HEV) causes feco-orally transmitted hepatitis and is responsible for more than 50% acute hepatitis cases in endemic countries. There is growing evidence of HEV emergence and re-emergence with an increasing number of indigenous cases in Europe. The main reservoirs of HEV are pigs, but the virus has been isolated from other animals as well. The most common sources of infection are contaminated drinking water and contaminated, undercooked food. While the prevalence of HEV in some animals (wild and domestic pigs) is well known, in other animals is rather unknown. This study will analyze the prevalence of HEV infection in different professionally exposed and unexposed population groups as well as different animal species. It will also analyze the risk factors for HEV infection including zoonotic transmission of HEV.

Materials and methods: This study is a cross-sectional study in which the occupational exposure to animals is a risk factor, and the seropositivity to HEV IgM antibodies (evidence of acute/recent infection) and to HEV IgG antibodies (evidence of previous infection) is an outcome. The occupationally exposed population is represented with 65 hunters, 50 forest workers and 45 veterinarians, while general, unexposed, population is represented with 75 adult asymptomatic persons. All participants will fulfill a questionnaire on living habits. In addition, serum samples will be taken from 384 horses and 282 dogs in order to estimate HEV prevalence and to determine the possible association between the source of infection in humans and animals by molecular diagnostics.

Results: From October 2016. to March 2017., a total of 37 serum samples were collected from forest workers, 25 samples from hunters and 116 samples from general population. HEV IgG antibodies were detected in 3 (8.1%) forest workers, one(4%) hunter and 3 (2.6%) adult unexposed participants from continental Croatia.

Discussion: The preliminary results confirmed that the seroprevalence of hepatitis E in Croatia is higher in occupationally exposed persons compared to general population which indicates that the animal contacts pose a risk factor for hepatitis E infection.

Acknowledgments: I would like to thank Nataša Janev Holcer, Ivka Djaković, Maja Vilibić and Vlatka Brumen for technical assistance.

MeSH/Keywords: Hepatitis E, prevalence, Croatia, risk factors

Poster code: R-C-1-37

EPIDEMIOLOGY OF THE HUMAN TICK-BORNE ENCEPHALITIS IN CROATIA IN PERIOD 1991 -2015

PhD candidate: Goranka Petrović, MD, Epidemiologist and Environmental Health Specialist

PhD Thesis: Significance of the tick-borne encephalitis seroprevalence in sentinel animals in the determination of natural foci and risk assessment of human infection

Mentor/s: 1. Assistant Professor Tatjana Vilibić-Čavlek, MD, PhD; 2. Associate Professor Ljubo Barbić, DVM, PhD

Affiliation: 1. University of Zagreb School of Medicine, Croatian Institute of Public Health, 2. University of Zagreb Faculty of Veterinary Medicine

Introduction: Tick-borne encephalitis (TBE) is the most important tick-borne neurotropic flavivirus infection occurring in natural foci in Europe and Asia, now being reported in previously non-endemic areas. As part of the research on possible use of sentinel animals in the determination of natural foci and risk assessment of human infection in Croatia, one of the specific aims is to investigate epidemiology of the human tick-borne encephalitis in Croatia during the period 1991 – 2015.

Materials and methods: Analysis of the incidence of the reported clinical cases of tick-borne encephalitis in people in Croatia based on the data collected through the mandatory notification system of communicable diseases in the period from 1991 to 2015 in the Infectious Disease Epidemiology Department at the Croatian Institute for Public Health.

Results: During the period 1991 – 2015 a total of 908 human cases of tick-borne encephalitis were reported in Croatia, of whom 612 (67.4%) in males and 296 (32.6%) in females. The number of cases varied from 11 (2007) to 87 (1994) cases, with an average of 36 cases annually. Significant difference in the geographical distribution of notified TBE cases was found, with 76% of cases being from four counties in north-western region of Croatia: Koprivnica - Križevci (260 cases, 29%), Bjelovar - Bilogora (194 cases, 21%), Krapina- Zagorje (130 cases, 14%) and Međimurje (110 cases, 12%) which is consistent with the previously documented natural foci of TBE in Croatia.

Discussion: In Croatia there are well documented natural foci of TBE in the north-western region, between the rivers Sava and Drava, and in the north-eastern region, Slavonija, as well as one natural focus in the area of Gorski kotar. Contrary to the TBE epidemiological situation in a number of the European countries, the results of our data analysis of the reported TBE cases do not show an increasing trend of TBE in Croatia during last 25-year period. Such finding can be explained by possible underestimation of the TBE infection in humans, especially considering the fact that mild and nonspecific clinical presentations remain unrecognized and undiagnosed. Moreover, since early 2000 vaccination against TBE of risk groups due to their professional exposure is highly recommended. Therefore, in order to determine natural foci more closely and further assess potential risk of human TBE infection, additional research of TBE seroprevalence in human population and sentinel animals is highly needed.

Acknowledgments: I would like to express my gratitude to Ms. Mara Glamočanin for her precious help in data gathering.

MeSH/Keywords: tick-borne encephalitis incidence, natural foci, Croatia, seroprevalence, sentinel animals

Poster code: R-C-1-55

PATTERNS IN NON-RESPONSING IN NATIONAL BREAST CANCER SCREENING PROGRAM IN POZEGA-SLAVONIA COUNTY

PhD candidate: Jasmina Kovačević, MD, Public Health specialist, MPH

PhD Thesis: Patterns in non-responsing in National Breast Cancer Screening Program in Pozega-Slavonia county

Mentor/s: Vesna Jureša, MD, PhD, Associate Professor

Affiliation: Public Health Institute of Pozega-Slavonia County

Introduction: Breast cancer is one of the leading Public Health worldwide. Accordingly, in Croatia, the National Breast Cancer Screening Program was implemented with a scope of early breast cancer detection so that it can be treated more effectively. The reasons for the mammography non-attendance are not sufficiently explored. Research objective is to determine patterns in non-responsing in the National Breast Cancer Screening Program in Pozega-slavonia County at third round of invitations. The research results should indicate presence of women's behaviour patterns and provide answers about the relations between education level, knowledge, socioeconomic factors and the mammography non-attendance.

Materials and methods: Data were collected by interviewing women 50-69 years of age included in the National Breast Cancer Screening Program in Pozega-Slavonia County who did not respond to mammography invitation. Interview was conducted by structured questionnaire which contained general information on women and their overall mammography attitude. Data were analyzed using Microsoft Office Excel.

Results: This research included 1.208 women who did not respond to mammography invitation in the National Breast Cancer Screening Program in City of Pozega, City of Pleternica and Brestovac Municipality. We visited 1.048 households/women (86,7%). In 48,1% households women were unavailable for interview, the reasons being: wrong address (48,0%), subject was not at home (30,5%), passed away (5,4%) or other (16,1%). Survey was carried out with 267 (22,1%) out of 1.208 women who did not respond to mammography invitation (25,5% out of all visited women), and 277 (26,4%) women declined interview.

Discussion: We covered 86,7% of all women who did not respond to mammography invitation by visit and collected all valuable information for all of them, although 48,1% of women were not available and 28,3% declined interview. We will have to take in account differences between women available or unavailable for interview, and those who declined survey for further analysis for all available data.

Acknowledgments: I would like to thank my mentor Professor Vesna Jureša for the knowledge she is always willing to share.

MeSH/Keywords: National Breast Cancer Screening Program, non-response, rural, urban

Poster code: R-C-2-41

IODINE INTAKE AND THYROID FUNCTION IN LACTATING WOMEN AND BREASTFED INFANTS AT THE REGION OF ZAGREB

PhD candidate: Marina Prpić

PhD Thesis: Iodine intake and thyroid function in lactating women and breastfed infants at the region of Zagreb

Mentor/s: Associate Professor Maja Franceschi, MD, PhD

Affiliation: University of Zagreb School of medicine, University Hospital Centre

Introduction: Lactating women and infants are one of the most vulnerable groups that may be affected by the long lasting consequences of iodine deficiency. As already well known, iodine is essential for the synthesis of thyroid hormones and lack of iodine during pregnancy and early childhood can lead to thyroid dysfunction and further cause permanent damage in fetal brain development thus impair mental functions.

Materials and methods: We enrolled in our investigation two population groups:1. lactating womenParticipants will be divided into two population groups:1.lactating women (between 18-44 years)
2. infants (between 2-26 months.Inclusion criteria:1.for lactating women generally healthy women, without chronicaldrug therapy and thyroid diseases. Methods: 1.a) Questionnaire for lactating women- to assess the inclusion criteria: history of use of iodized salt in home, consumption of processed foods containing iodized salt and foods rich in native iodine and consumption of iodine containing dietary supplements and specialized food products. b) Questionnaire for infants-birth data and infant feeding practice.2. Collection biological samples(blood, urine, breast milk)in order to assess laboratory levels of thyroid hormones, TSH, thyroglobulin as well as iodine concentration in urine (UIC) and breast milk (BMIC).

Results: Median UIC in lactating women is 35 (3, 127) μg/L and median BMIC is 124 (92, 188) μg/kg.Median UIC in infants is 239 (158, 385) μg/L.Median maternal and infant TSH is 0.3 (0.2, 0.5) and 0.5 (0.4, 0.8) mU/L,while median maternal and infant tT4 is 66 (47, 86) and 91 (66, 108) nmol/L.

Discussion: The present data obtained in lactating women with adequate iodine status suggest an increased fractional iodine excretion into breast milk at lower iodine intakes. Mothers with lower estimated overall iodine intake excreted a higher proportion in breast milk and a lower proportion in urine.Median BMIC appeared to be a more accurate indicator for iodine status in lactating women than median UIC. We therefore recommend that the median BMIC be included in studies assessing iodine status in lactating women. Recent data from an infant metabolic balance study suggest a BMIC of at least 92 μg/L (breast milk volume of 0.78 L/day)is able to meet the daily iodine requirement in infants. Median BMIC greater than 100 μg/L may indicate adequate iodine status in lactating women. More studies assessing infant and maternal UICs and BMIC, as well as their thyroid function, are needed to validate this proposed threshold.

Acknowledgments:

MeSH/Keywords: thyroid, iodine, iodine nutrition

Poster code: R-C-2-56

HOW MANY SPECIALISTS DOES CROATIA REALLY NEED?

PhD candidate: Danko Relić, MD

PhD Thesis: Development of a model for planning of specialist education of medical doctors in Croatia

Mentor/s: Prof. Jadranka Bozikov, PhD

Affiliation: University of Zagreb School of Medicine, Andrija Stampar School of Public Health

Introduction: Lack of proper policy planning and human resources management in many countries has resulted in an imbalance with multiple effects on employees in health care. Although the determination of the real ratio between the number of health workers and population size has become an aim of national policy on the human resources development in health care, in most cases remains a gap between plans and their realization. Croatian Medical Chamber reports that, since Croatiažs accession to the EU, more than 1300 medical doctors were issued certificates confirming their qualifications in order to work abroad. Long term systematic planning is absent at both, the total number of medical doctors and at the level of individual specialties.

Materials and methods: Developed model will be used as a tool for the simulation of different schemes for specialist education along with different scenarios of specialists' migration or retention flows in order to compare possibilities and options for the renewal of the Croatian healthcare personnel.

Results: Conceptual model was developed in consultations with experts. Model has been developed as multi-compartmental model with compartments or stocks corresponding to number of medical doctors with different qualifications (newly graduated, without specialization, at specialist education for different specializations, specialists of different specialities) across different age groups (one-year age groups will be used) and with flows between groups representing transitions between categories and aging.

Discussion: The significant lack of medical doctors in Croatia is a current problem that has become even bigger with the Croatian accession to the European Union in 2013. EUROSTAT data for 2014 shows that the average number per 1,000 inhabitants in EU is 3.4 specialists while corresponding number for Croatia is 2.9 which means that Croatia is missing 2,125 medical doctors. According to the criteria of World Health Organization (2011), Croatia lacks 4,300 medical doctors to reach average of EU countries that is 330 medical doctors per 100,000 inhabitants. Although the estimates of the Republic of Croatia population show probable decline in size, population aging might increase needs due to larger number of chronically ill and those seeking treatment or long-term care. Consequently demand for medical doctors will grow especially for certain specialties.

Acknowledgments: I would like to express my gratitude to my mentor, for her support and help.

MeSH/Keywords: medical doctors, modelling, specialisations, needs and demands for medical specialists

Poster code: R-C-2-99

SENSE OF COHERENCE AND QUALITY OF LIFE IN ADOLESCENTS AT THE BEGINNING OF SECONDARY EDUCATION

PhD candidate: Ivica Matić

PhD Thesis: Sense of coherence, health and quality of life in adolescents during secondary education

Mentor/s: Professor Vesna Jureša, MD, PhD

Affiliation: School of Nursing Mlinarska

Introduction: Adolescence is marked by numerous developmental tasks and constant adaptation to stressful situations. One such situation is the beginning of high school that many adolescents successfully overcome, while some experience a lowered quality of life. Thanks to the life orientation that determines one's perception of events in a logical manner, persons with a higher degree of sense of coherence become more resistant to stress and it is assumed that they have better life quality of life.

Materials and methods: The research is designed as longitudinal prospective cohort study. Preliminary results included the first measurement of the sense of coherence and life quality with 429 participants in the study. The research has been conducted based on a survey regarding their life orientation and life quality at the beginning of their schooling. The collected data were processed by methods of descriptive statistics. Mann-Whitney test was used for identifying the scale of variables' value significances between the two groups. The connection of questionnaires' results was identified by Spearman's correlation coefficient. The level of significance was α=0,05.

Results: The average sense of coherence among adolescents was 129 whether if they were accommodated in dormitories or not. There was a difference regarding sex, so the average sense of coherence for boys was 134 ± 21, and 125 ± 22 for girls. The results were similar with respect to life quality. The average life quality index for boys was 81 ± 15, and 76 ± 16 for girls. Analysis of the difference between groups according to the accommodation type shows no statistical difference in measured variables among groups. However, there were statistically significant differences between the results with boys and girls. Girls have significantly lower total coherence score (p=.000) and personal wellbeing (p=.001) in comparison to boys. Sense of coherence - total score was significantly positively correlated with personal wellbeing score.

Discussion: It should be noted that these are preliminary data that do not include a variable of self-estimated health and it is necessary to perform another measurement in the later period of students' life and do more detailed statistical analyses in order to examine the relationship between the sense of coherence, health and quality of life. These preliminary data suggest the need for implementing measures to raise the sense of coherence among adolescents.

Acknowledgments:

MeSH/Keywords: adolescence, sense of coherence, quality of life

Poster code: R-C-2-109

ANTIBIOTIC RESISTANCE IN URINARY TRACT PATHOGENS AND EVALUATION OF EMPIRICAL ANTIBIOTIC THERAPY FOR URINARY TRACT INFECTIONS IN UNIVERSITY CLINICAL CENTER KOSOVO

PhD candidate: Yllka Begolli Shehu MD

PhD Thesis: Antibiotic resistance in urinary tract pathogens and evaluation of empirical antibiotic therapy for urinary tract infections in University Clinical Center Kosovo

Mentor/s: Prof.ArjanaTambić Andrašević , MD, PhD , Prof .assoc.Gjyle Mulliqi Osmani

Affiliation: University of Zagreb School of Medicine , University of Prishtina Faculty of Medicine

Introduction: Introduction: Urinary tract infections (UTI) are the most frequent bacterial infections. E.coli is the most common urinary tract pathogen. Antibiotic resistance is a growing problem worldwide, and rates of resistance greatly depend on local antibiotic usage. Hypothesis: Antibiotic resistance rates in Kosovo are high particularly in Enterobacteriaceae. Extended spectrum beta-lactamases (ESBL) producing isolates are common but carbapenemases producers are rare. Aim: To investigate the level of resistance in major urinary tract pathogens and to evaluate treatment options for UTI. Specific Aims: To detect presence of specific beta-lactamases in third generation cephalosporin and /or carbapenem resistent Enterobacteriaceae.

Materials and methods: Materials: We will collect urine isolates from symptomatic patients hospitalized at the University Clinic Center Kosova in the period of six months. Antibiotic sensitivity testing will be done by disk diffusion according to EUCAST standards. Enterobacteriaceae resistant to 3rd generation cephalosporins and/or carbapenems will be analysed for presence of resistance mechanisms by phenotypic and molecular techniques.

Results: Preliminary results: We have collected samples from October to December 2016, of 912 samples, 34.2% had positive cultures.The most common isolates were E.coli 57.4%, Klebsiella pneumoniae 9.7%, Staphylococcus aureus 5.8%, Citrobacter freundi 5.1%. The antimicrobial resistance rates of 14 selected antimicrobial agents among two most frequent uropathogens (E.Coli and Klebsiella pneumoniae) are as follows: E.coli resistance to Ampicilin peaked with 76.4%, and Cotrimoxazole with 68.3%, Cefepime with 4.5%.

Discussion: The present study showed that the rate of UTI among hospitalized patients was more than reported previously, Enterobactericeae isolates were the dominant bacterial pathogens.

Acknowledgments:

MeSH/Keywords: UTI

Poster code: R-C-2-123

HOSPITAL ADMISSIONS IN THE POPULATION OF CROATIAN WAR VETERANS

PhD candidate: Pero Hrabač, MD

PhD Thesis: Long-term morbidity and mortality assessment in population of Croatian war veterans from the Homeland war

Mentor/s: Prof. Neven Henigsberg, MD, PhD

Affiliation: Croatian Institute for Brain Research, School of Medicine, University of Zagreb

Introduction: We report on number, type, duration and indication for hospital admissions in the population of Croatian veterans from the Homeland war. More than 20 years after the end of the war, mean age in the studied population has surpassed 55 years. Based on this fact alone, together with the relatively significant proportion of war veterans in Croatian population, hospital admissions of this cohort become an interesting public health issue.

Materials and methods: A team of experts from four institutions – School of Medicine, University of Zagreb, School of Public Health "Andrija štampar", Croatian Institute of Public Health and Ministry of Croatian Veterans has gathered and analysed data about more than 650.000 individual hospital admissions in this population. Methodologically, two major problems were encountered. The first was the issue of correct identification of the subjects, complicated by Croatian administration's transition from one type of unique identifier (JMBG, unique main citizen's number) to another (OIB, VAT number). The second was the change in the definition of hospital admission in the 2008 - 2010 period. Namely, one-day admissions or so-called "day hospital admissions" were introduced in this statistic only after 2009. Both of these issues complicate interpretation and direct comparison of pre- to post-2009 results.

Results: Expectedly, number of admissions per year increased steadily over the studied period. By month of the year, admissions were on average more common in the first half of the year. The highest proportion of admissions was seen in the Zagreb metropolitan area, followed by Split-Dalmatia and Osijek-Baranja counties. By indication for admission, the most common were mental and behavioural disorders (22,13%), followed by neoplasms (12,14%), diseases of the genitourinary system (11,85%), diseases of the circulatory system (9,33%) and injury, poisoning and certain other consequences of external causes (9,12%). More specifically, the most common cause for hospitalization was post-traumatic stress disorder (ICD10 code F43.1), followed by chronic renal insufficiency (N18) and chronic alcoholism (F10.2).

Discussion: All demographic parameters of the studied population including sex and age differ significantly to the general population. Any interpretation of the results should therefore be based on the range of standardization methods. Detailed analysis of both current results and (proposed) trends is laid out in the final poster, with conclusions of potentially far-reaching significance for public health system.

Acknowledgments:

MeSH/Keywords: Veterans, Hospital admissions, Croatia, Homeland war

Poster code: R-C-2-143

PHD THESIS PROPOSALS

Basic Medical Sciences – Thesis Proposals

EFFECT OF PENTADECAPEPTIDE BPC 157 ON VESICOVAGINAL FISTULA HEALING IN RATS

PhD candidate: Domagoj Rašić, MD

PhD Thesis: Effect of pentadecapeptide BPC 157 on vesicovaginal fisula healing in rats

Mentor/s: Associate professor Alenka Boban-Blagaić, MD, PhD, Research associate Marko Sever, MD, PhD

Affiliation: University of Zagreb School of Medicine, Department of Pharmacology

Introduction: Vesicovaginal fistula is anomalous connection between the bladder and the vagina which allows direct contact between these two separate organs and as such represents a great difficulty in healing. It occurs as a complication of surgical procedures on urogenital system, as a complication of childbirth, opstetric procedures and radiation of tumors of the genitourinary tract, and as such represents medical, social and economic problem that undermines the quality of life of women. Formed vesicovaginal fistula requires long-term treatment often with a number of surgical procedures in the presence of incontinence and frequent recurrence.

Hypothesis: The assumption is that BPC 157 administered parenterally or orally to the rat model vesicovaginal fistula can improve the healing of the same.

Aims: To show the effect of BPC 157 on healing of the vesicovaginal fistula.

Materials and methods: For the model of vesicovaginal fistula, female Wistar rats that weight 200 g will be used. After lower median laparotomy in deep anesthesia, an incision will be made on anterior wall of vagina and rear wall of urinary blader in the length of 4 mm and vesicovaginal fistula will be formed. Pentadecapaptide BPC 157 dissolved in saline solution will be applied in daily doses of 1 μg/kg, 10 μg/kg, 100 ng/kg, 10 ng/kg intraperitoneally during the entire duration of the experiment starting 14 days afer surgery (7, 14, 21, 28, 42 days) and the control group animals will be given daily equivalent amount of 0.9% NaCl ip. The animals will be in deep anesthesia during the sacrifice to measure the pressure required for leakage of fluid through fistula. After the sacrifice the diameter of the fistula, macroscopic changes and differences in fistula healing between groups will be observed and compared. Tissue will be taken for microscopic analysis.

Expected scientific contribution: It is known that vesicovaginal fistulas are huge medical problem considering that in many cases they require multiple surgical treatment with questionable outcome. There is currently no adequate pharmacological therapy in treating vesicovaginal fistulas and therefore we believe that the results of this research could lead to new insights in therapy and thus contribute to the success of treatment and improving the quality of life of patients with vesicovaginal fistula.

Acknowledgments: I would like to thank my mentors associate professor Alenka Boban-Blagaić, MD, PhD and research associate Marko Sever, MD, PhD as well as full professor Predrag Sikirić, MD, PhD for their great support and assistance

MeSH/Keywords: pentadecapeptide BPC 157, vesicovaginal fistula, rats

Poster code: T-A-4-11

BETA-CATENIN PHOSPHORYLATION STATUS, EXPRESSION LEVELS AND POTENTIAL MUTATIONS IN HUMAN GLIOBLASTOMA

PhD candidate: Andrej Desnica, MD

PhD Thesis: Beta-catenin phosphorylation status, expression levels and potential mutations in human glioblastoma

Mentor/s: 1 Goran Mrak, MD, PhD , 2 Nives Pecina Slaus, MD, PhD

Affiliation: Department of Neurosurgery, University Hospital Centre Zagreb, University of Zagreb, School of Medicine, Croatia

Introduction: Glioblastoma is the most frequent primary intrinsic brain tumour in humans. Despite the advances in genetic research, neurosurgical and oncological treatment, long-term survival in patients harbouring glioblastomas is very low. Recent Wnt signalling pathway studies revealed beta-catenin importance in oncogenesis of human glial tumours.

Hypothesis: Beta-catenin gene mutations are an important factor in glioblastoma oncogenesis, determining the beta-catenin expression and phosphorylation status in correlation with long-term patient survival.

Aims: The objective is to determine the presence and frequency of exon 3 beta-catenin mutations (Ser37 / Thr41), investigate the beta-catenin expression and phosphorylation status together with mutational IDH1 (isocitrate dehydrogenase 1 R132H) status and correlate the results with clinical parameters in patients with glioblastoma.

Materials and methods: The level of the beta-catenin protein expression and its phosphorylation status will be explored by monoclonal antibodies that recognize both phosphorylated and non-phosphorylated type of the protein in a sample size of 50 human glioblastomas (25 tumours with-, and 25 tumours without IDH1 R132H mutation). All relevant clinical and radiological imaging data will be correlated with molecular findings as well as with the presence/absence of the IDH1 R132H mutation.

Expected scientific contribution: Determining cellular molecular mechanisms responsible for glioblastoma initiation and progression presents a valuable scientific and clinical contribution. The research of the role of beta-catenin provides a foundation for understanding the role of Wnt signalling in glioblastoma. The results will clarify genetic changes in glioblastoma as well as help define subcategories of this disease regarding prognostic paradigms and, eventually, response to therapy.

Acknowledgments:

MeSH/Keywords: Wnt signal transduction pathway, Glioblastoma, Beta-catenin, CTNNB1 gene

Poster code: T-A-6-121

THE EFFECT OF NEUROFEEDBACK ON THE SEVERITY OF CLINICAL PRESENTATION OF THE DEORESSIVE DISORDER

PhD candidate: Ana Šečić, Master of Educational Rehabilitation

PhD Thesis: The effect of neurofeedback on the severity of clinical presentation of the depressive disorder

Mentor/s: Prof. Neven Henigsberg, MD, PhD

Affiliation: University of Zagreb, School of Medicine, University hospital

Introduction: According to the estimates of the World Health Organization by 2020 depression will become the second world health problem. Neurofeedback is a computerized method, based on the monitoring of the brain electrical activity (EEG) and giving feedback. In that frame, this study will examine and scientifically evaluate the possibilities of neurofeedback training as a non-pharmacological method in treatment of depression regarding to improvement of the patient condition due to the symptoms of depressive disorders.

