

Dan doktorata

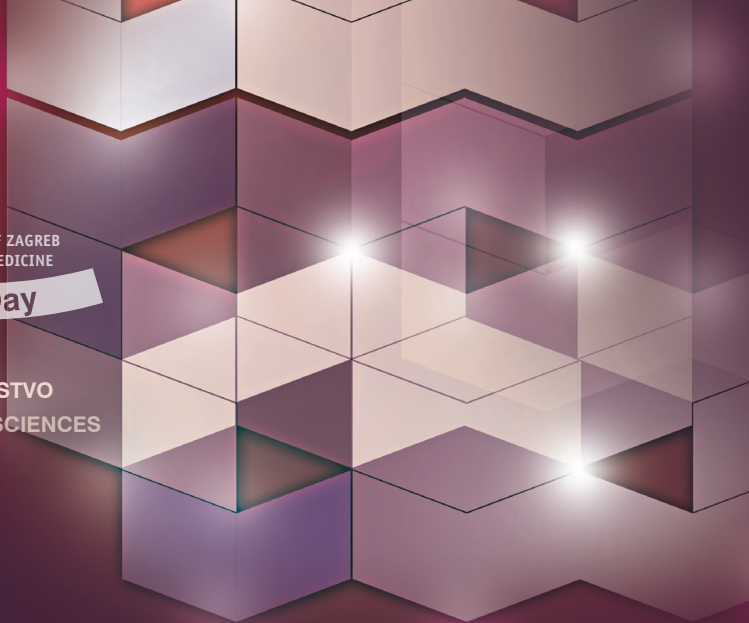
SVEUČILIŠTE U ZAGREBU
MEDICINSKI FAKULTET



UNIVERSITY OF ZAGREB
SCHOOL OF MEDICINE

PhD Day

DOKTORSKI STUDIJ BIOMEDICINA I ZDRAVSTVO
PhD PROGRAMME BIOMEDICINE AND HEALTH SCIENCES



DAN DOKTORATA

KNJIGA SAŽETAKA

PhD DAY
ABSTRACT BOOK

2015.

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

Doktorski studij Biomedicina i zdravstvo/PhD Programme
Biomedicine and Health Sciences

Dan doktorata 2015/PhD Day 2015

Knjiga sažetaka/Abstract Book

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Knjiga sažetaka/Abstract Book

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Doktorski studij Biomedicina i zdravstvo

PhD Programme Biomedicine
and Health Sciences

Dan doktorata 2015

PhD Day 2015

Knjiga sažetaka

Abstract Book

Medicinska naklada
Zagreb, 2015.

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PREFACE

PhD Day (Dan doktorata) started in 2012 and became a traditional annual event of PhD students at the School of Medicine University of Zagreb. The idea was to gather students, their mentors and distinguished guests from scientific community to help our students to improve their scientific work.

PhD Day is one day symposium which consists of a presentation of ongoing research of PhD students in a form of published abstracts, poster and selected oral presentations. It is mandatory for all the 2nd-year and 3rd-year students of the PhD programme Biomedicine and Health Sciences to participate in the PhD day and present their PhD theses projects and preliminary results.

PhD Day is an opportunity for PhD students 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.

PhD Day serves also as a motivation for PhD students to focus on their research because 3rd-year students have to present at least preliminary results of their research.

PhD Day also includes lectures from renowned scientists, which serves as a motivation for PhD students to finish their studies and to continue their research throughout their carriers, because science is an inseparable part of medicine. For the first time in 2013, selected abstracts were presented in oral form, which aroused great interest of participants. Last year, selected students presented their research through lectures and afterwards in informal communication shared their experiences and research work.

PhD Day serves as an opportunity to present research to colleagues and to encourage co-operation and interaction between scientists and yield even greater progress in their work. PhD Day is a public display of research activities and an opportunity of assessment of research work of PhD students and their mentors. For some PhD students this is maybe the first chance to give a talk and present their research in front of an audience.

Important part of PhD Days is also a motivation for mentors, because PhD Day also reflects activity of the mentors, which is crucial for research of PhD candidates. Therefore, we encourage participation of not only students, but also their mentors.

This year we are pleased to have an increasing number of abstracts which are presenting research results and not only abstracts with PhD theses presentation.

PhD Day is a day which celebrates science, research, co-operation and scientific friendship, gathering of PhD students, mentors and distinguished internationally recognized scientists as well as a great chance to share experiences and ideas in research and science.

*Marko Jakopović
Zdravko Lacković*

1. RESEARCH ABSTRACTS

1.1.

Basic Medical Sciences – Research Abstracts

Poster Title: EXPRESSION OF WNT 4 IN TRANSPLANT KIDNEYS

PhD candidate: Ines Mesar, MD

Part of the thesis: Expression of WNT 4 in transplant kidneys

Mentor/s: Professor Nikolina Bašić Jukić, MD, PhD

Affiliation: University Hospital Centre – Zagreb, Department of nephrology, arterial hypertension, dialysis and transplantation, Department of pathology

Introduction: Transplantation is the method of choice for patients with end stage renal disease. Thanks to modern pharmacology and new very potent immunosuppressants, rate of acute rejection is now very low. The most frequent cause of graft loss today is interstitial fibrosis and tubular atrophy. Better understanding of the processes that lead to it could in the future open up new therapeutic options to improve survival of transplant organs. WNT 4 is a secreted glycoprotein that is crucial for nephrogenesis during mesenchymal to epithelial transformation. Research in experimental models demonstrated its role in the process of kidney reparation during acute kidney injury, while on the other hand, there are experimental models in which WNT 4 participates in the formation of renal fibrosis. When will WNT 4 have protective effect on renal parenchyma and when will participate in the process of renal fibrosis has not yet been clarified.

Materials and methods: This is a retrospective study. Study group are the patients who had renal transplantation and graftectomy and control group are the patients who underwent nephrectomy due to localized renal carcinoma. In all the samples expression of the WNT4 will be done by immunohistochemical method. Expression will be quantified by the percent of positive tubule cells from O-III.

Results: At this time we have examined 45 samples, still no controls have been done. Most often reason for graft dysfunction was

chronic graft failure, then serious infection and vascular complications. Indications for graftectomy depended on the time when graftectomy was done. Depending on the graft survival we observed the most expression of the WNT 4 in those grafts which were removed in the first 3 months and in those after first year. Interestingly we observed that predominantly expression of the WNT 4 was correlated with some degree of graft rejection and some degree of interstitial fibrosis and tubular atrophy.

Discussion: This research would determine the localization patterns in humans of WNT 4, its expression in healthy kidney tissue as well as expression in kidney tissue after surgical removal of the transplanted organ. Still we lack of the control samples to be able to make some relevant conclusions but we can presume that expression of the WNT 4 will be in the relationship with rejection which is the trigger for later chronic changes in the kidney like interstitial fibrosis and tubular atrophy. Probably its expression begins with rejection and remains in the chronic kidney changes.

Acknowledgments: I would like to thank to Department of pathology UHC Zagreb, also many thanks to my mentor prof. Nikolina Bašić-Jukić

MeSH/Keywords: WNT 4, kidney, transplantation, tubulointerstitial fibrosis

Poster code: R-A-3-51

Poster Title: MALE AND FEMALE LACRIMAL GLANDS IN SF-1 KNOCKOUT MICE – PRELIMINARY RESULTS

PhD candidate: Kristina Šemanjski, MD

Part of the thesis: Sexual Dimorphism in Extraorbital Lacrimal Glands in Sf-1 Knockout Mice

Mentor/s: Professor Davor Ježek, MD, PhD, Professor Gregor Majdič, DVM, PhD

Affiliation: University of Zagreb, School of Medicine, Department of Histology and Embryology, University of Ljubljana, Veterinary Faculty, Center for animal genomics

Introduction: Sexual dimorphism (SD) represents all differences between males and females of the same species. SD of extraorbital lacrimal gland (GL) in the mouse is well documented. Also, a major effect of testosterone on the formation of “masculine” and “feminine” GL is proven. However, it remains unclear whether SD is solely determined by hormonal factors. Steroid factor-1 (SF-1) is nuclear receptor essential for embryonic survival of steroid organs. Mice with the knockout Sf-1 gene (Sf-1 KO) are born without gonads and adrenal glands and therefore are not exposed to sex hormones.

Materials and methods: This study included the tissue of extraorbital lacrimal gland of 10 Sf-1 KO male and 11 female mice and tissue of 8 Sf-1 KO male that received testosterone propionate in corn oil daily 2 weeks before sacrifice. C57BL/6J Sf-1 heterozygous mice were mated to produce homozygous Sf-1 KO offspring. To prevent death due to adrenal insufficiency all pups received daily subcutaneous injections of corticosteroids. Mice were genotyped by PCR assay of tail DNA on 6th or 7th day after birth. After genotyping, adrenal glands of WT littermates were excised and transplanted in Sf-1 KO pups. The animals were sacrificed after 6 months, GL removed and placed in Bouin’s fixative. The tissue was subjected to standard histological procedure. Paraffin sections were dyed with H-E, modified method by Masson and PAS

method and qualitative and quantitative measurements were done.

Results: Our histological analysis showed that in “male” GL acinar cells are polymorphous with irregular basophilic cytoplasm and nucleus located centrally. The borders between cells are indistinct. In contrast, “female” glands are more of uniform appearance, with nucleus located towards the basal part of the cell. The borders between cells are clearly visible. Also, we found pronounced lymphocytic infiltration in interlobular connective tissue and destruction of interlobular ducts in “male” GL. Our preliminary stereological results showed that in SF-1 KO mice the volume of lacrimal acini (per mm³ of the tissue) was higher in females. The volume and the length of the ductal system was higher in males, as was volume of connective tissue. Immunohistochemistry is yet to be done.

Discussion: According to our results we could conclude that sexual dimorphism in GL in SF-1 KO mice is present, although hormonal effects are excluded. This proves the impact of sex chromosomes on development of SD.

Acknowledgments: I would like to thank to Department of Histology and Embryology for help and support in my research.

MeSH/Keywords: sexual dimorphism, glandula lacrimalis extraorbitalis, testosterone, SF-1 KO mice

Poster code: R-A-3-57

Poster Title: THE ROLE OF GABA NEUROTRANSMITTER IN THE REGULATION OF THE ENDOCERVICAL MUCUS SECRETION

PhD candidate: Danijel Bursać, MD

Part of the thesis: The role of GABA neurotransmitter in the regulation of the endocervical mucus secretion

Mentor/s: Professor, Marija Ćurlin, PhD

Affiliation: Department of Obstetrics and Gynecology, University Hospital Merkur, Zagreb

Introduction: Infertility is an omnipresent problem of today's society. Reproductive system of woman and man is very sensitive and many factors affect and decrease the functionality of these systems. A significant, but in the research and treatment of infertility often overlooked factor of the women fertility is the uterine cervix. The cervix secretes cervical mucus, which prevents pathogen entering to uterus and also serves as a protective layer on the epithelium of the cervix and vagina. Cervical mucus plays an important role in fertility because it nourishes and keeps the sperms and guides them through the cervix and into the uterus. The mechanism of the regulation of the mucus production and release in the endocervical glands and the consequential change of the mucus properties during menstrual cycle is only partially explored. It is assumed that, besides estrogen and progesterone, neurotransmitter GABA also has a role in this regulation.

Materials and methods: Histological structure and secretory activity of the endocervical glands was analyzed and immunohistochemical detection and localization of the molecules involved in the GABA pathway of mucus secretion regulation was performed. Differences in the endocervical gland structure and activity and protein expression will be analyzed in relation to the day of the menstrual cycle and position of

the glands inside the cervical canal. The research was performed on the samples of the healthy human uterine cervix obtained after therapeutic operative procedures (usually hysterectomy).

Results: 39 uterine cervixes were analyzed immunohistochemically for GABA α receptor. The uteri were previously analyzed by a pathologist so the menstrual cycle phase could be determined. 22 out of 39 analyzed cervixes were labeled as 'proliferative phase', 10 as 'secretion phase', one as 'decidual reaction' and 6 were uncategorized. 10 out of 39 cervixes were positive for GABA α receptor. 6 were in proliferative phase, four in secretion and one uncategorized.

Discussion: The results prove existence of GABA receptor in the uterine cervix. At this moment it cannot be connected to the phase of menstrual cycle and further investigation is needed. Other components of the GABA secretion and action pathway need to be shown in order to prove a functional GABA system.

Acknowledgments: this research is supported by the grant of Ministry of science, education and sports, No. 108-1081870-1902

MeSH/Keywords: cervical mucus, GABA, infertility, cervix, menstrual cycle

Poster code: R-A-3-100

Poster Title: BIOREACTOR-ENGINEERED CARTILAGE GRAFT FOR OSTEOCHONDRAL KNEE LESION – STUDY IN SHEEP

PhD candidate: Andreja Vukasović

Part of the thesis:: Structural analysis of bioreactor – engineered autologous cartilage graft for treatment of osteochondral defects in sheep model

Mentor/s: Ass. Prof. Alan Ivković, MD, PhD

Affiliation: University of Zagreb School of Medicine, Department of Histology and Embryology University of Zagreb Faculty of Veterinary Medicine, Department of Surgery, Orthopedics and Ophthalmology

Introduction: The aim of this study was to produce tissue grafts from autologous nasal septum cartilage chondrocytes and biphasic scaffold in perfusion bioreactor, and use them for the treatment of osteochondral defects in a sheep stifle joint.

Materials and methods: Sixteen sheep were assigned to 4 treatment groups. All sheep underwent two surgical procedures. During the first procedure, chondral defects 4 mm in diameter were created on the weight bearing surfaces of both condyles of the right femur. After six weeks, all chondral defects were converted to osteochondral defects 6 mm in diameter and 5 mm deep. In groups NC (n=4) and AC (n=4) autologous three-dimensional osteochondral grafts engineered in perfusion bioreactor from bilayered scaffolds and nasal septum chondrocytes or articular chondrocytes, respectively, were implanted in the defect. In the CFS group (n=4) only bilayered scaffolds were implanted while CTR group (n=4) underwent only defect conversion (negative control).

Three months after treatment surgery, two sheep from each group were sacrificed. Remaining animals were sacrificed twelve months after treatment surgery. Tissue blocks of defect and surrounding healthy tissue were obtained for further analysis. The samples for histology analysis were fixed in 4% buffered paraformaldehyde and decal-

cified in 15% EDTA. Paraffin blocks were sectioned at 5 μ m and stained with hematoxylin-eosin, safranin O and picosirius Red. Immunohistochemistry was performed against collagen type I, II and aggrecan. Histology was evaluated with ICRS II histological score.

Results: Overall results showed that cartilage restoration was the best in NC group.

Discussion: Cell-based therapies for the treatment of cartilage defects are currently based on the use of chondrocytes derived from articular cartilage biopsies, which are known to possess high donor-to-donor variability. In vitro studies have shown that nasal chondrocytes could be more reproducible cell source. Our results showed that nasal septum cartilage chondrocytes have the capacity to restore articular cartilage in vivo. They could be a promising candidate for further tissue engineering studies.

Acknowledgments: The research leading to these results has received funding from the European Union's Seventh Framework Programme (FP7/2007-2013) under grant agreement n°278807.

MeSH/Keywords: perfusion bioreactor, cartilage, tissue engineering, osteochondral defects

Poster code: R-A-3-118

Poster Title: COMPARISON OF CLASSICAL AND ADVANCED DIAGNOSTIC TOOLS IN BONE TUMOR PATHOLOGY

PhD candidate: Ardita Qerimi

Part of the thesis: Comparison of classical and advanced diagnostic tools in bone tumor pathology

Mentor/s: Prof. Dr. Sven Seiwert

Affiliation: University of Zagreb

Introduction: Combination of immunohistochemical and molecular methods in bone tumor diagnosis can improve the diagnostic capacity in thesis changing also the therapeutic approach. 1. Re evaluate a group of bone tumors with giant cell morphology using classical, morphology-based diagnostic protocol and compare the results with the results obtained using advanced diagnostic techniques. 2. Re evaluate ES using classical, morphology-based diagnostic protocol and compare the diagnosis with the result obtained using advanced diagnostic techniques. 3. Testing of the predictive relevance of p16 at osteosarcomas.

Materials and methods: In the first part of the study will be included tumors with giant cell morphology diagnosed previously as Osteosarcoma with giant cell, Eosynophilic granuloma, giant cell tumour of bone and Aneurysmal bone cyst. Tumors will first be re evaluated using classical diagnostic tools (HE stain and radiologic – pathologic corre-

lation), than will be stained immunohistochemically for anti-CADM1, CD 68, p63, and CD 1a.

Results: First part of the study: Five of GCT from 15 were stained for CD68 and P63, two were negative for p63 but one was positive for CD1a (this marker is positive in EG) and the other is positive in P53. Nine EG were re- evaluated, six of them were stained for CD1a and CD68, diagnosis is same with classical tools and immunohistochemistry. Fifteen ABC were re-evaluate with classical tools, one was stained for CD68 to differentiate from GCT it was negative.

Discussion: For the rest of the cases we are waiting for results.

Acknowledgments: To my mentor

MeSH/Keywords: osteosarcoma, Aneurysmal bone cyst

Poster code: R-A-3-159

Poster Title: EFFECTS OF PENTADECAPEPTIDE BPC 157 ON SERIAL RIB FRACTURE HEALING IN RATS

PhD candidate: Goran Zukanović, MD

Part of the thesis: Pentadecapeptide BPC 157 has positive effect on serial rib fracture in rats

Mentor/s: Professor Predrag Sikirić, MD, PhD

Affiliation: Department of Pharmacology, Medical Faculty, University of Zagreb, Zagreb, Croatia

Introduction: Numerous studies have shown the beneficial effects of pentadecapeptide BPC 157 application in tissue healing. The hypothesis of this study was that the use of BPC 157 accelerates and improves healing of surgically induced serial rib fracture in rats. The objectives of this study were to analyze the effects of BPC 157 in healing of surgically induced injury in rats, on the level of clinical and functional outcomes and morphological changes in the examination of the macroscopic characteristics with the help of X-ray and computed tomography (CT).

Materials and methods: We used male Albino Wistar rats, 400 g body weight, kept under normal conditions, 10 rats at least per each experimental group and period, randomly assigned for all of the experiments, approved by our Local Ethics Committee. The method we used in causing serial rib fracture was the one described by Grills BL et al (1997.). In anaesthetized rats, an incision was made on the lateral aspect of the trunk between the eight and tenth rib. Previously mentioned ribs were located and fractured 2 cm from the vertebral column using a pair of fine scissors. Postoperatively the experimental animals were divided into two groups according to the mode of substance application. Then we divided the animals into treated (Group A1-experimental animals received 10 mg /kg BW of BPC 157

intraperitoneal once a day and Group B1 -experimental animals received 300 mg / l of BPC 157 dissolved in their drinking water) and the control group (A2-experimental animals received isotonic saline once a day applied intraperitoneally and group B2-experimental animals were given drinking water without any substance). The animals were sacrificed according to the study protocol on twentieth and on the sixtieth day after surgical rib fractures. After the sacrifice of the animals, macroscopic evaluation and further verification of the results by X-ray and CT was made.

Results: In animals treated with BPC 157 bridging occurs earlier in fracture crack, no overproduction of callus and creation of pseudoarthroses was found in later course of the healing process. We also found that the pleural adhesions in control group were significant unlike the treated group where we found no adhesions.

Discussion: The present macroscopic and radiological examinations results confirm our hypothesis but the histopathological analysis is still in progress.

Acknowledgments:

MeSH/Keywords: pentadecapeptide BPC 157, serial rib fracture, rats

Poster code: R-A-4-12

Poster Title: EFFECT OF PENTADECAPEPTIDE BPC 157 ON LIVER LESIONS INDUCED BY BILIARY OBSTRUCTION IN RAT

PhD candidate: Anita Zenko Sever, MD

Part of the thesis: Hepatoprotective effect of BPC 157 on model of biliary cirrhosis in rats

Mentor/s: Professor Predrag Sikirić, MD, PhD, Assistant Professor Marijana Ćorić, MD, PhD

Affiliation: University of Zagreb School of Medicine, Institute of Pathology, Department of pharmacology, University Hospital Centre Zagreb

Introduction: Biliary obstruction during longer period of time induces liver lesions leading to liver cirrhosis. Pentadecapeptide BPC 157 has already shown hepatoprotective effect on CCl₄-, alcohol- and NSAID-induced liver lesions.

Materials and methods: In our experiment male Wistar rats weight 180 – 200 g were used. Biliary obstruction was surgically induced by bile duct ligation. Animals were randomized to control and pentadecapeptide BPC 157 treated group. BPC 157 animals received pentadecapeptide BPC 157 in drinking water (10 µg/kg/day), control animals received equivalent water volume. At selected intervals (2, 4, 6 and 8 weeks after bile duct ligation) blood samples were analyzed for AST, ALT, bilirubine, and albumine serum levels as well as PT. After sacrifice at mentioned intervals macroscopic evaluation, liver weight, and microscopic analyses were performed.

Results: Since 4th week significantly higher serum levels of AST, ALT, bilirubine, albumine and prolonged PT were found in control group compared to pentadecapeptide BPC 157 group. Histologically, wider portal spaces with pronounced bile ductules proliferation and fibrosis were found in control group compared to BPC treated animals.

Discussion: Presented results clearly demonstrated hepatoprotective effect of pentadecapeptide BPC 157 on bile duct ligation induced liver lesion.

Acknowledgments: Professor Predrag Sikirić, Assistant Professor Marijana Ćorić. Professor Predrag Sikirić, Assistant Professor Marijana Ćorić.

MeSH/Keywords: Pentadecapeptide BPC 157, liver lesion, bile duct ligation, fibrosis

Poster code: R-A-4-41

Poster Title: EFFECT OF RETROBULBAR APPLICATION PENTADECAPEPTID BPC 157 ON EFFECT OF RETROBULBAR APPLICATION L-NAME IN RATS

PhD candidate: Mirna Zlatar, MD

Part of the thesis: Effect of retrobulbar application of BPC 157

Mentor/s: Professor Predrag Sikirić, MD, PhD

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

Introduction: Vasoconstriction of retinal arteries causes immediately or gradually loss of vision of the affected eye. Clinical picture depends on the involvement of the central retinal artery or its branches.

Materials and methods: 54 Wistar rats. The animals will be divided into 3 major groups with 6 rats in the test group. After retrobulbar application of L-NAME (2mg/kg), we monitored the effect of retrobulbar application of BPC 157 (2µg/kg, 2 ng/kg) on retinal arteries. Fundus of the eye was recorded with the USB microscope camera before retrobulbar application of L-NAME and BPC 157, after retrobulbar application of L-NAME and after retrobulbar application of BPC 157. Changes on the fundus of the eye was analyzed by computer program to analyze images and histopathologic analysis eyeball on standard sections, paraffin embedded and hemalaun eosin painted.

Results: During monitoring of the animals applied with BPC 157 retrobulbar, there was

no signs of retinal artery occlusion in the photographic and histological images, as compared with the controls. The animals which is applied BPC 157 had normal findings fundus with normal presentation choroidal circulation. On histological images, in the control group, retina was completely thinned and each layer is thinned as compared to animals treated with BPC 157.

Discussion: Our results suggest a protective effect of retrobulbar application of BPC 157 on the retinal blood vessels and the retina as a whole. The vasoconstrictor effect of retrobulbar application of L-NAME, causes retinal ischemia, while retrobulbar application of BPC 157 leads to retinal ischemia recovery and prevents its atrophy.

Acknowledgments:

MeSH/Keywords: BPC, L-NAME, vasoconstriction of retinal arteries

Poster code: R-A-4-71

Poster Title: THE EFFECTS OF BPC 157 ON HETEROTOPIC OSSIFICATION IN THE RAT

PhD candidate: Neven Starčević, MD

Part of the thesis: The effects of BPC 157 on heterotopic ossification in the rat

Mentor/s: Prof. Predrag Sikirić, MD, PhD, Prof. Žarko Rašić, MD, PhD

Affiliation: Department of Pharmacology, Medical Faculty University of Zagreb, Croatia

Introduction: Heterotopic ossification (HO) is a condition that can occur as a result of tissue trauma, and is characterized by mature bone formation outside of anatomic bone. In this study we will investigate the effects of pentadecapeptide BPC 157 on heterotopic ossification in rats.

Materials and methods: A mature bone and bone marrow cylinder was implanted in the quadriceps muscle of the hind leg. Pentadecapeptide BPC 157 dissolved in saline solution was applied „per os“ in doses of 10 µg/kg i 10 ng/kg according to the experimental group, the control group received drinking water. Throughout the duration of the experiment we conducted functional measurements (MFI- modified motor function index, shortening of the leg). After

ethanasia X rays were performed on the donor site and the locus of the induced HO.

Results: Formation of heterotopic bone was reduced on X-rays, the experimental fractures healed better and the function of the leg was improved in the treated group, the control group deteriorated in all of the aforementioned parameters.

Discussion: In conclusion, we can state that the preliminary results warrant further research into the effects of BPC 157 on heterotopic ossification in the rat.

Acknowledgments:

MeSH/Keywords: BPC 157, heterotopic ossification, rat

Poster code: R-A-4-77

Poster Title: PENTADECAPEPTIDE BPC 157 AND WOUND HEALING AFTER HIND LIMB ISCHEMIA

PhD candidate: Andrej Šitum, MD

Part of the thesis: Pentadecapeptide BPC 157 and wound healing after hind limb ischemia

Mentor/s: Professor Leonardo Patrlj, MD, PhD and Professor Predrag Sikirić, MD, PhD

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

Introduction: Recent studies have shown the positive effect of pentadecapeptide BPC 157 on lesions of various organic systems and its effect on the NO system. No study on the effect of the pentadecapeptide BPC 157 on hind limb wound healing in ischemic conditions has been published so far. We have, therefore, analysed its effect produced by permanent ligation of common iliac artery.