Hypothesis: The respondents involved in neurofeedback training shall demonstrate less severe depression symptoms and better cognitive functioning in comparison with respondents not involved in neurofeedback training.

Aims: To assess and scientifically evaluate the possibility of neurofeedback training and the effects of neurofeedback training on certain cognitive functions among persons suffering from depressive disorder.

Materials and methods: For the purpose of this research, a sample shall be formed made up of adult respondents (aged 18-80 years) suffering from depressive disorder (mild and moderate depressive episode). By applying the random choice method, the respondents shall be divided into one of the following groups: experimental and control group. The following tests shall be used: for depression degree (Beck's Depression Inventory –II-BDI-II and MADRAS – Montegomery-Asberg Depression Rating Scale), quality of life level (WHOQOL – BREF questionnaire), personality test (16 personality factors test – 16PF), cognitive functions (Test of Attention). The experimental group shall undergo the neurofedback treatment in duration of 45 minutes (15 sessions). Basic central and dispersive parameters shall be calculated for all variables. The normality of variable distribution shall be evaluated by applying the Kolmogorov-Smirnov test. The change of dependent variables within the experimental group shall be analyzed by applying the two-factor analysis of variance (group x time) with repeated measures on one factor (time) as well as the Kruskall-Wallis H test. The level of statistical significance shall be set at $p < 0.05$.

Expected scientific contribution: The obtained results shall be used to determine the effects of neurofeedback training on clinical presentation of depressive disorder. The insights based on results of this research could be used to implement a more successful neurorehabilitation of persons suffering from depressive disorder, and they shall contribute to development of future therapeutic programmes.

Acknowledgments: I would like to thank Professor Neven Henigsberg MD, PhD and Petra Kalember, MD for their unconditional professional and personal support. I would also like to thank the company Pamel for supplying the neurofeedback device.

MeSH/Keywords: depression, neurofeedback, cognitive functions

Poster code: T-A-9-6

PERINATAL AND EARLY POSTNATAL DEVELOPMENT OF BASAL TELENCEPHALON IN HUMAN

PhD candidate: Matea Baljkas Barković, MD

PhD Thesis: Perinatal and early postnatal development of basal telencephalon in human

Mentor/s: Ivica Kostović, Professor Emeritus, MD, DSc

Affiliation: Croatian Institute for Brain Research

Introduction: The nucleus basalis magnocellular complex has a key role in the cholinergic modulation of the cerebral cortex. Perinatal development, growth indicators of the basal telencephalon and possible perinatal and postnatal reorganization of the nucleus basalis cellular organization in humans are not known. Using MRI and morphometric software it is possible to quantify the area and volume of different brain structures.

Hypothesis: The main phase of the growth and the cytoarchitectonical differentiation of the basal telencephalon is completed in early postnatal development, and in further development partially follows the development of the hemispheres.

Aims: The aim of the study is to collect the new information about the development of the nucleus basalis and correlate this information with data on the development of the normal cerebral cortex in the human fetus, premature infants and term infants.

Materials and methods: Research will be carried on specimens from Zagreb Neuroembyological Collection (ZNC), scanned by In vitro MR (age range 15 weeks after conception to 1 year), as well as histological and histochemical sections. Normotypic premature infants (age range: 24-31 weeks) without lesions, and normal term infants without lesions will be analysed. In histological part of the study, post-mortem human brain from ZNC, age ranging from 15 weeks after conception up to one year, will be analyzed. Nissl stained serial sections will be used to determine the cytoarchitectonic boundaries of the nucleus basalis. Using a camera lucida (Zeiss), the single cell measurement and the differentiation stage determination of the macrocellular component will be performed. This method will also be used to find out the size distribution and the degree of cell differentiation. Using the AChE-histochemistry we will show whether the cells and the nucleus basalis neuropil are AChE positive. Cell densitometry will also be performed.

Expected scientific contribution: Results of the perinatal cytoarchitectonical differentiation and reorganization, as well as nucleus basalis MR volumetry, will be the important contribution to understanding the development of basal telencephalon and will complement the previous results of the research groups of the Croatian Institute for Brain Research. New growth indicators will clarify the the ratio of the growth of this area and the cerebral cortex, and also help to clarify the abnormal development after perinatal brain damage.

Acknowledgments: This work has been supported by CSF IK-4517

MeSH/Keywords: nucleus basalis, MRI, cholinergic neurons, perinatal development

Poster code: T-A-9-13

CHANGES IN MR SIGNAL INTENSITY AND MICROSTRUCTURE OF TRANSIENT FETAL ZONES AS INDICATORS OF GROWTH AND DEVELOPMENT OF AXONAL PATHWAYS IN THE HUMAN BRAIN

PhD candidate: Iris Žunić

PhD Thesis: Changes in MR signal intensity and microstructure of transient fetal zones as indicators of growth and development of axonal pathways in the human brain

Mentor/s: Kostović Ivica

Affiliation: Croatian Institute for Brain Research, School of Medicine, University of Zagreb

Introduction: Development of fiber pathways in the human brain is a complex process that can be disrupted by many different factors. Transient fetal zones play an important role in axonal growth, navigation, elongation and recognition of postsynaptic elements. Two key zones for axonal growth are subplate and intermediate zone (fetal white matter), but each of five segments of white matter, described by Von Monakow, has its relevance in normal and pathologic development of the brain. Different classes of fiber pathways have distinct periods of intensive growth and development, which leads to increase of vulnerability to noxious factors in these periods. Development of MRI techniques enabled us to visualize brain development in-vivo, and it became possible to diagnose various disorders of the fiber pathway growth in fetuses and prematurely born children. Fractional anisotropy (FA) and other MRI-DTI scalars are used to represent microstructural changes in different pathologies of white matter, both in adult and developing human brain. Although many studies investigated development of the fiber pathways, the spatial relationship between growing fiber pathways and subplate, and MR characteristics of normal and abnormal growth of fiber pathways are still unknown.

Hypothesis: Microstructural changes of MRI-DTI scalars along white matter segments (from ventricle to pia) will reflect certain organization of white matter, reveal differentiation of segments of white matter and relations to key neurogenetic events in developing human cerebral wall.

Aims: The goal of this study is quantification of microstructural changes of white matter segments during normal and disturbed processes of brain development, for the purpose of better understanding of background of neurodevelopmental disorders and clearer correlation between MRI-exam and clinical parameters.

Materials and methods: Current cohort of 52 prematurely born children are MRI examined at preterm and term equivalent age, third MRI will be performed at their second year of life. All of these MRI scannes will be analyzed by volumetric analysis and MRI DTI programmes.

Expected scientific contribution: Using MRI volumetric and microstructural analysis, clinical parameters and neurodevelopmental outcome, it is expected to make correlation between MRI and clinical outcome more tangible, especially in mild and merely to notice MRI developmental changes, during brain development.

Acknowledgments: Supported by CSF IK-4517

MeSH/Keywords: white matter segments, prematurity, DTI-MRI, FA

Poster code: T-A-9-34

HYDROCEPHALUS IN PATIENTS WITH ANEURYSMAL SUBARACHNOID HEMORRHAGE TREATED WITH ENDOVASCULAR COILING

PhD candidate: Ivan Jovanović, MD

PhD Thesis: Predictors of hydrocephalus in patients with ruptured intracranial aneurysm treated with endovascular coiling

Mentor/s: Professor Marko Radoš, MD, PhD

Affiliation: University of Zagreb School of Medicine, University Hospital Centre – Zagreb

Introduction: Intracranial aneurysm is a bulging, weak area in the wall of an intracranial artery occurring in about 1–2% of the population. Rupture of an intracranial aneurysm results in subarachnoid hemorrhage (SAH), a subset of stroke that occurs at a relatively young age compared with other stroke subtypes and carries high mortality and morbidity rates. In case of SAH, treatment options include surgical clipping and endovascular management, which when technically feasible should be the preferred technique because of better outcome in terms of survival free of disability. Hydrocephalus, defined as an abnormal expansion of brain ventricles, is a well-known complication of SAH which may aggravate initial injurious effects of SAH and lead to further neurologic deterioration and longer hospital stay. The overall risk of hydrocephalus after aneurysmal SAH varies between 6% to 67% in different series.

Hypothesis: Morphological parameters of ruptured intracranial aneurysm, baseline clinical status and initial head computed tomographic scan findings can be used as predictors of hydrocephalus development in patients treated with endovascular coiling.

Aims: To determine the incidence and risk factors for hydrocephalus in patients with aneurysmal subarachnoid hemorrhage treated endovascularly.

Materials and methods: Retrospective review of medical records and radiological findings of patients with aneurysmal SAH who underwent endovascular treatment during the period from January 2013 to December 2016 revealed a total of 207 patients. We will analyze demographic data (age and sex), baseline clinical features (neurological severity grading at SAH onset using Hunt and Hess scale) and neuro-imaging findings (CT and DSA images) to determine the potential risk factors predictive of hydrocephalus in patients with aneurysmal SAH treated with endovascular coiling. The initial and follow-up computed tomography (CT) images will be reviewed, and the amount and distribution of blood and the occurrence of hydrocephalus will be registered. Digital subtraction angiography (DSA) images will be reviewed to determine morphological parameters (size and location) of ruptured intracranial aneurysms.

Expected scientific contribution: Early recognition of hydrocephalus and therapeutic intervention based on better detection of risk factors can lead to improved clinical outcomes in patients with aneurysmal SAH treated with endovascular coiling.

Acknowledgments:

MeSH/Keywords: intracranial aneurysm, subarachnoid hemorrhage (SAH), endovascular treatment, hydrocephalus

Poster code: T-A-9-62

THE EXTRACELLULAR MATRIX PROFILE OF HIPPOCAMPUS IN DRUG-RESISTANT EPILEPSY

PhD candidate: Barbara Sitaš, MD

PhD Thesis: The extracellular matrix profile of hippocampus in drug-resistant epilepsy

Mentor/s: Professor Nataša Jovanov Milošević, PhD, and Assis. Professor Danijela Kolenc, MD, PhD

Affiliation: University of Zagreb School of Medicine, Croatian institute for brain research

Introduction: Epilepsy is one of the most common neurological diseases as approximately 50 million people have epilepsy worldwide. 20-40% of patients have epileptic seizures that cannot be controlled with conventional antiepileptic therapy and thus present a special challenge in neurology. They are usually candidates for neurosurgical treatment. Most common pathohistological diagnosis found in drug-resistant epilepsies are focal cortical dysplasia (FCD) and hippocampal sclerosis (HS) in 65-70% of cases with loss of pyramidal neurons (most prominent in CA1 region of hippocampus) and aberrant mossy fibers sprouting in dentate gyrus as hallmark features. The commonly accepted hypothesis of epileptogenesis is imbalance between excitatory and inhibitory circuits, hyperexcitability of dentate granule cells on the one hand and asynchronous inhibition on the other. In vivo experimental models have shown up or downregulation of certain extracellular molecules, components of the synapse, and dysregulation of their proteinases

Hypothesis: The expression of the extracellular molecules (ECM) in the hippocampus in drug-resistant epilepsy is changed towards juvenile pattern of expression.

Aims: To determine changed components of the ECM profile of hippocampus in drug-resistant epilepsy in comparison with the ECM profile of hippocampus without any neuropathological burden.

Materials and methods: The archived in 4% paraformaldehyde fixed, paraffin embedded brain tissues (include 80 HS and 7 FCD samples). As controls, postmortem archived samples from patients without a neurological or neuropathological diagnose are used. The 20μm thick sections were immunohistochemically processed for different ECM (neurocan, tenascin, CS-56, glypican, wisteria floribunda agglutinin), and common neuronal and glial markers, as well as Nissl staining for citoarchitectonics evaluation. The Imamge J was used for qualitative analysis of the ECM expression.

Expected scientific contribution: Better understanding of the changed ECM profile in epileptogenic human hippocampus has an important role in the understanding of the pathogenessis of pharmacoresistant epilepsies and thus could provide potential key candidates for development of new therapeutic targets.

Acknowledgments:

MeSH/Keywords: hippocampal sclerosis, metalloproteinases, neurocan, dentate gyrus, focal cortical dysplasia

Poster code: T-A-9-104

AUDITIVE PROCESSING IN CHILDREN WITH PERINATAL PERI-INTRAVENTRICULAR HEMORRHAGE (PV-IVH) OF I AND II DEGREE

PhD candidate: Dinah Vodanović, Msc SLP

PhD Thesis: Auditive processing in children with perinatal peri-intraventricular hemorrhage

Mentor/s: academician Ivica Kostović, prof.emeritus, prof Vlatka Mejaški Bošnjak

Affiliation: University of Zagreb School of Medicine, The Croatian Institute for Brain Research. University of Zagreb School of Medicine

Introduction: Brain development in humans is a complex process, therefore PV-IVH leads to disturbing that process. It is assumed that neurodevelopment in children after perinatal damage depends on interaction of current damage to the structures, compensatory processes and brain plasticity, preferably accompanied with correct and customized therapy procedures. PV-IVH are frequent in premature children and are localized in the area seen as a crossroad to the projection, associative and commissural pathways. Development of central auditory pathways starts prenatally, and continues its development postnatally. Every change to the brain, that includes hemorrhage leads to disruption in development of auditory system and possibly changes the way brain processes auditory information. Auditory processing is the way the brain receives, processes and interprets received sounds. It is estimated that about 3-5% of children have this disorder. It interferes with auditory stimuli and the integration of received verbal information. Listening is a binaural process which contributes to the premise of higher influence of bilateral damage to the refined function of auditory processing. There is no single definition of the disorder, but most of them emphasize neurological background of it, so the main point in this research is to find one.

Hypothesis: In the group of children diagnosed with PVL-IVH we expect significantly more mistakes in the categories of Auditory processing disorder 1.This kind of hemorrhage leads to slight changes in neurological structures responsible for auditory processing.

Aims: To determine if auditory processing disorder has its roots in neurological etiology. Further on to establish how much does it influences speech and language acquisition and skills

Materials and methods: A battery of auditory tests will be applied to the group of 30 children aged 6,5 up to 11,5 years of age. All participants early on are identified by the neuropediatrician on the intracranial ultrasonography with the PV-IVH of I and II degree. Subjects will be matched with equal number of controls. Performed battery will determine auditory competencies in controlled environment than subjects will be tested with auditory processing disorder 1 test

Expected scientific contribution: We expect to gain better insight in neurological etiology of this disorder. Main goal of this research is to make contribution to the early detection, consequently to adapt and tailor correct rehabilitation procedures to enable better outcomes

Acknowledgments:

MeSH/Keywords: Peri-intraventricular hemorrhage, auditory processing, rehabilitation

Poster code: T-A-9-77

THE EXPRESSION OF PERINEURONAL NETS IN THE FETAL AND PERINATAL HUMAN BRAIN

PhD candidate: Darko Orešković, M.D.

PhD Thesis: The expression of perineuronal nets in the fetal and perinatal human brain

Mentor/s: Professor Nataša Jovanov Milošević, PhD

Affiliation: University of Zagreb School of Medicine, Croatian Institute for Brain Research

Introduction: Perineuronal nets (PNNs), a specialized component of the extracellular matrix, rich in chondroitin-sulphate, and other proteoglycans and glycoproteins, condense and surround certain populations of neurons and initial part of their axons. Today it is known that they perform a wide variety of functions during the development, in synapse formation and functions, in neuroprotection and plasticity of neurons, and neuronal circuitries. The research conducted in vitro and on in vivo animal models, it has been demonstrated that during development the PNNs have, among others, an important role in neuroprotection, and even in formation of axons pathways, while in mature brain they inhibit neuron regeneration.

Hypothesis: The PNNs have a specific developmental spatio-temporal expression pattern during fetal and prenatal development of the human brain that correlate with the developmental processes of morphogenesis, differentiation and synaptogenesis and differ from mature pattern of PNN allocation.

Aims: The aim of this study is to show the PNNs in the fetal and perinatal human brain, to determine the period when they start to develop as well as their cellular, zonal, laminar and structural distribution in correlation with the processes of morphogenesis, differentiation and synaptogenesis.

Materials and methods: In this study, archive tissue samples of human fetal and perinatal brain will be used, where the PNNs will be shown by histochemical and imunohistochemical methods. Furthermore, the PNNs will be qualitatively and quantitatively analyzed in correlation with neuronal, synaptic, glial and ECM markers in the context of developmental differentiation processes of the neuron population which they surround.

Expected scientific contribution: The development of the PNN in the human brain, except for a few papers from the beginning of the 19th century, hasn't been described. The time frame and sequence of regional and areal appearance, and spatio-temporal distribution of the PNNs in the human fetal and perinatal brain is still unknown.

Acknowledgments: This work is supported by projects UNIZG-BM0054 and HIMRICO-Adris. We thank B. Popovic, M. Horvat and D. Budinscak for thier technical support.

MeSH/Keywords: chondroitin-sulphate proteoglycans, wisteria floribunda agglutinin, GABAergic neurons, subplate zone

Poster code: T-A-9-126

NEUROCOGNITIVE REPRESENTATION OF THE TIME: REPRODUCTION, DISCRIMINATION AND GENERATION OF SHORT TIME INTERVALS

PhD candidate: Ivan Šerbetar, PhD in Kinesiology

PhD Thesis: Neurocognitive representation of the time: reproduction, discrimination and generation of short time intervals

Mentor/s: Professor Zdravko Petanjek, MD, PhD / Professor Predrag Zarevski, PhD

Affiliation: Faculty of Teacher Education University of Zagreb

Introduction: Human ability to estimate time durations on different scales is crucial for anticipation, learning and adaptation to temporal regularities in the social and physical environment. Timing in the range of milliseconds is thought to be "automatic"-related to the motor control and neurally dependent on cerebellum. Supra-second or interval timing is considered to be cognitively controlled, associated with attention and memory and dependent on cortico-striatal circuits. The hallmark of the interval timing is scalar property, which shows that variability in timing grows proportionally to the mean of the timed interval. Therefore, coefficient of variation (SD/Mean) should remain constant across different durations or tasks. However, the previous studies did not confirm that uniquely. Accordingly, it is not clear whether the unified scalar timer is accounted for timing in motor and perceptual tasks, neither is clear whether unified or distinct timer i.e. neural network is accountable for different timescales.

Hypothesis: We assume that the significant differences in intra-individual variability will be observed between perceptual and motor timing tasks as well as between processing the duration in milliseconds and seconds, indicating that different timing tasks are under control of different timers.

Aims: The study aims to illuminate the relationships between performance of different temporal tasks, as well as the relationships across different time durations, to establish whether the same timing mechanism is responsible for perceptual and motor timing and whether the same scalar timer controls durations in sub and supra-second range.

Materials and methods: The 80 subjects aged 18-25 yrs of both sexes will be assessed. Experimental tasks of reproduction, discrimination and production of time intervals, but also reproduction task accompanied with working memory load, will be carried out on a computer using E-Prime software. Intra-individual differences between the tasks, expressed by CV and reflecting different processes of the time estimation, will be assessed by within subjects repeated measures ANOVA.

Expected scientific contribution: The study is expected to advance the understanding of how humans perform temporal tasks in perceptual and motor modalities. The study may also contribute to more accurate formulation of the timing theory, but also to the development of the diagnostic procedures and treatments for patients or elderly who suffer from disorders which include deficits in timing.

Acknowledgments:

MeSH/Keywords: interval timing, millisecond timing, intra-individual differences, scalar property

Poster code: T-A-9-110

Clinical Medical Sciences – Thesis Proposals

THE ASSOCIATION BETWEEN SEVERITY OF PSORIASIS AND OBESITY BASED ON THE ANALYSIS OF THE SERUM LEVELS OF TNF-α, IL-6, RESISTIN, OMENTIN AND AMOUNT OF VISCERAL FAT

PhD candidate: Kristina Žužul

PhD Thesis: The association between severity of psoriasis and obesity based on the analysis of the serum levels of TNF-α, IL-6, resistin, omentin and amount of visceral fat

Mentor/s: Assistant Professor Krešimir Kostović, MD, PhD and Professor Drago Batinić, MD, PhD

Affiliation: University of Zagreb School of Medicine, University Hospital Centre Zagreb

Introduction: Psoriasis is a chronic inflammatory skin disease associated with numerous comorbidities. Studies that have investigated the relationship of psoriasis to obesity proposed the association through a common pathophysiological mechanism of chronic low-grade inflammation. Adipose tissue, especially visceral fat, is an active endocrine organ that secretes adipokines involved in regulation of various metabolic processes. Until today, several adipokines have been identified that may contribute to the systemic inflammation present both in obesity and psoriasis, but their exact mechanism of action in both of these conditions is still not completely understood. This study will analyze the relationship of the serum levels of TNF-α, IL-6, resistin, omentin and amount of visceral fat, with the severity of psoriasis.

Hypothesis: Compared to control group, patients with psoriasis have increased amount of visceral fat, increased serum levels of TNF-α, IL-6, resistin, and decreased serum levels of omentin, with direct correlation of measured values to the severity of psoriasis.

Aims: To investigate the relationship of serum levels of adipokines (TNF-α, IL-6, resistin, omentin) and the amount of visceral fat with the psoriasis severity.

Materials and methods: The study will be conducted at the University Hospital Centre Zagreb and University of Zagreb School of Medicine, and will include at least 50 patients with histologically verified plaque psoriasis and at least 25 age and sex adjusted healthy volunteers as controls. After taking a detailed patient history, the patients will be clinically examined and severity of psoriasis will be assessed according to PASI (Psoriasis Area and Severity Index). The following parameters will be measured: height, weight, BMI, waist circumference, amount of visceral fat and serum levels of cytokines and adipokines. The amount of visceral fat will be measured by bioelectrical impedance analysis (BIA) using Tanita BC-418 Segmental Body Composition Analyzer. Peripheral venous blood samples (5 mL) will be collected and serum concentrations of TNF-α, IL-6, resistin and omentin will be determined with ELISA method, using commercial kits. Statistical analysis will be performed using STATISTICA software, version 13.0.

Expected scientific contribution: The results of this study could help clarify pathophysiology of psoriasis, and have a therapeutic role in improving psoriasis severity and protecting against comorbidities.

Acknowledgments:

MeSH/Keywords: psoriasis, obesity, cytokines, TNF-α, IL-6, resistin, omentin, visceral fat

Poster code: T-B-2-72

GLOMERULAR HYPERFILTRATION AS A PREDICTOR FOR RENAL IMPAIRMENT AND INCREASED CARDIOVASCULAR RISK IN PREHYPERTENSION

PhD candidate: Ana Jelaković, MD

PhD Thesis: Glomerular hyperfiltration as a predictor for renal impairment and increased cardiovascular risk in prehypertension

Mentor/s: Assistant professor Mario Laganović, MD, PhD

Affiliation: University Hospital Center Zagreb

Introduction: Prevalence of prehypertension (PHT) in general population is high and debate whether those subjects should be treated or not is going on.Glomerular hyperfiltration (HGF) is associated with more rapid progression to chronic kidney disease(CKD).It is considered to be an early marker of CKD in diabetes and hypertension.PHT is not a homogenous group.It was proposed that HGF might be one of prognostic biomarkers in this group as well.

Hypothesis: HGF is an independant predictor of CKD and increased CV risk in subjects with PHT.

Aims: Main: 1)To determine prevalence of HGF in general population and in BP subgroups.2)To analyze characteristics of subjects divided into GFR subgroups and calculate CV risk using risk chart scores.3)At the end of follow-up period analyze predictive value of HGF on renal function and CV morbidity and mortality. Specific:1) In PHT group determine risk factors for HGF.2)Analyse impact of risk factors(HGF,BP,heart rate,BMI,WC,insulin resistance,leptin,adiponectin)on progression of albuminuria and deterioration of eGFR and development of sustained hypertension.3)At the end of follow up period, in the PHT group analyze differences among eGFR subgroups 4) Determine which one of equations for eGFR is the most reliable (i.e. in concordance with cystatin C equation).

Materials and methods: In this prospective study (average 7.5 years of follow up) epidemiological, clinical and laboratory data on 954 subjects from general population will be analyzed. Subjects were enrolled in the period 2005-2010 (door-to-door method/participation rate 75%). Inclusion criteria: age=18 years, untreated hypertension, no previous CV morbidity. Exclusion criteria: treated hypertension, coronary heart disease, stroke, CKD, diabetes, pregnancy, dementia, disability. BP and heart rate will be measured following ESH guidelines using oscillometric device. PHT will be defined after ESH and JNC-7. Laboratory parameters will be determined in one laboratory: serum and urine creatinine, albuminuria, alpha-1Microglobulinuria, FBG, serum lipids, leptin, adiponectin. GFR will be estimated using 4 equations: MDRD, CKD-Epi, C-G and CKD-Epi cystatinC. HGF will be defined as mean 2SD, 95th percentile,5th quintile.Insulin resistance will be estimated using HOMA equation. CV risk will be determined using Framingham CV Risk Score and Heart Score.