Materials and methods: The experiment was performed on 255 male Wistar Albino rats. The animals underwent surgery aimed at the ligation of common iliac artery and hind limb wound under deep anaesthesia. The animals were randomly divided into 11 groups and were treated with saline, BPC 157, L arginine, L NAME and cream. The animals were sacrificed and assessed at the end of each single experimental period (24 hrs, 3,7,14 and 21 days). The assessed parameters were: macroscopic, functional and microscopic analysis of the hind limb skin wound.

Results: Contrary to controls, animals treated with BPC 157 showed better and faster healing of hind limb wounds, better wound contracture, less healing complications and better vascularization after common iliac artery ligation. Also, despite severe induced ischaemia, the status of hind limb ischaemia was promptly reduced and almost completely gone within 24 hrs.

Discussion: The combination of the BPC 157 and L-arginine strengthened the otherwise

mild positive effect of L-arginine. The negative effect of L-NAME (difficult and slower wound healing in comparison to the control group) was annulled by the effect of L-arginine and vice versa (L-NAME L-arginine reached control level), whereas the administration of BPC 157, besides annulling the negative effect of L-NAME, not only brought its damaging effect to regression but also resulted in a positive effect in the wound healing process (L-NAME BPC 157, L-NAME L-arginine BPC 157 resulted in a reduction below control level). All mentioned positive effects of the BPC 157 were achieved regardless of the dose and administration modality. Our study furthermore shows that the use of the pentadecapeptide BPC 157 in the treatment of ischemic ulcer of rats' skin is dose and administration modality independent. A similar effect was partly noticed in the administration of L-arginine, whereas the opposite was achieved by administering L-NAME.

Acknowledgments: I express my gratitude to my mentors Professor Leonardo Patrlj, MD, PhD and Professor Predrag Sikirić, MD, PhD for their guidance throughout my research.

MeSH/Keywords: pentadecapeptide BPC 157, NO system, wound healing, ischemia, hind limb, L-arginine, L-NAME

Poster code: R-A-4-89

Poster Title: THE EFFECTS OF ROSUVASTATIN, SIMVASTATIN AND FENOFIBRATE ON BRAIN MALONDIALDEHYDE IN RATS

PhD candidate: Antonija Vukšić, MD

Part of the thesis: The Effects Of Antilipid Drugs On Cholinesterase And Oxidative Stress Parameters In Biological Material Of Normolipemic And Hyperlipemic Rats

Mentor/s: Professor Vlasta Bradamante, MD PhD, Professor Jasna Lovrić, PhD

Affiliation: University of Zagreb School of Medicine, Department of Pharmacology, Polyclinic Bonifarm, Department of Clinical Pharmacology, Zagreb

Introduction: Free radicals can be involved in pathogenesis of Alzheimer disease (AD). While the literature data have shown that antilipemic drugs either decrease or have no influence on malondialdehyde (MDA) level, our previous unpublished results have shown that simvastatin (SIMV) reduce MDA in rat's brain. We decided to compare the influence of rosuvastatin (ROSU) and fenofibrate (FENO) on MDA level in the brain of normolipidemic rats and to repeat the experiment with SIMV.

Materials and methods: Ninety male Wistar rats were divided into five control groups (saline) and five experimental groups. One experimental group was on SIMV treatment (10 mg/kg/day), two groups on ROSU treatment (5 and 10 mg/kg/day) and remaining groups on FENO treatment (30 and 50 mg/kg/day). Agents and saline were given orally for the period of 3 weeks. Animals were sacrificed with ether 24 hours after the last dose and brain samples were rinsed with saline. MDA levels were measured by HPLC-MS method (Drury JA et al, 1997). Data were analysed by Dunn's Multiple Comparison Test.

Results: ROSU and SIMV in dose of 10 mg/kg/day decreased significantly MDA level ($\mu\text{mol/L}$) in brain of normolipidemic rats for

10% and 58% vs. control ($p < 0.05$, mean \pm SD) (ROSU 10 mg vs. control: 2.549 ± 0.2762 vs. 2.812 ± 0.2368 – SIMV 10 mg vs. control: 1.112 ± 0.2306 vs. 2.664 ± 0.2044), while lower dose of ROSU and FENO didn't influence MDA level vs. control. Higher dose of FENO indicated a decrease of MDA by 21% in comparison with control: FENO 50 mg vs. control: 2.282 ± 0.2012 vs. 2.891 ± 1.0181 .

Discussion: Our results have shown that rosuvastatin, simvastatin and fenofibrate decrease MDA level in brain of normolipidemic rats. As well, our previous results obtained with simvastatin are confirmed. According to these results we have suggested that protective effect of antilipemic drugs against AD may be the consequence of their antioxidative action.

Acknowledgments: I offer my sincerest gratitude to my mentors, Prof. Vlasta Bradamante and Prof. Jasna Lovrić for supporting me throughout my thesis with patience and knowledge whilst allowing me the room to work in my own way.

MeSH/Keywords: statins, fenofibrate, antioxidant activity, Alzheimer's disease.

Poster code: R-A-4-111

Poster Title: EARLY CHANGES OF ACETHYLCHOLINESTERASE ACTIVITY AND TAU PROTEIN PHOSPHORYLATION IN THE MOUSE MODEL OF SPORADIC ALZHEIMER'S DISEASE

PhD candidate: Andrija Lončar

Part of the thesis: Early changes in the brain induced by central administration of streptozotocin in the experimental model of sporadic Alzheimer's disease

Mentor/s: Melita Šalković Petrišić

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

Introduction: Intracerebroventricular (icv) administration of streptozotocin (STZ) generates a mouse model of sporadic Alzheimer's disease (sAD). Long term effects of STZ-icv treatment have been well documented but the acute neurochemical impairment have not been investigated thoroughly enough. We aimed to explore the appearance and development of the cholinergic deficits and tau protein hyperphosphorylation in the mouse brain within the 24 hours after the STZ-icv treatment.

Materials and methods: Adult male mice (strain C57Bl/6) were injected icv with STZ (1 and 1,5 mg/kg) or vehicle-citrate buffer (controls). The animals were sacrificed 15 min, and 1, 6 and 24 hours following the STZ-icv treatment. Acetylcholinesterase (AChE) activity in hippocampus (HPC) and parietal cortex (PC) was measured (all four time-points) spectrophotometrically by Ellman's method. Protein expression of phosphorylated tau protein (PHF13), phosphorylated glycogen synthase kinase 3 (pGSK3 β), in HPC and PC (time-point: 1 hour) was measured by SDS-PAGE electrophoresis, followed by Western blot analysis. Data were analysed by Mann-Whitney U test ($p < 0.05$).

Results: One hour after STZ-icv injection the expression of PHF13 was found significantly increased in HPC (26%) and PC (37%), while the ratio of phospho/total GSK3 β protein expression was found significantly decreased in PC (-19%) only. The AChE activity in PC was significantly increased at earliest 6 hours (10%) following the STZ-icv injection and was still increased after 24 hours (15.5%).

Discussion: Results indicate that changes in tau phosphorylation are occurring earlier than those in AChE activity, and that the changes in both parameters occur earlier in the PC than in the HPC. These data suggest that STZ-icv administration triggers specific early changes in the mouse brain which demonstrate post-treatment time – and brain region-dependency.

Acknowledgments:

MeSH/Keywords: Streptozotocin, tau protein, acetylcholinesterase, sporadic Alzheimer's disease.

Poster code: R-A-4-119

Poster Title: PENTADECAPEPTIDE BPC 157 AFTER 70% LIVER RESECTION IN RATS

PhD candidate: Dalibor Crvenković MD

Part of the thesis: Pentadecapeptide BPC 157 after 70% liver resection in rats

Mentor/s: Professor Predrag Sikirić MD PhD, Professor Žarko Rašić MD PhD

Affiliation: University of Zagreb School of Medicine

Introduction: Extensive liver resection leads to liver failure. At the moment there is no adequate medicament therapy that could prevent further hepatic damage and help liver regeneration to avoid liver failure. Objective was preserving of remaining hepatic tissue and function with improvement of regeneration after 70% liver resection in rats with gastric pentadecapeptide BPC 157, since it can rescue severe liver lesions after NSAID overdose, CCl₄ or chronic alcohol abuse.

Materials and methods: 70% rat liver resection was performed on 120 Wistar rats by ligation and resection of median and left lateral lobe. Animals were divided in BPC 157 (10 µg/kg or ng/kg i.p. or p.o.) and control groups (saline (i.p. or p.o.)). During sacrifice (at day 4,14,21,28) blood samples were taken and AST, ALT, LDH, bilirubine, albumin, PT levels were measured. Observation also included body weight, liver mass ratio, liver volume, macroscopic measurements and histolog. examinations.

Results: BPC 157-rats maintained the weight, exhibited better liver regeneration

based on better liver mass/body weight ratio (i.e. 14 days: 0.037 CI0.004 (BPC 157) vs. 0.023 CI0.005 (control), 28 days: 0.053 CI0.007 (BPC 157) vs. 0.03 CI0.004 (control) and larger liver volume in pentadecapeptide BPC 157-rats. Unlike constantly increased AST, ALT, bilirubine levels in controls, BPC 157-rats after a short post-surgery increase, mostly presented values comparable to non-resected animals (confirming functional liver regeneration). Microscopically, controls presented larger areas of liver steatosis focal necrosis and liver fibrosis unlike BPC 157-rats. Although binuclear cells were sporadically seen in controls, there were less hepatocytes with mitosis compared to all BPC 157 regimens.

Discussion: Pentadecapeptide BPC 157 induced better liver regeneration in rats with extensive liver resection

Acknowledgments:

MeSH/Keywords: BPC 157, liver resection, rat

Poster code: R-A-4-127

Poster Title: THE IMMEDIATE EFFECTS OF SOCCER GAME ON MARKERS OF MUSCULAR DAMAGE

PhD candidate: Antonela Devrnja, MD

Part of the thesis: Relationship between activity intensity and oxidative stress biomarkers in young soccer players

Mentor/s: Professor Branka Matković, MD, PhD

Affiliation: Department of Sport and Exercise Medicine, Faculty of Kinesiology, University of Zagreb, Horvačanski zavoj 15, 10000 Zagreb, Croatia

Introduction: Soccer, as one of the most popular modern sports, is played by men and women in many countries around the world, not only at a competitive level but also as a very popular recreational sports game. It is estimated that players cover approximately 8 to 13 km per game, including walking, moving backwards, jogging, running and sprinting. During the game soccer players experience a number of short accelerations and decelerations at near maximal or even maximal intensities that could represent an important source of muscle damage. The aim of the study was to determine biomarkers of muscular damage in young soccer players immediately after a match play.

Materials and methods: 19 male field players aged 18.05 ± 0.5 , members of two soccer teams competing on junior national level, participated in this research. All subjects signed informed consent. The study was carried out in accordance with and approved by the Research Ethics Committee of Faculty of Kinesiology University of Zagreb. 30 minutes before and immediately after the game blood samples were taken and creatine kinase, lactate dehydrogenase, aspartate transferase and myoglobin concentrations were determined. Focus X2 was used to analyze player on-field activities. Statistical

computations were performed using Statistica for Windows software. All data are presented as mean \pm SD and paired sample t-tests were used to analyze significant differences between pre- and post-match enzymatic values.

Results: On average players covered distances of 9811 ± 1779 m. They were walking for 3000 ± 419 m, jogging 3917 ± 1457 m, running 1756 ± 559 m and sprinting 1139 ± 413 m. All biochemical parameters increased after the match: CK 51%, myoglobin 119%, lactate dehydrogenase 71% and aspartate transferase 74%. Despite myoglobin increasing in all players, this was not statistically significant probably because of the large variability in values ($p=0.11$). All other changes were significant ($p=0.000$).

Discussion: These large increases in the biochemical parameters from pre-match to post-match are in agreement with other studies observing muscle damage changes in soccer players during the game. No correlation with distances covered were noticed.

Acknowledgments:

MeSH/Keywords: soccer, muscular damage, young soccer players

Poster code: R-A-5-76

Poster Title: CHANGES IN GENE STRUCTURE AND PROTEIN EXPRESSION OF DVL1, DVL2 AND DVL3 AND TRANSCRIPTION FACTORS TCF1 AND LEF1 IN GLIOBLASTOMA

PhD candidate: Anja Kafka BS, MS in biology

Part of the thesis: Changes in gene structure and protein expression of DVL1, DVL2 and DVL3 and transcription factors TCF1 and LEF1 in astrocytic brain tumors.

Mentor/s: Professor Nives Pećina-Šlaus, PhD

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

Introduction: Glioblastomas are the most common and the most aggressive tumors of central nervous system and are classified as grade IV astrocytoma by the criteria of the WHO. Wnt signalling pathway is basic cellular pathway whose misregulation plays important roles in tumorigenesis. Dishevelled (DVL) is cytoplasmatic phosphoprotein, who comes first in downstream Wnt signalling cascade from Frizzled (Fz) receptor. When the signalization mediated by DVL is disrupted, it consequently induce transcription of target genes regulated by transcription factors TCF1 and LEF1 which results in tumor development and progression.

Materials and methods: Genetic changes of DVL1, DVL2 and DVL3 were tested by PCR/loss of heterozygosity (LOH) method using D1S468 polymorphic microsatellite marker for DVL1 gene, D17S960 for DVL2 gene and D36S1262 for DVL3 gene. Protein expressions and localizations of DVL1, DVL2, DVL3, TCF1 and LEF1 were analyzed by immunohistochemistry.

Results: Our total sample comprised of 30 glioblastomas. LOH was observed in 11% of samples for the DVL1 gene, 6,25% for DVL2

gene and 39,3% for DVL3 gene. A type of genomic instability – MSI was also detected in 22% cases for DVL1, 25% for DVL2 gene and 6% for DVL3 gene. The results on protein expressions of DVL1, DVL2 and DVL3 showed moderate or strong expression in glioblastoma tissues in 65%, 73,5% and 67% of samples respectively. Glioblastomas were also characterized with strong TCF1 expression in 51.6%, and with strong LEF1 expression in 71% of cases. While transcription factors TCF1 and LEF1 were present exclusively in the nucleus, Dishevelled protein was visible predominantly in cytoplasm with occasional nuclear appearance.

Discussion: Our findings suggest that genetic and protein changes of DVL1, DVL2, DVL3 and transcription factors TCF1 and LEF1 are involved in glioblastoma etiology.

Acknowledgments: This study was supported by Croatian Science Foundation (Project Number: 6625, WNT4EMT)

MeSH/Keywords: Wnt signaling pathway, glioblastoma, Dishevelled (DVL), TCF1, LEF1

Poster code: R-A-6-122

Poster Title: APPLICATION OF MICRONUCLEUS ASSAY AND FLUORESCENCE HYBRIDIZATION IN ESTIMATION OF CHROMOSOME INSTABILITY AND OCCURRENCE OF REGULAR FORM OF DOWN SYNDROME IN YOUNG COUPLES

PhD candidate: Ana Vičić, MSc

Part of the thesis: Application of Micronucleus Assay and Fluorescence Hybridization in Estimation of Chromosome Instability and Occurrence of Regular Form of Down Syndrome in Young Couples

Mentor/s: Assisted Professor Feodora Stipoljev, MSc, PhD

Affiliation: University Hospital Sveti Duh

Introduction: Regular form of Down syndrome (trisomy 21) is the most common chromosomal abnormality, and the major genetic cause of mental retardation in human population. Despite that, its etiology still remains unclear. To date, the only risk factor associated with Down syndrome occurrence is advanced maternal age at the conception. Still, a large number of trisomy 21 pregnancies are detected among mothers aged 35 or younger. There are only a few reports in the literature regarding increased susceptibility to chromosome malsegregation among young couples who had one or more pregnancies and/or children with Down syndrome. Micronucleus assay has been proven as an ideal, i.e. reliable, fast and inexpensive method for investigation of genomic instability. The aim of study is to evaluate the application of micronucleus assay and fluorescence in situ hybridization in estimation of chromosome instability and occurrence of regular form of Down syndrome within young couples.

Materials and methods: Study will include 30 couples (60 examinees, mothers and fathers) in which women had previous pregnancy with regular form of Down syndrome at the age of 35 or less. Control group will

consist of 30 couples with two healthy children and no previous spontaneous abortions. Investigations will be carried out on peripheral blood samples. All examinees will fulfill questionnaire in order to get insight into their medical history and to identify factors which could have impact on micronucleus frequency. Methods used in this survey will be micronucleus assay, fluorescence in situ hybridization and mitomycin challenge assay.

Results: The study is currently in the phase of data collection. So far investigation was performed on 11 couples: 6 couples in the examined group and 5 in control group.

Discussion: According to the results, significance of micronucleus assay as a prognostic biomarker for assessment of risk of aneuploidies in subsequent pregnancies would be determined. Furthermore, this survey could have contribution in dismissal of etiology of Down syndrome.

Acknowledgments:

MeSH/Keywords: Down syndrome, micronucleus assay, fluorescence in situ hybridization, chromosomal nondisjunction

Poster code: R-A-6-142

Poster Title: THE FREQUENCY OF MICRONUCLEI IN BUCCAL EXFOLIATED CELLS OF WOMEN WITH CERVICAL CANCER

PhD candidate: Goneta Gashi, MD

Part of the thesis: The frequency of micronuclei in peripheral blood lymphocytes and buccal exfoliated cells in women with cervical cancer

Mentor/s: Prof.dr. Isa Elezaj, PhD. Prim.dr.sci. Vesna Mahovlic, MD, PhD

Affiliation: University of Prishtina, Faculty of Natural Science, Department of Biology and Faculty of Medicine, Institute of Pathology, University Hospital Petrova, Department of Cytology

Introduction: Cancer is a multistage process that results from an accumulation of multiple genetic changes. Therefore, it is imperative to use some biomarkers of DNA damage due to genetic instability to predict cancer risk as well as to identify high-risk individuals. Micronucleus (MN) is a biomarker of genotoxic events and chromosomal instability. Micronuclei are cytoplasmatic chromatin masses with the appearance of small nuclei that arise from chromosome fragments or intact whole chromosomes lagging behind at the anaphase stage of cell division. The aim of this study is to determine the association between different stages of cervical precancerous lesions and cervical cancer with the micronucleus frequency in buccal mucosa cells.

Materials and methods: The study was carried out at Gynecology and Obstetrics Hospital, University Clinical Centre of Prishtina, in which were included 10 women who were diagnosed and classified on the bases of the Papanicolaou (PAP) test and colposcopy/biopsy into: 4 patients with low grade squamous intraepithelial lesions (LGSIL), 3 patients with high-grade squamous intraepithelial lesions (HGSIL), 1 patients with invasive squamous carcinoma and 2 healthy per-

sons. From patients was taken buccal mucosa smears. Per each women MN in 2000 cells was analysed, according to the original authors (MN in buccal cells after Tolbert et al).

Results: In this preliminary study we have found that frequency of micronuclei in patients with LSIL was 5.75/2000 cells, in patients with HSIL was 7/2000, in patient with invasive squamous carcinoma was 11/2000 and in healthy persons is 3/2000.

Discussion: Increased number of MN in buccal cells of invasive cancer patient and patients with precancerous lesion compared to healthy persons was observed. Our preliminary data of MN number in buccal cells support the predictive value of micronucleus test as a biomarker of genetic instability for evaluation of risk level of cancer diseases.

Acknowledgments: To the Ministry of Education, Science and technology of Kosovo for financial support.

MeSH/Keywords: micronucleus, cervical cancer, buccal cells, cancer risk

Poster code: R-A-6-152

Poster Title: MICRONUCLEUS INDEX IN BUCCAL EXFOLIATED CELLS IN PATIENTS WITH PAPILLARY UROTHELIAL CARCINOMA

PhD candidate: Arjeta Podrimaj Bytyqi, MD

Part of the thesis: Micronucleus index in epithelial exfoliated cells of urothelium and buccal mucosa, and peripheral blood lymphocytes of patients with papillary urothelial carcinoma

Mentor/s: Prof.dr. Isa Elezaj, PhD, Dr. Ana Borovecki, MD, PhD

Affiliation: University of Prishtina, Faculty of Natural Sciences, Department of Biology and Faculty of Medicine, Institute of Pathology, University Hospital Merkur, Department of Pathology and Cytology

Introduction: Micronuclei (MN) are intracytoplasmic inclusion bodies, formed from chromatin fragments or whole chromosomes. Their presence in cells is a reflection of chromosomal aberration during cellular mitosis and also an important initiating event in cancer. Exfoliated epithelial cells have traditionally been used for cancer screening by cytopathologists and these cells also can be used for biomonitoring of the genotoxic effects in humans. The aim of this study is to show the correlation between MN index in buccal exfoliated cells with different tumor grades, in patients with papillary urothelial carcinoma.

Materials and methods: In this study were included 10 male patients aged from 32yr – 70yr, 3 patients diagnosed with Low grade papillary urothelial carcinoma, 3 patients with High grade papillary urothelial carcinoma and 4 healthy controls. MN assay was performed according to Tolbert et al. in buccal exfoliated cells, and the MN index was analyzed in 2000 cells per each patient.

Results: In this preliminary study was found that MN index in healthy control patients was 6.5/2000 cells, in Low grade and High grade papillary urothelial carcinoma patients was 11/2000 cells and 12.6/2000 cells, respectively.

Discussion: The preliminary results support our hypothesis that MN index in buccal cells increases with the histopathologic grade of the tumor. The MN index is higher in cancer patients for 1.69 -1.93 times compared to controls. Additionally, during evaluation of micronuclei in buccal cells, it is found that other nuclear abnormalities, like nucleoplasmic bridges, are more frequent in high grade cancer patients.

Acknowledgments: I would like to acknowledge the Ministry of Education, Science and Technology of Kosovo, for the financial support.

MeSH/Keywords: micronucleus, buccal exfoliated cells, papillary urothelial carcinoma.

Poster code: R-A-6-153

Poster Title: CHEMOKINE RECEPTOR PROFILE OF OSTEOCLAST PROGENITOR CELLS IN PATIENTS WITH RHEUMATOID ARTHRITIS

PhD candidate: Alan Šučur, M.D.

Part of the thesis: Phenotypic and functional characterization of osteoclast progenitors in patients suffering from rheumatoid arthritis

Mentor/s: Danka Grčević, M.D., PhD, associate professor

Affiliation: Department of Physiology and Immunology, University of Zagreb School of Medicine

Introduction: Rheumatoid arthritis (RA) is a chronic joint disease marked by persistent inflammation and osteodestruction. The mechanisms leading to joint destruction involve infiltration of osteoclasts, multinucleated cells derived from monocyte/macrophage lineage. Human osteoclast progenitors (OCPs) are contained among peripheral blood monocytes at low frequency even in healthy subjects. OCPs exhibit chemotaxis and, furthermore, synovial compartment of RA patients highly expresses different chemokines. The aim of our study was to define these chemotactic signals by analyzing expression of several chemokine receptors on OCPs in the peripheral blood, the levels of their respective ligands in serum and synovial fluid of RA patients and to assess differentiation potential of isolated OCPs.

Materials and methods: Mononuclear cells were separated from peripheral blood of healthy controls and RA patients. The phenotype of OCPs (CD3-CD19-CD56-CD11b CD14) was determined using flow cytometry for the following chemokine receptors: CCR1, CCR2, CCR4, CXCR4, C5AR1. Chemokine ligand concentrations (MCP-1/ CCL2, MIP-1 α /CCL3, MIP-1 β /CCL4, RANTES/ CCL5, MIG/CXCL9, IP-10/CXCL10) were measured in serum and synovial fluid of RA patients using flow cytometry bead based array. OCPs were sorted and cultured with M-CSF and RANKL. After two weeks, the cells were

stained for TRAP enzyme and positive, mature, osteoclasts were counted.

Results: Human peripheral blood OCPs similarly expressed chemokine receptors CCR1, CCR2, CCR4 and CXCR4 in RA and healthy subjects. However, CCL4 and CXCL10 concentrations were significantly higher in synovial fluid compared to serum levels in RA, while CCL2, CXCL9 and CXCL10 serum levels were higher in RA patients compared to the control group. Cell culture revealed no significant differences in mature osteoclast count between RA and control group.

Discussion: Although OCPs in RA have a differentiation potential similar to controls, levels of several chemokines are upregulated, indicating a possible chemotactic mechanism of OCP migration to affected joints. These results may help to reveal a migration mechanism of OCPs specifically associated with RA in order to develop more efficient therapeutic approaches.

Acknowledgments: I would like to thank my mentor, prof. Danka Grčević, and also our laboratory staff, Katerina Petrović Zrinski and Sanja Ivčević, for all of their time, support and help provided.

MeSH/Keywords: rheumatoid arthritis, osteoclast progenitors, peripheral blood, synovial fluid, chemotaxis

Poster code: R-A-7-3

Poster Title: THE ROLE OF AUTOPHAGY IN THE EFFECTS OF 5-AMINOIMIDAZOLE-4-CARBOXAMIDE RIBONUCLEOSIDE (AICAR) AND METFORMIN ON U937 CELLS

PhD candidate: Vilma Dembitz, MD

Part of the thesis: Autophagy and metabolic changes in differentiation of acute myeloid leukemia cell lines

Mentor/s: Professor Dora Višnjić, MD, PhD

Affiliation: Department of Physiology and Croatian Institute for Brain Research, School of Medicine, University of Zagreb, Salata 12, 10 000 Zagreb, Croatia

Introduction: Our recent study showed that AICAR, an AMP-activated protein kinase (AMPK) activator, inhibits proliferation, increases apoptosis and induces expression of differentiation markers in monocytic leukemia cell line U937. However, siRNA experiments suggested that AICAR-mediated effects in U937 cells were AMPK-independent. Autophagy has been recently described as an AMPK-independent AICAR-mediated effect in other cell types. Therefore, the aim of this study is to determine the role of autophagy in AICAR-mediated differentiation of U937 cells.

Materials and methods: U937 cells were incubated in the presence of AICAR, A76996, metformin, all-trans retinoic acid (ATRA), phorbol 12-myristate 13-acetate (PMA) and 3-methyladenine (3-MA). The number of viable cells was determined by hemocytometer. The expression of differentiation markers and cell viability were analyzed by flow cytometry (FACSCalibur, Becton Dickinson). Gene knock-down was performed using siRNA transfections (Neon transfection system, Invitrogen). Total cell lysates were analyzed for the level of LC3B-I and -II, Beclin 1, PI3KC3 and actin by Western blot. The data are shown as means±S.E.M. and analyzed using Student t-test or ANOVA.

Results: In concordance with our previous observation that differentiative effects of AICAR are AMPK-independent, AICAR-mediated increase in CD11b and CD64 was not

mimicked by the presence of A76996, a more specific AMPK-activator. Western blot analysis revealed an accumulation of the autophagy marker LC3B-II in U937 cells treated with differentiation inducers but not in cells treated with metformin for 48h. The pretreatment of cells with PI3KC3-inhibitor 3-MA inhibited AICAR-mediated increase in the expression of differentiation markers, decreased the number of viable cells, and increased the level of LC3B-II. Gene knock-down for autophagy regulators Beclin 1 and PI3KC3 did not abolish the differentiative effects of AICAR, ATRA and PMA. However, metformin-mediated decrease in cell viability was inhibited in cells with down-regulated Beclin 1.

Discussion: Differentiation inducers increase autophagy markers in U937 cells. Inhibitory effects of 3-MA on the expression of differentiation markers cannot be ascribed to selective inhibition of PI3KC3 and autophagy induction. Preliminary data suggest that the presence of Beclin 1 is more important for cytotoxic effects of metformin than differentiative effects of AICAR.

Acknowledgments: We thank Ms Dunja Tanković for valuable technical help and assistance. This study was supported by the University of Zagreb, grant BM1.48 (to Dora Višnjić).

MeSH/Keywords: acute myeloid leukemia, differentiation, autophagy, metabolism

Poster code: R-A-7-104

1.2 Clinical Medical Sciences – Research Abstracts

Poster Title: SYNERGISTIC EFFECT OF LOCAL ANESTHETICS ON HEMODYNAMIC CHANGES DURING THE APPLICATION OF A PARAVERTEBRAL BLOCK

PhD candidate: Miroslav Župčić

Part of the thesis: Synergistic Effect of Local Anesthetics on Hemodynamic Changes During Paravertebral Block

Mentor/s: Professor Ino Husedžinović, MD, PhD

Affiliation: Department of Anesthesiology, Reanimatology and Intensive Medicine, University Hospital Dubrava, Zagreb, Croatia

Introduction: In this study we will use ultrasound guided paravertebral block considering all contraindications. Many studies suggest performing anesthesia in surgery of the breast in just paravertebral block or in a combination with general anesthesia, although there is still no reliable data regarding hemodynamic events during the implementation of this type of block.

Materials and methods: The total number of 80 patients with ASA 1 and ASA 2 status of breast cancer will be divided into two groups: the solution of 0.5% levobupivacaine and 2% lidocaine (7,0 ml. on three levels of Th2, 3.4) will be given to the first (LLS-Group) while the second (LS - Group) will receive the solution of 0.5% levobupivacaine also of 7.0 ml at the previously mentioned levels. Intravenous anesthetics and muscle relaxants for the induction and the maintenance of anesthesia will be administered in both groups after applying paravertebral block. Measurements of hemodynamic parameters with the help of Vigileo / FloTrac System will be performed perioperatively. Postoperatively, the patient will be sent to the department where they will remain during the first 24 hours to track their recovery.

Results: During the research period, we have managed to include 37 patients, 19 in (LLS- Group) and 18 in (LS - Group). We used the Pearson Chi-Square Tests to assess dif-

ferences in categorical values and determined that there is a significant difference in the decline of mean arterial pressure (MAP) between the study (LLS- Group) and control group (LS - Group) - up to 42.1% compared to 0%. The significance of this difference in the form of p value is $p < 0.002$. Non-parametric Mann Whitney U test was used for the comparison of quantitative values between groups. The values obtained here show that low values of MAP are simultaneously accompanied by elevated levels of Stroke Volume Variation (SVV) in (LLS-Group) at $p < 0.005$ during the first 45 min of hemodynamics measurements.

Discussion: Preliminary results of our study are in favor of our hypothesis and show a significant difference in the decline of mean arterial pressure (MAP): the group that received a solution of two local anesthetics (LLS- Group) had significantly more frequent pressure drops compared to the group which received only one local anesthetic (LS - Group). Although the results are preliminary we hope that further statistical analysis of the total number of patients will fulfilled our predictions.

Acknowledgments:

MeSH/Keywords: paravertebral block, local anesthetics, hemodynamic monitoring

Poster code: R-B-1-7

Poster Title: CARDIOPULMONARY EXERCISE TESTING: ANALYSIS OF ITS INDICATION BASED ON PREOPERATIVE FEV1 IN THORACIC SURGERY PATIENTS

PhD candidate: Iva Milišić Jašarević

Part of the thesis: Cardiopulmonary exercise testing: analysis of its indication based on preoperative FEV₁ in thoracic surgery patients

Mentor/s: Professor Sanja Popović Grle, MD, PhD Jasna Špiček Macan, MD

Affiliation: University hospital centre Zagreb, Department of Anesthesiology and intensive care for thoracic surgery patients

Introduction: According to present recommendations, all patients undergoing pulmonary resection who's forced expiratory volume in 1s (FEV₁) was less than 80% during preoperative evaluation should perform cardiopulmonary exercise testing (CPET). In everyday clinical practice it has become evident that the above recommendations may not be sufficiently precise. With this research we aim to demonstrate that CPET should be performed in patients having much lower FEV₁ values than is currently recommended. The aim of this research is to examine the FEV₁ cut-off value which is an absolute indication for ergospirometry in order to identify those patients who could develop post-operative cardiorespiratory complications. The hypothesis of this research is that this value should be set below the currently proposed 80%.

Materials and methods: This research will include a total of 200 adult patients who underwent pulmonary resection procedure due to malignancy. All patients will have done ergospirometry. Patients who could not perform ergospirometry out of any objective or subjective reason were excluded from the study. This is a prospective study with parallel group design. All patients were informed about the study and have signed an informed consent. Following surgical indication for resection procedure, patients have undergone a preoperative anesthesiologic check up. Based on FEV₁ values, pa-

tients were divided into six parallel groups. Anesthesiologic work up for such procedures was done in an usual way. Following the procedure, all patients were placed in an ICU. During following 48 hours in ICU patients were monitored for development of cardiorespiratory complications, as well as while on ward and up until their release home.

Results: Partial data which are analysed so far are in line with the research hypothesis. This means that not all patients who had FEV₁ value less than 80% were indicated to do ergospirometry, and that this cut-off value is much lower.

Discussion: The study results obtained so far are not in line with majority of to date's research which holds that all patients with a FEV₁ value below 80% need to do ergospirometry.

The results of our study show that this value is significantly lower and the aim is to determine in which group of patients who are planned for pulmonary resection based on spirometric tests, ergospirometry should be mandatory.

Acknowledgments:

MeSH/Keywords: preoperative assessment, pulmonary function assessment, CPET, anesthesiology procedure, postoperative complications.

Poster code: R-B-1-137

Poster Title: PREOPERATIVE PERIPHERAL NERVE BLOCKADE IN THE PERIOPERATIVE PAIN MANAGEMENT AND EARLY MOBILIZATION FOR CRUCIATE LIGAMENT ARTHROSCOPIC ANTERIOR RECONSTRUCTION

PhD candidate: Ira Skok

Part of the thesis: Preoperative peripheral nerve blockade is better in the perioperative pain management and early mobilization than the usually used continuous parenteral analgesia.

Mentor/s: doc. dr. sc. Ivan Bojanic and doc. dr. sc. Visnja Neseck Adam

Affiliation: orthopedic surgeon and anesthesiologist

Introduction: One of the most often arthroscopic procedure in orthopaedic surgery is anterior cruciate ligament reconstruction and one of the most painful. Although arthroscopy is associated with less tissue trauma, postoperative pain is still a clinical concern during the first 24-postoperative hours.

Materials and methods: The aim of this study is to investigate the success rate of preoperative ultrasound-guided peripheral nerve blockade with low dose of local anesthetic. For this purpose, 150 patients scheduled for the anterior cruciate ligament reconstruction will be randomly chosen. They will be uniformly anesthetized, but the analgesia will be different: intravenous and two models of regional.

Results: We use descriptive analysis of the sample: gender, age, intraoperative sedative and opioid consumption, duration of the surgery. VAS analysis results (visual analog

scale of pain): intraoperative pain control, Tourniquet tolerance, postoperative pain control- group and analysis of subgroup (1-control, 2-femoralis, 3-saphenus) analysis according to variables quadriceps motor deficit, foot flexion, headache, postoperative nausea and vomiting- group and analysis of subgroup (1-control, 2-femoral, 3 saphenus). All the results will be presented with graphs and tables. MS Excel and SPSS are used for statistical analysis.

Discussion: There is a difference between the femoral and saphenus group (group 2 and 3) regarded to motor deficit and early mobilization.

Acknowledgments: to my mentors, nurses, orthopedic surgeons

MeSH/Keywords: anterior cruciate ligament reconstruction, ultrasound-guided peripheral nerve blockade

Poster code: R-B-1-165

Poster Title: THE CLINICAL PATTERN VARIATIONS OF TINEA CAPITIS ASSOCIATED WITH NEW AND ATYPICAL PATHOGENS

PhD candidate: Biljana Gorgievska-Sukarovska, MD

Part of the thesis: The clinical pattern variations and epidemiology of deep seated tinea capitis

Mentor/s: Prof. Mihael Skerlev, MD, PhD

Affiliation: University Department of Dermatology and Venereology, Zagreb University School of Medicine and Zagreb University Hospital

Introduction: Significant changes in epidemiology, aetiology and in the clinical pattern of fungal scalp infections caused by *Microsporum* spp. have been observed. The lesions are usually moderately inflammatory, but, most recently, cases of severe kerion like tinea capitis have been also registered. As the same fungal species might evoke different clinical patterns, interspecies polymorphism within *Microsporum* (*M.*) *canis* isolates might have been responsible for this phenomenon. The aim of this study was to identify the patients with deep seated tinea capitis caused by *M. canis*, to study the genotypic variability within isolates of *M. canis* from those patients and to compare these results with the isolates of *M. canis* from the patients with the superficial tinea capitis.

Materials and methods: Sixty strains of *M. canis* from patients with both superficial and deep seated tinea capitis have been isolated and identified to species using standard and advanced mycological procedure techniques. Morphological identification was confirmed by molecular methods RFLP (Restriction Fragment Length Polymorphism). After amplification of ITS1-5.8S-ITS2 region, the product was exposed to restric-

tion enzyme *Hinf*I. All strains of *M. canis* had identical pattern on gel electrophoresis. For subtyping of *M. canis* was used RAPD (Randomly Amplified Polymorphic DNA typing) using (ACA)₅ and (GACA)₄ primers.

Results: So far up to 40 strains were amplified using universal primers ITS1 and ITS4. Targeting ITS1-5.8S-ITS2 regions results revealed a pattern unique for *M. canis*. After RAPD amplification with (ACA)₅ primer, among all examined *M. canis* isolates we distinguished only one type. Using (GACA)₄ primer, several different band patterns were distinguished.

Discussion: Results of most molecular studies show that there is no clonal differentiation within *M. canis*. Using (GACA)₄ primer we distinguished several different band patterns. Further research and analyze of the results is perform.

Acknowledgments: I would like to thank Lidija Žele-Starčević, MD, PhD, for her help and contribution in this research.

MeSH/Keywords: *Microsporum canis*, tinea capitis, strain differentiation, RAPD method

Poster code: R-B-2-80

Poster Title: MULTIMODAL ANALGESIA AFTER TOTAL KNEE REPLACEMENT

PhD candidate: Darija Granec, MD

Part of the thesis: The influence of multimodal analgesia with metamizole on the postoperative pain and early postoperative rehabilitation in patient with total knee replacement

Mentor/s: Associate Professor Domagoj Delimar, MD, PhD

Affiliation: University of Zagreb School of Medicine, University Hospital Centre – Zagreb, Special Hospital for Medical Rehabilitation Krapinske Toplice

Introduction: Pain is a major limiting factor of early rehabilitation after total knee replacement (TKR). Multimodal analgesia enables to control pain better, with lower opioids dose. Optimal postoperative analgesia involves effective pain control and reduction of the inflammation. Data regarding optimal drug combination regimen during the first four weeks of rehabilitation in patients after TKR are insufficient.

Materials and methods: This prospective randomized open label study is planned to enrol 140 patients of both gender, aged 50-75 years, with indication for TKR due to primary osteoarthritis. Patients will be divided into two groups. All patients will receive oxycodone tablet 20mg oral BID, from 2.-20.postoperative day (POD). In the first group meloxicam tablet 15mg once a day oral is added, and in the second group metamizole 1000mg tablet TID. From 21-28.POD all patients will receive analgesics (1000mg of paracetamol oral and tramadol 50mg oral) given per need protocol. Standardised surgical approach, same model of prosthesis, analgesic protocol for the first POD, thromboprophylaxis and rehabilitation protocol are provided for all patients. Intensity of the pain at rest, during activity and during the night and patients satisfaction using VAS (0-100mm), range of motion of the knee (°) and the suprapatellar circumference of the knee (cm) will be monitored daily. Knee function and general health will be assessed (WOMAC, KSS, SF-36, 6MWT) prior to surgery and at the 28.POD. Data will

be presented using frequency tables, contingency tables and descriptive measures. Student's t-test or Mann-Whitney U-test will be used for discrete and consecutive measurements. Student's t-test for paired samples or the Wilcoxon test for unpaired samples will be used for the parameters with interval measuring.

Results: Data collection is in progress (expected end is in June 2015). Preliminary results point to a similar control of postoperative pain and functional outcome in two groups of patients 4 weeks after TKR.

Discussion: Postoperative pain after TKR depends on duration and intensity of preoperative pain, sex, age, anxiety and depression. There is no difference in pain control between the two investigated groups of patients with various multimodal analgesia. Functional outcome during and after four weeks of rehabilitation does not depend on postoperative pain in this period, but correlated with the preoperative functional status. Note-unexpected circumstances in the national health system prolonged this study.

Acknowledgments: I would like to thank Goran Bičanić, MD, PhD, and Miroslav Mayer, MD, PhD, for selfless and professional support in creation of this research

MeSH/Keywords: multimodal analgesia, metamizole, postoperative pain, total knee replacement, rehabilitation after total knee replacement

Poster code: R-B-3-109

Poster Title: AN ADEQUACY OF LOW MOLECULAR WEIGHT HEPARIN TREATMENT IN PATIENTS WITH HEREDITARY TROMBOPHILIA AS CAUSE OF MISSED ABORTIONS

PhD candidate: Vesna Sokol

Part of the thesis: Treatment with low molecular weight heparin improves perinatal outcome in women with hereditary trombophilia as cause of two or more missed abortions.

Mentor/s: Professor Marina Ivanišević, MD, PhD

Affiliation: Clinical Hospital Centre Zagreb, Department of obstetrics and gynaecology, Croatian Institute of Transfusion Medicine

Introduction: Approximately 5% of women trying to conceive experience early pregnancy loss, and in 50% of these women the cause of the preceding miscarriages still remains unknown. Inherited trombophilia could be associated with recurrent miscarriages. The goals of this research are to investigate the perinatal outcome in hereditary trombophilic patients with recurrent missed abortions after treatment with low molecular weight heparin. Nevertheless, this study will evaluate the prevalence of hereditary trombophilia in group of healthy patients with negative obstetric history and among these mutation carriers, investigate the perinatal outcome without treatment with LMWH.

Materials and methods: Ninety-eight patients with the history of early recurrent pregnancy loss and hereditary trombophilia are included in this study. The cause of their preceding miscarriages is unknown. All of them are treated with prophylactic dose of LMWH in period from visualisation of gestational sac till 2 weeks after delivery. The second group includes 98 healthy pregnant women that are examined for trombophilic mutations and nevertheless the results are without therapy with LMWH. In both group we observe the perinatal outcome.

Results: These are preliminary results of prospective study (from January 2012). During this period 53 patients with recurrent miscarriages and hereditary trombophilia were admitted to our Clinic. Among them, the most common type of the gene mutation

was homozygosity for PAI-1 and heterozygosity for MTHFR. Second most common type of mutation was prothrombin heterozygosity. 85% of women that underwent treatment with LMWH had successful perinatal outcome and 7.5% of suffered from another miscarriage. In the group of 33 healthy pregnant women with no obstetric history 27% of them were carriers of trombophilic mutation. The most common type was heterozygosity for PAI-1 polymorphism and MTHFR polymorphism. This group of women was not treated with LMWH. 6% of them had intrauterine growth retardation.

Discussion: Our results indicate the importance of heparin for successful perinatal outcome in women with recurrent miscarriages and hereditary trombophilia. This study also highlights the high percentage of inherited trombophilia in asymptomatic, healthy population of women and their good perinatal outcome even without heparin therapy. Additional studies on a larger sample are still needed to confirm this assumption.

Acknowledgments: I thank my mentor Prof Marina Ivanišević and Prof Josip Đelmiš. We acknowledge all patients and the staff of State Referral Centre for Diabetes in Pregnancy, at Hospital Medical Centre in Zagreb and all other collaborators who are contributing to the study.

MeSH/Keywords: hereditary trombophilia, recurrent miscarriages, low molecular weight heparin, perinatal outcome

Poster code: R-B-5-26

Poster Title: THE INFLUENCE OF MATERNAL PERSONALITY AND MOTHER – INFANT BONDING AND PERINATAL FACTORS ON BREASTFEEDING DURATION

PhD candidate: Neike Keller, MD

Part of the thesis: The influence of maternal personality and mother – infant bonding and perinatal factors on breastfeeding duration

Mentor/s: Professor Vesna Medved, MD, PhD

Affiliation: General hospital Varaždin, Department of gynecology and obstetrics, University hospital centre – Zagreb, Psychiatry Clinic

Introduction: In most delivery departments who have the certificate 'Baby – Friendly Hospital' breastfeeding is stimulated from the first hours upon childbirth. Studies conducted until now demonstrated the correlation of breastfeeding with socioeconomic and psychosocial factors. Activities for promotion of breastfeeding have gained limited effect. The factors truly influencing the breastfeeding from the perspective of maternal personality traits and mother – infant bonding and some possible obstetric and puerperal factors were examined in this research.

Materials and methods: Written informed consents were obtained from women who have terminated breastfeeding and fulfilled inclusion criteria with a child up to 2 years of age in the primary paediatric practice during their visits to the paediatrician and a number of 301 was included in the research. They were offered to complete a Big Five Personality Inventory, Postpartum Bonding Questionnaire and a structured questionnaire to examine basic sociodemographic status and breastfeeding duration. Also the information about the mode of delivery and possible obstetric and puerperal complications, maternal age, parity and sex of a child were collected through interview and medical data through a structured questionnaire. The research was carried out through a period of one year, between February 2014 and February 2015 as an observational cross – sectional study.

Results: The research is still in progress, so far with all of the planned data collected. The research is currently in the phase of statistical data analysis. At this moment, preliminary results are being statistically analyzed and there aren't any preliminary results available.

Discussion: We believe that the results of this research would examine the influences and correlation of factors so far not investigated on duration of breastfeeding in a determined population and thus help in due time through certain interventional programs to try to influence them in order to improve the overall breastfeeding practice according to WHO recommendations. Accordingly, it is of great importance for obstetricians to recognize mothers who are in need of more centered support and to provide it in close collaboration with psychologists who should be included in every delivery department/maternity ward.

Acknowledgments: Prof. Vesna Medved, mentor, and Giovana Armano, MD, primary paediatric practice where women have been recruited.

MeSH/Keywords: maternal personality, mother – infant bonding, obstetric and puerperal factors, breastfeeding

Poster code: R-B-5-44

Poster Title: EXPRESSION OF THE PLACENTAL VEGF IN NORMAL AND LATE-ONSET TERM IUGR PREGNANCIES

PhD candidate: Maja Grah

Part of the thesis: Expression of the placental VEGF and early neurological outcome of infants from pregnancies complicated with intrauterine growth restriction

Mentor/s: Aida Salihagić Kadić

Affiliation: Clinical Hospital „Sveti Duh“, Medical School, University of Zagreb, Zagreb, Croatia

Introduction: Vascular endothelial growth factor (VEGF) is a signal protein that has a major role in the physiological and pathological angiogenesis and vasculogenesis during placental development.

Materials and methods: In this study we compared the expression of VEGF in human placentas obtained from 11 term pregnancies complicated by intrauterine growth restriction (IUGR) with 11 placentas from normal term pregnancies. Immunofluorescence staining was used to quantify the VEGF expression in the placentas.

Results: There were no differences between the groups in the age and parity of the mothers. In normal placentas analysis showed negative or light VEGF staining in the endothelium of fetal blood vessels, villous stromal cells and syncytiotrophoblast. In IUGR placentas expression of VEGF was mild to strong, suggesting increased vasculogenesis, and localization of VEGF staining was the same as in normal placentas. Furthermore, in these pathological pregnancies

difference in VEGF expression in relation to neurological outcome of infant after birth was observed, but the sample is too small for statistical analysis. It is possible that the strongest expression of VEGF is associated with early postnatal functional or structural brain disorders.

Discussion: Caused by impaired placental development hypoxia occurs in placental tissue and we demonstrated increased placental expression of VEGF in IUGR placentas. However, there is no data whether the expression of placental VEGF correlates with neurological damage in IUGR, which is a condition known as neurorisk factor. The aim of our further research is to assess the difference in placental VEGF expression in relation to the early neurological outcome of neonates with IUGR.

Acknowledgments:

MeSH/Keywords: placenta, IUGR, VEGF, brain development,

Poster code: R-B-5-45

Poster Title: INFLUENCE OF OVERWEIGHT, OBESITY AND VISCERAL FAT ON SPERMIOGRAM AND HORMONAL STATUS

PhD candidate: Sonja Anić Jurica, MD

Part of the thesis: Overweight, obesity and visceral fat have negative impact on spermogram and hormonal status

Mentor/s: Miro Kasum, MD PhD

Affiliation: University Hospital for Gynecology and Obstetrics, University Hospital Center Zagreb, University of Zagreb School of Medicine

Introduction: Prevalence of overweight and obesity males of fertile age increased due to modern life style. Increased body weight is most often determined by body mass index (BMI), waist to hip ratio (WHR) and waist circumference (WC). Many studies pointed negative impact of obesity defined with BMI on fertility in men- high estrogen levels, low testosterone and gonadotropins, increased scrotal temperature, inflammation due to adipokines, obstructive sleep apnea. Very few studies considered that abdominal or visceral fat more often leads to hormonal changes and causes inflammation than fat in other body parts. Standard weight parameters give more data about subcutaneous fat tissue than visceral and depend on muscle mass. A method is developed that measures segmental body mass by bioelectrical impedance – higher impedance through fat tissues. Impact of excessive fat and visceral fat measured by different methods on men fertility is analyzed.

Materials and methods: Study population is selected within men in pursue of reproduction- men with pathological spermogram and the control group with good spermogram, age 22 to 48 years, those with additional risk factors excluded. Analysis includes ejaculate volumen, sperm concentration, progressive movement of sperms, sperm morphology, DNA fragmentation index, levels of gonadotropins, estradiol, sex hormone binding globuline, testosterone are determined. Overweight, excessive weight, vis-

ceral fat are determined by BMI, WHR, WC. Segmental part of fat tissue is determined by measuring bioelectrical impedance. Impact of weight parameters on spermogram and hormonal status is analyzed in two study groups and correlation of spermogram values with body parameters calculated.

Results: Data collected from study participants so far show a trend of pathological spermograms and slighter trend to adverse hormonal status in men with excessive weight especially in those with predominant abdominal fat distribution respectively more visceral fat measured by bioelectrical impedance. Number of participants (n=13) at this point is insufficient for adequate statistical analysis results.

Discussion: Preliminary results are in concurrence with the study thesis that overweight, obesity and visceral fat have negative impact on spermogram and hormonal status with visceral fat having a strongest impact. Different measuring methods more precisely determine quantity of visceral fat improving diagnostic approach in clinical practice.

Acknowledgments:

MeSH/Keywords: obesity, visceral fat, body mass index, bioelectrical impedance, spermogram

Poster code: R-B-5-90

Poster Title: PROGESTERONE LUTEAL SUPPORT IN INDUCED CYCLES

PhD candidate: Vlatka Tomić, MD

Part of the thesis: Progesterone luteal support in in-vitro stimulated cycles

Mentor/s: Miro Kasum, MD, PhD

Affiliation: Department of Gynecology and Obstetrics, County Hospital Mittleres Erzgebirge, Zschopau, Germany

Introduction: Controlled ovarian hyperstimulation in in-vitro fertilization cycles leads to abnormalities in the concentration of sex-steroid-hormones. There is strong evidence of the usefulness of luteal support in stimulated cycles but no consensus exist about the route, dose and duration of progesterone administration. Also it is not clear which route and sort of progesterone drugs favor patients themselves.