Expected scientific contribution: If HGF confirmed to be an independent factor for renal deterioration and would have prognostic value for CV morbidity it could be proposed as a new biomarker helping clinician to decide when to treat PHT.

Acknowledgments:

MeSH/Keywords: glomerular hyperfiltration, prehypertension, chronic kidney disease, cardiovascular risk

Poster code: T-B-9-2

THE ASSOCIATION OF QUALITY OF LIFE AND HIGH DOSE CHEMOOTHERAPY FOLLOWED BY STEM CELL RESCUE IN PATIENTS WITH HEMATOLOGIC MALIGNANCIES ACCORIDING TO THE PRESENCE OF DEPRESSIVE SYMPTOMATOLOGY

PhD candidate: Vibor Milunović

PhD Thesis: The association of quality of life and high dose chemootherapy followed by stem cell rescue in patients with hematologic malignancies accoriding to the presence of depressive symptomatology

Mentor/s: professor Slobodanka Ostojić Kolonić, MD, PhD professor Miro Jakovljević, MD, PhD

Affiliation: Division of Hematology, Clinical Hospital Merkur, Zargreb, Center for Psychiatry, Clinical Hospital Centere Zagreb

Introduction: High dose chemotherapy followed by stem cell rescue (ASCT) is one of most common procedures performed in first or second line in malignant hematology, primary lymphomas or multiple myelomas.. Despite that fact, the research on its association with quality of life in this population is only at the begining

Hypothesis: The depressive patients undergoing ASCT have worse QoL than those patients not suffering from depression.

Aims: The main aim of the study is to establish the association between ASCT, depression and QoL in the cohort of consecutive patients treated at single center (planned N=100) as a a function of time at multiple time points: prior ASCT, immediately upon hematopoietic recovery, 2 and 6 months after procedure. Secondary aim is to examine possible adverse prognostic factors of QoL in this group: levels of anxiety, perception of prognosis, coping mechanisms and pain.

Materials and methods: QoL will be assessed by self-reported scale European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 while depression will be assesed by Center for Epidemiologic Studies Depression Scale-Revised. Other prognostic factors will be examined by following questionnaires: Hospital Anxiety and Depression Scale (depression and anxiety), Perception of Treatment and Prognosis Questionnaire (prognosis perception), Mini-Mental Adjustment to Cancer Scale (coping mechanisms), Connor-Davidson Resilience Scale 25 (resilience) and visual-analogue scale of pain. Expected results are that ASCT is associated with the deterioration of QoL and that the proposed prognostic factor will be significant in its prediction

Expected scientific contribution: This will be one of the first studies using multidimensional approach in evaluating QoL in this group of patients.

Acknowledgments:

MeSH/Keywords: quality of life, depression, hematologic malignancy, stem cell transplantation

Poster code: T-B-9-3

BETA-FIBRINOGEN -455 G/A GENE POLYMORPHISM AND THROMBOSIS

PhD candidate: Petra Angebrandt, MD

PhD Thesis: The association of beta-fibrinogen – 455G/A gene polymorphism with left atrial thrombus in patient with atrial fibrillation

Mentor/s: Anton Šmalcelj, PhD

Affiliation: University of Zagreb, School of Medicine, University Hospital Center Zagreb, Department of cardiovascular disease

Introduction: Atrial fibrillation is the most commonly encountered rhythm problem in adult population. It is associated with increased long-term risk of stroke as well as heart failure and death. There are many external and genetic risk factors for tromboembolic events. One of them is a specific biomarker fibrinogen and it's polymorphism, as possible genetic marker of trombosis.

Hypothesis: Beta-fibrinogen gene -455 G/A polymorphism is more prevalent in patient with atrial fibrillation and left atrial thrombus than in those without left atrial thrombus.

Aims: Main research aims: To analyze prevalence of beta-fibrinogen gene -455 G/A polymorphism in patients with atrial fibrillation and thrombus in the left atrium detected with transesophageal echocardiographic exam and in those without thrombus formation. Specific research aims: To analyze correlation between fibrinogen concentration, gene polymorphism and prevalence of thrombus. Give answer whether high fibrinogen concentration is a result of a gene polymorphism or is connected with procoagulant state caused with thrombus formation in circulation by itself.

Materials and methods: Observational, analitic, case-control study was designed with patients with atrial fibrillation to whome genetic analysis for -455 G/A fibrinogen polymorphism will be done. Patients will be selected in two groups: 60 patients with thrombus in the left atrium and 60 patients without thrombus. As primary goal of this study will be the association of beta-fibrinogen -455 G/A gene polymorphism with left atrial thrombosis and serum fibrinogen concentration. As a second study goal will be to correlate hyperfibrinogenemia with gene polymorphism, as we know how hyperfibrinogenemia is a risk factor for many cardiovascular disease.

Expected scientific contribution: To prove how beta-fibrinogen -455 G/A polymorphism may be a promising marker of left atrial thrombosis in patients with atrial fibrillation and with our results to contribute in better clinical judgment when decision about the level of anticoagulant treatment is being made.

Acknowledgments:

MeSH/Keywords: atrial fibrilation, left atrial thrombosis, fibrinogen, polymorphism

Poster code: T-B-9-20

METABOLIC SYNDROME AND PROFESSIONAL SPORT

PhD candidate: Ana Majić

PhD Thesis: The effect of professional sport on the prevalence of metabolic syndrome and cardiovascular risk in retired sport players

Mentor/s: Asst. prof. Dario Rahelić, MD, PhD.

Affiliation: Department of Endocrinology, Diabetes and Clinical Pharmacology, Clinical Hospital Dubrava, Zagreb

Introduction: In terms of daily physical activity, persons engaged in professional sports are often presented to the public as a symbol of healthy lifestyle that should be followed. Several recent studies have showed another side of professional sports, particularly high prevalence of metabolic syndrome and cardiovascular risk factors in retired American football players.

Hypothesis: There is a significantly higher prevalence of metabolic syndrome and greater cardiovascular risk in people who were engaged in professional sports in relation to people who have never been envolved in professional sports.

Aims: To estimate the overall prevalence of the metabolic syndrome and to evaluate cardiovascular risk in professional athletes and people who have never been envolved in professional sports.

Materials and methods: This cross-sectional study will include 300 male professional athlets in football, handball, basketball or water polo, divided into three subgroups: 25 active professional athletes (who have been engaged in professional sports at least 5 years), 25 former professional athletes who retired 10 years ago and 25 former professional athletes who retired from the sport 20 years ago. The control group will consist of 75 men who correspond to the study group by age selected at regular medical examinations of the general population which are carried out daily at the University Hospital Dubrava. The following parameters of the metabolic syndrome will be determined for each subgroup: waist circumference, height, body weight, body mass index, systolic and diastolic blood pressure, plasma triglyceride concentration, HDL concentration and fasting plasma glucose. The risk of cardiovascular disease in the next 30 years will be estimated using the Framingham risk score. Additionally, the following parameters will be determined: total cholesterol, LDL cholesterol, C-reactive protein, fasting insulin, insulin resistance index (HOMA-IR) and glycated hemoglobin (HbA1c).

Expected scientific contribution: Raising awareness of the need for intensive health monitoring of active and former professional athlets.

Acknowledgments: I would like to thank my mentor for his continuous support.

MeSH/Keywords: metabolic syndrome, cardiovascular risk, retired sport players

Poster code: T-B-9-23

ENDOTHELIAL DYSFUNCTION AND ENDOTHELIAL LIPASE SERUM LEVELS IN NEWLY DIAGNOSED ARTERIAL HYPERTENSION PATIENTS AND INTRODUCTION OF AMLODIPINE/PERINDOPRIL AND NEBIVOLOL

PhD candidate: Krešimir Kordić, MD

PhD Thesis: Endothelial dysfunction and endothelial lipase serum levels in newly diagnosed arterial hypertension patients and introduction of amlodipine/perindopril and nebivolol

Mentor/s: Assist. Prof. Matias Trbušić, MD, PhD

Affiliation: KBC Sestre milosrdnice, Vinogradska cesta 29, 10000 Zagreb

Introduction: Endothelial lipase plasma level are increased in patients with arterial hypertension, metabolic syndrome and smokers. There is also a direct correlation with CRP and IL-6 levels. Atherosclerosis affects endothelial lipase plasma level, too. Endothelial dysfunction occurs in the early stages of atherosclerosis and is a predictor of future cardiovascular events. One of the methods to evaluate endothelial dysfunction is flow-mediated vasodilation. Antihypertensive drugs, especially ACE inhibitors, may improve endothelial dysfunction measured by flow-mediated vasodilation.

Hypothesis: Hypothesis is that the reduction of endothelial lipase plasma levels after 8 weeks of therapy with amlodipine/perindopril directly correlates with the improvement of endothelial dysfunction measured by flow-mediated vasodilation in patients with newly diagnosed arterial hypertension. Endothelial lipase plasma levels might be a predictor of endothelial function improvement.

Aims: The goal of the present study is to evaluate endothelial lipase plasma levels and endothelial dysfunction measured by flow-mediated vasodilation in patients with newly diagnosed arterial hypertension who are treated with amlodipine/perindopril and nebivolol for 8 weeks.

Materials and methods: Patients with newly diagnosed arterial hypertension according to the current ESC guidelines will be recruited from the Department of Cardiology, Department of Internal medicine and Emergency department of Sisters of Mercy University hospital center. Medical history will be recorded from all patients and blood samples will be taken for analysis using competitive ELISA test. Routine clinical data (ECG, echocardiography, routine blood tests) will also be used. Brachial artery flow-mediated vasodilation measurement will be performed according to current recommendations. Antihypertensive therapy with amlodipine, perindopril and/or nebivolol will be initiated at the first visit. Eight months later, blood samples will be taken for analysis using competitive ELISA test, and the brachial artery flow-mediated vasodilation measurement will be repeated. Study will be performed according to Good Clinical Practice and Helsinki Declaration principles.

Expected scientific contribution: Expected scientific contribution is further clarifying of the role and complex interactions of endothelial lipase, especially in early stages of atherosclerosis development. Endothelial lipase plasma levels might be a predictor of endothelial function improvement.

Acknowledgments: /

MeSH/Keywords: atherosclerosis, endothelial lipase, endothelial dysfunction, flow-mediated vasodilation

Poster code: T-B-9-30

ASSOCIATION OF PRO12ALA POLYMORPHISMS OF PPAR GAMMA AND MTHFR C677T WITH CLINICAL MANIFESTATION OF METABOLIC SINDROME IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME

PhD candidate: Marija Miletić, MD

PhD Thesis: Association of Pro12Ala polymorphisms of PPAR-γ gene and MTHFR C677T with clinical manifestation of metabolic syndrome in patients with primary Sjögren's syndrome

Mentor/s: Prof Jasenka Markeljević, MD, PhD

Affiliation: Clinical Hospital Sisters of Mercy

Introduction: Sjögren's syndrome (SS) is an interesting autoimmune disease (AID) in the light of the research of local and systemic immunity and early atherogenesis (AG). Patients with AID develop early and severe vascular atherosclerotic changes. Proinflammatory cytokines may act on the initiation and development of the AG. Metabolic syndrome (MS) is one of the strongest independent predictors of cardiovascular (CV) diseases, and it could constitute the connection between chronic inflammation and elevated CV risk in patients with AID. One of the key factors of adipogenesis is peroxisome proliferator-activated receptor gamma gene (PPAR-γ). PPAR-γ Pro12Ala polymorphism is associated with various metabolic disorders, but also with sicca syndrome. Methylenetetrahydrofolate reductase (MTHFR) is the most important enzyme involved in DNA methylation process. MTHFR deficiency has been associated with hyperhomocysteinemia, who has been recognized as a risk factor for several diseases such as atherosclerosis, AID.

Hypothesis: Pro12Ala polymorphisms of PPAR-γ and MTHFR C677T gene are associated with increased risk of development of metabolic syndrome in patients with primary Sjögren's syndrome.

Aims: To investigate the relationship between Pro12Ala polymorphisms of PPAR-γ and MTHFR C677T gene with the appearance of metabolic syndrome in patients with primary Sjögren's syndrome. One of the goals is to determine the prevalence of the MS in patients with pSS.

Materials and methods: The research plan to include a total of 90 patients suffering from pSS. Patients will be classified into groups based on the presence / absence of the MS. After anthropometric measurements, subjects will be asked to obtain the blood sample for the purpose of DNA isolation and biochemical analysis. We are going to extract DNA from blood samples and for the detection of polymorphisms we will use the polymerase chain reaction (PCR).

Expected scientific contribution: This research will allow a more rational diagnostic procedure and contribute to more precise diagnosis of early AG, monitoring of patients with AID and individualization of therapy in this patients.

Acknowledgments:

MeSH/Keywords: Sjoegren syndrome, metabolic syndrome, atherogenesis

Poster code: T-B-9-42

ASSESSMENT OF PARAVALVULAR REGURGITATION SEVERITY AFTER TRANSCATHETER AORTIC VALVE IMPLANTATION USING PLATELET AGGREGATION

PhD candidate: Zvonimir Ostojić

PhD Thesis: Assessment of paravalvular regurgitation severity after transcatheter aortic valve implantation using platelet aggregation

Mentor/s: Assit. Prof. Joško Bulum

Affiliation: Department of Cardiovascular Diseases, University Hospital Center Zagreb

Introduction: Transcatheter aortic valve implantation (TAVI) is globally approved method for treating sever aortic stenosis (AS) in patients whose surgical risk is too high. Paravalvular regurgitation (PVR) is most common complication after TAVI with incidence as high as 70%. Although majority of those are usually mild in severity, moderate or sever one is expected up to 20% of cases after first implantation. In those cases additional interventional procedures, such as balloon dilatation or implantation of another valve, can reduce PVR severity. Beside currently used fluoroscopic and echocardiographic methods for PVR assessment, recent studies indicate that platelet aggregation (PA) tests for Von Willebrand factor activity can be used for the same purpose. Different type of PA measurement, using ASPI-, ADP- and TRAP- test on Multiplate® analyzer have been widely used in detection of platelet disorders, tailoring antiplatelet therapy and stratification of bleeding risk. According to our knowledge, those PA tests have not been tested in assessment of PVR after TAVI.

Hypothesis: Patients with sever AS who underwent successful TAVI procedure, without significant residual PVR, will improve platelet aggregation.

Aims: Determine incidence and degree of PA dysfunction in patients with sever AS using ASPI-, ADP- and TRAP- test on Multiplate® analyzer. Determine extent of PA correction after TAVI using the same tests. Determine connection between PA and early bleeding and thromboembolic complications after TAVI.

Materials and methods: 40 patients who underwent TAVI procedure will be enrolled in this research. Their PA will be measured in several time points: first immediately after induction of anesthesia, second after administration of heparin and third 10 minutes after implantation of initial valve. If additional interventional procedures will be required another blood sample will be taken 10 minutes after final results. Last measurement will be done on third postoperative day.

Expected scientific contribution: Results of this research will indicate is it possible to use PA to determine efficacy of TAVI. Furthermore, possibility of using PA test, before and after TAVI, as predictive model for bleeding and thromboembolic complications will be assessed.

Acknowledgments:

MeSH/Keywords: Aortic stenosis, Transcatheter aortic valve implantation, Platelet aggregation

Poster code: T-B-9-52

N- GLYCOSYLATION OF IMMUNOGLOBULIN G IN ADULT PATIENTS WITH IMMUNE THROMBOCYTOPENIA

PhD candidate: Ena Ranković, MD

PhD Thesis: N-glycosylation of immunoglobulin G (IgG) in adult patients with immune thrombocytopenia (ITP) differs from N-glycosylation of IgG in adults who have normal platelet levels.

Mentor/s: [1]Assist. Prof. Dražen Pulanić, MD, PhD, [2]co-mentor Prof. Gordan Lauc, PhD

Affiliation: [1]University Hospital Center Zagreb and University of Zagreb Medical School; [2]Faculty of Pharmacy and Biochemistry, University of Zagreb, Zagreb, Croatia.

Introduction: ITP is an autoimmune disease characterized by a reduction in platelet counts below $100x10^9$/L. Glycosylation is one of the most common and variable post-translational modification of proteins. IgG is the most abundant glycoprotein in human plasma and the major effector molecule of the humoral immune system. Since ITP is an autoimmune disease analysis of glycosylation of IgG antibodies could have significant implications for understanding the pathophysiology of the disease and could potentially become an important biomarker of diagnosis, treatment decisions and follow up of patients with ITP.

Hypothesis: N-glycosylation of IgG in adult patients with ITP differs from N-glycosylation of IgG in adults who have normal platelet levels. There is also a difference in N-glycans of IgG between patients with ITP who will achieve remission or respond well to certain established forms of therapy and have mild clinical manifestations and patients who do not achieve remission nor good response or have severe clinical manifestations.

Aims: The aim of this study is to examine whether N-glycosylation of IgG in adult patients differs from N-glycosylation of IgG in adults who have normal platelet counts, as well as the difference in N-glycans between patients with ITP who have mild clinical manifestations, achieve remission or good response to therapy and patients with ITP who do not respond well or have sever clinical manifestations.

Materials and methods: Glycans of IgG will be analyzed from a sample of blood plasma of 50 adult patients with ITP and 25 adults in the control group. ITP patients will be longitudinally followed in several time-points.In patients with ITP demographic data, former course of the disease, treatment lines, quality of life, intensity, localization and frequency of bleeding, and routine laboratory tests will be evaluated. Blood plasma samples will be sent to the Genos laboratory where analysis of N-glycans will be conducted.

Expected scientific contribution: Glycan analysis in ITP represents a possible diagnostic, predictive and prognostic biomarker of ITP.

Acknowledgments: Division of Hematology, UHC Zagreb

MeSH/Keywords: Immune thrombocytopenia, N- glycosylation, immunoglobulin G, glycom, autoimmune disease

Poster code: T-B-9-53

THE ROLE OF FRACTAL ANALYSIS IN DIAGNOSTIC IMAGING OF METASTATIC NEUROENDOCRINE TUMORS

PhD candidate: Mateja Strinović, MD

PhD Thesis: Fractal analysis of computed tomography images in differentiating metastatic neuroendocrine tumors and colorectal carcinomas

Mentor/s: Associate Professor Milan Vrkljan, MD, PhD

Affiliation: Department of Endocrinology, Diabetes and Metabolic Diseases, "Mladen Sekso", University Hospital Center "Sestre Milosrdnice", University of Zagreb, School of Medicine

Introduction: Neuroendocrine tumors (NET) are epithelial neoplasms with neuroendocrine differentiation. The most common NETs are gastroenteropancreatic (GEP- NET) and lung NETs. GEP-NETs are rare tumors with an incidence between 1 and 8 per 100,000. These tumors have significantly increased incidence rates in the last 30 year due to rapid advance in diagnostic procedures. 60 to 75% of patients at the time of diagnosis have liver metastases. In 20 to 50% of cases it is difficult to localize the primary site of tumor and therefore the diagnosis is based on pathohistological analysis of metastatic lesions. There is no imaging method that would meet all expectations in the clinical detection of NETs. The latest research show that tumors have fractal structure which potentially enable development of non-invasive diagnostic methods based on fractal analysis of CT and MRI images that can help in distinguishing NETs from other tumors.

Hypothesis: The hypothesis of our research is that neuroendocrine tumors (NETs) and colorectal carcinomas could be distinguished using the fractal analysis of computed tomography (CT) images.

Aims: Our main goal is to investigate the differences in the values of fractal dimension and/or lacunarity between liver metastasis of NETs and colorectal carcinomas as well as to analyze connection between parameters of fractal dimensions and/or lacunarity with tumor aggressiveness, serum tumor markers, overall survival and progression free survival.

Materials and methods: The study will include a total of 50 consecutive and treatment naive patients with NETs as well as 50 consecutive and treatment naive patients with colorectal cancer with liver involvement. Patients in both groups will be divided into two subgroups according to the differentiation of the tumor into tumors of low and high grade. We will conduct fractal analysis of CT native and postcontrast images of liver metastases.

Expected scientific contribution: We expect that the identification of the characteristic values of fractal dimensions and/or lacunarity could have important role in differentiation of metastatic NETs from colorectal cancer. We also expect that results obtained with fractal analysis will help us predict the degree of tumor differentiation, the course of treatment and patients survival.

Acknowledgments:

MeSH/Keywords: neuroendocrine tumors, colorectal carcinoma, fractal analysis, lacunarity, CT images

Poster code: T-B-9-57

PROTEIN ADAMTS4 AS A NOVEL BIOMARKER IN CHRONIC KIDNEY DISEASE

PhD candidate: Ivana Kovačević Vojtušek, MD

PhD Thesis: Protein ADAMTS4 as a novel biomarker in chronic kidney disease

Mentor/s: Associate professor Lovorka Grgurević,MD, PhD, Assistant professor Mario Laganović, MD, PhD

Affiliation: University of Zagreb, School of medicine, University hospital centre Zagreb

Introduction: Chronic kidney disease (CKD) is characterized by progressive loss of kidney function, leading to end stage renal disease (ESRD). Progressive tubulointerstitial fibrosis is the final common pathway for all CKDs. Therapeutic interventions aiming to reverse kidney fibrosis have been unsuccessful until now. ADAMTS 4 is a member of ADAMTS proteases family, capable of binding to extracellular matrix components. In animal study ADAMTS4 was correlated with kidney function.

Hypothesis: We hypothesize that ADAMTS4 is a novel biomarker of CKD, which correlates with disease progression and histological parameters for kidney fibrosis.

Aims: The primary aim of the study is to detect ADAMTS4 in blood and urine of patients (pts) in different stages of CKD, including pts with ESRD on hemo- and peritoneal dyalisis and kidney transplant pts. Second aim is to correlate ADAMTS4 blood concentration with kidney fibrosis parameters.

Materials and methods: Total of 135 pts in 5 stages of CKD, including 30 pts with kidney transplant will be enrolled in the study after signing informed consent. 15 health volunteers will be enrolled as a control group The presence of ADAMTS4 in blood and urine will be detected by proteomic analysis and protein concentration will be determined by solid-phase enzyme immunoassay. Histological parameters of fibrosis will be analyzed in kidney biopsy samples of pts with clinical indication for the procedure. Statistical analysis of the data will be done in SPSS v.23 (IBM Corp.,SAD). The investigation is approved by Hospital and University ethical committees.

Expected scientific contribution: If ADAMTS 4 protein emerged as a new biomarker of CKD, correlated with the disease progression or an uremic toxin, new therapeutic intervention can be developed, including invention of ADAMTS 4 antibodies.

Acknowledgments: I would like to thank Marijana Čorić and Stella Bulimbašić for patohistological analyses

MeSH/Keywords: Chronic kidney disease, ADAMTS 4

Poster code: T-B-9-59

ASSOCIATION BETWEEN CXCL9 AND CXCL10 GENE POLYMORPHISMS AND ACUTE GRAFT REJECTION AFTER LIVER TRANSPLANTATION

PhD candidate: Ana Ostojić, MD

PhD Thesis: Association between CXCL9 and CXCL10 gene polymorphisms and acute graft rejection after liver transplantation

Mentor/s: Assistant Professor Anna Mrzljak, MD, PhD and Assistant Professor Tomislav Kelava, MD, PhD

Affiliation: School of Medicine, University of Zagreb and University Hospital Merkur, Zagreb

Introduction: Despite the improvement and optimization of the immunosuppression protocols, an acute cellular rejection (ACR) is still a frequent complication after liver transplant (LT). ACR is a result of an immune response in which cytokines, including chemokines CXCL9 and 10, have a pivotal role. It is established that certain single nucleotide polymorphisms (SNP) of previously mentioned chemokines genes have a predictive role in some infective and autoimmune diseases; however their role in ACR after LT has not been elucidated.

Hypothesis: CXCL9 and CXCL10 gene polymorphisms are associated with acute cellular rejection after liver transplant in patients with alcoholic liver disease (ALD).

Aims: Our aim is to analyze the association between CXCL9 and CXCL10 SNPs and biopsy-proven acute cellular rejection. This study will determine the frequency of SNPs of CXCL9/10 in patients transplanted for ALD, and explore their relationship with the grade of ACR according to Banff criteria, number of ACR episodes, ACR time frame after LT and relevant clinical and laboratory parameters.