Materials and methods: In a controlled ovarian hyperstimulation was used standard "step down" stimulation protocol with GnRH agonists. Ovarian response was measured by serum levels of E2 and ultrasound measures of follicle growth. Gonadotropin stimulation is terminated when at least two follicles had a diameter of 16-17mm. For the final follicular maturation was used hCG. After the successful fertilization embryos were transferred into the uterine cavity. Progesterone support of the corpus luteum lasted from aspiration of oocytes to the date of pregnancy test, or in the case of pregnancy until the 10-12 weeks of pregnancy.

Results: The similar rates of clinical pregnancies (33.1% vs. 30.9%) were obtained by using either Crinone 8% vag.gel or Utrogestan vag.capsules. Overall tolerability and

acceptability were significantly better in the Crinone-group than in the Utrogestan-group. The comparable rates of ongoing pregnancies were noted with use of combined-progesterone therapy (39.5%) and progesterone-monotherapy (33.5%). Abortion rate (6.4% vs. 15.6%) was significantly lower with the use of combined therapy. Tolerability and satisfaction of both supplements was almost equal. The on-going pregnancy rates were comparable between Crinone 8% vag. gel and oral dydrogesterone – Duphaston (28.1% versus 30.3%).

Discussion: Overall satisfaction and tolerability were significantly higher in the dydrogesterone-group than in the Crinone-group. Vaginal bleeding, interference with coitus and local adverse side effects such as vaginal irritation and discharge occurred significantly more in Crinone-group.

Acknowledgments: I would like to thank my grandparents Eugenija and Boris for being my constant support and my son Domagoj for inspiration.

MeSH/Keywords: in vitro fertilization, luteal phase support, progesterone, early pregnancy

Poster code: R-B-5-112

Poster Title: THE INFLUENCE OF TOBACCO SMOKE UPON BIOCHEMICAL CHANGES IN CERVICAL MUCUS OF WOMEN IN REPRODUCTIVE AGE

PhD candidate: Gordana Planinić Radoš, MD

Part of the thesis: Easily reachable material (cervical mucus) can provide useful information about the female genital tract.

Mentor/s: Željko Duić, MD, docent

Affiliation: University Hospital Merkur, Zagreb, Croatia

Introduction: Tobacco reduces the availability of vitamins and protective antioxidant mechanisms, enzymes and processes. A prospective study will examine possible connections between tobacco and fertility, by determining biochemical markers in cervical mucus. Mucus of presumably healthy women aged 18-35 years, smokers and non-smokers, fertile and those proven infertile, will be sampled in the first half of the menstrual cycle and markers of oxidative stress will be measured: total protein, vitamin C, thiocyanate, activity of cytochrome C oxidase, activity of rhodanese, cytochrome P450, and total antioxidant capacity.

Materials and methods: 120 women in reproductive age 18-35 years of life will be examined. The examinees will be divided into three groups: non-smokers, light smokers (up to 10 cigarettes a day) and heavy smokers (10 or more cigarettes a day). The gynecologic examination will include taking cervical mucus. Samples will be stored in a test tube containing 2 ml of phosphate buffer pH 7.5 to achieve maximum solubility. Homogenized samples will be centrifuged to separate the clear supernatant from the darker sediment. Further centrifugation will separate organelles which will be submitted to further processing.

Results: In women smokers, there is no statistical significant inverse correlation be-

tween vitamin C and the quantity of cytochrome P-450. A similar relationship exists between the amount of thiocyanate and the cytochrome P-450, where there is a positive correlation. Statistically significant difference at the $p < 0.001$ level exists only in relation of thiocyanate to vitamin C and the activity of the cytochrome c oxidase enzyme. Positive correlation between the concentration of thiocyanate and concentration of vitamin C shows that in women smokers the parameters that are statistically different at the $p < 0.001$ level, are inversely correlated. Increase in number of smoked cigarettes increases the concentration of thiocyanate and the amount of vitamin C is reduced.

Discussion: Tobacco smoke reduces the level of vitamin C secretion in cervical cells. Volume of vitamin C decreases with the increase in number of smoked cigarettes, and is lower in women who are heavy smokers. These tests show that increase in number of smoked cigarettes also increases the concentration of thiocyanate in the cervical mucus of women smokers.

Acknowledgments:

MeSH/Keywords: cervical mucus, smoke, biochemical, cytochrome oxidase, cytochrome P450, cytochrome c oxidase, rhodanese

Poster code: R-B-5-124

Poster Title: FEMALE PATIENTS WITH GENITAL CHRONIC GRAFT VERSUS HOST DISEASE – A COHORT ANALYSIS

PhD candidate: Tajana Klepac Pulanić, MD MSc

Part of the thesis: Demographic and clinical characteristics of female patients with genital chronic Graft-Versus-Host disease after allogeneic hematopoietic cell transplantation

Mentor/s: Prof. Dr. Slavko Orešković, MD, Prof. Dr. Steven Z. Pavletić, MD

Affiliation: National Cancer Institute, NIH, Bethesda, USA, Community Health Center Zagreb East, Zagreb, Croatia

Introduction: Female genital chronic Graft-versus-Host Disease (cGVHD) is an under-recognized late complication after allogeneic hematopoietic stem cell transplantation (alloHSCT). It is reported to occur in a quarter of long-term female survivors after alloHSCT impacting their quality of life. We prospectively analyzed a large cohort of adult female patients with cGVHD to determine their demographic characteristics, frequency of genital cGVHD, and severity of cGVHD.

Materials and methods: 130 female adult patients with cGVHD were enrolled on the National Cancer Institute cross-sectional natural history cGVHD study (04-C-0281, clinicaltrials.gov identifier: NCT00331968) from 2004 to 2014. All patients were evaluated by an interdisciplinary team during 4 days visit. Detailed history, physical examination and laboratory work-up were done. Diagnosis of cGVHD was made according to the NIH Consensus Criteria. NIH grading was used to determine global cGVHD score. History related to genital issues, gynecology examination and special questionnaire related to demographic parameters, genital symptoms and sexual activity was performed. Diagnosis of genital cGVHD was made according to Stratton-Turner criteria. Descriptive statistics and Chi square test for dichotomous variables were used in statistics. A p value <0.05 was considered to be statistically significant.

Results: Patients' median age was 44.5 year (range 18-70). Acute leukemias and MDS

were reason for alloHSCT in 66 (50.8%) patients. Myeloablative conditioning was performed in 70 (53.8%) patients. 105 patients (80.8%) received peripheral blood stem cells. Global cGVHD was severe in 97 (74.6%) and moderate in 32 (24.6%) patients. At the time of evaluation, 84 (64.6%) female patients had genital cGVHD. 53 (40.8%) patients with genital cGVHD had severe genital changes (vaginal adhesions, shortened vagina). More than one third of patients with genital cGVHD (34.5%) did not have any gynecological symptoms suggestive of genital cGVHD. There was no difference in age, myeloablative conditioning or stem cell source between patients with and without genital cGVHD. Patients with severe genital cGVHD were more likely to have severe global cGVHD score (p=0.035).

Discussion: Genital cGVHD should be considered and gynecologic assessment should be performed in all women with cGVHD, even if they are asymptomatic. Patients with severe global cGVHD score are more likely to present with genital manifestations.

Acknowledgments: Pamela Stratton, MD, Program in Reproductive and Adult Endocrinology, NICHD, NIH, Bethesda, MD, USA

MeSH/Keywords: allogeneic hematopoietic stem cell transplantation, female genital chronic Graft Versus Host Disease

Poster code: R-B-5-158

Poster Title: ULTRASOUND FOLLOW-UP OF LIPOATROPHY IN HIV-INFECTED PATIENTS TAKING ANTIRETROVIRAL THERAPY

PhD candidate: Ana Šoštarić Zadro, MD

Part of the thesis: Ultrasound follow-up of lipoatrophy in HIV-infected patients taking antiretroviral therapy

Mentor/s: Professor Josip Begovac, MD, PhD Kladija Višković, MD, PhD, senior scientific associate

Affiliation: University of Zagreb, School of Medicine, University Hospital for Infectious Diseases "Dr. Fran Mihaljević", Zagreb Special Hospital for Pulmonary Diseases, Zagreb

Introduction: HIV-associated lipoatrophy is a term used to describe a loss of subcutaneous fat in extremities and face. Changes in the distribution of adipose tissue along with metabolic changes, which also follow up application of antiretroviral therapy (ART) common form lipodistropy syndrome. Ultrasound (US) is a digital imaging method that is very acceptable in the diagnosis of lipoatrophy.

Materials and methods: We designed a follow-up study in which 151 HIV-infected patients treated at the University Hospital for Infectious Diseases "Dr. Fran Mihaljević" (UHID), Zagreb participated in ultrasound research of lipoatrophy in 2007th and 2008th and are taking antiretroviral therapy (ART) were measured by ultrasound after up to five years. So far, the control US measurement of subcutaneous fat were done in 77 participants, in the malar, brachial and crural region. The measured values were compared with the values determined by US in the same subjects, five years ago. The values of total cholesterol, LDL, HDL and triglycerides were also determined. A McNemar's test was performed to carry out a pairwise comparison. All patients provided written informed consent prior to enrolment. The Ethics Committee of UHID approved the protocol.

Results: Preliminary results show that seventy seven HIV-infected patients with baseline and five-year follow-up US measurements were assessed. There was a statistically

significant increase of subcutaneous fat in malar and brachial region ($p = <0.0001$, respectively), but no significant change in crural subcutaneous fat ($p = 0.3346$)

Discussion: Lipoatrophy is primarily associated with taking analogs of thymidine (stavudin, zidovudin) and it could be expected that a change in therapy has been increasing the amount of subcutaneous fat. In our study based on preliminary results of 77 examined participants, facial and brachial subcutaneous fat measured over 5 years of observation increased probably following a treatment-switch, but it didn't influence on crural subcutaneous fat. A potential limitation associated with the use of US may be the variation in the level at which the measurement was performed and external echoes from within adipose tissue that can make fascia difficult to visualize. The close proximity of tissue-muscle interfaces with bone can also produce multiple or confusing echoes, making measurement less accurate in severe lipoatrophy. In summary, our results, after follow-up examination of whole cohort will allow us to examine the predictive value of US as an objective tool in a longitudinal fashion.

Acknowledgments:

MeSH/Keywords: lipoatrophy, HIV-infection, ultrasound (US)

Poster code: R-B-7-46

Poster Title: APPROPRIATE ANTIBIOTIC THERAPY INFLUENCES PRESEPSIN LEVELS

PhD candidate: Ajete Aliu Bejta

Part of the thesis: Prognostic impact of increased presepsin concentrations on sepsis outcome

Mentor/s: Barsic Bruno MD, PhD, Dreshaj Shemsedin MD, PhD

Affiliation: Hospital for Infectious Diseases Zagreb, Clinic of Infectious Diseases Prishtine

Introduction: Presepsin (sCD14-ST) levels are specifically increased in septic patients and its concentration is more sensitive in comparison to other biomarkers, such as CRP and PCT. Compared to PCT, presepsin is more specific biomarker because its production is associated with bacterial phagocytosis. For risk stratification and predicting the prognosis of sepsis, scoring systems such as SOFA score and APACHE II score, are often used. Recent studies found a significant correlation between presepsin levels and SOFA score and presepsin levels and APACHE II score.

Materials and methods: The research is designed as prospective observational study that will include approximately 100 patients that fulfill defined criteria for sepsis. Patients will be divided into two groups: those with favorable and unfavorable outcome. Presepsin levels will be measured four times during the course of disease and will be compared to other sepsis markers: CRP and PCT and to prognostic scores: APACHE II and SOFA. Blood cultures will be taken in all participants. According to presepsin levels participants will be categorized as SIRS, sepsis and severe sepsis/septic shock.

Results: Blood samples from 15 consecutive patients that fulfilled the defined criteria are

collected and in 5 of them presepsin levels are measured. No statistical analysis is done because of low number of patients. So far we found higher levels of presepsin in patients with higher APACHE II and SOFA score. In one patient with documented sepsis, presepsin levels indicated septic shock while PCT levels were into the normal range. In two patients with unfavorable outcome presepsin levels were very high at admission and 72hrs after initial antibiotic therapy. In one of them blood culture results have demonstrated resistance of bacteria to initial therapy. As a result of administration of adequate antibiotic, presepsin levels decreased.

Discussion: Our initial results indicate the specificity and superiority of presepsin in diagnosing sepsis in comparison to PCT. In all patients, with administration of appropriate antibiotic therapy, presepsin levels decreased, indicating thus the impact of adequate antibiotic therapy in presepsin levels.

Acknowledgments: to "ProLab" laboratory staff for support.

MeSH/Keywords: presepsin, PCT, APACHE II, SOFA, antibiotic therapy

Poster code: R-B-7-106

Poster Title: LYME BORRELIOSIS FOLLOWING TICK BITE IN PRISTINA REGION, KOSOVO

PhD candidate: Albina Ponosheci Biçaku, MD

Part of the thesis: The risk of *Borrelia burgdorferi* infection following tick bite in Pristina region, Kosovo

Mentor/s: Assoc.Professor Goran Tešović, MD, PhD, Professor Salih Ahmeti, MD, PhD

Affiliation: University Hospital for Infectious Diseases, Zagreb University of Zagreb, School of Medicine, Clinic for Infectious Diseases at University Clinical Center of Kosovo - Pristina

Introduction: Lyme disease is a tick-borne multi-systemic disease caused by the spirochete *Borrelia burgdorferi* (Bb). Bb can attack various organs/systems such as skin, joints, nervous system, heart, and eyes. Lyme borreliosis (LB) manifestations can vary from subclinical – asymptomatic through mildly symptomatic to severe forms with significant organ damage resulting in death in severe Lyme carditis cases. LB occurs throughout Europe. Little is known about the prevalence and clinical significance of Lyme disease in Kosovo. To our knowledge very few cases have been recognized and no seroprevalence studies have been published yet. On the other side the presence of Ixodidae ticks which are the main vectors of Lyme borreliosis in Europe has been confirmed in Kosovo natural environment as well.

Materials and methods: The study will be conducted during two-year period (January 2015-December 2016) and will include all consecutive seronegative subjects older than 18 years of age bitten by Ixodes ticks (with embedded tick in the skin) in the region of Prishtina, Kosovo. Sample size will be around 500 patients. The risk of acquiring

LB after a tick bite will be assessed through serologic testing using ELISA. All subjects included in the study will be tested after the period of two months for seroconversion, and will be followed up for any clinical manifestation for the next six months.

Results: This is a prospective still ongoing study that started this year. Because of the seasonal nature of exposure to tick bites, by now we have enrolled 10 patients who fulfilled including criteria for our study. Two patients manifested erythema migrans and are treated with antibiotics. In period of two months subjects will undergo second testing for seroconversion, and will be checked for any clinical manifestation.

Discussion: In this small number of patients we had two cases with clinical manifestation of LB. Because of the early stage of the research no statistical analysis can be done.

Acknowledgments:

MeSH/Keywords: tick bite, Lyme borreliosis, Kosovo

Poster code: R-B-7-113

Poster Title: INVASIVE ASPERGILLOSIS IN PATIENTS TRANSPLANTED WITH ALLOGENEIC HEMATOPOIETIC STEM CELLS: INCIDENCE, RISK FACTORS AND IMPACT ON SURVIVAL – PRELIMINARY RESULTS

PhD candidate: Alen Ostojić, MD

Part of the thesis: Incidence and risk factors of invasive aspergillosis in patients with malignant hematologic diseases

Mentor/s: Professor Radovan Vrhovac, MD, PhD, Professor Zdenek Racil, MD, PhD

Affiliation: University Hospital Center Zagreb, Croatia, University Hospital Brno, Czech Republic

Introduction: Invasive aspergillosis (IA) is important cause of morbidity and mortality in immunocompromised patients (pts), especially in those treated with allogeneic hematopoietic stem cells transplantation (HSCT). Being difficult to diagnose it, prevention and prophylaxis of IA are the milestones in its management.

Materials and methods: This study was conducted on 148 consecutive pts (96 males) with median age of 38 years (range 3-63) treated with HSCT in period from January 2011 to December 2013, with 4 pts transplanted two times, counting a total of 152 HSCT (64% males). Most common diagnosis was acute leukemia (92 pts). Sixty percent of patient received myeloablative conditioning regimen. Sixty-one percent had peripheral blood, 38% bone marrow and 1% umbilical cord blood as the source of stem cells. Forty-eight percent of them had matched related donor (MRD). Diagnosis of IA was established according to EORTC/MSG criteria (DePauw et al. Clin Infect Dis. 2008) and categorized as proven, probable and possible IA. Kaplan-Meier survival function was used to calculate cumulative survival with log-rank test for survival comparison. Mann-Whitney test was used to compare non-parametric variables. Value of $p < 0.05$ was considered as statistically significant.

Results: Eighteen percent of pts developed IA (proven 3, probable 10 and possible 12

pts). In 14 of them IA was diagnosed in period of 100 days after HSCT. The most common isolate as cause of IA was *A. niger* (7 isolates). In two of pts only microbiological criteria was positive Galactomannan test. Majority of pts had pulmonary IA (17 pts), 3 disseminated, 3 sinusitis, 1 both sinusitis and orbital IA, and 1 both pulmonary IA and sinusitis. Patient receiving corticosteroids had significantly higher incidence of IA than those without it (31% vs 26%, $p = 0,003$). Pts with IA had significant shorter survival (1-year survival 38% vs 72% respectively, $p < 0,0001$).

Discussion: In this study using new EORTC/MSG IA diagnosis criteria, preliminary results show that incidence of IA in patients treated with HSCT is relatively high, representing still a significant cause of mortality. Use of corticosteroids is important risk factor of IA development. Further multivariate analysis of other possible risk factors is pending and could identify more risk factors and possibly result in creation of risk calculator which can help in deciding which preventive measures and what kind of antifungal prophylaxis should be used in certain group of pts.

Acknowledgments:

MeSH/Keywords: Aspergillosis, hematopoietic stem cell transplantation, hematologic malignancies

Poster code: R-B-7-121

Poster Title: SPECKLE TRACKING ECHOCARDIOGRAPHY IN TRANSPLANTED HEARTS

PhD candidate: Željko Baričević

Part of the thesis: Echocardiographic assessment of left ventricular myocardial deformation in heart transplant patients

Mentor/s: Professor Davor Miličić, MD, PhD, Professor Jadranka Šeparović Hanževački, MD, PhD

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

Introduction: Graft rejection and vasculopathy in heart transplant (HTx) patients require timely recognition, with endomyocardial biopsy and coronary angiography being the diagnostic gold standards. Finding a non-invasive alternative remains the major objective. Speckle tracking (ST) echocardiography permits early recognition of myocardial dysfunction. The reduction in strain has been shown to denote both rejection and vasculopathy. However, deformation indices are also reduced in "healthy" HTx recipients when compared with control subjects. Whether the reduction in strain is a chronic progressive process or the immediate result of transplantation has not been established. Hence, the lack of ST reference values in HTx population is one of the reasons that strain has not been used to follow-up these patients.

Materials and methods: 16 adult Htx patients with 1-year follow-up period were to be enrolled. However, up to now 3 patients were eligible for enrollment. Standard check-up visits included clinical examination, ECG, laboratory tests, endomyocardial biopsy and echocardiography. Coronary angiography was made at the end of the follow-up year. The study included "healthy" HTx patients only, which implied normal LV ejection fraction ($EF \geq 55\%$), normal ECG with sinus rhythm and $QRS < 120$ ms, lack of cellular rejection (ISHLT grade $\leq 1B$) and the absence of vasculopathy ($< 50\%$ epicardial artery stenosis). Patients with significant val-

ular disease, major cardiovascular events or poor quality echocardiographic records were excluded. Echocardiographic images were obtained with acquisition of apical views using high frame rates (50-90 frames/s) for adequate speckle tracking. Global and segmental strain values were determined and compared to normal subjects' reference values.

Results: Global longitudinal peak systolic strain (GLPSS) was $-15.65 \pm 0.55\%$ at baseline vs. $-15.93 \pm 0.55\%$ at the end of the follow-up year ($P = ns$). GLPSS was significantly lower in HTx patients compared to normal subjects' values (-15.65% and -15.93% vs. -19.7% , $P = 0.003$).

Discussion: In "healthy" HTx recipients we found no significant change of the GLPSS over time. The reduced strain exhibits soon after HTx and stays constant as long as the patients remain "healthy". The low enrollment does not justify conclusions, however the trend shows that early assessment of strain values in HTx recipients could serve as a reference, allow identification of post-HTx complications and might reduce the frequency of biopsy and coronary angiography in stable patients.

Acknowledgments: None.

MeSH/Keywords: Speckle tracking, myocardial deformation, strain, heart transplantation.

Poster code: R-B-9-9

Poster Title: SERUM ENDOTHELIAL LIPASE, LIPIDS AND INFLAMMATORY MARKERS IN ACUTE HEART FAILURE PATIENTS WITH METABOLIC SYNDROME

PhD candidate: Ines Potočnjak, MD

Part of the thesis: Elevated Serum Level of Endothelial Lipase, Inflammatory Markers and Lipid Profile in Metabolic Syndrome are Significant Prognostic Factors in Development of Acute Heart Failure.

Mentor/s: Professor Vesna Degoricija, MD, PhD

Affiliation: University of Zagreb School of Medicine, Sisters of Charity University Hospital Center, Zagreb, Croatia

Introduction: Heart failure (HF) is defined as an abnormality of cardiac structure or function lesion leading to failure of the heart to deliver oxygen at a rate commensurate with the requirements of the metabolizing tissues, despite normal filling pressures. Metabolic syndrome (MS) is a tendency of concomitant risk factors to group: central obesity, elevated serum triglycerides, lowered HDL-cholesterol, glucose intolerance and hypertension. Aim is to investigate whether elevated serum level of endothelial lipase, inflammatory markers and lipid profile can predict worse outcome in patients with AHF and overlapping MS.

Materials and methods: Study was performed as observational, prospective study on AHF pts recruited from the Emergency Department (ED) from January 2014 to January 2015. Participants were divided in two groups depending on presence of MS and compared according to levels of lipids and biomarkers. Pts were treated by standard protocol for AHF by ESC Guidelines. Study was approved by local Ethics committee. Pts' history, clinical presentation, diagnostic procedures and laboratory tests were recorded. Additionally, serum biochemical analysis will be performed at Medical University Graz, Austria.

Results: Analysis included data for 100 pts presenting with AHF. Interestingly there were 53% female pts and 47% male, average age 73 years. Most common clinical presentation of AHF was acute worsening of chronic HF. Unexpectedly, 90% of pts had high (III or IV) New York Heart Association (NYHA) Functional Classification. Increased BMI was observed for 70% of pts, 40% were classified as obese with BMI >30 kg/m², 23 of them were male. It was ob-

served that 89% pts had hypertension, 54% diabetes mellitus, 42% hypercholesterolaemia, 40% hyperlipidaemia and 30% anemia. Remarkably, 59% of investigated pts had MS, equally by gender. Average cholesterol level was 4.11 (mmol/L), 4.12 for pts with MS, 4.08 for pts without MS. Average HDL level for pts with MS was 0.943, 1.05 for patients without MS, average triglyceride level was 1.22 (mmol/L), 1.33 for pts with MS, 1.05 for pts without MS. 30-day mortality was 15%. Clinical improvement was most common recorded outcome.

Discussion: The results should determine investigated increased laboratory markers as predictors of morbidity and mortality. MS is important concomitant factor in development of AHF. Excitingly, pts in our study had highly elevated BMI, NYHA score and overlapping MS. The results of this research offer MS as treatment focus for improving outcome of AHF pts.

Acknowledgments: I would like to thank team members for collaboration on this project: Vesna Degoricija^{**1,2}, and Saša Frank^{**3}. ^{**1}Sisters of Charity University Hospital Center, Zagreb, Croatia, ^{**2}University of Zagreb, School of Medicine, Zagreb, Croatia, ^{**3}Institute of Molecular Biology and Biochemistry, Center of Molecular Medicine, Medical University Graz, Austria. A special appreciation for informatics support goes to Dubravko Rutalj. I would like to emphasise special gratitude for collaboration with Institute of Molecular Biology and Biochemistry, Center of Molecular Medicine, Medical University Graz, Austria (Austrian Science Foundation (FWF, grant) 2013-2016).

MeSH/Keywords: heart failure, metabolic syndrome, lipase, lipids, markers

Poster code: R-B-9-11

Poster Title: CIRCULATING DIPEPTIDYL PEPTIDASE-4 ACTIVITY IS ASSOCIATED WITH DIABETIC RETINOPATHY IN TYPE 1 DIABETIC PATIENTS

PhD candidate: Kristina Blaslov

Part of the thesis: Circulating dipeptidyl peptidase-4 activity is associated with diabetic retinopathy in type 1 diabetic patients

Mentor/s: Lea Smirčić Duvnjak, MD, PhD, Professor

Affiliation: Medical School University of Zagreb, Croatia

Introduction: Diabetic retinopathy (DR) is the most frequent complication among patients with type 1 diabetes mellitus (T1DM). Dipeptidyl peptidase-4 (DPP4) is a protease with elevated activity in patients with T1DM. Several studies indicate that DPP4 inhibitors might have beneficial effect on nonproliferative retinopathy (NPR) development as well as on its progression to proliferative retinopathy (PR). We aimed to explore the relationship between serum DPP4 activity and DR in patients with T1DM.

Materials and methods: This cross-sectional study recruited 44 patients with T1DM. The DPP4 activity was measured by colorimetric assay in a microplate reader. Photodocumented retinopathy status was made according to the EURODIAB protocol.

Results: A total of 28 (63.6%) patients were men, mean age 45.36 years, diabetes duration 23.71 years, glycated hemoglobin A1c (HbA1c) 7.4%. Patients were stratified into 2 groups according to retinopathy prevalence.

Group 1 comprised 14 (31.85%) patients with DR absence while the second group consisted of 30 (68.15%) patients with both PR and NPR. Group 1 had lower fasting serum DPP4 activity (25.85 vs 33.84 U/L, $p < 0.001$) when compared to the second group. In the binary logistic regression model adjusted for age, sex, diabetes duration, and HbA1c level, DPP4 activity was associated with DR prevalence (odds ratio 1.887 [1.073-3.321]).

Discussion: Serum DPP4 activity may be independently associated with both DR types in patients with T1DM. Further study is warranted to elucidate whether there is an association between DPP4 activity and DR severity and/or progression.

Acknowledgments: None.

MeSH/Keywords: Diabetic retinopathy, dipeptidyl-peptidase-4, type 1 diabetes mellitus

Poster code: R-B-9-14

Poster Title: ONE-YEAR FOLLOW-UP AFTER IRRIGATED MULTI-ELECTRODE RADIOFREQUENCY ABLATION OF PERSISTENT ATRIAL FIBRILLATION

PhD candidate: Nikola Pavlović

Part of the thesis: Comparison of Irrigated Multi-Electrode Radiofrequency Ablation and point-by-point ablation for Pulmonary Vein Isolation in Patients with Persistent Atrial Fibrillation

Mentor/s: Diana Delić Brkljačić, Christian Sticherling

Affiliation: University Hospital Centre "Sestre milosrdnice"

Introduction: The electrical isolation of the pulmonary veins (PVs) remains the cornerstone of treatment in patients undergoing ablation of atrial fibrillation (AF). Irrigated multi-electrode ablation (IMEA) is a novel tool to perform pulmonary vein isolation (PVI). The aim was to compare IMEA with point-by-point radiofrequency (RF) ablation in patients with persistent atrial fibrillation (AF) undergoing PVI.

Materials and methods: Forty-nine patients (age 60.9 years, 82% male) were studied. In 24 patients, the IMEA catheter was used in conjunction with an electroanatomic mapping system. Twenty-five patients undergoing RF point-by-point ablation (RF-PVI) served as a control group. Validation of PVI based on the IMEA catheter was performed using a standard circular mapping catheter.

Results: Ninety-two of 94 pulmonary veins (PVs) (98%) were isolated using IMEA alone. Procedure time was 125.23 min in the IMEA group and 127.31 min in the RF-PVI group (P 0.79). Fluoroscopy time was 12.2 (11–16.1) min with IMEA compared with 5.2

(4.1–9.3) min in the RF-PVI group (P 0.001). Net ablation time was 11.8 (10.2–15.4) min in the IMEA group compared with 33.6 (30.3–40.1) min in the RF-PVI group (P 0.001). Of 94 PVs presumed to be isolated after IMEA ablation, validation using a standard circular mapping catheter showed persistent PV potentials in 33 PVs (35%), requiring additional IMEA ablation. At 12 months, 16 of 24 patients (67%) in the IMEA group compared with 17 of 25 patients (68%) in RF-PVI group were free from AF (P 0.99).

Discussion: With similar total procedure duration, IMEA-PVI was associated with shorter net ablation time and longer fluoroscopy time. Irrigated multi-electrode ablation recordings were not sufficient to confirm isolation in 35% of PVs. Single-procedure efficacy after 12 months was similar between the two groups.

Acknowledgments:

MeSH/Keywords: Radiofrequency catheter ablation

Poster code: R-B-9-21

Poster Title: RENAL DISORDER IS MORE FREQUENT AMONG DECEASED PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) – ANALYSIS OF DATA FROM A SINGLE-CENTER REGISTRY

PhD candidate: Ivan Padjen, MD

Part of the thesis: Analysis of causes of death of patients with systemic lupus erythematosus followed-up in a tertiary hospital center during a ten-year period (2002-2011)

Mentor/s: Professor Branimir Anić, MD, PhD

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

Introduction: The number of fulfilled classification criteria is not a measure of disease severity in patients with SLE, however the fulfillment of particular criteria may be associated with a severe clinical course. In this study we compared the number of fulfilled ACR (American College of Rheumatology) criteria between SLE patients identified and not identified as deceased in the period from 2006 to 2011.

Materials and methods: Data were retrieved from our hospital-based registry of SLE patients. Patients with a diagnosis of SLE and at least one visit to the Centre in the 2006-2011 period or death in the same period were analyzed. Deceased patients were identified using the registry and death certificates. The number of fulfilled ACR criteria was counted. The chi-square test and Fisher exact test, as well as the Student t-test were used to evaluate differences between categorical and continuous variables, respectively.

Results: The number of identified SLE patients with at least one visit to the Centre in the 2006-2011 period was 702. The frequency of ACR criteria was available for

693/702 patients. We identified 48 deceased patients (31 females and 17 males). Data on the year of diagnosis and fulfillment of ACR criteria were not available for 4 deceased patients. The length of follow-up of deceased patients was 12.09 ± 7.38 years. The frequency of renal disorder and discoid rash was significantly higher in the deceased patient group compared to patients not identified as deceased (21/44 vs. 167/665, $\chi^2=9.702$, $p=0.002$ and 20/44 vs. 128/665, $\chi^2=15.610$, $p<0.001$). No difference in frequencies of other criteria was observed.

Discussion: The higher frequency of renal disorder among deceased SLE patients may be in line with the more pronounced disease severity in SLE patients with renal affection. The finding of a higher frequency of discoid rash among deceased patients requires further elucidation.

Acknowledgments: I would like to thank my mentor and all members of the Division.

MeSH/Keywords: systemic lupus erythematosus, classification criteria, death, registry

Poster code: R-B-9-22

Poster Title: QUALITY OF LIFE AFTER LIVER TRANSPLANTATION

PhD candidate: Nino Kunac, M.D.

Part of the thesis: Role of Transplantation and Clinical parameters in Quality of life change in Patients with Liver Cirrhosis

Mentor/s: Assistant professor Tajana Filipec Kanižaj, M.D., Ph.D., Full professor Vesna Medved, M.D., Ph.D.

Affiliation: University hospital Merkur¹ University hospital center Zagreb

Introduction: Liver transplantation is an established medical procedure for patients with liver cirrhosis. Considering the achievement of high patient and graft survival after liver transplantation, attention of research has focused on health related quality of life in transplant recipients and on factors affecting it.

Materials and methods: Quality of life will be evaluated by the Medical outcomes Short form (SF-36) (Croatian version) and Chronic liver disease questionnaire (CLDQ) in 100 patients before and 6 and 12 months after liver transplantation. We will investigate the association of pretransplantation (liver cirrhosis etiology, CTP and MELD score) and peri- and posttransplantation parameters (antiHBc donor status, DRI, vascular and biliary graft complications, infection, episodes of acute graft rejection, liver disease recurrence, new onset diabetes mellitus and immunosuppression protocol) with post-transplantation quality of life.

Results: At the moment we have 20 patients enrolled, with 5 of them undergone liver transplantation in period from March 1st

2015 until now. Because of the very early stage of research and small number of data collected so far, no relevant statistical analysis was done.

Discussion: The aim of this study is to evaluate the impact of pre- and posttransplantation clinical condition of patients and liver graft quality on quality of life after liver transplantation. Better clinical parameters are associated with better quality of life after liver transplantation. Identifying clinical parameters associated with positive and negative quality of life change after liver transplantation, would help to achieve a more purposeful and effective plan of precious graft distribution, and contribute to more precise and systematic posttransplantation patient care.

Acknowledgments: I would like to thank both of my mentors for advices and support during this investigation.

MeSH/Keywords: liver cirrhosis, liver transplantation, quality of life

Poster code: R-B-9-88

Poster Title: QUALITY OF LIFE AND PSYCHOLOGICAL STATUS OF PATIENTS WITH IMPLANTIBLE CARDIOVERTER DEFIBRILLATORS

PhD candidate: Ivan Bitunjac

Part of the thesis: Quality of Life and Psychological Status of Patients With Implantible Cardioverter Defibrillators

Mentor/s: Professor Martina Lovrić Benčić, MD, PhD, Assistant Professor Anita Lauri Korajlija, professor of psychology, PhD

Affiliation: General Hospital Dr. Josip Bencevic, Slavonski Brod

Introduction: The implantable cardioverter defibrillator (ICD) is a life saving device for individuals with life threatening ventricular arrhythmias. Nevertheless, shock delivery may be painful and frightening which causes psychological distress and deterioration of perceived quality of life. The clinical efficacy of implantable cardioverter-defibrillators (ICDs) has been convincingly proven in clinical trials but the impact of ICDs on recipients' quality of life (QOL) have hardly been studied.

Materials and methods: Three self-administered questionnaires will be used. Quality of life will be evaluated using SF-36. The 21-item DASS questionnaire will be used to assess the severity of the core symptoms of Depression, Anxiety and Stress. Third one is 11 item questionnaire designed to assess correlation between patient's subjective perception of ICD activity and objective analysis of the device. The first assessment will take place a day after implantation, the remaining three at 1, 6 and 12 months after discharge. Levels of anxiety, depression, stress and deterioration in quality of life will be measured regarding delivered therapy, indications for implantation, age and gender of patients.

Results: At the moment we have 29 patients enrolled, with ICD implanted in period from

June 1st 2014 until now. Because of the very early stage of research and small number of data collected so far, no relevant statistical analysis was done.

Discussion: The aim of the study is to evaluate quality of life and psychological well-being, and the prevalence of, and changes in, affective disorders of patients who did or did not experience defibrillatory shocks in the first 12 months of follow up period after ICD implantation. Quality of life and psychological well-being deteriorates over time in ICD recipients, respective of whether they experienced defibrillatory shocks. There is also higher prevalence of symptoms of anxiety and depression in the group of patients who experienced shocks. We expect that collected data and results will contribute to determine whether psychosocial interventions may be warranted for ICD patients.

Acknowledgments: I would like to thank both of my mentors for advices and support during this investigation.

MeSH/Keywords: implantable cardioverter-defibrillator, ICDs, defibrillation shocks, quality of life, affective disorder, anxiety, depression

Poster code: R-B-9-92

Poster Title: IMPACT OF DELAYED GRAFT FUNCTION ON LONG TERM KIDNEY TRANSPLANT OUTCOMES

PhD candidate: Bojana Maksimović, MD

Part of the thesis: The impact of delayed graft function on long term graft survival and progression of chronic histological changes in kidney transplant recipients

Mentor/s: Mladen Knotek, assistant professor

Affiliation: Renal Division, Department of Medicine, University of Zagreb Medical School and Clinical Hospital Merkur, Zagreb, Croatia

Introduction: Delayed graft function (DGF) is a manifestation of acute kidney injury. It has usually been defined as the need for dialysis within 7 days of the transplant. Incidence of DGF has increased over the time in deceased donors probably because of more often use of expanded criteria donors (ECD) and in some countries of donors after cardiac death (DCD). The incidence is approximately 30% in recipients of standard criteria deceased donor kidneys, 50 % for recipients of ECD and up to 70% recipients of DCD kidneys. The dominant cause of DGF is acute tubular necrosis. Risk factors for DGF are well defined, and they include cold ischemia time that exceeds 24 hours, calcineurin inhibitors use in the induction regimen and also factors related to the donor such as hypotension and dehydration. It is also known that there is higher incidence of acute rejection when DGF is present. The complex relationship between DGF and allograft survival and patient survival is still poorly understood.

Materials and methods: Two groups of patients with transplanted kidney or combined kidney pancreas and kidney liver transplantation, transplanted between 2003-2012 were included in the study. Group with established DGF compared to the group of patients without DGF. Glomerular filtration rate was estimated by MDRD equation, at 6 months and one year after transplantation.

Renal histology will be assessed at 0, 1, 6 and 12 months after transplantation in latter analysis. Impact of DGF on GFR and progression on chronic histological scores as defined by Banff classification will be analysed.

Results: DGF rate was 38,4%. There were 117 patients without DGF, 48 female, 69 male, and 73 patients with DGF, 30 male and 43 female. Average age at time of transplantation was 41,8 - 11,4 in group without DGF and 46,5 -12,5 in DGF group ($p < 0,05$). There was significant difference in eGFR between patients with DGF and without DGF (59,8 ml/min versus 64,1 ml/min and 58,5 ml/min versus 66,0 ml/min) at 6 months and one year after transplantation.

Discussion: Although early and short term results show statistically significantly lower eGFR in DGF group compared with the non-DGF group, we think that this difference might disappear after longer observation period (at 5 year). In the latter analysis we are going to show impact of renal histology and adjust results for chronic histological scores.

Acknowledgments:

MeSH/Keywords: kidney transplant, delayed graft function, kidney biopsy

Poster code: R-B-9-107

Poster Title: IMPACT OF EARLY STEROID WITHDRAWAL (ESW) ON PROGRESSION OF CHRONIC BIOPSY SCORES AFTER KIDNEY TRANSPLANTATION

PhD candidate: Karlo Mihovilović

Part of the thesis: Impact of early steroid withdrawal (ESW) on progression of chronic biopsy scores after kidney transplantation

Mentor/s: Associate Professor Mladen Knotek, MD, PhD

Affiliation: University of Zagreb School of Medicine, Clinical Hospital Merkur, Zagreb

Introduction: Long-term effects of ESW on development of chronic pathohistology changes in kidney allograft is unclear.

Materials and methods: In this study we compared chronic scores on protocol biopsies in Caucasian kidney recipients (N=41) without DGF with ESW vs. continuous steroids on top of CNI and MMF. Induction consisted of IL-2RA or ATG. Protocol biopsies were done on day 0 and 1 year after transplant. Chronic scores (ci, ct, cg, mm, cv and ah) were analyzed by Banff 97 classification.

Results: ESW was not associated with changes in ci, ct, cg, mm and cv scores, but slight progression of ah score was noticed in

ESW group (0.49 ± 0.51 vs. 0.21 ± 0.41 $p=0.02$). In multivariate analysis including recipient age and gender, donor age, type of donation (living or deceased) and type of transplant (kidney or kidney/pancreas), ESW was independently associated with progression of ah score ($p=0.049$).

Discussion: In conclusion, ESW may cause progression of ah score during first 12 months posttransplant, without impact on other chronic scores.

Acknowledgments:

MeSH/Keywords: kidney transplantation, chronic allograft nephropathy

Poster code: R-B-9-108

Poster Title: LEFT VENTRICULAR LONGITUDINAL FUNCTION IN HYPERTENSIVE PATIENTS WITH SEPTAL BULGE

PhD candidate: Vlatka Rešković Lukšić

Part of the thesis: Poremećaj deformacije miokarda u hipertroničara s hipertrofijom interventrikulskog septuma u izgonskom traktu lijeve klijetke

Mentor/s: Prof.dr.sc. Jadranka Šeparović Hanževački

Affiliation: University Hospital Center Zagreb

Introduction: In patients with arterial hypertension, due to chronic pressure overload, structural concentric remodeling occurs. Hypertrophy pattern is determined by fiber orientation, interaction with local wall stress and is the most prominent in the region of basal interventricular septum. By analyzing standard echocardiographic parameters, no reduction in global ventricular function is to be found in this early phase of geometric changes, but longitudinal fibers are known to be affected and longitudinal function could already be reduced.

Materials and methods: 30 patients with essential arterial hypertension, no other comorbidities and preserved LV ejection fraction were enrolled. Complete standard echocardiographic examination was done, along with 2D speckle tracking analysis of longitudinal strain. Patients were divided into two groups depending on presence of the basal interventricular (iv) septal bulge. Three patients were excluded from the study because of poor acoustic echo window. In 16 patients, iv septal bulge was present, and in 11 of them was not. Regional values of longitudinal strain were measured for each LV segment and data was compared between groups.

Results: In no bulge group, there was equal number of males (5 pts) and females (6 pts), but in septal bulge group, majority of patients were male (10 out of 16). There was no significant difference in patient's age be-

tween groups (45,7 god \pm 12,9 years in no bulge and 48,4 \pm 9,9 years in bulge group). Mean duration of hypertension was 8,1 \pm 8,9 years in no bulge and 6,2 \pm 8 years in bulge group. We found no statistically significant difference in regional longitudinal strain values, except in the region of medial interventricular septum (-21.4 \pm 3,1% vrs -18,3 \pm 3.02%, P=0,26), which was significantly reduced in patients with basal iv septal bulge. This is the area closest to the region most prominent to pressure overload and hypertrophy and significance of this finding should be investigated further on.

Discussion: In patients with hypertension and preserved ejection fraction, even in early stages of hypertensive heart disease, subtle changes in LV longitudinal function can be found. Interventricular septal hypertrophy could be a macroscopic marker for this changes and could help us in identifying patients in greater risk for developing heart failure. This data should be confirmed on larger number of patients and with particular focus on septal segments and correlation between regional longitudinal and radial function.

Acknowledgments:

MeSH/Keywords: Echocardiography, speckle tracking, longitudinal deformation, arterial hypertension, interventricular septal bulge

Poster code: R-B-9-115

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

PhD candidate: Dajana Katičić, MD

Part of the thesis: Serum phosphorus as a risk factor for cardiovascular morbidity in patients with diabetes mellitus typ 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 therapy with oral hypoglycemic 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 hypoglycemic 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 whether there is a correlation between serum phosphorus level and traditional risk factors for cardiovascular disease (age, gender, hypertension, hyperlipidemia, smoking, BMI Framingham Heart Score). Glomerular filtration rate will be assessed 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 separate measurements, or the use of hypoglycaemic agents (oral agents and/or insulin). Hypertension will be defined as blood pressure $\geq 140/90$ mmHg or taking antihypertensive therapy. Cardiovascular event will be defined as fatal or non-fatal heart attack, angina pectoris (stable or unstable), cardiac 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 sample of twenty patients, 10 in control group and 10 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 disease (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: No acknowledgments

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

Poster code: R-B-9-117

Poster Title: AORTIC ELASTICITY IN CHILDHOOD CANCER SURVIVORS

PhD candidate: Blanka Glavaš Konja, MD

Part of the thesis: Late Effects Of Childhood Cancer Treatment On Aortic Elasticity

Mentor/s: Academician Davor Miličić, MD, PhD

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

Introduction: Childhood cancer survivors are at higher risk for chronic disease and premature death, in particular from cardiovascular diseases. There is association of aortic stiffness with left ventricular hypertrophy and with future cardiovascular events. Conventional and tissue Doppler imaging (TDI) echocardiography have been shown to be useful methods in the evaluation of global ventricular functions and elastic properties of the aorta but it has not been evaluated in childhood cancer survivors.

Materials and methods: 13 adult childhood cancer survivors (6 women and 7 men, aged 21 ± 3 year) are matched 15 healthy volunteers (7 women and 8 men, aged 22 ± 4 year). Aortic elasticity is examined by using echocardiography device. Systemic arterial blood pressure is measured by sphygmomanometer in supine position, simultaneously with the echocardiographic examination of the ascending aorta. The index of aortic stiffness is calculated and statistically analyzed. Data are presented as mean \pm standard deviation for continuous variables. Differences between groups are assessed by Student t test.

Results: The healthy control group had a significantly ($p < 0.01$) lower stiffness index (2.28 ± 0.6) than the chemotherapy treated

(4.22 ± 2.31) group. In both groups systolic and diastolic heart function is considered normal. There was no significant difference in arterial blood pressure between the groups.

Discussion: Cardiovascular mortality is higher in long-term cancer survivors. Individual risk prediction of cardiotoxicity progression is difficult. Aortic stiffness is already determined as a risk factor for the development of hypertension and hypertensive heart disease. Also, it is connected to coronary heart disease. The results of this small study show increased aortic stiffness in the chemotherapy treated group what supports the thesis that aortic elasticity changes measured by echocardiographic methods can be useful in early cardiotoxic risk assessment.

Acknowledgments: I would like to thank to professor Jadranka Šeparović Hanževački, MD, PhD who is the leader of the project Myocardial Doppler in Early Detection and Follow up of Cardiovascular Diseases that is supported by the Ministry of Science, Education and Sport of the Republic of Croatia

MeSH/Keywords: aortic stiffness, childhood cancer survivors

Poster code: R-B-9-131

Poster Title: PLASMINOGEN ACTIVATOR INHIBITOR 1 IN ACUTE MYOCARDIAL INFARCTION

PhD candidate: Marin Pavlov

Part of the thesis: Prognostic value of plasminogen activator inhibitor 1 on long term outcome in patients with acute myocardial infarction with ST elevation treated with primary percutaneous coronary intervention

Mentor/s: Vesna Degoricija, MD, PhD, professor

Affiliation: Sestre milosrdnice University Hospital Centre, Zagreb

Introduction: Cardiovascular diseases are the main cause of death in Croatia. Acute myocardial infarction is the most severe form of coronary artery disease. Contemporary treatment of eligible patients includes primary percutaneous coronary intervention (PCI). Plasminogen activator inhibitor-1 (PAI-1) is the main inhibitor of plasminogen activation. It is secreted by endothelial cells and platelets, and in some circumstances by other cells. By reviewing recent data, no reference on PAI-1 value in prediction of long-term outcome for patients with acute myocardial infarction treated with primary percutaneous coronary intervention could be found.

Materials and methods: Patients treated with primary PCI for acute STEMI were included in the study, while those with altered immune response due to medical treatment, acute inflammatory illness or malignancy were excluded. PAI-1 activity was determined at arrival and after 24 hours. CPK levels were determined every 6 hours until drop. Outcomes were determined by telephone interview.

Results: A total of 87 patients were enrolled in the study with average age of 60 and male predominance (71%). Risk profile was observed as follows: 67% with medical history of hypertension, 15% of diabetes, 53% of smokers and 65% of dyslipidemia. Diagnosis of CAD was already established in 13% of patients, while prior PCI was performed in 8%. Long term usage of aspirin was reported by 15%, beta blockers by 15%, ACE

inhibitors by 24% and statins by 7% of patients. On presentation, heart failure was present in 10%, cardiogenic shock in 3%, ventricular fibrillation occurred in 13% of patients. All patients received aspirin and clopidogrel, while eptifibatide was used in 73% of patients. Most common culprit lesion was in right coronary artery (49%) followed by left anterior descending (39%) and circumflex artery (12%). Initial TIMI flow of 0 was observed in 78%, stents were implanted in 95% and final TIMI III flow was obtained in 79% of patients. Two patients died during initial hospitalization. Average value of PAI-1 activity on arrival was 3.25 U/ml, and after 24 hours 4,71 U/ml (an increase of 45%). Data on follow up could not be reported.

Discussion: The inclusion period is finished. The study population resembles one typical of STEMI patients with high incidence of hypertension, smoking and dyslipidemia. Other descriptive characteristics of study population are also as expected. The main study results can not be presented due to incomplete follow up.

Acknowledgments: I would like to thank professor Vjeran Nikolic Heitzler, who headed the original scientific project and who let me use a part of original data for this study.

MeSH/Keywords: plasminogen activator inhibitor-1, acute myocardial infarction, primary percutaneous coronary intervention, long term outcome, no reflow phenomenon

Poster code: R-B-9-134

Poster Title: THERMOGRAPHY IN ULCERATIVE COLITIS – A CASE REPORT

PhD candidate: Tonći Božin

Part of the thesis: Association between Clinical, Laboratory and Thermographic findings in Patients with Ulcerative Colitis

Mentor/s: Associate Professor Marko Banić, MD, PhD

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

Introduction: Ulcerative colitis represents a chronic condition occurring in relapsing and remitting fashion with uncertain outcome and requires lifelong treatment with considerable side effects. Diagnostic methods currently in use give an insight into disease activity, but are possibly associated with significant discomfort for the patient. For that reason there is a need for a noninvasive, biologically inert method for evaluation of disease activity in inflammatory bowel disease. The aim of this paper is to present the potential of thermography in surveillance of ulcerative colitis.

Materials and methods: For the purpose of this paper a female patient underwent standard diagnostic workup for ulcerative colitis (UC) and thermography. The thermographic measurements were done in two interval times: before initiating the therapy and after the patient had reached the remission of colitis, according to clinical, laboratory and endoscopic evaluation.

Results: Severe inflammatory activity of the disease correlated nicely with the pattern of thermographic infrared pictures, taken before treatment. After four weeks of intensive treatment the patient entered the remission of the disease, documented with significant clinical, laboratory and imaging improvement in disease activity. This finding, indicating the remission of active colitis corre-

lated with taken thermographic pictures showing only mild abnormalities with the significant decrease in abdominal surface temperature pattern, compared to initial thermographic examination.

Discussion: The findings in this case report indicate the correlation of standard laboratory and imaging tests and infrared imaging in evaluating the initial activity of acute severe pancolitis, in this particular patient. In addition, after four weeks of intensive treatment with anti-inflammatory drugs, the documented clinical, laboratory and imaging improvement in disease activity correlated with pattern of taken thermographic pictures. We believe that blood vessel activity during the process of active inflammation induces the increase in body surface temperature that would be higher than in normal tissue. Our findings point out to diagnostic potential of infrared thermography as a feasible and noninvasive method in evaluation of disease activity, in the patient with severe inflammatory bowel disease, such as acute pancolitis.

Acknowledgments: I wish to thank Professor Banic and dr. Antonini for helping me prepare this paper.