Materials and methods: The study will enroll 250 patients transplanted for ALD. Apart from alcohol-induced cirrhosis, all other causes of liver disease were excluded, including patients with previous solid organ transplantations. Episodes of ACR are defined as biopsy-proven, Banff score =3 within first 6 months after LT. In case of multiple ACR episodes, ACR with the highest Banff grade will be evaluated. Sera of 250 patients will be collected to determine SNPs for CXCL9 (rs10336) and CXCL10 (rs3921 and rs8878) using PCR. Clinical and laboratory data will be collected for all study patients. Statistical analysis will be performed by SPSS v19, $p < 0.05$ will be considered statistically significant.

Expected scientific contribution: CXCL9 and CXL10 single nucleotide polymorphisms may increase the reliability in assessment of ACR after LT and could serve as non-invasive genetic biomarkers. Those biomarkers could be used to individualize risk stratification and immunosuppression adjustment in order to prevent or minimize ACR after liver transplantation.

Acknowledgments:

MeSH/Keywords: acute cellular rejection, liver transplantation, gene polymorphisms, chemokines

Poster code: T-B-9-68

END-STAGE CHRONIC KIDNEY DISEASE IN ROMA ETHNICITY

PhD candidate: Ema Ivandić

PhD Thesis: Roma ethnicity is connected to younger age for development of end-stage renal disease, worse outcome during renal replacement therapy and kidney transplantation as well as worse outcome after kidney transplantation compared to general population.

Mentor/s: prof. dr. sc. Nikolina Bašić Jukić

Affiliation: Department of nephrology, arterial hypertension, dialysis and transplantation, University hospital centre Zagreb

Introduction: The Roma population is the largest ethnic minority group in Europe and includes around 10-12 million people. 16975 Roma people live in Croatia according to the last census. Scientific community has started examining that population for the last few years because of a higher cardiovascular mortality in this group compared to the general population, which is partially explained by higher presence of risk factors such as arterial hypertension, diabetes, metabolic syndrome and obesity. Data about prevalence of end-stage renal disease in this group is limited. Some studies have shown that chronic kidney disease is three times higher in Roma people compared to the general population. Besides that, Roma people start renal replacement therapy (RRT) with dialysis up to 10 years earlier if compared to general population. Renal transplantation in this group is very challenging due to higher morbidity with functional grafts compared to general population.

Hypothesis: Roma ethnicity is connected to younger age for development of end-stage renal disease, worse outcome during RRT and kidney transplantation as well as worse outcome after kidney transplantation if compared to general population.

Aims: To establish the prevalence of end-stage renal disease in Roma people and their morbidity and mortality during RRT, as well as the peri and post transplantation period. To determine the average age when end-stage renal disease develops, causes of renal failure and comorbidities. To analyse post-transplantation course, proportion of acute and chronic graft dysfunction and their loss, as well as specific causes of death after kidney transplantation.

Materials and methods: Collect data about percentage of Roma people receiving RRT in Croatian dialysis centers as well as percentage of patients who had kidney transplantation with a specifically designed questionnaire. Analyze the data to determine the start of RRT, determine the cause of kidney failure, complications during RRT, incidence of graft dysfunction (acute and chronic), reaching and maintaining immuno-suppression level, causes of death during RRT and after transplantation. Finally, compare the data with general population.

Expected scientific contribution: This research will facilitate better understanding of the causes of morbidity and mortality in Roma people and will help steer the interventions in order to decrease the risks which are present in this population.

Acknowledgments:

MeSH/Keywords: Roma people, end stage renal disease, renal replacement therapy, renal transplantation

Poster code: T-B-9-74

USE OF TRANSABDOMINAL DYNAMIC COLOUR DOPPLER ULTRASOUND AND STRAIN ELASTOGRAPHY IN THE DETECTION OF COLON CANCER AT DIFFERENT STAGES (DUKES' A-D)

PhD candidate: Nives Tarle Bajić,MD

PhD Thesis: Compare transabdominal colour Doppler ultrasound and strain elastography in the detection of colon cancer

Mentor/s: Professor Nadan Rustemović, MD, PhD

Affiliation: Private Family medicine practice Petrinjska 52 Zagreb Croatia, Department of Gastroenterology and Hepatology, Endoscopy Unit, University Hospital Centre Zagreb, Kispaticeva 12, 10000, Zagreb, Croatia

Introduction: This research aims to present new possibilities for the diagnosis of colon cancer by demonstrating reproducibility of transabdominal colour Doppler ultrasound (TCDU) and strain elastography.

Hypothesis: Transabdominal ultrasound imaging of colon cancer appears markedly different in B-mode and strain elastography, as do differences in vascular flow in the cancer-affected colon wall at different stages (Duke's A-D).

Aims: The objective of this paper is to present colon cancer in B mode, compared with the strain elastography, and then measuring the vascular flow in cancer affected colon wall through TCDU.

Materials and methods: This retrospective-prospective study will include patients whose colon cancer was detected through B-mode and strain elastography and confirmed by colonoscopy. When colon cancer was not detected in colonoscopy, MRI (magnetic resonance imaging) or MSCT (multi-slice computed tomography) were used. The study excluded all patients whose diagnosis of colon cancer was not confirmed. Following the power analysis of the author's previous research "Use of colour Doppler ultrasound in the detection of colon cancer" (Tarle Bajic N., Bajic I., 2014), which was presented at the Annual Congress of the British Institute of Radiology in London, this study will include 120 subjects, 30 per each cancer stage. The first step will be to establish colon cancer in B-mode and to compare in strain elastography. After identifying colon cancer, measure vascular flow in the cancer-affected wall of the colon and spectral analysis will be used. Measurements of vascular flow using three parameters – PSV (peak systolic velocity m/s), EDV (end diastolic velocity m/s) and RI (resistance index) will be compared and analysed to determine whether there is a significant difference at Duke´s stages (A-D). Stages of colon cancer will become known postoperatively.

Expected scientific contribution: Expected proof of significant differences in quantitative Doppler parameters (PSV, EDV and RI) at different stages (Duke's A-D), could prove useful of Doppler ultrasound and strain elastography in a staging of colon cancer and extraluminal colon cancer (GIST), which are not visible through colonoscopy.

Acknowledgments: I thank to Professor Rustemović for his great help

MeSH/Keywords: transabdominal colour Doppler ultrasound of colon cancer, strain elastography of the colon cancer,

Poster code: T-B-9-76

MITOCHONDRIAL QUALITY CONTROL DISORDER IN PATIENTS WITH HEART FAILURE

PhD candidate: Tomo Svaguša

PhD Thesis: Mitochondrial quality control disorder in patients with heart failure

Mentor/s: Filip Sedlić

Affiliation: University of Zagreb, Faculty of Medicine

Introduction: Despite the high incidence and prevalence of heart failure little is known about it cause, which is reflected in the inability of the target therapeutic effect. Heart failure is a consequence of the molecular, structural and functional disorders of the myocardium that reduces cardiac function. The heart is rich in mitochondria. Each mitochondria is associated with other mitochondria in a way to make the mitochondrial network. Normal functioning of the mitochondrial network is vital for every cell because any deviation can lead to extreme production of toxic products (free radicals) that can lead to the cell death. Therefore, quality control of mitochondria within the mitochondrial network is a major regulatory mechanism of normal mitochondrial function.

Hypothesis: Heart failure is associated with mitochondrial quality control disorder of which is reflected by changing the expression of genes whose products participate in this process.

Aims: The aim of this study is to compare the mitochondrial quality control in myocardium with and without signs of heart failure.

Materials and methods: In patients who are recipients of heart in heart transplant procedure, samples would be taken from the failing heart which is removed. In the study we would use samples of heart tissue that represent biological waste, directly after removal of the heart and after taking the sample for histopathological analysis. Samples of healthy heart tissue, with no significant cardiac pathology, would obtain in the organs explantation process from organ donors, in a situation where it is established that the heart can't be used for transplantation solely for medical reasons or technical reasons, or lack of a suitable recipient. Several mitochondrial genes group would be analyzed in study by PCR: genes involved in proteostasis, mitochondrial fission and fusion, mitophagy and transport of peptide/protein through the mitochondrial membrane. Genes that would be observed are:YME1L1, OMA1, OPA1, HSPA9, HSPD1, HSPE1, EIF2AK4, LONP1, UBL5, eIF2, HTRA2, DDIT3, CEBPB, JUN, SPG7, mTOR, MFN2, DAPK2, MAP1LC3B, TIMM44, TIMM17A, TIMM17B, TIMM23, FOS, TIMM22, TIMM9, TIMM10, park2, PINK1, parl, RHOT1, BECN1, MAP1LC3A, BNIP3, BNIP3L, FUNDC1, LAMP2, ULK1, PAM16, TPCN1, TPCN2, PPARGC1A, SIRT1.

Expected scientific contribution: The scientific contribution of this study is to better understand the pathogenesis of heart failure in people. The difference in the expression of genes could reveal possible disorders that are responsible or involved in the pathogenesis of heart failure in people.

Acknowledgments: none

MeSH/Keywords: mitochondria, gene expression, heart failure, heart transplantation

Poster code: T-B-9-117

COMBINED DEVICE THERAPY FOR ADVANCED HEART FAILURE

PhD candidate: Nina Jakus, MD

PhD Thesis: Combined device therapy for advanced heart failure

Mentor/s: Assist. prof. Maja Cikes, MD, PhD

Affiliation: University of Zagreb School of medicine, UHC Zagreb, Zagreb, Croatia

Introduction: Heart failure (HF) is a growing concern due to the increasing age of the population and extensive modalities of treatment of cardiovascular disease, partially leading to chronic HF. Treatment options in advanced HF include devices such as ventricular assist devices (VAD), implantable cardiac defibrillators (ICD), cardiac resynchronization therapy (CRT) and heart transplantation. As HF is characterized by its progressive course, more than one treatment modality is often utilized simultaneously in the same patient. The survival benefit of each device alone is well documented, but little is known about combined device therapy.

Hypothesis: Advanced heart failure treated by LVAD implantation might require additional device (ICD/CRT) implantation in a subset of patients. Combined device therapy may improve outcomes in a selected population of patients. Cardiac resynchronization therapy might provide additional clinical benefit to patients with LVADs. ICD implantation and/or generator replacement in LVAD carriers might reduce total mortality.

Aims: The aim of the study is to obtain better insight to outcomes of combined treatment strategies in advanced HF patients through a European network of HF centres.

Materials and methods: This observational study will include 250 patients with advanced HF, treated by implantation of an LVAD and/or CRT/ ICD. Patients will undergo an echocardiographic examination, laboratory testing and quality of life assessment, before and 6 months after the time of the last device implantation, as well as an assessment of outcomes during 1 year.

Expected scientific contribution: The results of this study should aid in creating clinical recommendations/guidelines regarding ICD/CRT/CRT-D implantations in LVAD recipients, as well as provide guidance on device (de-)activation, potential upgrades or battery replacement strategies in patients receiving an LVAD, that are already implanted with an ICD/CRT/CRT-D device, thus filling the current gap in knowledge on the matter. Results of this study could carry great practical implications in every day treatment of this growing patient population.

Acknowledgments:

MeSH/Keywords: Advanced heart failure, cardiac resynchronization therapy, implantable cardioverter defibrillator, left ventricular assist device.

Poster code: T-B-9-122

THERMAL CHANGES DURING HEALING OF CLAVICLE IN CHILDREN

PhD candidate: Filip Jurić, MD

PhD Thesis: Thermal changes during healing of clavicle in children

Mentor/s: Professor Anko Antabak, MD, Phd

Affiliation: Children's hospital Zagreb

Introduction: Bone can heal in two ways: primary or direct heling and secondary or indirect healing. Primary healing occurs when the fracture ends are anatomically reduced without any gap between and fracture parts are fixed with stable osteosynthesis. Secondary healing of bone occurs when these conditions are not met. It is the most common way of bone healing. Indirect bone healing consists of four phases: inflammation, soft callus formation, hard callus formation and remodeling.

Hypothesis: During the inflammation phase of bone healing blood flow is increased because of angiogenesis and the temperature of the surrounding tissue rises. As the callus is formed, the blood flow will decrease and therefore the temperature. With the formation of stable callus, the temperature should drop to normal values.

Aims: The general aim of this study is to determine temperature changes during the healing of the fractured clavicle compared to the healthy side. The temperature changes will also be compared with findings on the ultrasound to determine the connection between temperature change and callus formation.
The specific aim of this study is to determine correlation between temperature change and callus formation process.

Materials and methods: Prospective study of children with clavicle fracture will be conducted. The study will include at least 50 children aged between 1 and 18 years of both genders. The temperature of the skin above both clavicles will be measured with Keysight TrueIR U5855A thermal camera. Thermographic measurements will be performed in the same room with constant climate. Skin temperature above fractured and healthy side will be compared. Ultrasonographical imaging of fracture will also be performed with every thermographic measurement to determine callus formation. Each patient will be measured at 4th, 8th, 15th and 22nd day after trauma. The collected data will be statistically analyzed.

Expected scientific contribution: This study should determine difference and dynamics of temperature in the fractured clavicle. It should also determine connection between temperature change and callus formation. Possible clinical benefit of the study could be the use of IR thermography as a diagnostic non-invasive method for determination of stable callus formation instead of radiography which is used today. This is especially significant in children because it could reduce number of necessary x-ray images during follow up.

Acknowledgments:

MeSH/Keywords: thermography, clavicle fracture, pediatric,ultrasonography

Poster code: T-B-10-21

DETERMINING ANATOMICAL RELATIONS OF POSTERIOR FOSSA AND CRANIOCERVICAL JUNCTION IN PATIENTS WITH CHIARI MALFORMATION TYPE ONE

PhD candidate: Petra Barl, MD

PhD Thesis: Determining anatomical relations of posterior fossa and craniocervical junction in patients with Chiari malformation type one

Mentor/s: Professor Josip Paladino, MD, PhD

Affiliation: Clinic of Neurosurgery, University Hospital Center – Zagreb, University of Zagreb School of Medicine, Croatia

Introduction: Chiari I malformation is a well known clinical entity frequently amenable to surgical treatment. The descent of cerebellar tonsils toward the foramen magnum presents a morphological problem.

Hypothesis: Anatomic relationships of bone structures of the skull base and the position of the anatomical structure of the brain stem, medulla and cerebellum have been changed in patients with Chiari I malformation compared to healthy population due to the difference in the interconnection and the corners of the skull base and clivus causing disturbance in the foramen magnum.

Aims: The objective was to investigate the anatomical relationships skull base and brain structure (cerebellar tonsils, brain stem) with bone structures (clivus, occipital bone, anatomical structures of the spine, Atlas, Axis).

Materials and methods: The study will include patients in whom the magnetic resonance (MR) demonstrated Chiari I malformation (n = 30) and control group (N = 200) with normal MR of endocranium and craniocervical junction. To analyze the mediosagittal, coronary and transverse images of endocranium and craniocervical junction with magnetic resonance in different sequences of recording.

Expected scientific contribution: To explain the contributions of angulation of the skull base to the interface between the bone structure and the posterior fossa and foramen magnum towards the medulla and cerebellar structures and explain the causes of Chiari I malformation. Better knowledge of anatomical structures and their relations will contribute to choosing the best surgical procedure to solve the problem and extent of surgery.

Acknowledgments:

MeSH/Keywords: Chiari I malformation, magnetic resonance, posterior fossa, craniocervical junction, foramen magnum, clivus

Poster code: T-B-10-31

THE IMPACT OF THE ABSORBABLE AND NON-ABSORBABLE INTRADERMAL SUTURE ON POSTOPERATIVE SCAR FORMATION

PhD candidate: Matija Miletić

PhD Thesis: The impact of the absorbable and non-absorbable intradermal suture on postoperative scar formation

Mentor/s: prof. Zdenko Stanec, MD, PhD.

Affiliation: University Hospital Dubrava. Department of plastic, reconstructive and aesthetic surgery

Introduction: The thesis will examine the impact of 2 type of sutures that we use in closing the operative wound in intradermal continuous fashion on later scar appearance. Surgical incisions are from 10 to 30 cm in diameter including mastectomies, abdominoplasties and other larger incisions on the front side of the thorax and abdomen. Each half of it will be closed by different suture, one absorbable, and the other non-absorbable. The scar will be analysed in regular intervals.

Hypothesis: Intradermal suturing using absorbable and non-absorbable material do not show any difference in scar formation.

Aims: To determine which suture is more supreme for good aesthetic result on postoperative incisions on the front side of the thorax and abdomen.

Materials and methods: Here we talk about randomized controlled study. Among 30-50 patients who undergo the operation in general endotracheal anesthesia on the front side of the thoracic and abdominal wall, we will examine the quality of scar formation in regular intervals. The subcutaneus tissue will be closed with polyglactin 910 4-0 with interrupted suture technique and dermal layer will be closed using intradermal continuos fashion with glycolide dioxanone trimethylene carbonate 3-0 and polypropylene 3-0. Subcutaneus layer of the whole incision will be closed with polyglactin 910 4-0 and one half of dermal incision will be closed with glycolide dioxanone trimethylene carbonate 3-0 and the other half with polypropylene 3-0. Skin will be disinfected with 70% medical alcohol and sterile cotton swabs will be placed on the wound. Non-absorbable dermal suture will be extracted on 14th postoperative day. The scar will be evaluated using Vancouver scar scale by 3 other surgeons in my department in regular intervals. Follow up is one year. Patients in this study are selected by age (from 30-50 years), localisation of operation, BMI and diameter of incision. Criteria for exclusion are wound dehiscence, autoimmune diseases, connective tissue diseases, cheloid formation and diabetes type 2. Postoperative wound treatment after 14th day of surgery include using of unique neutral creme for each patient.

Expected scientific contribution: To determine optimal usefull suture (monofilament non-absorbable polypropylene or absorbable glycolide dioxanone trimethylene carbonate) which is ideal for closing postoperative incisions on the front of thoracic and abdominal wall in goal of supreme aesthetic result, price and quality of suturing material and aspect of economity.

Acknowledgments: prof. Zdenko Stanec, MD, PhD, prof. Rado Žic, MD, PhD, prof. Davor Mijatović, MD, PhD, doc. Krešimir Bulić, MD, PhD.

MeSH/Keywords: suturing material, operative incision, scar, polypropylene, glycolide dioxanone trimethylene carbonate.

Poster code: T-B-10-91

PREDICTING FACTORS FOR ANASTOMOTIC DEHISCENCE IN COLON RESECTION SURGERY

PhD candidate: Bojan Kljaić, dr.med.

PhD Thesis: Predicting factors for anastomotic dehiscence in colon resection surgery

Mentor/s: prof.dr.sc. Žarko Rašić, dr.med, doc.dr.sc. Višnja Nesek Adam, dr.med.

Affiliation: Klinika za kirurgiju KB Sveti Duh Zagreb, Klinika za anesteziologiju i intenzivno liječenje KB Sveti Duh Zagreb

Introduction: The large bowel, also called the large intestine, is a part of the digestive system. It runs from the small bowel to the rectum, which receives waste material from the small bowel. Its major function is to store waste and to absorb water from waste material. It consists of the following sections, any of which may become diseased: the cecum, the ascending colon, the transverse colon, the descending colon, the sigmoid colon, and the rectum. Colon resections (colectomies) are surgical procedures in which all or part of the large intestine is resected. The remaining portions of the colon are then connected, usualy by a mechanical stapler. Colon resections are performed to treat and prevent diseases and conditions that affect the colon, one of those being colon cancer. Colon resections are among the more common procedures performed in abdominal surgery, and like all surgical procedures include some complications that can occur. Those complications can be divided into intraoperative and postoperative complications. Most postoperative complications include wound infection, anastomotic dehiscence, ileus and bleeding.

Hypothesis: Our hypothesis is that there will be a statistically relevant conection between anastomosic dehiscence and various patient and operative factors.

Aims: The aim of this study is to assess the conections between anastomosic dehiscence and various patient and operative factors.

Materials and methods: Patients who had undergone a resection of a large bowel segment with an anastomosis performed by a mechanical stepler between October 2016 and October 2017 will be identified. Patients will be devided in two groups, those whose anastomosis functioned as intended, and those who suffered anastomosis dehiscence in the follow-up period (4 weeks postoperatively). Patient factors and surgical factors will be analised, evaluated, and compared between these two groups of patients.

Expected scientific contribution: To our knowledge such a study has not been performed in our institution or even in Croatia, and this study has great significance to the further mode of treating patients with an operative resection of the colon. By obtaining clear data on the significance and impact of the examined factors in the formation of dehiscence we can give our patients better health intreventions and care, and have the opportunity to reduce the morbidity and mortality associated with surgery resection of the colon.

Acknowledgments: I would like to thank my mentors and colleagues.

MeSH/Keywords: Anastomotic dehiscence, Colon cancer, Colon resection, Risk factors.

Poster code: T-B-10-60

INFLUENCE OF IMPLEMENTING THE ARTIFICIAL CERVICAL INTERVERTEBRAL DISC ON THE BIOMECHANICS OF THE CERVICAL SPINE

PhD candidate: Ivan Domazet

PhD Thesis: Influence of implementing the artificial cervical intervertebral disc on the biomechanics of the cervical spine

Mentor/s: Prof. Miroslav Vukic, MD, PhD

Affiliation: Department of Neurosurgery, University Hospital Centre Zagreb

Introduction: Implantations of the artificial cervical intervertebral disc (arthroplasty) came into use as a modern method of treatment of cervical spine diseases at the beginning of this century. When performing cervical arthroplasty the artificial cervical disc is implanted in the intervertebral space after discectomy. The advantage of arthroplasty is in sustaining the mobility of functional spinal unit.

Hypothesis: The hypothesis of this study is that the artificial cervical disc implantation increases the range of motion of the operated cervical spine, comparing radiographically measured range of motion of cervical spine before and after surgery.

Aims: The objective of this study is to define the influence of the arthroplasty on the biomechanics of the cervical spine.

Materials and methods: This study is currently being performed at the Department of Neurosurgery, University Hospital Centre Zagreb. The participants of this study will be divided in two groups. The group of patients who underwent cervical arthroplasty will be consisted of 25 patients who were operated at the Department of Neurosurgery, University Hospital Centre Zagreb in the time period between August 2011 and May 2014. The control group will be consisted of 25 healthy volunteers. Static and dynamic cervical radiographs of patients that had cervical arthroplasty because of one-segmental cervical disc herniation are going to be compared with the cervical radiographs of the same patients before the surgery, and with the radiographs of the control group. The range of motion of the cervical spine will be calculated after the computer analysis of the static and dynamic cervical radiographs.

Expected scientific contribution: We expect to define the influence of the cervical arthroplasty on the range of motion of the cervical spine.

Acknowledgments:

MeSH/Keywords: Arthroplasty, Cervical spine, Range of motion

Poster code: T-B-10-64

FECAL INCONTINENCE AFTER ANTERIOR RECTAL RESECTION

PhD candidate: Branko Bakula, MD

PhD Thesis: The impact of colorectal anastomosis hight on anorectal function after anterior resection

Mentor/s: Žarko Rašić, MD, PhD, Dragan Jurčić, MD, PhD

Affiliation: University of Zagreb School of Medicine, Clinical Hospital Sveti Duh, University of Osijek School of Medicine, Clinical Hospital Sveti Duh

Introduction: Anterior resection of rectum is a standard surgical procedure for treating malignant tumors of rectum and rectosigmoid junction. Postoperatively, many patients who undergo the anterior resection procedure present with increased daily bowel movements, urgency for defecation, and a variable degree of incontinence. These symptoms that were just described define the "anterior resection syndrome". Clear pathophysiological mechanism is still not completely clear. Anorectal manometry is an objective means of assessing the resistance to spontaneous defecation provided by the anorectal sphincter mechanism and the sensory capabilities of the rectum to provide a feeling of imminent defecation.

Hypothesis: The hight of colorectal anastomosis has a significant influence on postoperative fecal incontinence in patients with anterior rectal resection for cancer.

Aims: The aim of the study is to evaluate clinically and manometrically patients with anterior rectal resection.

Materials and methods: Our prospective study will include all patients of our department with histologically proven operable adenocarcinoma of rectum or rectosigmoid junction that are scheduled for anterior resection procedure. Preoperative diagnosis will be proven by colonoscopy, pathohistological examination and abdominal MSCT. Patients with major postoperative complication like anastomosis dehiscence, intraabdominal abscesses or haematoma formation will be excluded from the study. Patients with preoperative problems with continence will also be excluded from study. Participants will undergo procedure of standard anterior rectal resection with formation of anastomosis with circular stapling device (29-31mm). Oncologic principles like central ligation of inferior mesenteric artery and total mesorectal excision will be followed. Six months after surgery patients will be readmitted to evaluate fecal continence status. Clinical parameters of incontinence will be gathered by standard questionnaires for fecal incontinence (Jorge-Wexner Incontinence score) and anterior resection syndrome. Objective parameters of anorectal dysfunction will be tested by manometry of anorectum. After all results are gathered we will divide our patients in groups according to distance of anastomosis from anal verge measured with rigid rectoscope and analyze the impact of anastomosis hight on level of anorectal disfunction.