MeSH/Keywords: Ulcerative colitis, Thermography, Colonoscopy

Poster code: R-B-9-139

Poster Title: EFFECT OF IMMUNOSUPPRESSIVE AGENTS ON PLATELET AGGREGATION IN RENAL TRANSPLANT PATIENTS

PhD candidate: Željka Martinović

Part of the thesis: Immunosuppressive agents have different effect on platelet aggregation

Mentor/s: Professor Nikolina Bašić Jukić, MD, PhD

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

Introduction: Renal transplantation is the treatment of choice for patients with end stage renal disease meaning better survival and quality of life. The success of transplantation depends largely on immunosuppressive therapy. The major immunosuppressive agents that are currently being used in various combination regimens are corticosteroids, azathioprine, mycophenolate mofetil (MMF), cyclosporine, tacrolimus, everolimus, and sirolimus. Immunosuppressive therapy is associated with an increase risk of thromboembolic complications and overall increased risks of morbidity and mortality from cardiovascular disease.

Materials and methods: The study included renal transplant patients which were controlled in the Department of Nephrology, Hypertension, Dialysis and Renal Transplantation in Clinical Hospital Center Zagreb, during 3 months period. During regular visit, together with blood sampling for standard laboratory parameters, an additional 2 ml of blood was taken from all patients who met the inclusion criteria. Platelet function testing was performed on platelet function analyzer (PFA-200) that „in vitro“ simulates the process of aggregation and platelet activation. Results are reported as the closure time in seconds for COL-EPI and COL-ADP cartridges. The ranges for control subjects were 85–165 s for the COL - EPI closure time, and 71–118 s for the COL -ADP. Data for analysis

for renal transplant patients were taken from the medical records. Control group included healthy individuals.

Results: The study included 85 renal transplant patients (50 male and 35 female, median age 54 (29-76), divided into four groups based on the type of different immunosuppressive agent (cyclosporine, tacrolimus, everolimus, and sirolimus). All values of „in vitro“ closure times (s) with COL-EPI test were within the reference range, but patients in tacrolimus group had significantly lower values compared to controls ($p=0,006$), and compared to cyclosporine group ($p=0,031$). With COL/ADP test, patients in sirolimus group had significantly lower values compared to controls ($p=0,010$).

Discussion: Although, all the values of „in vitro“ closure times with both tests (COL-EPI and COL-ADP) were within reference range, tacrolimus and sirolimus group showed significantly lower values compared to controls. The sensitivity of the test and clinical relevance of these findings should be further investigated.

Acknowledgments:

MeSH/Keywords: platelet aggregation, immunosuppression

Poster code: R-B-9-141

Poster Title: VALIDATION OF CLASSIFICATION CRITERIA FOR SYSTEMIC LUPUS ERYTHEMATOSUS

PhD candidate: Marija Bakula, MD

Part of the thesis: Validation of Classification Criteria for Systemic Lupus Erythematosus

Mentor/s: Nada Čikeš, MD, PhD

Affiliation: University of Zagreb School of Medicine, University Hospital Centre Zagreb, Department of Internal Medicine, Division of Clinical Immunology and Rheumatology

Introduction: American College of Rheumatology (ACR) classification criteria for SLE developed in 1982, were revised in 1997 and since then have been used for standardisation of patients for clinical research. However, many SLE patients, especially in the early stage of the disease, do not fulfill the essential requirement of 4 out of 11 criteria for classification. Therefore, a new set of criteria (SLICC criteria) has been derived and validated, with the same specificity, but greater sensitivity in comparison with the ACR criteria. We applied the SLICC criteria on our group of patients with SLE and incomplete SLE (<4 ACR criteria). As expected, the SLICC criteria recognized SLE patients with high sensitivity and specificity and showed greater sensitivity in comparison with the ACR criteria in the early stage of the disease.

Materials and methods: Medical documentation of patients with diagnosis of SLE and other conditions related to SLE (antiphospholipid syndrome, mixed or undifferentiated connective tissue disease, overlap syndrome) treated at our Division was assembled (1918 patients). Documentation of patients with SLE and incomplete SLE was sorted out (968 patients). Patients not examined in the last 3 years were excluded from the investigation. SLICC criteria were tested on the first group of 60 patients. For every patient the criteria were applied on the date of patient's first visit and the total

score (at the last visit) was counted. The scores were compared with the ACR criteria.

Results: Applied at the early stage of the disease, SLICC criteria have shown greater sensitivity. Serological, hematological and cutaneous criteria are better defined and some neurological manifestations included. Therefore, in a number of patients with „incomplete“ SLE according to ACR criteria, diagnosis of SLE could be established at earlier stage. The exception was one patient who presented with cutaneous lupus, in this case ACR criteria showed greater sensitivity than SLICC criteria. By applying new criteria, some ambiguous cases were clarified and the group that was tested is now better defined.

Discussion: Current classification of SLE patients has not shown enough sensitivity. By applying SLICC criteria on our group of patients we determined that they are a better diagnostic tool for SLE, especially in the early stages of the disease. Forming a well defined group of patients is the specific aim of this dissertation, which will be useful in further clinical research.

Acknowledgments:

MeSH/Keywords: systemic lupus erythematosus, ACR criteria, SLICC criteria, criteria validation

Poster code: R-B-9-147

Poster Title: THE ROLE OF ADIPOCYTOKINES IN NEW ONSET DIABETES AFTER LIVER TRANSPLANTATION

PhD candidate: Iva Košuta

Part of the thesis: The role of adipocytokines in new onset diabetes after liver transplantation

Mentor/s: Assistant prof. Anna Mrzljak, MD, PhD, Marijana Vučić Lovrenčić, PhD

Affiliation: Department of Medicine, Merkur University Hospital, Zagreb, Croatia

Introduction: The development of New-Onset Diabetes After Transplantation (NODAT) has the highest negative impact on long-term survival of liver transplant (LT) patients. It is associated with increased infection, chronic kidney disease and cardiovascular risk. NODAT pathogenesis is most likely similar to that of type 2 diabetes mellitus. Adipocytokines, active products of adipose tissue, influence insulin resistance and beta-cell function and contribute to diabetes development in the general population. However their function is poorly understood in liver-transplanted patients.

Materials and methods: This prospective study will follow the metabolic status and development of NODAT in 150 patients undergoing liver transplantation at the Merkur University Hospital in the first postoperative year. Nondiabetic patients, regardless of liver failure etiology, will be included. Clinical and demographic data will be gathered prior to liver transplantation, together with an initial metabolic screening (serum leptin and adiponectin included). Metabolic reevaluation will take place at 3, 6 and 12 months post-LT, with the diagnosis of NODAT being made in concordance with WHO/ADA criteria.

Results: 34 patients (9 female) were included in the preliminary testing of preoperative and 3-month post-LT metabolic status.

(1) A significant decrease in insulin resistance (lower concentrations of insulin/c-peptide, HOMA-IR and HbA_{1c}, an increase of HOMA-IS) was found (all $P < 0,05$), with unchanged levels of fasting glycemia. (2) Also, a mild but statistically significant increase in HbA_{1c}, within a reference range, was observed. (3) Finally, 3 months post-LT there was a significant decline in adiponectin and leptin concentration ($P = 0,001$ and $0,043$, respectively), while adiponectin to leptin ratio remained unaffected ($P = 0,46$).

Discussion: (1) The preliminary results indicate an improvement of metabolic status 3 months post-LT with lower concentrations of insulin needed for maintaining euglycaemia. (2) The rise in HbA_{1c} can be accounted for in two ways: a) As an effect of immunosuppressive agents, b) As an effect of anemia correction after LT. (3) The observed decrease of adiponectin and leptin concentrations is most likely related to the improvement of insulin resistance, but further follow-up on the dynamics of the biomarkers, as planned by the study protocol, is needed for conclusive results.

Acknowledgments: ...

MeSH/Keywords: Liver transplantation, New Onset Diabetes After Transplantation, NODAT, Adipocytokines, Adiponectin, Leptin

Poster code: R-B-9-154

Poster Title: CLINICAL CHARACTERISTICS AND CYTOKINE PROFILE OF PATIENTS WITH RHEUMATOID ARTHRITIS IN KOSOVO

PhD candidate: Blerta Rexhepi, Medical Doctor, Resident in Rheumatology

Part of the thesis: Clinical characteristics and cytokine profile of patients with rheumatoid arthritis in Kosovo

Mentor/s: 1. Nada Cikes 2. Vjollca Sahatciu-Meka

Affiliation: 1. University of Zagreb, School of Medicine Dpt. for Internal Medicine, Div. for Clinical Immunology and Rheumatology 2. University of Prishtina, Medical Faculty

Introduction: Rheumatoid arthritis is a chronic inflammatory rheumatic disease with prevalence 0.5 to 1% of adults in the developed world. There is no data about the prevalence and clinical characteristics of RA patients in Kosovo. The aim of this study is to define the clinical characteristics and cytokine profile of RA patients in Kosovo population.

Materials and methods: This study will involve 100 patients with RA, divided into two groups. Patients with RA will fulfil ACR/EULAR Rheumatoid Arthritis Criteria. In both groups will be evaluated history of the disease, evaluation of number of swollen and tender joints, health assessment questionnaire (HAQ), global pain visual analogue scale (VAS), disease activity score (DAS-28), erythrocyte sedimentation rate, C-protein reactive, Rheumatoid factor, antibodies to citrullinated peptide and concentration of interleukin-6, interleukin-17, tumour necrosis factor- α will. Radiological status of patients will be evaluated. Patients will be treated with NSAIDs, DMARDs and glucocorticoids. The daily dose of glucocorticoids will be not more than 10 mg. Biologic therapy will not be given in any of the patients with RA. Routine laboratory findings will be done. Blood volume that will be taken from cubital vein for IL6, IL17, TNF, RF, CRP, ACPA will be 7 ml. All patients will be given Informed Consent form to fulfil. The group of patients with RA will be defined by

ACR/EULAR Criteria. They will be divided in two groups: patients with disease duration less than two years and patients with disease duration from three to ten years. Filling in the questionnaire in both groups, as well collection of data of comorbidity. We will evaluate criteria prevalence in patients with RA from Kosovo. Comparison of results from questionnaire in two groups of RA patients will be done. All data will be statistically analyzed.

Results: Patients after ambulatory visits were hospitalised in University Clinical Center of Kosovo, Rheumatology Clinic To do further investigations. Until now we have set the diagnosis to the collected patients fulfilling ACR/EULAR Criteria. After collecting the total number of patients for the study we will start to do additional laboratory tests IL-6, IL-17 and TNF- α .

Discussion: Because of the very early stage of research and small number of data collected so far, no relevant statistical analysis was done.

Acknowledgments: I would like to thank my mentors professor Nada Cikes and professor Vjollca Sahatciu-Meka for their guidance and the Director of Rheumatology Clinic in Prishtina professor Sylejman Rexhepi for the suport.

MeSH/Keywords: Rheumatoid arthritis, characteristics, epidemiology

Poster code: R-B-9-156

Poster Title: UROMODULIN IN PREHYPERTENSION

PhD candidate: Josipa Josipović

Part of the thesis: Uromodulin urinary excretion is independent risk factor for the development of prehypertension

Mentor/s: Professor Bojan Jelaković, MD, PhD

Affiliation: University Hospital Centre Sestre Milosrdnice, Vinogradska c29, 10000 Zagreb

Introduction: The cardiovascular risk (CVR) is increased in individuals with prehypertension (PH) (BP 130-139/85-89 mmHg). A reliable clinical marker for the assessment of prehypertension progression hasn't been established yet. In some studies lower urinary uromodulin levels were associated with the lower risk for hypertension. The plan of this study is to analyze potential value of uromodulin as a new biological marker in prehypertension

Materials and methods: The study group includes 125 adults age 18-45 with PH and control group are 125 adults matched for age with hypertension stage 1. Blood pressure with electronic device and ABPM will be measured. Samples of the vein blood will be collected for routine biochemistry measurements, spot urine will be collected for spec. gravity, albumin, alfa-1-microglobulin, creatinine and 24hours urine will be collected for uromodulin, creatinine, sodium and potassium. It will be done ECG, echocardiogram, measurement of pulse wave velocity and augmentation index value and determination of total peripheral resistance.

Results: Until this date we have included 13 adults, 8 men and 5 women. The median age was 37 years, 34% were current smokers, mean waist circumference was 76 +/- 8 cm. Family history of hypertension was positive in 76 % patients, diabetes in 23%,

dyslipidemia in 7%. There were 15 % patients who consume alcohol, 61% drank one cup of coffee daily, 15% two cups, 15 % three, and 7 % four cups of coffee per day. 46% patients didn't know about weekly physical activity, 38% practiced mild physical activities (less than 200 minutes weekly), 15% moderate (200-300 minutes weekly) and 7% practiced extreme physical activity (more than 300 minutes weekly). The average office blood pressure was 135/88 mmHg. Results of ambulatory blood pressure monitoring were: the average blood pressure was 131/82 mmHg, the average daytime blood pressure was 134/85 mmHg, the average nighttime blood pressure was 127/78 mmHg. Laboratory and other measurements are going to be done.

Discussion: We are going to examine a potential role of uromodulin as novel biomarker in categorization of prehypertensives in regards to cardiovascular risk and pharmacotherapeutic options. Until now, we have examine a small number of participants and biochemistry and other test are have to be done yet.

Acknowledgments:

MeSH/Keywords: prehypertension, uromodulin, cardiovascular risk, hypertension

Poster code: R-B-9-161

Poster Title: CARDIAC ALLOGRAFT VASCULOPATHY AFTER HEART TRANSPLANTATION

PhD candidate: Jana Ljubas Maček

Part of the thesis: The role of ischemic time, platelet function and cellular and humoral graft rejection on the development of coronary allograft vasculopathy after heart transplantation

Mentor/s: Academician Davor Miličić, MD, PhD

Affiliation: University Hospital Centre Zagreb

Introduction: Cardiac allograft vasculopathy (CAV) contributes to higher mortality after heart transplantation (HTx). Higher troponin T (TnT) values are found in more severe graft damage and longer ischemic time, whereby graft becomes more immunogenic and potentially liable to development of CAV. The aim is to examine the predictive significance of TnT for the development of CAV, especially "early" TnT during the first 4 months after HTx. Earlier and more severe CAV predisposes to graft dysfunction and cardiac death after HTx.

Materials and methods: 120 HTx patients are included in retrospective analysis and 20 patients in the prospective study. Pretransplantation workup (general patient data and standard laboratory, HLA typization, echocardiography, Swan-Ganz catheterization) and posttransplantation follow-up will be conducted, including standard laboratory with PCR cytomegalovirus and donor-specific antibodies, regular myocardial biopsies, echocardiography, coronary angiography, platelet aggregometry, 24-h Holter blood pressure and ECG monitoring. Variables will be analysed with student t-test, hi-square test and logistic regression analysis (SPSS software).

Results: 52 patients had all the required data for analysis. We found no significant correlation between higher values of "early" TnT and the development of CAV generally ($p=0,093$), nor the correlation to higher incidence of cardiac death vs. all-cause death ($p=0,46$). "Early" TnT did not predict earlier development of CAV (in the first 2 years after HTx, $p=0,87$), but it significantly indicated the risk of later CAV development (after 2 years postransplant, $p=0,027$).

Discussion: Higher troponin T values in early period after HTx, related to longer graft ischemic time, predict later development of vasculopathy, whereas early vasculopathy is not significantly triggered by early graft damage. Other immunological factors contribute more to early vascular damage after HTx.

Acknowledgments:

MeSH/Keywords: heart transplantation, cardiac allograft vasculopathy, troponin T, graft dysfunction, ischemic time.

Poster code: R-B-9-169

Poster Title: ASSOCIATION OF SEROTONIN TRANSPORTER GENE POLYMORPHISMS WITH CROHN'S DISEASE (CD) PHENOTYPES

PhD candidate: Katja Grubelić Ravić, MD

Part of the thesis: Association of serotonin transporter gene polymorphisms with Crohn's disease (CD) phenotypes

Mentor/s: Professor Boris Vucelić, MD, PhD

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

Introduction: Serotonin (5-HT) is a key mediator in intestinal peristalsis, secretion, vasodilatation and sensory signalling. The serotonin-selective reuptake transporter protein (SERT) terminates the action of 5-HT. Human SERT is encoded by a single gene on chromosome 17q11. Two important polymorphic sites in the SERT gene are: variable number tandem repeats in the gene's second intron (SERTin2), and an insertion/deletion in the promoter region (SERTPR). Consistent with the effects of 5-HT in the gut, SERT polymorphisms could potentially be involved in the development of different phenotypes of Crohn's disease.

Materials and methods: The study included 200 Crohn's disease patients who were genotyped for SERTPR and SERTin2 variants. Regarding to clinical presentation (behaviour), Crohn's disease (CD) has 3 different phenotypes but the reason for this differentiation isn't understood yet. According to Vienna classification 200 CD patients were phenotyped in three groups: inflammatory (group 1), penetrating (group 2), and stricturing (group 3). SERT genotyping was performed by the PCR method.

Results: By using univariate logistic regression (only on SERTin2 level), it has been discovered that the carriers of SERTin2 1s genotype have almost 3 times more chances for

developing ileocolic Crohn's disease compared to the ones with SERTin2 ss genotype (OR=2.78 95% CI=1.26 – 6.15). It has also been discovered that the carriers of SERTin2 ll genotype have over 2 times more chances for developing ileocolic Crohn's disease compared to the ones with SERTin2 ss genotype (OR=2.36 95% CI=1.04 – 5.34). CD patients and controls did not differ significantly in SERTPR or SERTin2 variants, but SERTin2 haplotype might be a useful genetic marker in distinguishing between these three clinical groups.

Discussion: Up to now there is no data available that confirmed relationship between inflammatory bowel disease and 5-HTT genetics. However, there is data available that confirms relationship between irritable bowel syndrome and SERT polymorphisms. This research shows that SERT gene polymorphisms is associated with CD phenotype and that will enable us in differentiating between different disease phenotypes from the beginning of the disease.

Acknowledgments: Professor Boris Vucelic, Professor Nada Bozina

MeSH/Keywords: Crohn disease, SERT gene, polymorphisms

Poster code: R-B-9-171

Poster Title: CHANGES IN THE ELECTRICAL POTENTIAL OF BONE DURING SURGICAL TREATMENT OF FRACTURES

PhD candidate: Tomislav Žigman

Part of the thesis: Intraoperatively measured electrical potential of the bone is an independent predictor of bone healing.

Mentor/s: prof.dr.sc. Slavo Davila

Affiliation: Medical School, Zagreb University

Introduction: Bone electrical potentials change with the force applied. Areas under compression develop negative potentials, as opposed to the positive potential that can be measured at the areas of tension. Negative potential is associated with deposition of bone, and positive with resorption. Also, fracture alters the bone electrical potential, so it becomes more electronegative. These potentials have an important role in fracture healing, bone growth and remodelling. Literature data on the influence of fracture operative treatment on bone electrical potentials, and possible consequences of this influence, are sparse. The objective of this study is to establish a method of intraoperative bone potential measurement, and to try to find a correlation between electrical potential and fracture type, osteosynthesis method and prognosis.

Materials and methods: 100 patients with a pertrochanteric fracture will be included in the study. Bone electrical potentials are measured intraoperatively using a thin Kirschner wire introduced through bone cortex at the selected point and pointed to opposite cortex, not penetrating it. Kirschner wires are connected using clamps to multimeter. Neutral electrode (inductive rubber) is placed behind ipsilateral gluteus. Two more Kirschner wires are introduced percutaneously, distant from the fracture site, with the aim to obtain control values. Patients are divided into groups depending on the type of fracture (AO classification). Publicly available soft-

ware R is used for statistical methods of data analysis (multiple linear regression). Treatment outcome is dependant variable, and fracture type, potentials, age, sex, ASA, anaesthesia are predicting variables.

Results: At the time of writing this abstract, 67 patients were fully examined, including the follow-up period of 6 months. Another 33 patients are included. Measured potentials at fracture site are dependent on the fracture type: -260mV measured in A1 group, and -305 in A2 group (corrected potential -111/-160 mV). This differences are not expressed at control sites. Also, during the operation potential at fracture site becomes more electronegative (from average -275 mV to -335mV), as oposed to control sites, where it doesn't change at all, or becomes less electronegative.

Discussion: Bone potentials, caused by fracture, can be measured intraoperatively the operative procedure appears to influence their generation. Measured potentials depend on the fracture type, and could be correlated with prognosis.

Acknowledgments: I thank to my menthor professor Davila.

MeSH/Keywords: Bone electrical potential, Bone plates, Bone metal implants, Fracture healing, Electric stimulation, Internal fracture fixation, Femoral fracture, Corrosion, Bone electricity, Intraoperative period.

Poster code: R-B-10-15

Poster Title: THE ROLE OF PENTADECAPEPTIDE BPC 157 ON INCISIONAL VENTRAL HERNIA PREVENTION AND WOUND TENSILE STRENGTH IMPACT

PhD candidate: Alen Pajtak

Part of the thesis: The Role of Pentadecapeptide BPC 157 and NO-system on Incisional Ventral Hernia Prevention and Wound Tensile Strength Impact

Mentor/s: 1.Prof Predrag Sikirić, PhD 2.Prof Janoš Kodvanj, PhD

Affiliation: 1.University of Zagreb, School of Medicine 2.University of Zagreb, Faculty of Mechanical Engineering and Naval Architecture

Introduction: Pentadecapeptide BPC 157 has proven positive effect on skin wounds and muscle-tendon damage healing, but its effect on laparotomy wounds, incisional hernia prevention as well as wound tensile strength impact has not yet been studied.

Materials and methods: Ingrained method (described by Dubay in 2004.) of early wound failure induction (with satisfactory incisional hernia incidence) was performed on Wistar rats. Rats were divided in Control group and two experimental groups (BPCmcg2w and BPC4w). According to experiment protocol rats in experimental groups were treated with BPC 157 (10mcg/kg, 0.16mcg/mL, 12mL/day/rat, per os), while control group did not receive any treatment. Rats in BPCmcg2w group were sacrificed 14 days and rats in BPCmcg4w group 28 days after initial operation. After sacrifice of tested animals clinical presence of incisional hernia was monitored. Muscle diastasis greater than 2mm was considered hernia. For tensile strength measurement 5mm broad samples (no significant thickness difference between Control group and experimental groups, $p=0.341$) were taken from the proximal part of laparotomy wound (sutured in 4:1 ratio elongated suture). Samples were analyzed on Beta 50-5 (Messphysik, Austria) Testing Machine.

Results: In Control group 70% of rats developed hernia while 20% of rats in BPCmcg2w

group and 20% in BPCmcg4w showed hernia presence. Hernia width in BPCmcg2w group was not significantly different from hernia width in Control group ($p=0.126$), while hernia width in BPCmcg4w was significantly smaller ($p=0.049$). BPCmcg2w group tensile strength was not significantly different ($p=0.679$) while BPCmcg4w tensile strength showed significant difference to Control group ($p=0.073$, p value 0.1 is taken significant because of few non-correctable external factors).

Discussion: Pentadecapeptide BPC 157 has evident hernia prevention effect. No significant hernia size difference in groups monitored for 14 days versus significant hernia size difference in 28 days monitored animals pinpoints over time hernia growth prevented by BPC 157. Tensile strength significant difference in 28 days monitored groups implies prolonged BPC 157 healing impact, through all three (inflammation, proliferation, maturation) wound healing phases.

Acknowledgments: I would like to express my gratitude to my mentors, for their support and help.

MeSH/Keywords: Incisional hernia, BPC 157, Early wound failure, Tensile strength

Poster code: R-B-10-18

Poster Title: MEDICAL DRILL WITH OPEN TYPE INTERNAL COOLING IN BONE AND JOINT SURGERY

PhD candidate: Tomislav Bruketa

Part of the thesis: Our newly constructed drill made out of medical steel with open type internal cooling lowers the temperature at the site of drilling the bone below the critical temperature of 47°C

Mentor/s: Goran Augustin, MD, PhD, research associate

Affiliation: Faculty of Mechanical Engineering and Naval Architecture, University of Zagreb. Faculty of Veterinary Medicine, University of Zagreb. University Hospital Centre – Zagreb

Introduction: During bone drilling in bone and joint surgery, the rise of temperature on the site of drilling is registered. Temperatures above 47°C cause osteonecrosis which can lead to loosening of the osteosinthetic materials. Current method of cooling the site of drilling is external cooling (pouring coolant on the drill). Use of the drill with open type internal cooling will lead the coolant to the site of drilling and will reduce the rise of the temperature. It is our hypothesis that newly constructed drill made out of medical steel with open type internal cooling system lowers the temperature at the point of drilling of the bone below the critical temperature of 47 °C and thus minimizes the possibility of thermal osteonecrosis.

Materials and methods: Research is carried out on pig cadaveric femur. The temperature on drilling site is measured with thermocouples which are located at distance of 5 mm from the drilling site. Drilling is performed with drill made out of medical steel with and without open type internal cooling with various stages of drill wear. Diameter of drill used in research is 4,5 mm with cylindrical canal 0,3 mm in diameter. As a coolant a saline at 26°C will be used. Dynamics of temperature is recorded and analyzed.

Results: Preliminary measurements were made with drill made out of medical steel

with and without open type internal cooling. Median temperature at the drilling site during drilling with drill made out of medical steel with and without open type internal cooling was 37,20°C and 55,31°C respectively.

Discussion: Temperatures above 47°C at the site of drilling of the bone can cause thermal osteonecrosis. Current methods of cooling are insufficient in reducing temperature at the drilling site below 47°C. Our newly constructed drill with open type internal cooling can reduce that temperature to satisfying level. In our preliminary results the recorded temperatures at drilling site when drill with open type internal cooling was used were around 10°C under the critical temperature while the temperatures with ordinary drill were about 8°C above critical. It is in our opinion that drill with open type internal cooling can lower the temperature under critical and thus minimize the possibility of thermal osteonecrosis.

Acknowledgments:

MeSH/Keywords: bone drilling, thermal osteonecrosis, open type internally cooled drill

Poster code: R-B-10-28

Poster Title: HEMOSTATIC ALTERATIONS DURING ADULT EXTRACORPOREAL LIFE SUPPORT USING POINT-OF-CARE TESTS

PhD candidate: Lucija Svetina

Part of the thesis: Impact of extracorporeal life support on blood clot viscoelastic properties and platelet aggregation

Mentor/s: Bojan Biočina, MD, PhD

Affiliation: Department of Cardiac Surgery, University Hospital Center Zagreb, University of Zagreb, Zagreb, Croatia

Introduction: Extracorporeal life support based on extracorporeal membrane oxygenation is the end-stage treatment of heart failure or cardiogenic shock. Its main aim is to reduce tissue hypoperfusion. Anticoagulation therapy is mandatory to avoid thromboembolic complications. Despite normal results of standard blood clotting tests, haemorrhage and thromboembolic incidents are common, contributing to negative outcome. Routinely performed laboratory blood clotting tests and platelet number do not offer sufficient understanding whether qualitative platelet dysfunction is present in a particular patient nor does it denote hypercoagulability, hyper or hypofibrinolysis. The aim of the study is to evaluate the effect of extracorporeal life support on blood clotting viscoelastic properties and platelet function through specific coagulation and aggregation tests. The results would be correlated with ischemic and haemorrhagic events during postoperative recovery. Point-of-care tests (POC) for coagulation, thromboelastometry (ROTEM®) and platelet aggregometry (Multiplate®) can provide specific, reliable, and timely information during bleeding and thromboembolic episodes and could improve outcomes.

Materials and methods: Adult VA-ECMO patient

Results: Eleven patients with VA-ECMO were studied over 400 days. Daily laboratory coagulation profile, transfusion history and

near-daily thromboelastometry (ROTEM®) and platelet aggregometry (Multiplate®) were performed.

A majority of TEM values were within the normal range, except for FIBTEM values, which were higher over longer ECMO runs. MEA tests had lower values, particularly in the adenosine diphosphate assay. There was correlation between laboratory and POCT as well as good correlation between the clot firmness after 10 minutes (A10) and the maximum clot firmness in ROTEM.

Discussion: Transfusion of allogeneic blood products is associated with increased morbidity and mortality in ECLS patients. Early and specific diagnosis and effective and targeted therapy of the underlying hemostatic pathology are of high clinical relevance. Point-of-care tests for coagulation enable detailed analysis of primary hemostasis and platelet dysfunction, are performed bedside, from whole blood samples, may speed up diagnosis of coagulopathies and improve management during bleeding and thromboembolic episodes, reduce the transfusion of inappropriate blood product and predict thromboembolic events thus improving outcomes.

Acknowledgments: None

MeSH/Keywords: Extracorporeal life support, aggregation, coagulation, ROTEM delta, Multiplate

Poster code: R-B-10-83

Poster Title: VALIDATION OF A COMPUTATIONAL MODEL OF A HUMAN THORACOLUMBAR SPINE SEGMENT

PhD candidate: Krešimir S. Đurić

Part of the thesis: Biomechanical stability analysis of transpedicular screws combined with sublaminar hook-rod system on a computed finite element model

Mentor/s: prof. Marin Stančić, prof. Jurica Sorić

Affiliation: Department of Neurosurgery, University Hospital Center Zagreb Faculty of Mechanical Engineering and Naval Architecture, University of Zagreb

Introduction: To test our hypothesis biomechanical analysis is to be performed and chosen method to do so is finite element method analysis. Finite element analysis starts with 3D computational modeling of Th11, Th12, L1 and L2 vertebra including intervertebral discs and ligaments. After the model is finished range of motion (ROM) under physiological loading simulation is performed in order to validate the model.

Materials and methods: Computational model of a spine segment ThXI, ThXII, LI, LII with intervertebral discs, anterior and adjacent ligaments is created. Each vertebra is segmented separately. Intervertebral discs are modeled separately as a void in between adjacent vertebrae. Linear elastic material characteristics were used according to the literature. Modeled parts are imported in the ABAQUS software and assembled in a single assembly. In order to validate the model an experiment done by Markloff et al. (1972) was recreated in silico. Relative rotation of the model of a FSU THXII-LI under various loads was measured and compared with relative rotation under the same loading conditions as Markloff described. Model of the FSU was loaded in such a way to simulate flexion, extension, lateral bending and torsion.

Results: Functional segment unit was loaded with 3 rotational moment increments: 1,3Nm, 2,7Nm and 4Nm to achieve flexion, extension, lateral bending and tor-

sion. The mean difference between Markloff and calculated results for flexion, extension, lateral bending and torsion is 5,39%, 43,98%, 8,41%, 82,8% respectively.

Discussion: Our results are showing similar range of motion for flexion and lateral bending when comparing with Markloff's. Main difference in the ROM is observed in extension and torsion. Our model is showing increased range of motion in extension what is from mechanical point of view expected on our model but in vivo experiments are showing different results. This could be explained by the difference between mechanical properties exhibited by ligaments and intervertebral disk in vivo and on our model. Difference in the torsion results can be explained by the nonlinear behavior and non-homogeneous morphology of the disk. In reality annulus fibrosus is fibers reinforced composite material consisting of viscoelastic matrix reinforced with fibers that are orientated in a certain angle.

Acknowledgments: This study is done by Krešimir S Đurić and Josip Rauker under close mentorship of prof. Marin Stančić and prof. Jurica Sorić. Therefore Josip Rauker should be acknowledged as one of the leading author in this work.

MeSH/Keywords: Spine, Mechanics, Investigative Techniques, Finite Element Analyses

Poster code: B-10-133

Poster Title: THE ROLE OF MAGNETIC RESONANCE IMAGING AND THE EXPRESSION OF MMP-9 AND COX-2 PROTEINS IN THE ANALYSIS OF CAROTID ATHEROSCLEROTIC PLAQUES IN PATIENTS WITH INDICATED CAROTID ENDARTERECTOMY

PhD candidate: Davorin Šef

Part of the thesis: Part of a Thesis: Analysis of Carotid Atherosclerotic Plaques in Patients with Indicated Carotid Endarterectomy

Mentor/s: Assistant Professor Anita Škrtić, MD, PhD, Assistant Professor Vinko Vidjak, MD, PhD.

Affiliation: Department of Cardiovascular Surgery, Magdalena Clinic for Cardiovascular Diseases

Introduction: Atherosclerosis is a major cause of stroke. Majority of strokes are ischemic with carotid artery atherosclerotic disease representing an important risk factor. Patients with hemispheric transient ischemic attack or stroke are considered symptomatic. Magnetic resonance imaging (MRI) can analyse the components of carotid atherosclerotic plaque. Current studies suggest that MRI can reliably distinguish between stable and unstable carotid plaque, and furthermore improve patient selection for surgery or stenting. Matrix metalloproteinase 9 (MMP-9) and COX-2 protein have a role in remodelling of atherosclerotic plaques and correlate with the presence of unstable plaques.

Materials and methods: Minimum of 60 patients for carotid endarterectomy will be included in the study, 30 asymptomatic and 30 symptomatic patients. Preoperatively carotid MRI, laboratory analysis of biomarkers of inflammation, coagulation factors and lipid status will be performed. MRI will be performed on Toshiba Excelart Vantage 1.5T MRI machine, and AHA classification of atherosclerotic plaque will be applied. Excised carotid plaque will be analysed mor-

phologically using HE and special histochemical trichrome staining. Semi quantitative analysis of collagen fibres will be performed. Immunohistochemical staining of MMP-9 of COX-2, semi quantitative analysis of CD68 PG-M1 marked macrophages, SMA marked smooth muscle cell as well as micro vessel density using CD34 will be obtained. Expression and intensity of MMP-9 and COX-2 immunohistochemical staining in macrophages and smooth muscle cells will be semi quantitatively analysed.

Results: Research is at the stage of patient and data collection.

Discussion: Further patient and data collection is needed to proceed with a discussion.

Acknowledgments: to ward and laboratory staff. This study was financially supported by Croatian Ministry of Science (044-0000000-3356) and by INEL – medicinska tehnika d.o.o.

MeSH/Keywords: Carotid endarterectomy, unstable carotid atherosclerotic plaque, magnetic resonance imaging, matrix metalloproteinase 9, COX-2.

Poster code: R-B-10-172

Poster Title: FREQUENCY OF AGT, ACE, AGTR1, ADRB1, UMOD and ADIPOQ GENETIC POLYMORPHISM IN PREHYPERTENSION – STUDY STATUS

PhD candidate: Livija Šimičević

Part of the thesis: Frequency of AGT, ACE, AGTR1, ADRB1, UMOD and ADIPOQ genetic polymorphism in prehypertension

Mentor/s: Prof. Bojan Jelaković, MD, PhD, Prof. Jasna Lovrić, MD, PhD

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

Introduction: Approximately 33% of the adult Croatian population has high normal blood pressure (BP), or prehypertension, which may develop into arterial hypertension (AH). However, the role of individual genes as well as their interactions with external factors in the development of AH has not yet been elucidated. The aim of this study is to assess the frequency of AGT, ACE, AGTR1, ADRB1, UMOD and ADIPOQ genes polymorphism, known to have a role in AH and metabolic syndrome, in prehypertensive patients and compare certain haplotypes with their clinical status and lifestyle.

Materials and methods: The study will include a total of 600 patients: 300 prehypertensive patients (130-139/85-89 mmHg) and 300 normotensive subjects as a control group. All subjects will fulfill a questionnaire detailing family history, drug therapy, lifestyle and socio-economic status. BMI, BP will be measured and the following blood tests, alongside genotyping, determined: glucose, creatinine, lipid status, adiponectin, leptin, and aldosterone. Urine samples will be tested on albumin, alpha-1-microglobulin and creatinine.

Results: Till now, 1/10 of each group of subjects has been enrolled. The prehypertension group consists of 32 (median age 36, range 21-45), and the control group of 37 subjects (median age 32, range 20-45). All subjects have fulfilled questionnaires, their BMI, sys-

tolic and diastolic BP have been measured. Urine and blood samples have been tested on biochemistry parameters. Statistical analysis has not yet been initiated due to the small sample size. Genotyping will commence when half of the subjects will be enrolled, however the validation of the genotyping methods is underway.

Discussion: The study results will better define the clinical and epidemiological characteristics of prehypertension, correlating cardiovascular and renal risk factors to the gene polymorphisms involved in the disease. Also, they will determine whether certain polymorphisms differ in their frequency among prehypertensive and normotensive subjects, shedding light into the importance of genetic predisposition and gene-gene and gene-environment interactions in the development of prehypertension into AH. Despite the small population, we can preliminary conclude that the relatively low median age of patients in the prehypertension group is indicative of the importance of gene-environment interactions in the development of AH.

Acknowledgments: /

MeSH/Keywords: prehypertension, arterial hypertension, genetic polymorphism

Poster code: R-B-11-132

Poster Title: FOXP3 POSITIVE LYMPHOCYTES IN CYTOLOGIC SMEARS OF LYMPH NODE ASPIRATES AND THEIR ASSOCIATION WITH PROGNOSTIC MARKERS IN PATIENTS WITH LYMPHOMAS

PhD candidate: Biljana Jelić-Puškarčić, MD

Part of the thesis: Foxp3 positive lymphocytes in cytologic smears of lymph node aspirates and their association with prognostic markers in patients with lymphomas

Mentor/s: Assist. Prof. Ika Kardum-Skelin, MD, PhD

Affiliation: University Hospital Merkur, Zagreb, Croatia

Introduction: The CD4, CD25 positive T regulatory (Treg) lymphocytes expressing Foxp3 transcription factor account for a relevant portion of tumor microenvironment in patients with Hodgkin's (HL) and non-Hodgkin's lymphomas (NHL). An increased number of tumour-infiltrating Treg cells has been associated with negative prognostic factors and an adverse clinical outcome in patients afflicted with solid tumours. On the contrary, in patients with classical HL and follicular NHL, increased numbers of tumour-infiltrating Treg cells have been associated with a better prognosis.

Materials and methods: In this prospective investigation, the number of immunocytochemically Foxp3 positive lymphocytes in lymph node aspirates from classical HL and NHL patients (100 patients) will be compared with a control group of patients (30 patients) with reactive hyperplasia (RH). In classical HL and NHL patients, the Foxp3 positive lymphocyte count will also be correlated with prognostic factors relevant for the clinical course of lymphoma. Anti-FOXP3 antibody (Abcam) and LSAB System-HRP visualization kit (Dako) is used for immunocytochemical staining. The number of Foxp3 positive cells per 100 lymphocytes (% Foxp3 positive lymphocytes) will be quantified, counting an average of a minimum of 10 counts per a cytological smear.

Results: This is an ongoing investigation. Up to now, 26 patients with RH, 18 with HL and

30 with NHL have been included in the study. Immunocytochemical staining was performed in all patients included. In patients with RH and HL %Foxp3 positive lymphocytes were determined, while analysis of the frequency of Foxp3 positive cells in patients with NHL is still in progress, as well as collection of clinical data. In the subjects included so far affected with HL a higher number of Foxp3 positive lymphocytes (19.61 ± 9.80) was found compared to the control group of patients with RH (11.15 ± 3.82). These are preliminary results, the patients pool included into the study so far and the data collected are insufficient for a detailed statistical analysis.

Discussion: To date, the expression of Foxp3 in patients with lymphomas has mainly been evaluated using immunohistochemistry and flow-cytometry techniques. In our study, the number of Foxp3 positive cells is assessed by immunocytochemistry on the smears of the lymph node aspirates. The results of this research could contribute to the understanding of the microenvironment effect on disease development and progression.

Acknowledgments: I would like to thank my mentor and my colleagues.

MeSH/Keywords: Foxp3, T regulatory lymphocytes, lymphomas

Poster code: R-B-12-135

Poster Title: THE INFLUENCE OF CYP3A4 AND CYP2D6 POLYMORPHISMS ON SERUM CONCENTRATIONS OF RISPERIDONE AND 9-HYDROXYRISPERIDONE IN PSYCHIATRIC PATIENTS

PhD candidate: Lana Ganoci, MMedBiochem

Part of the thesis: Impact of pharmacogenetic variations of CYP2D6 and ABCB1 on the long-acting risperidone treatment

Mentor/s: Nada Božina

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

Introduction: An increased risk of adverse effects and discontinuation of the long-acting risperidone (RIS-LAI) therapy is observed in patients with schizophrenia. Risperidone (RIS) is metabolized to its active metabolite 9-hydroxyrisperidone (9-OH RIS), mainly by the enzyme CYP2D6 and, to a lesser extent by CYP3A4. Its antipsychotic effect is assumed to be related to the active moiety of RIS and 9-OH RIS. The aim of this study is to investigate the role of genetic variations of CYP2D6 *dupl, *3, *4, *5, *6, including additional data of CYP2D6*41, and CYP3A4*22 on serum concentrations of RIS and 9-OH RIS in patients using RIS-LAI.

Materials and methods: 55 patients with schizophrenia treated with RIS-LAI (dose range 25-75 mg) were genotyped, and their serum steady-state concentrations of RIS and 9-OH RIS were measured on 5th and 14th day following risperidone injection. Pharmacogenetic analysis for CYP2D6 *dupl and allele *5 was performed by PCR, while real-time PCR analysis by TaqMan® assays was performed for genotyping of CYP2D6 alleles *3, *4, *6, *41 and CYP3A4*22. Serum concentrations of RIS and 9-OH RIS were measured by high-performance liquid chromatography-diode array detection (HPLC-DAD).

Results: The genotype distribution for CYP2D6 was: 28 extensive metabolizers, 14 intermediate metabolizers, 6 poor metabolizers, 2 ultrarapid metabolizers and 5 du-

plications of variant alleles. The median active moiety concentrations were on 5th day 69.4 nmol/L (95%CI=38.9-99.9), and on 14th day 43.9 nmol/L (95%CI=34.4-53.4). The median active moiety concentration for ultrarapid CYP2D6 metabolizers on 5th day was 26.8 nmol/L and on 14th day 31.1 nmol/L which is below recommended therapeutic range (50-150 nmol/L). The active moiety concentrations on 14th day were significantly different according to CYP2D6 genotype ($p=0.0455$). The additional genotyping of CYP2D6*41 revealed 3 patients to be poor metabolizers. No significant influence of CYP3A4*22 variant on concentrations and C/D ratios was found.

Discussion: The CYP2D6 genotypes had a strong influence on the steady-state serum levels of RIS, 9-OH RIS and active moiety. The additional genotyping of CYP2D6*41 is very important for detection of CYP2D6 poor metabolizers. CYP3A4*22 did not show influence on the steady-state serum drug concentrations. Results pointed to the large interindividual differences in RIS-LAI concentrations that can lead to therapy failure.

Acknowledgments: I would like to thank Assistant Professor Marina Šagud, Assistant Professor Igor Filipčić and Maja Živković, MD, PhD

MeSH/Keywords: pharmacogenetics, CYP2D6, CYP3A4, risperidone, schizophrenia

Poster code: R-B-13-145

Poster Title: MOLECULAR EPIDEMIOLOGY OF HEPATITIS C VIRUS IN PRISHTINA REGION OF KOSOVO

PhD candidate: Xhevat Jakupi, MD

Part of the thesis: Molecular epidemiology of Hepatitis C Virus in Prishtina region of Kosovo

Mentor/s: Adriana Vince PhD, MD

Affiliation: Department of Microbiology, National Institute of Public Health of Kosovo

Introduction: Infection with hepatitis C virus (HCV) is a global health problem. The study aimed to provide data with regard to HCV prevalence among specific groups of population and HCV genetic diversity in Kosovo which are currently scarce.

Materials and methods: This was a cross-sectional study in which total of 514 anti-HCV positive samples have been included, majority of them (354) coming from dialysis units, followed by injecting drug users - IDUs (100), 50 from HCV chronic patients in treatment and 10 from blood donors. Anti-HCV testing has been conducted with ELISA HCV test. HCV RNA detection was conducted by PCR and genotype determined by sequencing core region of viral genome on the 3500 Genetic Analyzer (Applied Biosystems) and with the NCBI Genotyping tool. The NS5b region of viral genome was sequenced using genotype specific primers, alignments made using BioEdit package and maximum likelihood phylogenetic trees constructed by using PhyML 3.0

Results: HCV RNA was detected in 378 (73.5%) samples, ranging from 60% among blood donors, up to 77.4% in dialysis patients. The HCV genotype 1a has been most frequently detected (59%), followed by 4d (25%), 3a and 1b both with 7% and 2c with

1%. The genotype 1a was most frequent among dialysis patients (62%) and among IDUs (65%). HCV genotype 4d was mainly present among dialysis patients (33%), while 3a was mainly present among IDUs (33%). Phylogenetic trees of HCV genotypes 1a and 4d presented HCV clusters among dialysis units and HCV genotype 3a clustering among IDUs

Discussion: The HCV prevalence among dialysis patients in Kosovo with 53% is higher compared to IDUs (37%) and blood donors (0.05%) and among highest in Europe among dialysis patients. Presence of HCV genotypes 1a and 3a follows European pattern of distribution. High prevalence of HCV genotype 4d in dialysis units should be investigated further since this is not common picture for Europe.

Acknowledgments: Highest appreciation for support to Mario Poljak, PhD, MD and his staff at the Reference Laboratory of HIV and Hepatitis, Institute of Microbiology and Immunology, Faculty of Medicine, University of Ljubljana

MeSH/Keywords: Hepatitis C Virus, prevalence, genotype, sequencing, Pristina, Kosovo

Poster code: R-B-16-101

Poster Title: SOMATOSTATIN RECEPTOR SCINTIGRAPHY IN NEUROENDOCRINE TUMOUR PATIENTS USING TECHNETIUM-99M OCTREOTIDE WITH SINGLE PHOTON EMISSION TOMOGRAPHY AND COMPUTED TOMOGRAPHY – PRELIMINARY RESEARCH RESULTS

PhD candidate: Mate Trogrlić, MD

Part of the thesis: Somatostatin receptor scintigraphy in neuroendocrine tumour patients using Technetium-99m octreotide with single photon emission tomography and computed tomography

Mentor/s: Stanko Težak, MD, PhD

Affiliation: Clinical Department of Nuclear Medicine, University Hospital Centre, Zagreb, CROATIA

Introduction: Neuroendocrine tumours (NETs) are rare tumours overexpressing somatostatin receptors. Technetium 99m hydrazinonicotinyl-tyrosine(3)-octreotide (Tc-99m HYNIC-TOC) is increasingly gaining acceptance as a new radiopharmaceutical for the diagnosis of NETs. Tc-99m HYNIC-TOC SPECT/CT (Single photon emission computed tomography/computed, x-ray tomography) is an excellent imaging modality for evaluation of NET-s in terms of sensitivity, specificity and diagnostic accuracy. Aim is to evaluate the potential usefulness of Tc-99m HYNIC-TOC SPECT/CT in patients with NETs.

Materials and methods: These are preliminary results of 21 patients with known NET and with at least one year follow up. Whole body and tomographic acquisition were taken 2 and 4 hours after administration of 666 MBq of Tc-99m HYNIC-TOC. All the patients underwent SPECT/CT 4 hours after injection of the tracer. SPECT/CT results were compared to SPECT alone, whole body scintigraphy and with conventional imaging methods (CT, MRI, EUS).

Results: Our analysis showed that SPECT/CT provided additional information for image interpretation in 52% (11/21) of cases. In most of these (8/21), the CT data improved localization of abnormal and physiologic findings. Diagnostic certainty was improved

in 7/21 cases (33%) and image interpretation was beneficially altered in 4/21 cases (19%). Somatostatin receptor positive lesions were found in 9 of 21 (43%) patients and negative in 12 of 21 (57%) patients. SPECT/CT results were true-positive in 8 cases, true-negative in 12 and false-positive in 1 case. Tc-99m EDDA/HYNIC-TOC had an overall sensitivity of 100%, specificity of 92%, a positive predictive value (PPV) of 89%, and a negative predictive value (NPV) of 100%. The diagnostic accuracy of Tc-99m EDDA/HYNIC-TOC SPECT/CT was 95%.

Discussion: The fusion of anatomical and functional information by hybrid SPECT/CT positively impacts image interpretation and adds diagnostic value over SPECT alone. SPECT/CT improves localizations of NETs and thereby improve the overall diagnostic accuracy of this modality in the assessments of NETs by adding information about lesion localisation not available when only whole body or only SPECT were performed.

Acknowledgments: I express my warm thanks to my mentor for his support and guidance.

MeSH/Keywords: neuroendocrine tumours, receptors somatostatin, tomography, emission-computed, single-photon, technetium Tc 99m hydrazinonicotinyl-Tyr (3)-octreotide

Poster code: R-B-17-33

Poster Title: CAN WE PREDICT CORNEAL GRAFT REJECTION BASED ON PRO-ANGIOGENIC CYTOKINES LEVEL AT THE TIME OF TRANSPLANTATION?

PhD candidate: Maja Pauk Gulić, MD

Part of the thesis: The role of pro-angiogenic cytokines and its receptors in development of corneal neovascularisation after penetrating keratoplasty

Mentor/s: Professor Iva Dekaris, MD, PhD

Affiliation: 1. Special Eye Hospital "Svjetlost" in Zagreb, Department of Ophthalmology, School of Medicine in Rijeka, University of Rijeka, Croatia 2. Institute Ruđer Bošković, Zagreb, Croatia

Introduction: Corneal transplantation (CT) in a recipient eye devoid of inflammation and neovascularisation (NV) is the most successful of all transplantations, with a success rate of over 90%. CT performed in an inflamed or vascularised bed, has a much lower success rate of 20-40%. The risk of corneal graft rejection in such eyes has been shown to correlate with the number of corneal quadrants with NV. Vascular endothelial growth factor (VEGF) is one of the most important mediators of angiogenesis and plays a crucial role in corneal NV. The purpose of the study is to evaluate whether the VEGF and its receptors in the recipient cornea measured at the time of penetrating keratoplasty (PK) can act as a prognostic factor for corneal graft reaction development.

Materials and methods: Study included 20 eyes scheduled for PK. Patients were divided into two groups: inflammatory and non-inflammatory group. Donor corneas obtained from cadaver eyes which were unsuitable for clinical use represented the control group (n=20). Quantity of angiogenic growth factors and their receptors: VEGF, sVEGFR1 and sVEGFR3 were analysed using an enzyme-linked immunosorbent assay. Patients were followed-up for 3 postoperative years in order to monitor the symptoms of graft reaction/rejection and degree of corneal NV.

Results: There was a statistically significant difference in the levels of VEGF-A protein between the recipient corneal buttons ob-

tained from eyes with inflammation and those from the non-inflammatory group and controls ($p < 0.01$). Overall quantity of VEGF-A was 287.74 pg/ml (SD=129.181) in the inflammatory group, 115.37 pg/ml (SD=105.93) in non-inflammatory group and 142.28 pg/ml (SD=93.081) in controls. sVEGFR1 and sVEGFR3 were present in significantly higher concentrations in corneas of the non-inflammatory as compared to inflammatory group. Eyes with graft reaction had a significantly higher level of VEGF-A (307.4 pg/ml, SD= 100.058) as compared to those without any signs of graft reaction (182.8 pg/ml, SD=124.987). Statistical analysis was done by t-test.

Discussion: Our results suggest that patients with higher levels of VEGF-A in their corneas at the time of penetrating keratoplasty are expected to have corneal graft reaction/ rejection more often than those with low amount of VEGF-A. Soluble forms of VEGF receptor, which were elevated in non-inflammatory diseases, may act as a sink for VEGF and thus act in fact as suppressors of angiogenesis and consequent graft reaction.