Expected scientific contribution: During our research we plan to clarify pathophysiological mechanisms of anorectal dysfunction in patients with anterior rectal resection.

Acknowledgments:

MeSH/Keywords: rectal resection, incontinence, anal manometry

Poster code: T-B-10-81

INFLUENCE OF PERIOPERATIVE NORMOXEMIA ON NEUROCOGNITIVE OUTCOME AFTER CORONARY ARTERY BYPASS GRAFTING

PhD candidate: Marko Borojević

PhD Thesis: Influence of perioperative normoxemia on neurocognitive outcome after coronary artery bypass grafting

Mentor/s: doc.dr.sc. Bojan Biočina

Affiliation: University Hospital Centre Zagreb, Department of Cardiac Surgery

Introduction: Oxygen in certain medical conditions (critical illness) saves lives, but used in high concentrations can be toxic. Hyperoxia while performing cardiac surgical procedure and immediately after in the intensive care unit is a daily routine practice. Conditions of high partial pressure of oxygen (PaO 2) and activation of systemic inflammatory response as consequences of extracorporeal circulation application lead to extremely large oxidative stress. Creation of significant quantities of free radicals causes dysfunction and organe damage. The brain is particularly sensitive in such conditions.

Hypothesis: Normoxemia (P02 10-15kPa) during the perioperative period of cardiac surgery procedures provides better neurocognitive outcome.

Aims: The primary outcome of the research is to determine witch PO2 target value (normoxemia vrs. hyperoxemia as a standard routine 25-30kPa) during cardiac procedures provides better neurocognitive outcome. The secondary outcomes are determination of end organ damage, evaluation of oxidative stress on lipid peroxidation, neurological injury and inflamation and evalution of quality of life.

Materials and methods: In order to achieve neurocognitive outcome we will conduct neurocognitive testing before and on the seventh postoperative day after cardiac surgery. In our previous research incidence of neurocognitive damage amounted to 53% at the seventh postoperative day. For the purpose of proving the difference in reducing the incidence of neurocognitive damage from 50% to 30% it is the necessary to include 75 subjects per group, with a power of 80% o and $\alpha = 0.05$. The impact of oxidative stress on lipid peroxidation, neurological damage and inflammation will be estimated by measuring concentration of specific biomarkers in cerebrospinal fluid (S100, NSE, IL-6, IL-10, isoprostanes). Assessment of quality of life will be done with questionnaire SF-36 before and 6 months after surgery.

Expected scientific contribution: Oxygen is one of the most frequently used drugs in the hospital practice. While the risks associated with hypoxia are well known, there is growing concern that also hyperoxia may cause harmful effects on a complete organism, especially the brain, which is one of the most vulnerable organs. Therefore, ensuring adequate target value of the partial pressure of oxygen is one of the priorities of good clinical practice.

Acknowledgments:

MeSH/Keywords: oxygen tension, cardiac surgery, neurocognitive decline

Poster code: T-B-10-85

YOGA IN RHEUMATOID ARTHRITIS

PhD candidate: Silva Pukšić, MD

PhD Thesis: Impact of yoga on health-related quality of life and markers of inflammation in rheumatoid arthritis patients

Mentor/s: Professor Jadranka Morović Vergles, MD, PhD

Affiliation: Division of Clinical Immunology, Allergology and Rheumatology, Department of Internal Medicine, University Hospital Dubrava, University of Zagreb School of Medicine

Introduction: Rheumatoid arthritis (RA) is a chronic disabling inflammatory disease that substantially impacts health-related quality of life (HRQOL) of patients. In addition to pain, fatigue and physical disability the disease also affects psychological health. Yoga, a mind-body therapy, integrates physical exercises with relaxation and meditation. Published data suggest its beneficial effects on both physical and mental health in various chronic conditions. The true biological mechanism underlying these effects is not well known. Recent research suggests potential modulation of the immune system and inflammation-related gene expression changes.

Hypothesis: Yoga program based on Yoga in daily life system has positive impact on clinical and biologic outcomes in RA patients.

Aims: To determine the impact of a 12-week yoga program on measures of psychological distress, HRQOL, fatigue, pain, disease activity, levels of circulating inflammatory markers and proinflammatory gene expression.

Materials and methods: 50 RA patients, aged 18-65 years, on stabile standard pharmacological treatment will be randomly assigned to a 12-week yoga intervention or arthritis-education control. Yoga classes will be conducted 2xweekly/ 90 minutes and consist of physical exercises (asanas), breathing exercises (pranayama), relaxation and self-enquiry meditation based on Yoga in daily life system. Arthritis-education classes will be conducted 1xweekly/ 120 minutes and consist of lectures on arthritis and related issues followed by group discussion. Self-administered questionnaires will be used to assess quality of life (SF-36), depressive symptoms and anxiety (HADS), fatigue (FACIT-F), RA impact of the disease (RAID), perceived stress (PSS), and pain (VAS). Blood samples will be collected for measurement of CRP and hsCRP and RT-PCR analysis of expression of 5 proinflammatory genes (IL-1β, IL-6, TNFα, NFκB1, RELA). Disease activity will be assessed by DAS28CRP score. Baseline, post-treatment and 3 month follow-up assessment will include questionnaires, DAS28CRP and hsCRP measurement and baseline and post-treatment only for genomic analysis.

Expected scientific contribution: This research will provide information on potential efficacy of yoga program in improving physical and psychological outcomes in persons with RA and explore its influence on immunological system. If proved effective this intervention could be used as complementary nonpharmacological method in management of RA patients aimed at promoting their physical and psychological health.

Acknowledgments:

MeSH/Keywords: rheumatoid arthritis, yoga, gene expression, inflammation, health-related quality of life

Poster code: T-B-14-47

CLINICAL FEATURES OF PATIENTS WITH RHEUMATOID ARTHRITIS AND ATRIAL FIBRILLATION

PhD candidate: Melanie-Ivana Čulo, MD

PhD Thesis: Correlation between chronic systemic inflammation and development of FA

Mentor/s: Professor Jadranka Morović Vergles, MD, PhD

Affiliation: University Hospital Dubrava, University of Zagreb School of Medicine, Department of Internal Medicine, Division of Clinical Immunology, Allergology and Rheumatology, Avenija Gojka Šuška 6, 10 000 Zagr

Introduction: Atrial fibrillation (FA) is the most common sustained arrhythmia in clinical practice strongly correlated with cardiovascular diseases (CVD). There are lot of known risk factors for development of FA and recently, new studies have shown that systemic inflammation is also independent risk factor for development and maintenance of FA. Histological studies have shown the presence of inflammation in atrium of patients and experimental animals with FA. Many studies have also shown the positive correlation between CRP, IL-6 and TNFα levels with development and maintenance of FA. Rheumatoid arthritis (RA) is a chronic sistemic inflammatory disease that primarily affects joints. The cytokines involved in development and maintenance of RA are TNFα, IL-1, IL-2, IL-6, IL-17 etc. It is well known that cardiovascular morbidity and mortality are significantly increased in RA patients and RA is independent risk factor for development of CVD since 2009. For that reason patients with RA may have an increased risk for development of FA. Recent data have shown the importance of systemic inflammation in pathogenesis of FA. If the systemic inflammation is one of the risk factors of FA, patients with chronic systemic diseases might have an increased risk for development of FA regardless of CVD. Having this in mind, development of FA in RA patients could be the consequence of increased prevalence of CVD in RA and consequence of direct effect of chronic systemic inflammation. Two main conducted studies showed the opposite results. The cohort study conducted by Lindhardsen et al. showed that patients with RA have 40% increased risk for development of FA while Kim et al. showed that patients with RA don't have an increased risk for development of FA.

Hypothesis: Positive correlation between disease activity in patients with rheumatoid arthritis measured by DAS28CRP and atrial fibrillation.

Aims: To determine the prevalence of FA in patients with RA and in patients with osteoarthritis (OA). To asses the correlation of FA and RA disease activity measured by DAS28CRP.

Materials and methods: Multicenter, cross-sectional study on group of patients with RA and OA with existing database from our Clinic. Data includes 627 patients with RA and 352 with OA. All patients have EKG recorded, measured CRP levels, noted comorbidities and demographic data and measured DAS28CRP.

Expected scientific contribution: This study will help to determine the prevalence of FA in RA and OA patients in Croatia and will establish if FA is positively correlated with RA disease activity.

Acknowledgments:

MeSH/Keywords: Atrial fibrillation, rheumatoid arthritis, cardiovascular disease, proinflammatory cytokines, osteoarthritis

Poster code: T-B-14-67

THE IMPACT OF IODINE INTAKE ON FUNCTIONAL PARAMETERS OF THE THYROID IN PREGNANT WOMAN

PhD candidate: Vedrana Gladić Nenadić, MD

PhD Thesis: The impact of iodine intake on functional parameters of the thyroid in pregnant woman

Mentor/s: Asst.Prof.Tomislav Jukić, MD,Phd

Affiliation: University Hospital Center Sestre milosrdnice

Introduction: According to the recommendations of the WHO/ICCIDD /UNICEF optimal daily intake of iodine in pregnant women is 250 mg,corresponding to the concentration of iodine in the urin(UIC)between 150 and 249 g/L.Studies have shown that even in the countries with longtime programs of USI,there is always a proportion of pregnant women who have insufficient iodine intake.The American Thyroid Association (ATA) issued a recommendation that all women during pregnancy need to take supplements rich in iodine at a dose of 150 mg per day.However,these recommendations are not routinely accepted in practice.Epidemiological studies conducted in 2009 Croatia has shown that a significant number of pregnant women had a median UIC below the recommended level of 150μg/L,suggesting insufficient iodine intake.Therefore,further research are needed to assess whether there is a need for additional iodine intake in pregnant women.

Hypothesis: Pregnant women not taking supplements iodine have lower values of the urine iodine concentration and thyroxine, and higher values of thyrotropin, thyroglobulin and thyroid volume.

Aims: 1.Identify whether there is a significant difference between the studied parameters in test groups and the importance of including these parameters in routine control during pregnancy. 2.To determine whether pregnant women in tested area should take preparations rich in iodine

Materials and methods: The research will include 2 groups healthy pregnant women in the 1,.2.,and 3.trimester of pregnancy. 1. Pregnant woman who do not take supplements containing iodine; 2. Pregnant woman who take supplements containing iodine. The research includes: 1. Questionnaire with medical history information about previous pregnancies, complications of pregnancy, delivery, personal history of previous thyroid disorders and severe disease, family history of thyroid disease, drug therapy, dietary supplements with iodine and eating habits and iodized salt. 2. Ultrasound examination of the thyroid to determine thyroid volume 3. Sampling urine to determine UIC modifying the method of Sandell-Koltoff 4. Collection of blood samples for determination of TSH, FT4, Tg, TPOAt,TPOAb. TSH and FT4 in serum will be determined using the chkemoluminiscency, and Tg and TPOAb, TPOAt elektrochkemoluminiscency method.

Expected scientific contribution: Results of the research are to publish national guidelines for the use of iodine preparations in pregnancy, and the importance of including measured parameters in a routine.

Acknowledgments: I thank my mentor Ass.Prof.Tomislav Jukic for their helpful advice and support.

MeSH/Keywords: Iodine deficiency, pregnancy, thyroid hormones, iodination of salt

Poster code: T-B-17-35

LOWER EYELID TARSUS THICKNESS – UNIFORM OR NOT

PhD candidate: Ana Bišćan Tvrdi

PhD Thesis: Lower eyelid tarsus thickness – uniform or not

Mentor/s: Sanja Masnec, MD, PhD[1] Prof. Biljana Kuzmanović Elabjer, MD, PhD[2]

Affiliation: [1]Ophthalmology department, Clinical Hospital Center Zagreb, School of Medicine, University of Zagreb, Croatia; [2]Ophthalmology department, Clinical Hospital

Introduction: Tarsus or tarsal plate is a structural part of the upper and lower eyelid of both eyes. It is composed of dense connective tissue that gives strength and maintains the shape of the eyelid. In normal anatomic relationship with surrounding eyelid structures it ensures their adherence to the eyeball. Regardless of whether the upper or lower eyelid, current literature states that thickness of the tarsus is around 1 to 1.5 mm, but does not specify is there any difference in thickness along its length. At the same time, the known data on the thickness are mainly related to Asian population, with very few research on population of whites, and existence of anatomical difference of eyelids between races is already established. Tarsus, as the only solid eyelid structure, plays an important role in the development of various ophthalmic morbidity, especially the lower eyelid, of which the most important are involutive changes such as entropy and ectropion. Knowing the tarsus thickness in our population and the existence of possible differences along its length will help to better understanding of the occurrence of various pathologies of the lower eyelid, and access to appropriate treatment.

Hypothesis: Lower eyelid tarsal plate thickness is not equal throughout its length.

Aims: Known data on the thickness are mainly related to Asian population, with very few research on population of whites, and existence of anatomical difference of eyelids between races is already established. Tarsus, as the only solid eyelid structure, plays an important role in the development of various ophthalmic morbidity, especially the lower eyelid, of which the most important are involutive changes such as entropy and ectropion.

Materials and methods: Measuring of the lower eyelid tarsus thickness will be conducted, during autopsy at the Institute of Pathology and Cytology in University Hospital "Sveti Duh", in 25 consecutive cadaver over 60 years of age. The method includes excision of both full thikness lower eyelids. Collected samples will be fixed in 10% formalin. Measures will be performed on ocular micrometer by a single pathologist.

Expected scientific contribution: Knowing the tarsus thickness in our population and the existence of possible differences along its length will help to better understanding of the occurrence of various pathologies of the lower eyelid, and access to appropriate treatment.

Acknowledgments:

MeSH/Keywords: tarsus, tarsus thickness, lower eyelid, involutive changes

Poster code: T-B-18-51

EVALUATION OF QUALITY OF LIFE IN PATIENTS AFTER VITRECTOMY FOLLOWING IDIOPATHIC EPIRETINAL MEMBRANE

PhD candidate: Gentian Bajraktari MD

PhD Thesis: Evaluation of quality of life in patients after vitrectomy following idiopathic epiretinal membrane

Mentor/s: Ass. Prof. Tomislav Jukić MD PhD

Affiliation: Department of Ophthalmology, University Hospital Center, Zagreb, Croatia

Introduction: Idiopathic epiretinal membrane (IEM) is a fibrocelular, nonvascular proliferation that develops on the surface of the internal limiting membrane. This can decrease visual acuity and cause metamorphopsia as a result of retinal wrinkling resulting from traction in the macular region. When asymptomatic, patients are usually only on observation. If patient is bothered by reduced visual acquity or metamorphopsia, pars plana vitrectomy (PPV) using intraocular tamonades (IT) with epiretinal peeling should be considered. The goal of surgery is to optimize visual acquity, reduce metamorphopsia and restore binocularity if it was affected preoperatively.

Hypothesis: Although there is an improve in quality of life and visual functions in patients following PPV for IEM treatment, the improvment will be better in one of the three different IT that will be used.

Aims: 1.To evaluate the effects of three types of IT, used during PPV, following IEM on patients' quality of life and visual functions. 2.To compare between three types of IT, used during PPV, on the quality of life and visual functions among patients with IEM.

Materials and methods: In this randomized cohort study, we will include 90 patients, that have been diagnosed properly with IEM. Patients with glaucoma, previous cataract surgery in 6 months, age-related macular degeneration, diabetic retinopathy and macular hole, will be excluded. Patients will undergo PPV using three different types of tamponades. In 30 patients we will perform PPV using sulfur hexafloride (SF6), in 30 other patients PPV using air, and in 30 remaining patients PPV using balanced salt solution (BSS). Quality of life assesment will be performed using The Natonal Eye Institute 25 Item Visual Function (VFQ-25), a self rated quastionnaire, that will be applied one week prior surgery (baseline) and will be repeated one month after surgery (short term post evaluation) and 6 months after surgery (medium term post evaluation). Collected data will be processed and presented using appropriate statistical methods.

Expected scientific contribution: By this study we will determine the effects of the PPV procedure in patients' quality of life and visual function. In addition, it will be defined if any of the IT used, will show advantage or even disadvantage over the other. And based on results, we might recommend the procedure that benefit the most, in terms of quality of life and visual functions.

Acknowledgments:

MeSH/Keywords: Idiopathic epiretinal membrane, pars plana vitrectomy, quality of life.

Poster code: T-B-18-106

PSEUDOPHAKIC CYSTOID MACULAR EDEMA IN PATIENTS WITH NON-PROLIFERATIVE DIABETIC RETINOPATHY

PhD candidate: Anđela Jukić, MD

PhD Thesis: The effect of topical bromfenac in prevention of pseudophakic cystoid macular edema in patients with non-proliferative diabetic retinopathy.

Mentor/s: Associate Professor Miro Kalauz , MD, PhD

Affiliation: Ophthalmology Clinic, University Hospital Center Zagreb, Department of Ophtalmology, University Hospital Dubrava

Introduction: Pseudophakic cystoid macular edema (PCME) occurs as a complication 6-10 weeks after cataract surgery. It is the main cause of vision loss after cataract surgery and could lead to permanently impaired central vision owing to altered outer photoreceptor features. This study will investigate the effect of topical nonsteroidal anti-inflammatory drugs (NSAIDs) and topical corticosteroids on intraocular interleukin 6 (IL-6) concentration and on incidence of pseudophakic cystoid macular edema (PCME) in patients with non-proliferative diabetic retinopathy.

Hypothesis: Topical NSAIDs reduce intraocular concentration of interleukin 6 (IL-6) and reduce the incidence of pseudophakic cystoid macular edema (PCME) in patients with non-proliferative diabetic retinopathy.

Aims: To determine the effect of topical nonsteroidal anti-inflammatory drugs (NSAIDs) and topical corticosteroids on intraocular concentration of interleukin 6 (IL-6) and the incidence of pseudophakic cystoid macular edema (PCME) in patients with nonproliferative diabetic retinopathy.

Materials and methods: We will include 90 patients with cataract and nonproliferative diabetic retinopathy. We will divide them into three groups. One group will recieve topical bromfenac seven days before cataract surgery and three weeks postoperatively. Second group will recieve topical dexametasone seven days preoperatively and three weeks postoperatively and third group will recieve topical placebo seven days preoperatively and three weeks postoperatively. All three groups will recieve topical corticosteroids and topical antibiotics three weeks postoperatively. On the day of the surgery we will take a sample of aqueous humor from the anterior chamber (0.2 mL) from all patients and analyze the intraocular concentration of interleukin 6 (IL-6). Visual acuity, slit lamp biomicroscopy, aplanation tonometry and central retinal thickness (measured by optical coherence tomography-OCT) will be measured 7 days prior to surgery, on the day of surgery and on 1, 7, 30, 90 and 120 postoperative day. The study will include patients with mild to moderate nonproliferative diabetic retinopathy by the ETDRS classification.

Expected scientific contribution: There are no studies that compare the effect of NSAIDs and corticosteroids on the intraocular concentration of pro-inflammatory mediator interleukin-6 (IL-6) and the incidence of pseudophakic cystoid macular edema (PCME) in patients with diabetic retinopathy.

Acknowledgments:

MeSH/Keywords: pseudophakic cystoid macular edema (PCME), phacoemulsification, interleukin 6 (IL-6), optical coherence tomography (OCT), non-steroidal anti-inflammatory drugs (NSAID)

Poster code: T-B-18-132

THE ROLE OF TUMOR HYPOXIA IN PATIENTS WITH ENDOMETRIAL CANCER

PhD candidate: Zrinka Rendić Miočević, MD, radiotherapy and oncology specialist

PhD Thesis: The role of tumor hypoxia in patients with endometrial cancer

Mentor/s: prof. Lidija Beketić Orešković, MD, PhD, radiotherapy and oncology specialist

Affiliation: University hospital for tumors, Clinical Hospital Centre Sestre milosrdnice, Zagreb. Clinic for gynecology and obstetrics, Clinical Hospital Centre Zagreb, Zagreb.

Introduction: Tumor hypoxia is one of the most important microregional factors of tumor growth, but impact of hypoxia in endometrial cancer is still not sufficiently investigated. CAIX, carboanhydrase IX, is considered to be one of the best biomarkers for tissue hypoxia. Often is overexpressed in human epithelial tumors and is usually indicator of a bad prognosis.

Hypothesis: Subgroups of patients with endometrial cancer which have stronger expression of hypoxia (CAIX) and tumor agressiveness indicators (p53 and Ki67) will experience worse disease prognosis.

Aims: This study will analyze immunohistochemical expression of tissue hypoxia indicator CAIX and indicators of tumor agressiveness (p53 and Ki67) as prognostic and predictive parameters in patients with endometrial adenocarcinoma. Mutual correlation of the tested parameters will be analyzed, as well as their correlation with standard clinical and histopathological parameters. Simultaneous analysis of the tumor tissue from the curretage and after radical hysterectomy might provide the possibility of better prognosis determination in certain subgroups of patients, which might finally have an impact on treatment choice.

Materials and methods: The study will enroll 100 patients with endometrial cancer diagnosed between 2007. and 2012. For each patient a paired tissue sample will be analyzed (a tissue specimen after curretage and after hysterectomy) for expression of CAIX, Ki67 and p53. Analysis will be based on immunohistochemical reaction after administering compatible mouse monoclonal antibody. Expression of the analyzed parameters will be assesed based on intensity of reaction as well as percentage of cells with positive reaction. The results of the immunohistochemical analysis will be correlated with the clinical (age, adjuvant therapy, survival) and histopathological features (histologic subgroup of endometrial cancer, tumor grade, size, FIGO stage) of that same patient. The results will be statistically processed, statistical significance starts at the level of $p<0,05$. The study is retrospective.

Expected scientific contribution: This study would further determine the biological role and mechanisms of tumor hypoxia in endometrial cancer. Correlation of expression of tumor hypoxia parameter (CAIX) and factors of tumor aggressiveness (Ki67 and p53) to standard clinical and histopathological factors might determine the role of tumor hypoxia and CAIX as prognostic and predictive parameter in patients with endometrial cancer.

Acknowledgments:

MeSH/Keywords: Endometrial Neoplasms, Tumor Hypoxia, Immunohistochemistry

Poster code: T-B-19-19

THYROID HORMONES AND AGGRESSIVNESS OF PROSTATE CANCER

PhD candidate: Petra Petranović Ovčariček, MD

PhD Thesis: Thyroid function in patients with newly diagnosed prostate cancer

Mentor/s: Asst. Prof. Tomislav Jukić, MD, PhD

Affiliation: University Hospital Centre Sestre milosrdnice, Clinical Hospital Sveti Duh, Zagreb

Introduction: Numerous studies are trying to find a biomarker that would differentiate aggressive from indolent forms of prostate cancer. The prostate has receptors for thyroid hormones, which can potentially affect cellular proliferation and be the trigger in carcinogenesis. This research will study the connection of hormones (T3, fT4 and TSH) and patohistological findings of prostate cancer ("Grade Group"). In that way we will try to indicate potential biomarkers for aggressive prostate cancers.

Hypothesis: The concentrations of total triiodothyronine (T3) and the free fraction of thyroxine (FT4) are higher, while the concentration of thyrotropin (TSH) is lower in patients with histologically aggressive prostate cancer.

Aims: To determine the relationship between the thyroid function and prostate cancer for the purpose of better understanding of carcinogenesis and detection of potential biomarkers in the occurrence of histologically aggressive prostate cancers.

Materials and methods: Subjects will be divided into 2 research groups. The first group will include patients with postoperative patohistological findings of prostate cancer Grade Group 1 and 2, while the second group will include patients with prostate cancer of Grade Group 3, 4 and 5. The number of patients in each group will be around 70. The criterion for inclusion of subjects is biopsy-proven prostate cancer scheduled for radical prostatectomy, without evident distant metastases. Patients will be 60 to 70 years old, without known thyroid disease, that were not receiving iodine contrast in the past year, patients that do not take medications that could affect the thyroid function, patients without history of the external radiation of the cervical region and without serious comorbidity. Preoperatively we will take a blood sample to determine concentration of T3 (total triiodothyronine hormone), fT4 (free fraction of thyroxine hormone), TSH (thyroid-stimulating hormone), Anti-TPO (antibodies to thyroid peroxidase) and Anti-Tg (antibodies to thyroglobulin). Blood samples for T3, fT4 and TSH will be analysed using Immunoassay CLIA-Chemoluminiscent at XPI Siemens Immulite 2000, while anti-TPO and anti-Tg will be measured with ECLIA -Electrochemoluminiscent Immunoassay at Roche COBAS e411.

Expected scientific contribution: The purpose of this study is to find biomarkers that will help us in distinguishing aggressive from indolent forms of prostate cancer. Reducing the mitotic effect of triiodothyronine and thyroxine could be a new possible additional treatment of prostate cancer.

Acknowledgments: I would like to thank my mentor, asst. prof. Tomislav Jukić, MD, PhD, for providing me support in this research.

MeSH/Keywords: prostate cancer, thyroid function, patohistology

Poster code: T-B-19-28

THE ROLE OF SPECIFIC PLURIPOTENCY GENES AND BCL2 ONCOGENE ACTIVITY IN MALIGNANT PLEURAL MESOTHELIOMA

PhD candidate: Fran Seiwerth, MD

PhD Thesis: Oncogenic pathways in malignant mesothelioma

Mentor/s: prof. Marko Jakopović, MD[1], PhD, assist. prof. Filip Sedlić, MD, PhD[2]

Affiliation: [1]UHC Zagreb, Department for respiratory diseases Jordanovac, [2] University of Zagreb, School of medicine, Department of pathology

Introduction: Malignant mesothelioma is an agressive mesenchimal tumor, originating from the pleural or peritoneal serous mesothelial cells. Available therapeutic options proved as ineffective, resulting in a median overall survival of patients with pleural mesothelioma of 9 - 12 months. The grade of cell differentiation and pluripotency-related gene expresion in mesothelioma cells corelates with poorer overall survival and greater resistance to chemoterapeutic agents.

Hypothesis: The expression of specific pluripotency genes and oncogenes as well as the activity of the signaling PI3/AKT pathway corelates with poorer clinical outcome in patients with malignant pleural mesothelioma (MPM).

Aims: To investigate the corelation between the PI3/AKT pathway activitiy, BCL2 oncogene as well as Sox2, Nanog and Oct4 pluripotency genes expression and the therapeutic outcomes in malignant pleural mesothelioma.

Materials and methods: The analysis will be performed on tissue samples of patients with MPM from the archive of the Department of pathology, School of medicine, University of Zagreb. All samples will be re-analyzed by two independent pathologists to classify them to epitheloid, sarcomatoid and biphasyc subtype. Imunohistochemistry analysis will be performed to define the percentage of cells with specific gene expression. The results will be scored by semiquantified sistems using computer protocols. Patients' medical histories will be analyzed for clinical data, including demographics, tumor staging, treatment and patient survival time from diagnosis, among others. All data will be analyzed using lycensed statistical tools.

Expected scientific contribution: This kind of resarch of oncogenic pathways in malignant pleural mesothelioma has not be performed on patient tissue samples, according to available databases. Our goal is to provide useful data on specific oncogene expression and signaling pathways activity in MPM tissue samples, which can potentially be used as biomarkers in prognosis and therapeutic options selection in patients with MPM.

Acknowledgments: to the Department of pathology, Zagreb school of medicine and the Department for respiratory diseases Jordanovac, University hospital centre Zagreb

MeSH/Keywords: malignant mesothelioma, pluripotency genes, oncogene

Poster code: T-B-19-43

THE ROLE OF SERUM INTERLEUKIN-7 LEVELS AS BIOLOGICAL MARKER IN BREAST CANCER

PhD candidate: Faton Sermaxhaj MD

PhD Thesis: The role of serum Interleukin-7 levels as biological marker in breast cancer

Mentor/s: 1) Prof. Ass. Natalija Dedic Plavetic, 2) Prof. Dr. Damir Vrbanec

Affiliation: University of Zagreb School of Medicine, University Hospital Centre-Zagreb, Department of Medical Oncology

Introduction: Breast cancer is a major public health problem worldwide, whose incidence is increasing dramatically. There are some indicators that may be used to redirect the prognosis of the disease as well as follow the patients more effectively. Based on the fact that Interleukin-7 induces growth and proliferation of breast cancer cells, as well as lymphangiogenesis, the potential use of Interleukin-7 as biological marker could help in this regard.

Hypothesis: Working Hypothesis: Serum level of Interleukin-7 in the patients diagnosed with breast cancer is in a direct correlation with the tumor size, low cell differentiation, lymphovascular invasion, negative hormone receptors status, lymph node methastasis and Ki-67 status. In addition, no difference in the serum levels of IL-7 exists between the patients recruited in Croatia and Kosovo, respectively.
Null Hypothesis: No correlation between the serum level of Interleukin-7 in the patients diagnosed with breast cancer and histopathological and clinical (age, menopausal status) findings exists.

Aims:
To evaluate, if there any elevation of the serum level IL-7 in the patients diagnosed with breast cancer. To evaluate the correlation between the serum level of IL-7 in the patients with breast cancer and clinicopathological findings. To evaluate possible differences in clinicopathological characteristics of Croatian and Kosovo subcohorts. To evaluate serum IL-7 levels differences between Croatian and Kosovo subcohort of patients with newly diagnosed breast cancer.

Materials and methods: This cross-sectional, observational analytic study will include patients diagnosed with early, operable breast cancer. The participants will be 200 patients with breast cancer (100 from Croatia and 100 from Kosovo) and 60 healthy controls (30 from Croatia and 30 from Kosovo). To evaluate the level of IL-7, blood samples will be taken from patients prior to surgical intervention. In addition, after the surgical intervention, the hystopathological specimen examination will be performed to investigate tumor size, grade, hormone receptors status, nodal status, Ki-67 status and lymphovascular invasion.

Expected scientific contribution: The results of this study will help the global discussion in order to use IL-7 as a biological tumor marker. It also we contribute to evaluate and compare clinicopathological characteristics of breast cancer patients in Kosovo, with Croatian cohort.

Acknowledgments:

MeSH/Keywords: Interleukin-7, interleukins, breast cancer.

Poster code: T-B-19-61

THE ROLE OF PITTING CORROSION IN WEAKENING OSTEOSYNTHETIC IMPLANTS MADE OF STAINLESS STEEL 316L

PhD candidate: May Labidi, MD

PhD Thesis: The role of pitting corrosion in weakening osteosynthetic implants made of stainless steel 316L

Mentor/s: 1. Associate Professor Ivan Dobrić, MD, PhD 2. Professor Janoš Kodvanj, Mechanical Engineer, PhD

Affiliation: Faculty of Mechanical Engineering and Naval Architecture, Zagreb University. Working at General Hospital "dr.Tomislav Bardek"

Introduction: Usage of metal implants in orthopaedic and trauma surgery has been practiced for many decades, the development of different metal materials and their specifications is still in progress. 316L stainless steel is one of the most frequently used and until now there are many uncertainties to be resolved about implant breakage, one of them is metal corrosion and specifically the most common pitting corrosion.

Hypothesis: Biological media affects the integrity of osteosynthetic 316L implants due to pitting corrosion microstructural changes which finally results in mechanical weakening of the implants.

Aims: By assessment of surgical stainless steel 316L we would like to confirm the effect of bilogical liqud media (SBF-Stimulated Body Fluid) of weakening it due to pitting corrosion.

Materials and methods: Using fourty eight (n=48) stainless steel 316L implants samples divided into four groups of a certain number of samples after randomization: the first group not immersed, second immersed in SBF(saline 0.9% NaCl), third group immersed in SBF with added lactic acid to obtain a pH value of 5.0, and fourth group immersed in SBF with added lactic acid to obtain a pH value of 6.0 . The morphology and dimentions of corrosion defects analyzed by SEM-Scanning Electron Microscope, biomechanical tests performed at the beginning and end of the study. Evaluation of corrosion changes by the SEM will be held in four different stages: first at day ten, second at day 28 (four weeks), third at day 168 (six months), and the last at day 365 (one year later). Evaluation intervals are in accordance with bone healing dynamics and changes in acidity. A control evaluation will be performed at day zero. The effect of pitting corrosion in changing mechanical properties of the implant will be evaluated in the control group initially, and in the remaining three groups after the last evaluation of corrosion changes with the SEM at static and cyclic loading. Statical loading assessment will be performed on a tensile testing machine model Messphysik Beta 50-5. As for the dynamic loading assessment a servo hydraulic testing machine model Walter Bai LFV-50-HH will be used. Loading, frequencies and magnification on the SEM will be specified during the reaserch.

Expected scientific contribution: This research is aimed to favour optimization of implants made out of 316L stainless steel used in orthopaedic and trauma surgery.

Acknowledgments:

MeSH/Keywords: Osteosynthetic implants, 316L, corrosion surgical stainless steel

Poster code: T-B-20-125

PRESENCE OF BRAF V600E MUTATION AND LACK OF CPSF2 EXPRESSION AS PROGNOSTIC MARKERS FOR PAPILLARY THYROID CANCER

PhD candidate: Irena Makovac, MD

PhD Thesis: Presence of BRAF V600E mutation and lack of CPSF2 expression as prognostic markers for Papillary Thyroid Cancer

Mentor/s: Associate Professor Drago Prgomet, MD, PhD

Affiliation: University of Zagreb School of Medicine, University Hospital Centre – Zagreb

Introduction: Papillary thyroid carcinoma is the most common form of thyroid gland malignancy and it constitutes about 80% of all the thyroid carcinomas (1,2). Substantial increase in incidence last two decades all over the world (3,4) raised interest on identifying prognostic biomarkers that enable us to identify the aggressive forms of papillary cancer in early stage of the disease and thus also allowing us better strategy in treatment planning and exploring novel targeted treatments for metastatic papillary thyroid cancer. BRAF mutations (from eng. žB - rapidly accelerated fibrosarcoma") are important in cell and tumor progression and are most common genetic events in thyroid cancer (11). Many studies aim to determine the correlation between the presence of BRAF V600E mutation and aggressive behavior of papillary thyroid cancers but also emphasize wide variation in the prevalence of the BRAF V600E mutation in PTC which varies between 30% and 80% depending on geographic region and iodine consumption (12-18, 24-35). Genome-wide expression (GWE) analysis in PTC samples performed by Nilubol et al. (2011.) identified five genes (CPSF2, LARS, AURKC, TRNT1 and BCL11A) that were differentially expressed in patients with PTC-associated mortality, giving that CPSF2 expression has the highest predictive value (36). Cleavage and Polyadenilation Specificity Factor Subunit 2 is the 100 kDa subunit of CPSF(37). Low protein expression of CPSF2 (cleavage and polyadenilation specificity factor subunit 2) is associated with increased cellular invasion, increased markers of thyroid cancer stem cells (CD44 and CD133 expression) and predicts a poorer clinical outcome (38).

Hypothesis: BRAF V600E mutation and protein expression of CPSF2 in papillary thyroid carcinoma is associated with the development of metastasis and aggressive form of the disease.

Aims: To evaluate the prevalence of BRAF V600E mutation and protein expression of CPSF2 in papillary thyroid cancer patients who underwent surgical treatment at our Department.

Materials and methods: The expression of CPSF2 protein will be evaluated by immunohistochemistry (dilution 1:100-200, Abcam) and the presence of the BRAFV600E mutation by cobas® 4800 BRAF V600 Mutation Test, both retrospectively in formalin-fixed, paraffin-embedded (FFPET) human PTC tissue samples in 40 PTC without (control) and 90 with (study group) metastasis to regional lymph nodes of the neck.

Expected scientific contribution: Improving detection of risk factors, preoperative planning and targeted treatment options for patients with PTC

Acknowledgments: I would like to thank professors Sven Seiwerth, Srećko Gajović and Dražen Huić for their help and guidance, my dear friend and colleague dr. Antonia Jakovčević for her great effort on this project and at last to dr. Suzana Kober (Medical Director at Roche Pharmaceuticals) for her faith, commitment and support in all possible ways, without whom all this would not be possible.

MeSH/Keywords: BRAF, CPSF2 protein, PTC, papillary thyroid cancer, prognostic markers

Poster code: T-B-21-141

EXPRESSION OD D2-40 CLONE IN LYMPHANGIOGENESIS OF SUBLINGUAL CARCINOMA AND LINGUAL CARCINOMA CONSIDERING EXTRACAPSULAR SPREAD OF OCCULT NECK METASTASIS

PhD candidate: Igor Čvrljević

PhD Thesis: Expression od D2-40 clone in lymphangiogenesis of sublingual carcinoma and lingual carcinoma considering extracapsular spread of occult neck metastasis

Mentor/s: Associate Professor Ivica Lukšić, M.D., PhD Co-mentor: Danko Muller, M.D., PhD

Affiliation: University of Zagreb School of Medicine, University Hospital Dubrava, Zagreb

Introduction: Malignant intraoral tumors metastasize primarily lymphogenic, neck status being one of the most important predictive factor, and tumors of the tongue and sublingual region mestasize most often. Podoplanin, D2-40 clone is a reliable lyphangiogenesis marker in squamous cell carcinoma of head and neck with a connection between podoplanin expression and regional metastasis occurance.

Hypothesis: Expression of D2-40 clone is directly associated with lymphangiogenesis of primary squamous cell sublingual carcinoma and lingual carcinoma and higher rate of extracapsular spread in occult neck metastasis.

Aims: General aim is to determine the expression od D2-40 clone in sublingual and lingual carcinoma and connection with extracapsular spread in occult neck metastasis. Specific aims: 1. Determine the rate of occult metastasis in sublingual and lingual carcinoma. 2. Determine the expression of D2-40 clone in primary carcinoma and significance considering clinical and patohistological factors of primary tumor and neck dissection specimen. 3. Determine prognosis and survival rate depending on clinical and patohistological factors and considering primary tumor lymphangiogenesis.

Materials and methods: A retrospective study will be conducted in University Hospital Dubrava. For all patients, data will be researched from tumor database (tum2/dBaseIII) developed in Maxillofacial surgery Clinic of University Hospital Dubrava. Tumor staging will be determined according to the newest TNM classification from 2010. Including criteria will be: histological verification of squamous cell carcinoma, sublocalization tongue and sublingual region, primary surgical treatment in Maxillofacial Surgery Clinic University Hospital Dubrava and clinically negative neck status. An imunohistochemical analysis of patohistological specimen will be conducted based on D2-40 clone expression. Lymph node density in primary tumor will be used as a lymphangiogenesis indicator.

Expected scientific contribution: Objective is to determine the role of clinical and patohistological factors of the primary squamous cell carcinoma of sublingual and lingual region considering the rate of extracapsular spread in elective neck dissections. Results could help to determine guidelines for clinical practice and therapy, especially regarding elective neck dissection. Imunohistochemical determination of podoplanin expression in primary tumor would have a direct influence on disease prognosis, especially survival, choice of optimal therapy and disease understanding.

Acknowledgments: I would like to thank my mentors for their guidance and patience and my family for support

MeSH/Keywords: D2-40 clone, podoplanin expression, intraoral carcinoma, extracapsular spread, occult metastasis

Poster code: T-B-21-142

EARLY DETECTION OF DIABETIC NEPHROPATHY IN CHILDREN

PhD candidate: Bernardica Valent Morić, MD

PhD Thesis: Ambulatory blood pressure monitoring and biomarkers of renal damage in early detection of diabetic nephropathy in children

Mentor/s: Bojan Jelaković, MD, PhD, professor, Gordana Stipančić, MD,PhD, assistant professor

Affiliation: Clinical Hospital Center Sestre milosrdnice

Introduction: The morbidity associated with type 1 diabetes (T1D) is mainly related to the development of long-term vascular complications the most common of which is diabetic nephropathy (DN). Microalbuminuria as a marker of glomerular damage is the most widely used early indicator of DN. However, recent research has shown that it's predictive value is limited because many T1D patients become normoalbuminuric at follow-up. The current data also suggest that subtle but early elevations of blood pressure antedate the development of microalbuminuria thus playing a key role in DN development. Recently, it has been shown that tubular damage is an important factor in progression of DN with neutrophil gelatinase-associated lipocalin (NGAL) being the most promising tubular marker.

Hypothesis: In children and adolescents with T1D tubular damage preceeds albuminuria and is related with changes in ambulatory blood pressure monitoring (ABPM) parameters.

Aims: The general aims are to determine the characteristics of ABPM parameters in children with T1D and to establish do children with T1D have an elevated tubular injury marker NGAL in urine compared to healthy controls. The specific goals are to determine the relationship between ABPM, tubular injury marker NGAL and albuminuria and analyze the factors which have an impact on both urinary markers.

Materials and methods: In this cross-sectional study we plan to include 200 children and adolescents of both genders, aged 5-20 years with T1D of at least 1 year duration. A control group of 100 children will be formed in order to establish a normative values of NGAL in urine. The exclusion criteria for both groups are: hypertensive patients, receiving medication that affects blood pressure, pre-existent kidney disease, acute or chronic inflamatory disease and abnormal urinary sediment. In study group a blood sample will be taken for HbA1c and creatinine. Three first-morning urine samples for albumin/creatinine ratio will be collected along with additional sample for NGAL and urinary sediment analysis. Urinary NGAL will be analysed in both study and control group using ELISA (enzyme-linked immunosorbent assay). ABPM will be performed using oscillometric device Mobilgraf MO1100120, I.E.M.GmbH. The following ABPM parameters will be analysed: systolic/diastolic BP and BP load over 24 h, during daytime and nigthtime and nocturnal dipp.

Expected scientific contribution: We expect to confirm the role of ABPM and tubular injury marker NGAL as the earliest indicators of diabetic nephropathy in children.

Acknowledgments:

MeSH/Keywords: ambulatory blood pressure monitoring, albuminuria, NGAL, type 1 diabetes, children

Poster code: T-B-24-9

EVOLUTION OF INFLAMMATORY ARTHRITS: ROLE OF ULTRASOUND AND OTHER BIOMARKERS IN PREDICTING OF DEVELOPMENT JUVENILE IDIOPATHIC ARTHRITIS (JIA)

PhD candidate: Edi Paleka Bosak, MD

PhD Thesis: Evolution of inflammatory arthritis: role of ultrasound and other biomarkers in predicting of development juvenile idiopathic arthritis

Mentor/s: Professor Miroslav Harjaček, MD, PhD

Affiliation: Clinical hospital centre - Sestre Milosrdnice, University of Zagreb School of Medicine

Introduction: Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease in children. Classification identifies different subtypes based on clinical and laboratory features including number of affected joints and presence of few known biomarkers in blood of the patient. Undifferentiated arthritis (UA) in early phase of the disease does not fulfil criteria for any category or is excluded by fulfilling criteria for more than one category. UA can progress into chronic rheumatic disease or even completely withdraw. To this date, number of biomarkers have shown limited potential for predicting clinical phenotype, disease activity and severity and response to treatment and detecting of new and reliable biomarkers presents a challenge in further researches.

Hypothesis: Outcome of patients with UA can be predicted by combining newly detected biomarkers and continuously Power Doppler ultrasonography monitoring (PDUS).

Aims: To identify diagnostic or/and prognostic biomarkers from blood, stool and saliva samples in patients with UA that have a potential to predict disease course and distinguish patients with JIA and their correlation with PDUS findings.

Materials and methods: The study will include 50 patients age <16 years with UA according to ILAR Criteria for JIA after given informed consent. The assessment of the activity of arthritis will be made by the following tools: Juvenile Arthritis Disease Activity Score (JADAS) and Childhood Assessment Score (CHAQ). PDUS will be performed at every visit for 10 joints according to OMERACT instructions and graded on the scale 0-3 for vascular signal. Blood, stool and saliva samples will be collected at the baseline and after 3, 6 and 12 months for routine laboratory analysis as well as for high-resolution mass spectrometry (MS). Synovial fluid will be analysed with MS in patients where possible or needed for intra-articular steroid injections. Patients diagnosed with JIA during the study will be treated according to Croatian Society for Rheumatology guidelines. Enzyme-Linked Immunosorbent Assay (ELISA) will be performed for 15 proteins after detailed analysis of data collected from MS.

Expected scientific contribution: We anticipate that the biomarkers indentified in this study may support the development of a biomarker panel that could help to predict disease course in patients with UA and lead to improvement in JIA classification and response to medication.

Acknowledgments: Croatian Science Foundation

MeSH/Keywords: JIA, Undifferentiated arthritis, Biomarkers, Power Doppler ultrasonography

Poster code: T-B-24-36

BIOCHEMICAL AND RADIONUCLIDE EVALUATION OF RENAL DAMAGE IN THE CHILDREN AND YOUNG ADULTS SUFFERING OF HAEMOPHILIA A AND B

PhD candidate: Zrinko Šalek, MD

PhD Thesis: Biochemical and radionuclide evaluation of renal damage in the children and young adults suffering of haemophilia A and B

Mentor/s: Assoc. Prof. Ernest Bilić, MD, PhD, Prof. Danko Milošević, MD, PhD

Affiliation: University Hospital Centre Zagreb, Department of Pediatrics

Introduction: Haemophilia is rare, inherited bleeding disorder with incidence of 2-4 new newborn boys per year. Haemophilia is treated with factor VIII/IX concentrates. Today we have better health care for the patients with haemophilia, and new uncertainties arise such as kidney pathology. The literature about haemophilia and kidney diseases is very rare, especially in children and young adults with haemophilia.

Hypothesis: Kidney damage in patients with haemophilia depends on the duration of disease, presence of microhaematuria, patient compliance, additional renal anomalies and the severity of the disease by a certain level of FVIII and FIX.

Aims: The aim of the study is to determine the incidence of kidney damage in haemophilia A/B, and determine which are risk factors for the development of kidney damage in children and young adults (up to 30 years of age) (duration of haemophilia, level of activity of FVIII or FIX, the presence of inhibitors of the F VIII/IX, macrohematuria, urinary tract malformations, etc.).

Materials and methods: We plan to enroll 50 patients suffering of haemophilia A and B
The data of subjects will be collected using standard laboratory and radiological methods. We plan to perform kidney ECHO (power Doppler, resistance index) to detect renal anomalies. If there is a suspition of renal anomalies we plan to do renal scintigraphy.

Expected scientific contribution: The results will show if there is kidney damage in children and young adults with haemophilia and which are the most important risk factors for the development of kidney damage.

Acknowledgments: None

MeSH/Keywords: haemophilia, bleeding, kidney damage, children

Poster code: T-B-24-66

CAUSES OF SEPTICEMIA IN NEONATES CAUSED BY URINARY TRACT INFECTIONS AND CURRENT BACTERIAL RESISTANCE IN MATERNITY WARDS AND INTENSIVE CARE UNITS IN CROATIA: A NATIONAL SURVEY

PhD candidate: Ana Meyra Potkonjak

PhD Thesis: Causes of septicemia in neonates caused by urinary tract infections and current bacterial resistance in maternity wards and intensive care units in Croatia: a national survey

Mentor/s: Professor Boris Filipović Grčić, MD, PhD, Professor Danko Milošević, MD, PhD

Affiliation: University Hospital Centre Zagreb, Department of pediatrics

Introduction: Resistance to antibiotics that treat infections of the urinary system (UTI) is increasing, while the incidence of UTI in situations of suspected and proven sepsis in neonates is 6%. Improperly treated UTI can lead to long-term complications. With respect to resistance of microbial environment in each region it is necessary to selectively choose antibiotics in order to optimize therapy, and based on the existing trends of bacterial sensitivity, examine the feasibility of treatment and to set the foundations of guidelines for the therapy, which primarily take the bacterial resistance in newborns into account.

Hypothesis: In the last 10 years in Republic of Croatia there is a change of bacterial sensitivity / resistance which causes the urinary tract infections in newborns, with a possible regional difference in antimicrobial sensitivity / resistance.

Aims: In the time period from 2005 to the end of 2015, the goal on a national level is to determine the overall incidence of urinary tract infections in the early and late neonatal sepsis, the most common causes of these infections and their response to standard anitmicrobial therapy. The specific aim is to compare regional microbiological conditions of hospital centers in Croatia, as well as differences of sensitivity to antibiotics between neonates who were treated in hospital conditions and general pediatric population. Outcomes of antimicrobial treatment will be compared and the justification for applying double-standard therapy will be examined.

Materials and methods: The subject of the research is a national multicenter retrospective analysis which will include neonates with urinary tract infections from maternity hospitals with intensive care units for newborns (regional and subregional perinatal centers). The analysis of urosepsis in individual respondents considered will include microbiological test results with corresponding antibiograms and results of routine laboratory tests. Additional nephrological analysis will be used to detect the presence of urinary tract anomalies. These parameters will be retrospectively analyzed in groups of neonates born in 2005 and 2015. The data will be statistically analyzed using the Mann-Whitney statistical test for independent variables.

Expected scientific contribution: The results of comparative analysis can serve as an indicator of bacterial resistance in neonatal population and also as a starting point for therapeutic guidelines and analysis of the cost-effectiveness of applied therapy.

Acknowledgments:

MeSH/Keywords: antibiotics, neonates, bacterial resistance, urinary tract infection, urosepsis, therapy

Poster code: T-B-24-130

ASSOCIATION OF GALLSTONE DISEASE WITH PERSONALITY DIMENSIONS

PhD candidate: Tatjana Jukić, MD

PhD Thesis: Association of gallstone disease with personality dimensions

Mentor/s: Branka Aukst Margetić, MD, PhD

Affiliation: Neuropsychiatric Hospital Dr. I. Barbot, Popovača

Introduction: Until now only few studies have investigated the connection between gallstones and personality traits. Studies have shown that women with gallstones have a higher risk of developing depression and emotional instability. Also, most previous research indicates association between personality traits with disturbances in lipid and/or glucose metabolism, which is indirectly associated with the development of gallstones. However, personality in gallstone disease was not assessed. For the assessment of personality, the Temperament and Character Inventory (TCI) was chosen, being one of the most widely used instruments for the assessment of personality in current psychiatric research.

Hypothesis: The presence of gallstone disease is associated with higher levels of personality dimensions harm avoidance and novelty seeking compared to the control group.

Aims: To determine if there is difference in personality dimensions between the group with gallstones and healthy control group.

Materials and methods: Participants will be consecutive outpatients of Neuropsychiatric Hospital Popovača, aged 18 to 65 years. Estimated sample size is 140 patients (70 patient with ultrasound verified gallstones and 70 healthy control subjects matched for age and gender). Inclusion criteria will be the presence of gallstones. According to these criteria participants will be assigned in two groups: participants with gallstones and participants without gallstones (control group). Both groups will be measure body mass index, waist circumference, blood glucose, lipidogram and CRP. Differences between two groups will be analyzed by the test set including: Dimensions of personality will be assessed with Temperament and character questionnaire (TCI-140), depression will be assessed with Center for Epidemiologic studies Depression Scale (CES-D) and sociodemographic questionnaire.

Expected scientific contribution: This is the first study to examine the relationship of gallstones with personality dimensions. The results of this research could point to, so far, unexplored factors in the formation of gallstones but also emphasize the need for prevention in the field of psychological health because of long-term mental problems can lead to the formation of somatic disturbances. The same can apply and in clinical practice.

Acknowledgments:

MeSH/Keywords: gallstone disease, personality dimensions

Poster code: T-B-25-118

IMMUNOHISTOCHEMICAL ANALYSIS OF CANCER/TESTIS ANTIGENS IN NONINVASIVE DUCTAL BREAST CANCER

PhD candidate: Ana Roguljić

PhD Thesis: Immunohistochemical analysis of cancer/testis antigens in noninvasive ductal breast cancer

Mentor/s: Božena Šarčević, MD, PhD Antonio Juretić, MD, PhD

Affiliation: University of Zagreb School of Medicine, Department of Oncology- Pathology
University of Zagreb School of Medicine, Department of Oncology

Introduction: Breast cancer is the most common cancer in women. Epithelial tumors can be divided in invasive and noninvasive tumors. Cancer testis (C/T) antigens are encoded by group of genes expressed physiologically in human germ line cells and aberrantly in various malignancies. The most important among antigens are „melanoma-associated antigens"(MAGE) and antigen NY-ESO-1 which discovery gave necessary momentum to the attempts of applying immunotherapy. Noninvasive ductal breast cancer is not one entity but a heterogeneous group of at least four subtypes, and intertumoral heterogeneity (mixed histology within a lesion) may be observed. There have been a lot of controversy about treatment of DCIS but if there is expression of steroid receptors adjuvant hormonal therapy might be used. Tumor infiltrating lymphocytes in tumor tissue are possible sign of immune response and might associate with better clinical outcomes.

Hypothesis: Cancer/testis antigens expression correlates with tumor aggressiveness. Their expression in noninvasive ductal breast cancers (DCIS- Ductal carcinoma in situ) could be associated with aggressiveness of tumors, and could show which type of ductal noninvasive breast cancer has more chance to become invasive.

Aims: Immunohistochemistry will be performed on tumor samples and expression of cancer/testis antigen (MAGEA and NY-ESO-1) will be determined. The results will be correlated with standard pathohistological parameters for noninvasive ductal breast cancer (tumor size, tumor grade, expression of estrogen and progesterone receptors, necrosis and margin). Evaluation of tumor-infiltrating lymphocytes (TILs) will be also performed and (defined as exist or not).

Materials and methods: This study will include pathohistological material from patients with noninvasive cancer (DCIS) operated at the University Hospital for Tumors, University Hospital Centre Sisters of Mercy from 2007.-2014. Immunohistochemistry will be performed on tumor samples and expression of cancer/testis antigen (MAGE-A and NY-ESO-1) will be determined. Results will be determined semi quantitatively.

Expected scientific contribution: If there is correlation between expression of cancer/testis antigen and standard pathohistological prognostic values or if expression is independent prognostic value for noninvasive ductal breast cancer, expression could be used for definition of biological behavior of the tumor and evaluation of tumor infiltrating lymphocytes (TILs).

Acknowledgments:

MeSH/Keywords: non-invasive breast cancer, cancer/testis antigene, MAGE, NY-ESO-1

Poster code: T-B-26-44

EFFECTIVENESS OF LOCAL ANESTESIA IN ESWL

PhD candidate: Duje Rako, MD, FEBU

PhD Thesis: Effectiveness of Subcostal Anesthetic Block in Treatment of Nephrolithiasis with Extracorporeal Shock Wave Lithotripsy

Mentor/s: Professor Željko Kaštelan, MD, PhD

Affiliation: Department of Urology, University Hospital Dubrava and School of Medicine University of Zagreb

Introduction: Worldwide incidence of urolithiasis is close to 10% and risk of relapse is up to 80% in ten years period. Most of the patients are treated with ESWL and majority of treatments are carried out with analgesia and without anaesthesia. One of the factors reducing treatment success is pain and possibilities of local anaesthesia haven't been adequately investigated.

Hypothesis: Application of local anesthesia by subcostal block can reduce pain during ESWL and thus enable delivery of more shocks with higher power resulting in better fragmentation rate.

Aims: Determine effectiveness of subcostal block in reducing pain during ESWL treatment by measuring pain level, number of shocks delivered, maximum power of shocks and totally delivered energy level as well as difference in the rate of radiologically demonstrated immediate fragmentation of treated calculi.

Materials and methods: Double blind, randomised controlled trial including 108 adult male and female patients with solitary calculus measuring 6 to 20mm and not greater than 300mmx^2 in upper or middle part of left kidney will be allowed to enrol. Prior to scheduled ESWL treatment enrolled patients will receive two 5mL subcostal injections of either physiological solution (placebo arm) or 2% lidocaine (treatment arm). Both patient and investigator will be blinded until the end of the study.

Expected scientific contribution: To demonstrate safety and effectiveness of novel approach by using subcostal local anesthesia block for patients undergoing ESWL treatment.

Acknowledgments: This research was conducted entirely in University Hospital Dubrava with financial support from Department of Urology.

MeSH/Keywords: urolithiasis, ESWL, local anaesthesia

Poster code: T-B-28-4

THE EFFECT OF PHARMACOGENETIC VARIATIONS OF P-GLYCOPROTEIN AND INOSINE-5'-MONOPHOSPHATE DEHYDROGENASE ON TREATMENT OUTCOMES IN PATIENTS WITH KIDNEY TRANSPLANT

PhD candidate: Luka Penezić, MD

PhD Thesis: The effect of pharmacogenetic variations of P-glycoprotein and inosine-5'-monophosphate dehydrogenase on treatment outcomes in patients with kidney transplant

Mentor/s: Associate professor Željko Kaštelan, MD, PhD, Associate professor Nada Božina, MD, PhD

Affiliation: University of Zagreb School of Medicine, University Hospital Center Zagreb

Introduction: Interindividual and intraindividual variability in clinical response to immunosuppressants – mycophenolic acid and calcineurin inhibitors, is well documented. Numerous studies investigated pharmacogenetic associations of P-glycoprotein and IMPDH SNPs on kidney transplantation clinical outcomes.

Hypothesis: Genetic polymorphisms of IMPDH2 (rs11706052) and P-glycoprotein (rs1128503, rs2032582 and rs1045642) decrease the efficacy and increase the incidence of adverse effects of immunosuppressive therapy in kidney graft recipients.

Aims: Primary aim is investigation of IMPDH2 and P-glycoprotein SNPs' influence on kidney transplantation outcomes. Specific aims: determination of IMPDH2 SNP frequency in recipients and P-glycoprotein SNPs' frequency in donors and recipients, investigation of IMPDH2 and P-glycoprotein SNPs' influence on acute rejection, graft function, graft and patient survival during first 12 months after transplantation and subsequent follow-up, examination of IMPDH2 and P-glycoprotein SNPs' association with adverse effects, tumors and infections incidence and exploration of gender associated frequency differences among SNPs and determination of their effect on outcomes.

Materials and methods: Study will retrospective and include 250 patients transplanted at the Department of Urology, Clinical Hospital Center Zagreb, from January 2011 onward. Inclusion criteria are: capability for informed consent and the availability of DNA. Exclusion criteria are: early postoperative complications that result with graft loss. Genotypization will be performed form recipients' blood samples and donors' archived materials. We'll review recipients' medical documentation for clinical outcomes and laboratory measurements during the initial and minimum 3 years follow up. Basic data such as sex, age, BMI, miss match, cold ischemia time, concomitant medication, etc. will be collected along with relevant clinical (graft function, graft loss, death, BPAR according to Banff classification, infections, lymphocele, tumors, etc.) and laboratory (creatinine, whole blood count, electrolytes, urinalysis, immunosuppressive drug concentrations, etc.) data. DNA extraction will be done by salting-out method according to Miller and the genotypization using Real-Time PCR.

Expected scientific contribution: Determination of IMPDH2 and P-glycoprotein SNPs' influence on long term kidney transplantation outcomes in population of Croatian kidney graft recipients for the benefit of better individualization of immunosuppressive therapy.

Acknowledgments: I would like to thank The University Hospital Center Zagreb Kidney Transplantation Team for their approval of this study and my family for support.

MeSH/Keywords: Kidney transplantation, immunosuppressive agents, pharmacogenetics, single nucleotide polymorphism, IMP dehydrogenase, P-glycoprotein

Poster code: T-B-28-16

UROTHELIAL CARCINOMA OF UPPER URINARY TRACT, ENDEMIC NEPHROPATHY AND HLA GENES

PhD candidate: Damir Dittrich,MD

PhD Thesis: The association of HLA region with endemic nephropathy and upper tract urothelial carcinoma in Croatia.

Mentor/s: Professor Željko Kaštelan, MD, PhD, Professor Zorana Grubić, PhD.

Affiliation: University of Zagreb School of Medicine, University of Zagreb Faculty of Science

Introduction: Endemic nephropathy (EN) is a chronic tubuloinsterstitial renal disease. Studies made over the years have shown that EN is associated with the development of cancer of the upper urynari tract (UUC). The purpose of the present study is to investigate the differences between EN patients with and without UUC given the prior history (age, age at onset of the disease, gender), and the diversity of HLA genes between these two subgroups. The study will include 80 patients aged 58-88 years treated at the General Hospital "Dr. Josip Benčević" Slavonski Brod, divided into 2 subgroups (patients with/without UUC), 50 healty family members and 150 healthy control subjects.

Hypothesis: The HLA genes are associated with a risk of EN and urothelial carcinoma of the upper urinary tract in patients with EN.

Aims: The aim of the study is to answer the question whether the HLA genes are susceptible/protective for the development of EN or UUC.

Materials and methods: Diagnosis of EN will be established on the basis of medical history, clinical and laboratory parameters. Diagnosis of UUC will be established on the basis of red blood cell and/or malignant cells in urine, intravenous urography or CT, MR urography. Five milliliters of peripheral blood anticoagulated with EDTA of patients treated at the Urology Department and Dialysis Department in the period from 2005 to 2018, in the hospital, "Dr. Josip Benčević" in Slavonski Brod, will be used for determining the DNA polymorphism of HLA class I and class II. HLA genes detection will be done with Polymerase Chain Reaction - Sequence Specific Oligos probe. Data will be analyzed by descriptive statistics. Allele frequencies will be determined with the help of Genera Program (http://geneva.unige.ch/ahpd/). The program PyPop (http://www.pypop.org) will be used to calculate Hardy-Weinberg equilibrium (HWE),and analysis of haplotypes two loci. The same program will be used to calculate the imbalance of association. Haplotypes HLA-AB-DRB1 will be analyzed with the help of a computer program PHASE.

Expected scientific contribution: The study of genetic etiology of endemic nephropathy and urothelial cancer of the upper urinary tract will contribute to better understanding of the mechanisms of these diseases, and possibly, in the future and to new ways of prevention and therapy. The presence of susceptible HLA genes among family members will indicate the healthy subjects who are at increased risk of disease and include them in the program of preventive examinations.

Acknowledgments:

MeSH/Keywords: endemic nephropathy,upper urinary tract cancer,HLA genes

Poster code: T-B-28-87

DIAGNOSTIC VALUE OF SERUM CHEMOKINE CXCL13 CONCENTRATION IN PATIENTS WITH PROSTATE CANCER

PhD candidate: Marjan Marić, MD, Urologist

PhD Thesis: Chemokine CXCL13 in prostate cancer

Mentor/s: Prof. Željko Kaštelan, MD, PhD, Urologist

Affiliation: University Hospital Centre Zagreb, University of Zagreb School of Medicine

Introduction: Prostate cancer is second most common cancer in men. Usually is adenocarcinoma, and for patologicall scoring Gleason score (GS)is used and also International Society of Urological Pathology (ISUP)classification in 5 grades. Chemokines are low molecular weight basic pro-inflammatory proteins implicated in a variety of diseases. They have been associated with acute and chronic inflammation as well as with immunologically mediated diseases and various malignant diseases. Few recent studies showed biological and clinical significance of receptor CXCR5 and it's chemokine ligand CXCL13 in prostate cancer.

Hypothesis: Serum concentration of chemokine CXCL13 is higher in patients with prostate cancer and corelates with histological findings expressed in GS and grading according to ISUP classification.

Aims: GENERAL AIM: To determine serum concentration of chemokine CXCL13 and it's diagnostic value in patients with prostate cancer. SPECIFIC AIMS: 1. To determine if patients with diagnosed prostate cancer have higher serum concentration of CXCL13 in comparison to the control group of patients (with normal prostate biopsy specimen). 2. To determine whether patients with more agressive form (higher GS and ISUP grade) of prostate cancer have higher serum levels of CXCL13. 3. To determine if serum concentration of CXCL13 and/or multimarker approach (CXCL13 and PSA) is better predictor of more aggresive form of prostate cancer than prostate specific antigen (PSA) alone. 4. To determine cut-off value of serum CXCL13 concentration which has high sensitivity and specificity in selectioning patients with prostate cancer.

Materials and methods: Study is designed as a case-control study which will include 150 patients (75 with biopsy proven prostate adenocarcinoma and 75 with normal prostatic tissue on transrectal prostate biopsy specimen (control group)). Chemokine concentrations will be measured according to standardized enzyme immunotests.

Expected scientific contribution: If we confirm our hypothesis and find a cut-off value of CXCL13 with high diagnostic properties in diagnosing prostate cancer, clinical application and introduction of serum chemokine CXCL13 concentration in diagnostic algorithm of prostate adenocarcinoma is possible.

Acknowledgments:

MeSH/Keywords: chemokine CXCL13 prostate cancer

Poster code: T-B-28-135

THE DIFFERENCES IN REASONS FOR USING SCHIZOPHRENIA INTERNET FORUMS AND DEPRESSION INTERNET FORUMS IN CROATIA

PhD candidate: Nikola Žaja, MD

PhD Thesis: The differences in reasons for using schizophrenia internet forums and depression internet forums in Croatia

Mentor/s: Assistant Professor Tea Vukušić Rukavina, MD, PhD

Affiliation: University of Zagreb School of Medicine, University Psychiatric Hospital Vrapče

Introduction: Searching the Internet is one of the main sources for obtaining health and medical information. When searching the Internet, users can find information published by various organizations, companies, agencies or institutions and also information posted by users on the user-oriented Internet platforms, such as forums, blogs, and various social networks. There are no single, standardized mechanisms to ensure the truthfulness, objectivity, credibility and comprehensibility of health information available on the Internet.

Hypothesis: There are differences in reasons for using schizophrenia Internet forums and depression Internet forums in Croatia. Users of depression Internet forums more often seek emotional support from other users than users of schizophrenia Internet forums. Users of schizophrenia Internet forums more often seek information support from other users than users of depression Internet forums.

Aims: The study will determine the frequency of seeking emotional and informational support and also frequency of other reasons for using schizophrenia Internet forums and depression Internet forums in Croatia. Subsequently, comparison of the reasons for each forum and sub-group of users will be made.

Materials and methods: User-generated posts will be qualitatively analyzed using thematic analysis with pre-defined categories, emotional support and informational support and during the analysis new categories and sub-categories will be identified in the process of coding and grouping of the posts (inductive approach to thematic analysis). Study sample comprises user-generated posts (mentally ill, family and friends) on the Internet forum www.forum.hr, on "Shizofrenija – opća tema" (Schizophrenia – general topic) and "Depresija-opća tema" (Depression – general topic) themes, which were posted between June 1 st 2015 and June 1 st 2016.

Expected scientific contribution: No study has ever been conducted to compare the reasons for using schizophrenia Internet forums and depression Internet forums. So far, in Croatia, no study has been conducted to explore the reasons for using Internet forums on mental health. This research will enable us to better understand issues faced by patients and thus contribute to the creation of the Internet model for interventions for people with schizophrenia and depression. Knowing which information is needed by their patients would enable doctors the possibility of giving those information timely and thus establishing better doctor-patient relationship.

Acknowledgments:

MeSH/Keywords: Internet forums, mental health, schizophrenia, depression, Croatia

Poster code: T-B-29-17

THE EFFECT OF LIGHT THERAPY ON CLINICAL AND BIOLOGICAL INDICATORS IN PATIENTS WITH TREATMENT-RESISTANT DEPRESSION

PhD candidate: Biljana Kosanović Rajačić, MD, psychiatrist

PhD Thesis: The effect of light therapy on brain-derived neurotrophic factor plasma levels and interleukin-6 serum levels in patients with treatment-resistant depression

Mentor/s: Professor Dražen Begić, PhD, MD, psychiatrist

Affiliation: University Hospital Center Zagreb

Introduction: In clinical practice and on the basis of recent research, favorable therapeutic effect of light therapy in depressive disorder has been observed, but the effect of phototherapy on brain-derived neurotrophic factor (BDNF) and interleukin-6 (IL-6) levels in treatment-resistant depression (TRD) has not been explained yet. The aim of this research is to investigate the effect of phototherapy on BDNF and IL-6 levels and its correlation with clinical picture and quantitative EEG (qEEG) results. The research will encompass patients with diagnosed TRD, at the Department of Psychiatry and the Department of Laboratory Diagnostics, University Hospital Center Zagreb.

Hypothesis: Phototherapy leads to the increase of BDNF plasma levels and the decrease of IL-6 serum levels in patients with TRD. The significant reduction of depressive symptoms is correlated with increased levels of BDNF and decreased levels of IL-6.

Aims: The primary objective is to determine the effect of phototherapy on the BDNF plasma levels and the IL-6 serum levels in patients with TRD. We will determine whether there is a correlation between the increase of BDNF and the decrease of IL-6 with improvement in depressive symptoms. As the secondary objective we will investigate the changes in the qEEG before and after phototherapy, and the correlation of these changes with the outcome of treatment.

Materials and methods: The study will include 60 patients, according to power analysis, suffering from depressive disorder who have shown resistance to antidepressants in previous treatment. The examiner will perform a psychiatric interview, confirm the diagnosis in accordance with ICD-10 and DSM-5, and take socio-demographic data. Participants will continue to take antidepressants. Then, just before the start and after 4 weeks of phototherapy will apply HAMD-17 and MADRS scales, take out blood to measure the concentration of BDNF and IL-6, and do qEEG. The study will be carried out during 2017. and 2018.

Expected scientific contribution: Better understanding of TRD and new insights into the connection between biological and clinical indicators are expected, which will enable us to further research, and more efficient and faster treatment of depressed patients.

Acknowledgments: I would especially like to thank Assistant Professor Marina Šagud, the leader of the project 'The impact of religiosity on the outcome of treatment of depression: clinical and biological indicators' in which my research is carried out, and also my mentor Professor Dražen Begić and Professor Alma Mihaljević-Peleš for their support and help.

MeSH/Keywords: treatment-resistant depression, light therapy, BDNF, IL-6, qEEG

Poster code: T-B-29-24

SERUM CONCENTRATIONS OF ZINC, ALBUMIN, C-REACTIVE PROTEIN AND INTERLEUKIN-6 IN PATIENTS WITH MAJOR DEPRESSIVE DISORDER AND DEPRESSIVE EPISODE OF BIPOLAR DISORDER

PhD candidate: Tihana Bagarić, MD

PhD Thesis: Serum concentrations of zinc, albumin, C-reactive protein and interleukin-6 in patients with major depressive disorder and depressive episode of bipolar disorder

Mentor/s: Professor Alma Mihaljević Peleš, MD, PhD

Affiliation: University Hospital Centre Zagreb, University of Zagreb, School of Medicine

Introduction: Due to the similarity in the clinical presentation of major depressive disorder and depressive episodes of bipolar disorder, it is often in clinical practice that bipolar disorder is misdiagnosed and therefor incorrectly treated. Unrecognized bipolar patients are in this case treated with antidepressants, which is not only ineffective, but may lead to worsening of bipolar disorder. From the literature it is known that there are certain biological indicators that could help in the distinction between these two entities, but for now none is sufficiently reliable.

Hypothesis: There is a difference in biological parameters (zinc, albumin, C-reactive protein, interleukin-6) between the patients with major depressive disorder and patients in the depressed phase of bipolar disorder.

Aims: To determine concentrations of zinc, albumin, C reactive protein and interleukin-6 in the serum of patients with major depressive disorder and in patients in depressive episode of bipolar disorder.

Materials and methods: The research will include total od 128 participants of both sexes, aged 18 to 60, fulfilling the criteria for major depressive disorder and depressive episode of bipolar disorder according to ICD 10 and DSM 5. Research will be conducted individually using sociodemographic questionnaire. The severity of depressive symptoms will be measured by the Montgomery Asberg Rating Scale (MADRS) and the Hamilton Depression Scale (HAM-D-17). Clinical Global Impression Severity Scale (CGI-S) will be used to assess severity of the disorder. Blood samples will be obtained from a brachial vein from each study participant,in order to determine serum concentrations of zinc, albumin, CRP and IL-6.

Expected scientific contribution: It is expected that this research will contribute to the timely recognition and diagnosis of major depressive disorder and depressive phases of bipolar disorder. Possible contribution is reflected in connecting the observed biological parameters and clinical characteristics of the studied disorders.

Acknowledgments:

MeSH/Keywords: major depressive disorder, bipolar disorder, zinc, albumine, C reactive protein, interleukin 6

Poster code: T-B-29-101

SHAME AND NARCISSISM

PhD candidate: Marija Eterović, MD

PhD Thesis: The association between shame and grandiose and vulnerable narcissistic personality traits

Mentor/s: Professor Vesna Medved, MD, PhD and Assistant Professor Vedran Bilić, MD, PhD

Affiliation: University of Zagreb School of Medicine, University of Zagreb Faculty of Humanities and Social Sciences, University of Zagreb Faculty of Kinesiology, Clinical Hospital Dubrava

Introduction: Empirical studies of shame and narcissism assess narcissistic pathology as a categorical construct characterized by indicators of grandiosity. This framework ignores the complexities of the construct that also include vulnerability, which should be appreciated as dimension of narcissism, together with grandiosity.

Hypothesis: Narcissistic grandiosity is associated with rigid and totalistic denial of shame. On the contrary, narcissistic vulnerability is associated with flexible and non-totalistic affirmation of shame.

Aims: To explore the association of grandiose, as well as vulnerable narcissistic personality traits, with shame proneness, variability of responses to different shame-inducing situations, and sensitivity to the increased intensity of these situations.

Materials and methods: A minimum number of 300 students will be enrolled into the study. We plan to: 1. Translate into Croatian language using forward- and back-translation processes, adapt, and make preliminary validation of the measures of shame- and guilt- proneness (TOSCA-3), grandiose narcissistic personality traits (NPI), and vulnerable narcissistic personality traits (HSNS). 2. Add the situations of increased intensity to the original situations of the TOSCA-3 measure. Apply them together with TOSCA-3, NPI, HSNS, and demographic questionnaire to all subjects. 3. Examine the association of the total NPI score and the NPI-domains with the score on the TOSCA-3 shame-domain. 4. Examine the association of the HSNS score with the score on the TOSCA-3 shame-domain. 5. Examine the association of the total NPI score, as well as the HSNS score, with variability of the responses on the TOSCA-3 shame-domain. 6. Calculate the differences between responses to TOSCA-3 shame-inducing situations of different intensity (effect of provocation). Examine the association of the total NPI score, as well as the HSNS score, with the effect of provocation.

Expected scientific contribution: Elucidating the complex interplay between shame and narcissism while appreciating the complementarity and dimensionality of grandiose and vulnerable expressions of narcissism, hereby, generating a more expanded narcissism construct that should have increased utility for clinicians. The methodological novelty is exploring the pattern of responses on the original measures and their modification.

Acknowledgments:

MeSH/Keywords: shame, narcissism, grandiosity, vulnerability

Poster code: T-B-29-129

MULTIMODAL EVOKED POTENTIALS IN THE ASSESSMENT OF FATIGUE IN PATIENTS WITH RELAPSING-REMITTING MULTIPLE SCLEROSIS

PhD candidate: Gorana Vukorepa, MD

PhD Thesis: Multimodal evoked potentials in the assessment of fatigue in patients with relapsing-remitting multiple sclerosis

Mentor/s: Assistant Professor Mario Habek, MD, PhD

Affiliation: University Hospital Centre-Zagreb

Introduction: Fatigue is a common and extremely disabling symptom in patients with multiple sclerosis for which there are no adequate biomarkers. The most commonly used in the evaluation of fatigue are rating scales among which psychometrically most roboust is Neurology Fatigue Index, and as electrophysiological marker evoked potentials are used.

Hypothesis: Patients with fatigue have increased number of pathological evoked potentials

Aims: The aim of this study was to compare the number of pathological visual, auditory, somatosensory and vestibular evoked potentials and the sum of the EP with a degree of fatigue according to the results obtained in fatigue assessment scales.

Materials and methods: Total of 100 patients with MS (50 with and 50 without symptoms of fatigue) will first be given Beck depression scale and Epworth Sleepiness Scale to exclude patients with depression or sleepiness disorders. Patients will be divided into two groups depending on numerological fatigue level on Neurology Fatigue Index-NFI-MS. Patients with sum =18 will be in fatigued group, while patients with sum <18 in non-fatigued group. Every enrolled patient will do following tests and diagnostic work up: neurological exam quantified in EDSS form, rating scales: Neurology Fatigue Index-NFI-MS, Visual Analogue Scale, Fatigue Severitiy Scale-9, Modified Fatigue Severity Scale-21, evoked potentials: VEP, AEP, SSEP n.tibialis and n.medianus, VEMP. For all evoked potentials latencies and amplitudes will be determined as well as EP and VEMP score and compared with laboratory normatives.

Expected scientific contribution: Results of this study will determine the importance of evoked potentials as a biomarker of fatigue. There are no published studies in patients with RRMS regarding correlation of fatigue severity with results of multimodal EP, EP and VEMP score. Results of this study could as an outcome have use of multimodal evoked potentials as objective fatigue biomarker with diagnostic and therapeutical implications in RRMS patients.

Acknowledgments: I would like to thank to Tereza Gabelić, MD, PhD for her support in design of this study

MeSH/Keywords: fatigue, multiple sclerosis, evoked potentials

Poster code: T-B-30-46

AUTONOMIC DYSFUNCTION IN PATIENTS WITH CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY

PhD candidate: Rujana Šprljan Alfirev, MD

PhD Thesis: Autonomic dysfunction in patients with chronic inflammatory demyelinating polyneuropathy

Mentor/s: Assoc. Prof. Ervina Bilić, MD, PhD

Affiliation: University of Zagreb School of Medicine, University Hospital Center Zagreb, Department of Neurology

Introduction: Chronic inflammatory demyelinating polyneuropathy (CIDP) is an acquired immune disorder of peripheral nerves and nerve roots. Immunogenetic variations are the probable cause of different phenotypic variants in the CIDP spectrum. The inflammatory process affects mainly large, myelinated fibers. In contrast to acute autoimmune polyneuropathies (e.g. Guillain Barre syndrome), autonomic nervous system (ANS) testing is not included in the standardized workup for chronic forms. Data about autonomic dysfunction in these patients are lacking. Most previously published studies found that autonomic dysfunction is a rare manifestation of CIDP. On the other hand some recent studies suggest a higher prevalence of autonomic dysunction in CIDP.

Hypothesis: CIDP affects autonomic system nerve fibers, especially small myelinated fibers, which can be detected by standardized ANS testing.

Aims: The aim of this research is to determine the prevalence and type of autonomic dysfunction in CIDP patients using standardized ANS testing. We will also determine the clinical and electrophysiological characteristics of CIDP and try to correlate autonomic dysfunction symptoms quantified by validated questionaire scores with objective scores of ANS testing.

Materials and methods: We aim to recruit a total of 31 adult patients with the diagnosis of idiopathic CIDP (European Federation of Neurological Societies/Peripheral Nerve Society criteria), meeting previously established inclusion and exclusion criteria. The research will be conducted in the University Hospital Center Zagreb, Department of Neurology. After signing an informed consent, all patients will be carefully neurologicaly examined, detailed patient history will be taken, and two standardized diagnostic procedures will be performed. These procedures are clinical electromyoneurography using needle and surface electrodes and ANS testing consisting of Valsalva maneuver, deep breathing test and tilt table test. Clinical symptoms will be scored by validated questionaires. Acquired data will be statistically analysed.

Expected scientific contribution: We expect our results to show that autonomic dysfunction is prevalent in CIDP and establish a correlation between clinical symptoms and ANS testing recordings. This would prompt clinicians to include ANS testing in managing this group of patients since unrecognized and untreated autonomic dysfunction could lead to poorer disease outcome and lower quality of life.

Acknowledgments:

MeSH/Keywords: chronic inflammatory demyelinating polyradiculoneuropathy, autonomic dysfunction, autonomic nervous system testing

Poster code: T-B-30-65

INCIDENCE AND CHARACTERISTICS OF NEUROPATHY IN PATIENTS WITH CHRONIC GRAFT VERSUS HOST DISEASE

PhD candidate: Branimir Ivan Šepec, MD

PhD Thesis: In a significant proportion of cGVHD patients clinical and/or electrophysiological signs of neuropathy are present.

Mentor/s: Prof. Ervina Bilić, MD PhD[1], Assist. Prof. Dražen Pulanić, MD PhD[2]

Affiliation: University of Zagreb School of Medicine and University Hospital Centre Zagreb, Department of Neurology[1], Division of Hematology, Department of Internal Medicine[2]

Introduction: Chronic graft-versus-host disease (cGVHD) is a major late complication after allogeneic stem cell transplantation (alloSCT), which affects from 30 to 70% of long term survivors. Most frequent involved organs are the skin, eyes, mouth, lungs, gastrointestinal tract, liver, but also joints/fascia and genital tract. Although neurologic manifestations in cGVHD patients may involve the central nervous system (vasculitis, demyelination, encephalitis), the peripheral nervous system (polyneuropathy), the neuromuscular junction (myasthenia gravis) or the muscle (myositis), there are no diagnostic neurologic criteria for cGVHD. Only myositis and polymyositis are considered as "distinctive" for cGVHD, while different forms of polyneuropathy and myasthenia are regarded as "associated features".

Hypothesis: Most cGVHD patients have clinical or electrophysiologic signs of peripheral neuropathy. Neuropathic pain occurs when C fibers are affected.

Aims: To detect lesions of the peripheral nervous system in patients with cGVHD, describe their incidence, characteristics and favouring factors.

Materials and methods: We will include 45 patients with cGVHD after alloSCT and 30 controls (patients after alloSCT but without cGVHD). cGVHD will be assessed and scored according to the NIH criteria. Electrophysiologic: Electroneurography, quantitative sensory testing. Neurologic examination. Questionnaires: Pain detect questionnaire, total neuropathy score. Laboratory: Ca, Mg, P, K, PTH, vitamin D, vitamin B12, folic acid, Cu, Zn, Se.

Expected scientific contribution: To detect the incidence, characteristics and favouring factors of neuropathy in patients with cGVHD after alloSCT, with possible conclusions regarding prevention and treatment for neuropathy, neuropathic pain and muscle cramps.

Acknowledgments: Snježana Švedi, Milica Jug.

MeSH/Keywords: Polyneuropathy, cGVHD, muscle cramps

Poster code: T-B-30-69

DIAGNOSTIC ACCURACY OF SERUM BIOMARKERS OF INFLAMMATION, STRESS AND ISCHEMIA IN DIFFERENTIANTIG BETWEEN SEIZURES AND PSYCHOGENIC NONEPILEPTIC ATTACKS

PhD candidate: Ana Piršić, MD

PhD Thesis: Diagnostic accuracy of serum biomarkers of inflammation, stress and ischemia in differentiating between seizures and psychogenic nonepileptic attacks

Mentor/s: Professor Igor Filipčić, MD, PhD, Professor Ana-Maria Šimundić, PhD

Affiliation: Sveti Duh University Hospital, Sveti Ivan Psychiatric Hospital, University Hospital Centre Zagreb, University Hospital Dubrava

Introduction: Seizure (S) is defined as transient signs and/or symptoms due to abnormal excessive synchronous neuronal activity of the brain. Psychogenic nonepileptic attack (PNEA) is an abrupt paroxysmal change in behavior or consciousness semiologically resembling S, without typical accompanying changes in electroencephalogram (EEG), with psychogenic process as a causative factor. In a clinical context, distinguishing S (as part of epilepsy) from PNEA is extremely important due to the different therapeutic approach, but is often difficult in spite of available diagnostic tests. Consequently, research of novel biomarkers for differentiating between the two is ongoing.

Hypothesis: Due to different characteristics of motor activity and due to differences in the pathophysiological processes including sympathetic and parasympathetic dysfunction, S and PNEA differ in the level of inflammatory response, stress and ischemia.

Aims: To examine the diagnostic accuracy of biochemical markers (copeptin, calprotectin, lactate, troponin, creatine kinase, creatine kinase-MB and myoglobin) in distinguishing S from PNEA.

Materials and methods: The study is planned as applied, observational, multicenter and cross-sectional study of diagnostic accuracy. Accessible population, from which will be sampled, will consist of patients during continuous video-EEG monitoring, clinically presenting with motor semiology. The consecutive sample of patients, according to the admission in centers, will consist of 40 patients with S episode and 40 patients with PNEA episode. Lactate concentration will be determined from the capillary blood 30 minutes after the episode while the venous blood will be sampled after four hours, stored at -20 ° C for the subsequent analysis of serum biomarkers: copeptin, calprotectin, troponin, creatine kinase, creatine kinase - MB and myoglobin, whose analysis will be performed after having completed the sampling of scheduled number of patients. The episode will subsequently be classified into S or PNEA according to the assessment of an experienced neurologist and psychiatrist.

Expected scientific contribution: Theoretical contribution will be a better understanding of pathophysiological changes during and immediately after the episodes, while the clinical purpose is improvement in diagnostic accuracy.

Acknowledgments: This study is financially supported by the project of Centre of Integrative Psychiatry (NCT02773108), Sveti Ivan Psychiatric Hospital. I would like to thank my mentors for their guidance.

MeSH/Keywords: seizure, psychogenic nonepileptic attack, diagnostic accuracy, biochemical marker

Poster code: T-B-30-73

MARKERS OF APOPTOSIS IN THE CEREBROSPINAL FLUID AND SERUM OF PATIENTS WITH CONVULSIVE STATUS EPILEPTICUS

PhD candidate: Lejla Ćorić, M.D.,neurologist

PhD Thesis: Elevated apotosis markers in the serum and cerebrospinal fluid of patients with convulsive status epilepticus

Mentor/s: Professor Željka Petelin, M.D., Ph.D., neurologist

Affiliation: Department of Neurology, UHC

Introduction: Epileptic status (ES) is the most serious instance of epileptic seizures that represents an emergency medical state. It is well known that prolonged excitation activity in brain cells during epileptic seizures can lead to brain damage and death. The production and accumulation of reactive compounds can result in damage and death of cells by activating apoptotic and/or necrotic pathways in cells. Apoptosis is a process of programmed cell death that occurs intrinsically, intracellularly or extrinsically, extracellularly. Molecules important for the initiation and implementation of programmed cell death belong to the superfamily of proteins called the tumour necrosis factor (TNF), one of which is the Fas (CD95/Apo-a) receptor, onto which Fas ligand is bound, initiating the process of apoptosis.

Hypothesis: This research sets three hypotheses: 1) there is a significant difference in the levels of markers of extrinsic and intrinsic apoptotic pathways in the cerebrospinal fluid and serum of patients with convulsive epileptic status, compared to a control group of subjects. 2) There is no statistically significant difference in levels of markers of extrinsic and intrinsic apoptosis in the cerebrospinal fluid and serum with convulsive epileptic status. 3) There is a statistically significant difference in the levels of markers of apoptosis in the serum of patients with convulsive epileptic status before and after receiving treatment.

Aims: This research aims at establishing the presence of markers of intrinsic and extrinsic apoptotic pathways in the serum and cerebrospinal fluid of patients with convulsive epileptic status, and at exploring the difference in the concentration of markers in extrinsic apoptotic pathways (sFAS) and markers of intrinsic apoptotic pathways (Bcl 2) in the cerebrospinal fluid and serum of patients with convulsive epileptic status. Finally, the research aims to determine whether there is a difference in the levels of markers of apoptosis in the serum of patients with a convulsive epileptic status prior to and after received treatment.

Materials and methods: The purpose of this study is to analyse the data collected from the blood of 40 adult patients with history of convulsive status epilepticus, and to compare them with compatible number of patients of the control group. Criteria for inclusion in this investigation will be diagnosis of convulsive status epilepticus. Level of sFAS / APO 1 in serum and cerebrospinal fluid, Bcl protein, will be determined with enzyme-specific linked immunosorbent assay (ELISA) whales. Results will be presented as the mean value and the standard deviation. The normality of the distribution variables will be tested by the Kolmogorov-Smirnov test. The difference between the groups will be calculated by Student t test. The connection between the sFAS / APO1 levels in serum and CSF, and level of Bcl proteins in serum and cerebrospinal fluid will be tested by Pearson's correlation coefficient. Student's t-test for paired samples will be used in order to compare repeated measurements of continuous variables within the group.

Expected scientific contribution: Research biochemical markers in epileptic status in humans will contribute to a better understanding of the domination of certain pathogenic mechanisms of prolonged epileptic activity to draw attention to the possible further development of epileptogenesis.

Acknowledgments: I would like to thank my all my colleagues for support.

MeSH/Keywords: epileptic status, adults, seizures, apoptosis, TNF, Bcl-2, sFAS.

Poster code: T-B-30-79

Public Health and Health Care – Thesis Proposals

PREVALENCE OF ALLERGIC DISEASES AMONG SCHOOL CHILDREN OF NATURAL PARK LONJSKO POLJE AND CITY OF ZAGREB

PhD candidate: Iva Topalušić, MD

PhD Thesis: Prevalence of allergic diseases among school children of Natural park Lonjsko Polje and City of Zagreb

Mentor/s: Prof. Asja Stipić Marković, MD, PHD

Affiliation: 1 Children´s Hospital Zagreb, 2 Clinical Hospital Sveti Duh

Introduction: Prevalence of allergic diseases in industrialised countries, as well as in Croatia, has dramatically increased. Although etiology of allergic diseases is not fully understood, it is believed that it is strongly influenced by enviromental factors, especially microorganisms. Large population studies, epigenetic and imigration studies have shown higher prevalence of allergic diseases in urban and highly industrialised areas, comparing to microbiota rich, rural enviroment. According to biodiversity hypothesis, loss of the macrodiversity is associated with alterations of the indigenous microbiota, which leads to the loss of imunotolerance.

Hypothesis: The prevalence of symptoms of allergic rhinitis, atopic dermatitis and asthma among school children, as well as allergic sensibilisation is higher in The City of Zagreb than in the rural Area of Natural Park Lonjsko Polje.

Aims: The aim of the study is to compare the prevalence of allergic disease symptoms and sensibilisation in rural (Lonjsko polje) and urban area (City of Zagreb) using standardisied ISAAC (Internatinal Study of Allergy and Asthma in Childhood) methodology, in correlation with enviromental life-style characteristics.

Materials and methods: A total random sample of 1500 school-children aged 6-7, 10-11 and 13-14 years old from both City of Zagreb and Lonjsko polje will be included. Parents will be asked to complete ISAAC questionnaires about symptoms of allergic rhinitis, atopic dermatitis and asthma, child´s demographic characteristics, enviromental factors and life- style in the present and in the past. All children will be examined on skin signs of atopic dermatitis and will be performed skin prick test on standard set of inhallant allergens. The difference between investigated groups will be calculated with Chi square test. A probability value of $p<0.05$ (two-tailed) indicates a statistically significant difference. Univariate regression and multiple linear models and logistic regressions will be used.

Expected scientific contribution: The study will give information on prevalence of allergic diseases among school children in Lonjsko polje and City of Zagreb. A comparison of results and correlation with enviromental factors and life style will help to understand the etiology of atopic diseases and to build future prevention strategies.

Acknowledgments: We declare no confflict of interest

MeSH/Keywords: epidemiology of allergic disease, biodiversity, ISAAC studies, prevention

Poster code: T-C-1-114

ANALYSIS OF OUT-OF-HOSPITAL EMERGENCY MEDICAL SERVICE SYSTEM REGARDING THE OUTCOME OF RESUSCITATION PROCEDURE

PhD candidate: Damir Važanić, RN, MSN

PhD Thesis: Analysis of out-of-hospital emergency medical service system regarding the outcome of resuscitation procedure

Mentor/s: Professor Ingrid Prkačin, MD, PhD, Assistant Professor Višnja Nesek Adam, MD, PhD

Affiliation: Croatian Institute of Emergency Medicine

Introduction: In Republic of Croatia 8.346 cardiac arrests have been noted in outpatient conditions during 2016. Out of overall number of cardiac arrests, out-of-hospital Emergency Medical Service (EMS) has begun cardiopulmonal resuscitation in 3.098 cases of, out of which 549 patients have been handed over to hospital with the return of spontaneous circulation (ROSC). Overall analysis of EMS system factors and their mutual interconnection could result with solutions for detection of those factors which influence on better outcome of resuscitation procedure.

Hypothesis: Reduction of time intervals from cardiac arrest to hospital handover of patients with ROSC affect on resuscitation procedure outcome for out-of-hospital cardiac arrest.

Aims: 1. Determine the influence and mutual interconnection of EMS system factors regarding outcome of cardiopulmonal resuscitation in out-of-hospital settings, 2. Determine relationship between resuscitation procedure outcome and different time intervals from call reception to hospital handover, 3. Determine outcome of cardiac arrest regarding bystanders resuscitation, dispatcher assisted CPR, first monitored cardiac rhythm, day or night working shift.

Materials and methods: This prospective research will include adults with out-of-hospital sudden cardiac arrest. Data will be collected in time frame of one year from out-of-hospital EMS information database through Utstein template and time interval data set. Collected data will be processed based on relevant statistical methods. The results will be interpreted at the 5% significance level.

Expected scientific contribution: Overall analysis of EMS system will determine factors which affect on resuscitation procedure outcome in out-of-hospital settings until hospital handover. As a research result, a basis for new EMS system tool analysis regarding the outcome of resuscitation procedure will be obtained.

Acknowledgments:

MeSH/Keywords: emergency medical service, system, resuscitation, cardiac arrest, outcome

Poster code: T-C-2-7

SIGNIFICANCE OF TRADITIONAL MASCULINITY FOR THE PREDICTION OF INJURIES IN MALE ADOLESCENTS

PhD candidate: Natko Gereš

PhD Thesis: Significance of traditional masculinity for the prediction of injuries and accidents in male adolescents

Mentor/s: Aida Mujkić, Pamela Orpinas

Affiliation: Andrija Štampar School of Public Health, Zagreb School of Medicine, University of Zagreb

Introduction: Health Promotion and Behavior, College of Public Health, University of Georgia, USA

Hypothesis: Risk from injuries and accidents is increased for men in comparison to women. Young men are especially at risk. There is a complexity of interactions between environmental and personal factors (masculinity, impulsivity, depression and indicators of socioeconomic status, micro and macro environment) in relation to risky behaviors and injuries and accidents. Men have higher incidence of risky behaviors (for instance, alcohol use) that contribute to injuries. Existing studies put emphasis on exploring traditional masculine attitudes as factors contributing to this trend.

Aims: Expressed traditional attitudes measured through 5 dimensions (avoidance of femininity, self-reliance, aggression, status and restrictive emotionality) are significant predictors of risky behaviours with students of high schools in the age of 16 and 17 in the city of Zagreb.

Materials and methods: Analyse existence of the correlation between expressed traditional masculine attitudes and personal and environmental factors with risk behaviours related to safety and experiences of injuries and accidents with 16 and 17-year-old high school students from the city of Zagreb.

Expected scientific contribution: The research was implemented by using, among other instruments, already existing validated tools on 1. Injuries and accidents: Youth Risk Behavior Survey-YRBS (CDC, 2013), 2. Masculinity: Male Role Norm Inventory-Adolescent-revised (Levant et al., 2008) and 3. Experiences of injuries and accidents using Injury Checklist (Jelalian, 1997). Respondents were 2nd and 3rd-grade high school students (n=4230).

Acknowledgments:

MeSH/Keywords: Natko Gereš, prof.dr.sc. Aida Mujkić, prof.dr.sc. Pamela Orpinas

Poster code: T-C-2-32

INTERACTION OF CONSTITUTIONAL AND OCCUPATIONAL RISK FACTORS ON THE INCIDENCE OF OCCUPATIONAL CONTACT DERMATITIS IN HAIRDRESSING APPRENTICES DURING VOCATIONAL TRAINING

PhD candidate: Zrinka Franić, MD

PhD Thesis: Interaction of constitutional and occupational risk factors on the incidence of occupational contact dermatitis in hairdressing apprentices during vocational training

Mentor/s: Professor Suzana Ljubojević Hadžavdić, MD, PhD, Jelena Macan, MD, PhD, scientific advisor

Affiliation: Institute for Medical Research and Occupational Health

Introduction: The most common occupational skin diseases are irritative contact dermatitis (ICD) and allergic contact dermatitis (ACD) primarily located on the hands, with occupational contact to irritants (wet work) and allergens from hairdressing chemicals. Pilot study on Croatian hairdressing apprentices showed that work-related skin symptoms were present in 40% of apprentices at clinical examination on their 3rd year of education. Regarding skin protection measures, gloves are used regularly during treatment of hair with chemicals, but are rarely used during hair washing.

Hypothesis: Occupational exposures to physical and/or chemical hazards are ethio-pathogenetically related to the development of ICD and ACD. Development of ICD and ACD is influenced by the level and duration of exposure to occupational physical and/or chemical hazards and by constitutional characteristics. Filaggrin gene (FLG) polymorphism has a significant role in ICD and ACD development.

Aims: The main goal of this research is to estimate the prevalence and 3-year incidence of ICD and ACD in hairdressing apprentices that represent high-risk population, and to assess occupational and constitutional factors (FLG polymorphism and factors related to the function of skin barrier) with the impact on development and course of these diseases.

Materials and methods: Prospective cohort study will be conducted on 500 apprentices, starting at the beginning of their vocational education, with follow-up of skin condition at the end of each school year. The prevalence of self-reported skin symptoms will be assessed by a translated Nordic Occupational Skin Questionnaire. Skin examination will include Osnabrueck hand eczema severity index. Buccal swabs will be used for genotyping FLG-2282del4 and FLG-R501X alleles. Allele variations will be detected through the TaqMan SNP method using an Applied Biosystems 7500 Fast Real-Time PCR System. Skin pH and TEWL (transepidermal water loss) measurements will be performed by commercial devices. Standard patch testing will be applied in individuals with reported skin symptoms, with European baseline series and additional hairdresser series.

Expected scientific contribution: To estimate prevalence of genetic polymorphisms considered to be in relation with the appearance of ICD and ACD in Croatian population, accompanied by the potential for defining individual indicators of susceptibility to the development of analyzed ICD and ACD in exposed apprentices.

Acknowledgments:

MeSH/Keywords: occupational contact dermatitis, prevention, safety at work, filaggrin gene polymorphism, contact sensitization

Poster code: T-C-3-93

QUALITY OF LIFE AND BURDEN IN FAMILY MEMBER CAREGIVERS OF PATIENTS WITH DEMENTIA

PhD candidate: Jelena Lucijanić, MD

PhD Thesis: Quality of Life and Burden in Family Member Caregivers of Patients with Dementia

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Introduction: With aging of population dementia is becoming growing global health problem affecting both patient with dementia and his/her family members. Patient's family should be included in the disease management process due to long duration of disease. Although health care is focused on a patient, additional care should be given to caregivers-family members. People that care about family members with dementia are exposed to additional emotional, physic, social and financial stressors.

Hypothesis: Caregivers family members of patients with dementia have poorer quality of life than general population of Croatia, especially if patients exhibit behavioral symptoms of dementia.

Aims: Aim of this study will be to estimate quality of life and caregiver burden in a population of caregivers family members of patients with dementia and to estimate associated factors in patients and caregivers.

Materials and methods: Cross-sectional study will be carried out in a town of Zagreb. Total of 130 families that include patient with dementia and one member that is a dominant caregiver will be analyzed. Zarit caregiver burden scale will be used to estimate caregiver burden and SF-36 questionnaire will be used to estimate quality of life.

Expected scientific contribution: Better understanding of factors associated with impaired quality of life and increased caregiver burden in caregivers family members of patients with dementia. Obtained results will be used in planning future interventions in this population.

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