Acknowledgments:

MeSH/Keywords: penetrating keratoplasty, corneal neovascularisation, VEGF, soluble VEGF receptor, graft rejection

Poster code: R-B-18-38

Poster Title: THE ROLE OF RAREBIT PERIMETRY IN EVALUATION OF FUNCTIONAL OUTCOME AFTER SUCCESSFUL MACULAR HOLE SURGERY

PhD candidate: Lana Dujmović, MD

Part of the thesis: The role of Rarebit perimetry in evaluation of functional outcome after successful macular hole surgery

Mentor/s: Zoran Vatauvuk, MD, PhD

Affiliation: University Department of Ophthalmology, University Clinical Centre Sestre Milosrdnice

Introduction: Recovery of visual acuity after macular hole surgery is a complex and not fully understood process. Optical coherence tomography (OCT) analysis of retinal morphology is not always able to explain the discrepancy between anatomical and functional outcomes. Rarebit fovea test (RFT), a novel microperimetry technique, has been developed to sensitively detect early neural damage. The aim of our study was to correlate morphological and functional outcomes after successful macular hole surgery.

Materials and methods: We have performed a prospective case series of 13 consecutive cases. All eyes underwent best corrected visual acuity testing, optical coherence tomography and rarebit fovea testing at baseline, one week, one month and three months after the surgery.

Results: We found a statistically significant increase in best corrected visual acuity from 0.1 to 0.4 at the final follow up visit

($p=0.006$).

There was no statistically significant change in Rarebit fovea test scores during follow up ($p=1.0$), and no correlation between Rarebit fovea test and visual acuity scores.

Discussion: Rarebit fovea test has been shown to be sensitive in detecting early neural damage in glaucoma and diabetic retinopathy. In our study no correlation between Rarebit perimetry and visual acuity after successful macular hole surgery was established, despite obvious improvement in visual acuity. Possible explanation for this might be that stimulus in Rarebit fovea test is too small for such an extensive neuroretinal damage.

Acknowledgments: n/A

MeSH/Keywords: macular hole, rarebit perimetry

Poster code: R-B-18-63

Poster Title: CONVERGENCE INSUFFICIENCY AND ATTENTION DEFICIT DISORDER SYNDROME (ADD) IN CHILDREN

PhD candidate: Barbara Dawidowsky MD

Part of the thesis: The correlation between convergence insufficiency and attention deficit disorder syndrome in children

Mentor/s: Branimir Cerovski MD, PhD

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

Introduction: ADD syndrome (attention deficit disorder) is a disorder that consists of problems with attention span. One of the symptoms is a disturbance in reading and writing, and a nonspecific visual disturbance that a child or a parent cannot precisely describe. That state is often recognized in school age as the expectation of abilities that consist of longer concentration and better attention arise. Convergence insufficiency (CI) is the inability to maintain binocular vision while working at near distance. It results in loss of binocular vision and problems in working at near distance. We noticed that children diagnosed with ADD had a high incidence of CI. The symptoms of these two conditions can overlap and both can interfere with reading and learning.

Materials and methods: Children between 8 and 14 years with ADHD sy (attention deficit/hyperactivity disorder) subtype ADD (diagnose verified by a children's psychiatrist) had an ophthalmologic exam (visual acuity measured with Snellen optotips, convergence in cm, stereovision with synoptophore, Lang test I and II, Titmus test) to establish ophthalmologic status. The patients are tested for concentration and attention degree with d2 Test of Attention. The exercises for improving their convergence and stereovision are performed at home and at orthoptic dpt. After the period of 3 and 6 months, the ophthalmologic exam as well as psychology testing are repeated in order to

verify children's psychological status and measure changes.

Results: The preliminary results suggest that improvement of convergence and binocular vision strongly influence the attention span in children diagnosed with ADD. However, the number of patients is insufficient for proper statistical analysis, since 2/3 of targeted number of cases has not been completely processed. After the gathering of the results, the analysis of variance will be used to analyze the differences among the numeric values of the three measuring. Difference in distribution of qualitative values among different measuring will be tested with Stuart-Maxwell test of marginal homogeneity.

Discussion: After ophthalmologic exercises the improvement of convergence results in the improvement of binocular function too. The results of psychology testing initially show the improvement in concentration and attention. Since the patients during those 6 months had no other therapy but ophthalmologic exercises, we may suppose that the enhancement of convergence and binocular vision also improve their attention

Acknowledgments:

MeSH/Keywords: convergence insufficiency, binocular vision, attention deficit disorder

Poster code: R-B-18-93

Poster Title: ASSOCIATION BETWEEN CATARACT SURGERY AND TYPE OF IMPLANTED INTRAOCULAR LENS WITH SLEEP QUALITY

PhD candidate: Ivan Škegro, MD

Part of the thesis: Association between cataract surgery and type of implanted intraocular lens with sleep quality

Mentor/s: Assistant professor Rajko Kordić, MD, PhD

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

Introduction: With aging, the natural human lens opacifies and prevents passage of light to retina, and that may influence on entrainment of circadian rhythms. The human eye has several non-image forming functions: alteration of core body temperature, regulation of pupil constriction and entrainment of the circadian rhythm. With time, the natural lens of the eye acquires a yellow-brownish discoloration because of chromophores that absorb short wavelength region of visible spectrum. People with impaired vision have sleep disorders, also sleep disorders are more frequent in elderly population. Intraocular lenses with blue light filter were developed in order to prevent adverse effects of blue light to retina.

Materials and methods: We contacted 126 patients who had an appointment for cataract surgery. Of these, we included 48 of them. 26 patients were allocated to a group that will receive the conventional IOL and 22 patients in group with implantation of IOL that filters blue light. 1 month prior and 2 months after the operation they completed ophthalmological examination and filled in the Pittsburgh Sleep Quality Index questionnaire. Inclusion criteria were age over 60. Non-inclusion criteria were verified sleep disorders, taking of psychopharmacological drugs, previous eye surgeries, diseases and disorders of the retina, only one eye, opaqueness of optical media, eyelid ptosis and terminal forms of glaucoma. Exclusion

criteria were complications of surgery, change of the type or dose of medication and taking of new drug after primary examination.

Results: The results show improvement in all 7 components of the questionnaire after surgery. The greatest improvement occurred in the sleep latency. The distribution of good and bad sleeper before and after surgery varies significantly. Before we had 86% of poor sleepers, or the subjects with overall scores on the questionnaire 5 and higher. After surgery, the rate of poor sleepers decreased to 52%. Rank sum test showed a statistically significant improvement in overall results of questionnaire after cataract surgery in both groups. If we compare the improvement in the quality of sleep with student t test, no statistically significant differences between groups with different type of IOL.

Discussion: Cataract surgery effectively improves quality of sleep, there is no difference in improvement of sleep quality between implantation of conventional and yellow IOL and blue-light-filtering IOLs have no adverse effect on circadian rhythm.

Acknowledgments:

MeSH/Keywords: sleep quality, intraocular lens, blue light, phacoemulsification

Poster code: R-B-18-97

Poster Title: PROGNOSTIC VALUE ANALYSIS OF STRUCTURAL CHANGES IN THE OPTIC NERVE AND RETINA IN THE EARLY DETECTION OF GLAUCOMA IN PATIENTS WITH EXFOLIATIVE SYNDROME

PhD candidate: Sonja Jandroković MD

Part of the thesis: Prognostic value analysis of structural changes in the optic nerve and retina measured with optical coherence tomography in the detection of glaucoma in patients with exfoliative syndrome

Mentor/s: Associate Professor Smiljka Popović Suić MD, PhD

Affiliation: Department of Ophthalmology, University Hospital Centre Zagreb, Croatia, Kišpatićeva 12

Introduction: Exfoliative syndrome (EXS) is a systemic disease with ocular manifestations. EXS is the most common known cause of glaucoma. Exfoliative glaucoma (EXG) is characterized by an aggressive clinical picture with progression. Spectral OCT uses optical coherence tomography method to obtain high-resolution images of the retina and optic nerve head and enables the visualization and measurement. The proposed study will analyze the OCT data of patients who have EXS without elevated intraocular pressure and patients with EXG. The data obtained will be compared with perimetry data. All data will be compared with the control group.

Materials and methods: We are going to recruited 60 patients with EXS and they will be divided into two groups with 30 patients: exfoliative syndrome (EXS) group and exfoliative glaucoma (EXG) group. Subjects will be divided into three groups according the stage of the exfoliation and glaucoma symptoms. There will be control group. All patients will underwent OCT optical coherence tomography SOCT Copernicus (Optopol Technology SA) and SAP (Haag Streit Octopus 900, G program). The discrimination power of each OCT parameter will be statistically evaluated in all groups and all data will be compared.

Results: Initial results indicate that the rim area showed the strongest correlation with glaucoma in optic nerve head ONH analysis.

It is well known that the disk size has an impact on the results of OCT examinations, therefore all groups had equal average size of the disk. Comparison of parameters for the cup area and cup volume has shown that there is a difference that was statistically significant between the control group and exfoliation glaucoma group. Unfortunately the exfoliative syndrome group was too small sample and statistical significance can not be calculated. Anyway, early progression of EXS to EXG clearly show the differences in certain parameters obtained with OCT.

Discussion: Imaging technologies provide objective and quantitative measurements that are highly reproducible and show very good agreement with clinical estimates of optic nerve head structure and visual function. As with other technologies, imaging may produce false identification of glaucoma and clinicians should not make management decisions based solely on the results of one single test or technology. There is a need for an individualistic approach to the management of patients with exfoliative syndrome because it may be converted to glaucoma.

Acknowledgments: I would like to thank my mentor Professor Smiljka Popović Suić MD, PhD

MeSH/Keywords: Exfoliative syndrome, exfoliative glaucoma, neuroretinal rim, rim volume, optical coherence tomography, perimetry

Poster code: R-B-18-103

Poster Title: REFRACTIVE SURGICAL METHODS FOR PRESBYOPIA TREATMENT: IS THERE HOPE?

PhD candidate: Lidija Andrijašević, MD

Part of the thesis: Can the available refractive surgery methods achieve satisfying visual acuity at near and distance at the same time?

Mentor/s: Vladimir Trkulja, Mladen Bušić

Affiliation: Medical School Zagreb, Univeristy Hospital

Introduction: Presbyopia correction can be achieved by glasses and contact lenses, and more recently by surgical methods. There are two main surgical approaches which attempt to correct the vision at near and distance – multifocal approach and monovision. Both approaches are applicable for cornea (laser) and lens (phakic and aphakic lenses). These are new methods and evidence on postoperative visual acuity and the actual independence of optical aids after the surgery are necessary. A systematic review of research that show the results of the mentioned methods should provide evidence about their effectiveness.

Materials and methods: Electronic databases Pubmed MEDLINE, Ovid MEDLINE, EBM Reviews, Scopus – Health Sciences, ISI Web of Knowledge, EBSCO were searched. The research was ment to be primarily sensitive, and not specific to identify all the articles relevant for validation of each of the method of interest. All studies were included, regardless the country of origin, language or publication year that a) deal with presbyopia, b) have goal to achieve satisfying visual acuity at near and distance, c) include patients treated with one of the meth-

ods of interest, d) are not duplicates, e) provide data about at least one outcome relevant to this research. First performed level of screening was based on the title and abstract, and the second level was based on article full text.

Results: We have identified 27905 studies in the first literature search. 264 studies were selected for further analysis based on title and abstract. There were 4 meta-analyses and 16 randomized controlled trials, and the remaining were studies of lower level of evidence (controlled and non-controlled observational studies of variable quality). Qualitative data analysis has shown that most of the studies are of questionable quality and quantitative data synthesis is yet to be performed.

Discussion: There is a body of evidence on refractive surgical methods, but it still remains to test the quality and level of evidence these data offer.

Acknowledgments: -

MeSH/Keywords: presbyopia, monovision, multifocal, visual acuity

Poster code: R-B-18-116

Poster Title: TREATMENT OPTIMIZATION IN ADVANCED ESOPHAGEAL CANCER

PhD candidate: Blanka Jakšić, MD

Part of the thesis: Treatment optimization and prognostic factors in advanced esophageal cancer

Mentor/s: Associate Professor Ana Fröbe, MD, PhD

Affiliation: UHC Sestre milosrdnice

Introduction: Patients with advanced stage of esophageal cancer have a poor quality of life and high mortality, despite therapeutic interventions. Up till now, use of high-dose rate intraluminal brachytherapy, external beam radiotherapy and sequential chemotherapy has never been tested systematically and prospectively, with the primary objective to improve local control of the disease and quality of life.

Materials and methods: Forty patients with the advanced stage of esophageal cancer, who are not candidates for radical treatment, are included in this study. All patients have received two applications of intraluminal high-dose rate brachytherapy, 800 cGy per application, and external beam radiotherapy, 3000 cGy in 10 fractions or 2000 cGy in 5 fractions. Twenty patients have received sequential cisplatin/5-fluorouracil based chemotherapy and twenty patients did not receive any additional therapy. Influence of these different treatment protocols on the symptoms of dysphagia, odynophagia, regurgitation, chest/back pain and quality of life was evaluated according to a developed scales for each of these symptoms and quality of life. Time to pro-

gression of the symptoms of the disease and impact on survival was also evaluated.

Results: Preliminary results of this study show that sequential use of chemotherapy after high-dose rate brachytherapy and external beam radiotherapy improves symptoms of dysphagia, odynophagia, regurgitation and chest/back pain, prolongs time to progression of the symptoms of the disease and improves quality of life but it does not have an effect on the overall survival of patients with the advanced stage of esophageal cancer who are not candidates for radical treatment.

Discussion: This study supports sequential use of high-dose rate brachytherapy, external beam radiotherapy and cisplatin/5-fluorouracil based chemotherapy in patients with advanced stage of esophageal cancer who are not candidates for radical treatment.

Acknowledgments:

MeSH/Keywords: esophageal cancer, dysphagia, quality of life

Poster code: R-B-19-16

Poster Title: BONE MORPHOGENETIC PROTEIN 6 (BMP-6) EXPRESSION IN ORAL SQUAMOUS CELL CARCINOMA (OSCC)

PhD candidate: Petar Suton, M.D.

Part of the thesis: Prognostic significance of bone morphogenetic protein 6 (BMP-6) expression in oral squamous cell carcinoma

Mentor/s: Associate Professor Ivica Lukšić, MD, PhD, Professor Lovorka Grgurević, MD, PhD

Affiliation: 1) University Hospital Dubrava, 2) University of Zagreb School of Medicine, Laboratory of Mineralized Tissues, 3) University Hospital for Tumors

Introduction: Bone morphogenetic proteins, BMPs, are growth and differentiation factors, originally isolated as molecules which stimulate ectopic bone and cartilage formation in vivo. The role of BMP-6 protein in the process of bone remodeling and metabolism is a well-known one. Despite its increased expression in various malignant tumors the prognostic significance of BMP-6 expression in oral squamous cell carcinoma (OSCC) remains unknown.

Materials and methods: This retrospective study included 120 patients with clinically T1-T3N0 OSCC who were primary surgically treated at the Department of Maxillofacial Surgery of the University Hospital Dubrava. The pathologist revised all pathologic specimens following standard histopathologic evaluation of paraffin embedded specimens. For each carcinoma, one representative section including central and peripheral portions of the tumor was selected for BMP-6 immunohistochemistry.

Results: Out of 48 processed primary tumor sections, forty-two (87,5%) cases showed cytoplasmic immunoreactivity for BMP-6. The obtained values will be correlated with

clinical (age, gender, tumor size and sublocalization) and pathohistological (tumor size, depth of invasion, tumor grade, perineural/perivascular invasion, periosteal involvement and bone invasion, total number and the lowest region of pathologically involved lymph nodes, extracapsular spread) factors, disease recurrence and survival, by use of univariate and multivariate statistical methods. This approach is expected to identify statistically significant and independent factors relevant for survival. The study is expected to be concluded by September 1, 2015.

Discussion: Our results will provide evidence and clarify the role of BMP-6 as well as the identification of clinical and pathohistological factors predictive for recurrence and survival in patients with OSCC.

Acknowledgments:

MeSH/Keywords: head and neck, oral squamous cell carcinoma, bone morphogenetic protein 6, prognostic factor, immunohistochemistry

Poster code: R-B-19-30

Poster Title: INTERACTION OF CRP AND FIBRINOGEN AS PREDICTOR OF CHEMOTHERAPY OUTCOME IN TREATMENT OF LOCALLY ADVANCED AND METASTATIC NON-SMALL CELL LUNG CANCER (NSCLC)

PhD candidate: Sonja Badovinac

Part of the thesis: Predictive significance of nonspecific inflammatory laboratory parameters in patients with locally advanced and metastatic non-small cell lung cancer treated with chemotherapy

Mentor/s: Marko Jakopović

Affiliation: University Hospital Centre – Zagreb

Introduction: Lung cancer is the leading cause of cancer death and the non-small-cell lung cancer represents 80%. When diagnosed, in most cases the cancer is in locally advanced or metastatic stage of the disease (stage IIIB and IV) and chemotherapy is the standard therapeutic strategy. Due to the heterogenic biology of the disease the search for adequate predictive factors to define patients with better response to the therapy is still in progress. Objective of this study was to explore predictive value of CRP and fibrinogen on the response to frontline chemotherapy.

Materials and methods: In this retrospective cohort study a total of 170 adult patients with locally advanced and metastatic non-small cell lung cancer in stage IIIB and IV were included. Demographic data, laboratory data at the time of diagnosis, chemotherapy type, and response to chemotherapy were documented and analyzed.

Results: CRP and fibrinogen values were statistically significantly correlated at the beginning of chemotherapy (Spearman's rank correlation, $\tilde{r}=0.67$ $P < 0.001$). After the adjustment for age, sex, cytological/histological type, chemotherapy protocol and antibiotic, CRP, fibrinogen, and their interaction were independently significantly associated with disease control at re-evaluation. Planned post-hoc analysis revealed that below 10th percentile of fibrinogen values

(≤ 3.3 mmol/L) higher CRP values was statistically significantly associated with progression of disease. At higher levels of fibrinogen, CRP was not statistically significantly associated with DCR. By Johnson-Neyman technique we found that below fibrinogen value of 3.5 mmol/L CRP is significantly associated with DCR. Above this fibrinogen value the association of CRP and DCR is lost.

Discussion: Different aspects of inflammation appear to regulate all phases of malignant disease. Elevated CRP level is a proven marker of different infection types but could be found in cancer patients without infection. Mechanism of inflammation in cancers is partially explained by neoplastic inflammation, inflammatory reaction on tumor necrosis or damages of adjacent tissue, and tumor release of proinflammatory cytokines. In this study we explored whether the level of non-infectious inflammation has the predictive value on the therapy response and found the correlation of the elevated level of CRP and fibrinogen and the poorer response to frontline chemotherapy of IIIB and IV NSCLC. These findings should be explored in the prospective studies.

Acknowledgments:

MeSH/Keywords: non-small-cell lung cancer, C-reactive protein, fibrinogen

Poster code: R-B-19-32

Poster Title: CHEMOBRAIN-COGNITIVE DEFICITS ASSOCIATED WITH CHEMOTHERAPY

PhD candidate: Ivana Kukec, MD

Part of the thesis: Adjuvant chemotherapy of breast cancer patients is connected with impairment of cognitive functions

Mentor/s: 1. Professor Stjepko Pleština, M.D, PhD., 2. Lovorka Brajković, Clinical Psychologist, PhD.

Affiliation: Clinic Of Oncology, University Hospital Centre Zagreb, Croatia

Introduction: Increasing number of cancer patients are concerned about cognitive problems. Cancer patient need to be aware of potential cognitive effects of cancer treatment to make informed treatment decisions. This research of cognitive functions associated with adjuvant chemotherapy women with breast cancer has goal to explore when cognitive deficits occur, and how long they last. Results could help us with modifications of treatment regimens that reduce cognitive deficits while maintaining treatment efficacy. Also development and implementation of cognitive rehabilitation simultaneously with oncology treatment could improve the daily functioning of cancer patient.

Materials and methods: In this prospective study women with breast cancer, while waiting their adjuvant chemotherapy to prepare, are examined cognitive functions. After they gave Informed Consent they underwent testing of general intellectual status before the start of oncology treatment. Further testing of cognitive functions is done after second and fourth cycle of chemotherapy. Further planned testing are not yet done. Used Tests are: Demographic questionnaire (created for this research), Standard Progressive Matrices (SPM - test of general intellectual status), Beck Anxiety Inventor (BAI), Beck Depression Inventor (BDI-II), Hopkins Verbal Learning Test-Revised (HVLTR), Trail Making Test (TMT – visual-spatial search and psychomotor speed),

Controlled Oral Word Association Test (COWAT – verbal fluency).

Results: We collected data for 12 of planned 120 women which are treated with adjuvant chemotherapy for breast cancer. Our candidates were divided into groups by chemotherapeutic regimens (antracyclines/taxanes). We noticed cognitive deficits after application of second and progression after fourth cycle of chemotherapy. Given that in these candidates have not yet been provided all planned testing of cognitive functions and that for now they are few, use of statistical methods would be unjustified. On the basis of incomplete data cannot be made valid conclusions.

Discussion: Some chemotherapeutic regimens are more toxic than others so our study will separate candidates by chemotherapeutic regimens. Existing researches indicate that a subgroup of patient (older and with lower pretreatment cognitive reserve) with breast cancer experience long-term cognitive changes after adjuvant treatment. Age, education, pretreatment cognitive reserve are considered in our research.

Acknowledgments: I would like to thank my family and mentors especially Lovorka Brajković.

MeSH/Keywords: cognitive functions, adjuvant chemotherapy, chemobrain

Poster code: R-B-19-59

Poster Title: FLUOROPYRIMIDINE AND IRINOTECAN TOXICITY PARTLY EXPLAINED BY DIHYDROPYRIMIDINE-DEHYDROGENASE (DPD) AND UDP-GLUCURONYL TRANSFERASE (UGT) GENOTYPING

PhD candidate: Ivan Bilić, MD MSc

Part of the thesis: The role of dihydropyrimidine-dehydrogenase and UDP-glucuronyl transferase polymorphisms in fluoropyrimidine and irinotecan toxicity

Mentor/s: Professor Nada Božina, MD PhD

Affiliation: University of Zagreb School of Medicine, Department of Pharmacology and University Hospital Centre Zagreb, Department of Laboratory Diagnostics

Introduction: Treatment with fluoropyrimidines (FP) and irinotecan is still the pillar of oncologic approach to patients with colorectal cancer. Dihydropyrimidine-dehydrogenase (DPD) is the rate-limiting enzyme of the FP metabolism, responsible for bulk degradation of injected FP (up to 90%). Irinotecan is to similar extent inactivated by glucuronidation through UDP-glucuronyl transferase (UGT1A1). Patients with partial or complete enzyme-deficiency are at increased risk for toxicity. Here we present single-institution patient cohort genotyped for some major DPYD- and UGT-polymorphisms and tested for toxicity during FP and/or irinotecan therapy.

Materials and methods: The patients are genotyped for two DPYD- and one UGT variant: DPYD*2A (IVS 14 1 G>A), M166V (496 A>G) and UGT1A1*28, respectively. Side-effects are followed-up for three months (because enzymatic deficiency is supposed to give early toxicity). Experimental group is defined with higher toxicity-grade (III and IV) and control group grade I or II or none. Genotyping of polymorphisms of DNA isolated from patient whole blood samples is performed by real-time PCR. The data were analyzed by statistics package SPSS 19

Results: The report includes preliminary study data on 78 analyzed subjects (28 in experimental and 50 in control group). We found only one DPYD*2A (IVS 14 1 G>A) polymorphism: the patient was homozygous and suffered high grade toxicity with lethal outcome (death of grade IV neutropenia with mucositis and sepsis). Frequency of M166V (496 A>G) poly-

morphism was 34,8% in experimental vs. 22,2% in control group. The difference was not significant ($p=0,09$). All control subjects with M166V variant were heterozygotes. In experimental group we detected 3 homozygotes with M166V variant. UGT1A1*28 homozygotes (Gilbert syndrome) were found in 21,7% in experimental vs. 10,9% in control group, whereas UGT heterozygotes were found in total of 27 cases, evenly distributed among groups.

Discussion: This preliminary report suggests that both tested polymorphisms could influence clinical course of chemotherapy among sample group. Therefore it appears that genotyping of DPYD and UGT1A1 can improve individualization of cancer-therapy. Whether patients should be tested prior to FP treatment is still a matter of debate among health authorities due to its high cost. From clinician's point of view, upfront testing is highly recommended as lethal outcome can occur even in adjuvant (preventive) treatment-setting, if patients are given chemotherapy unselectively.

Acknowledgments: I would like to show gratitude to my mentor professor Nada Božina and to professors Damir Vrbanc and Stjepko Pleština for their support, as well as all my constructive colleagues and co-workers at Medical School and Department of oncology in the University Hospital Center Zagreb that helped in designing the study and acquiring the data.

MeSH/Keywords: DPD-deficiency, DPYD, UGT1A1, fluoropyrimidines, fluorouracil, 5-FU, irinotecan, chemotherapy, pharmacogenomics, cancer-therapy, side-effect, adverse event

Poster code: R-B-19-70

Poster Title: COMPARISON OF BIOMECHANICAL PROPERTIES OF THE PLANTARIS AND GRACILIS TENDONS FOR MEDIAL PATELLOFEMORAL LIGAMENT RECONSTRUCTION

PhD candidate: Josip Vlaić, MD

Part of the thesis: Comparison of biomechanical properties of the plantaris and gracilis tendons for medial patellofemoral ligament reconstruction

Mentor/s: Assistant Professor Mislav Jelić, MD, PhD

Affiliation: Division of Pediatric Orthopedic Surgery, Children's Hospital Zagreb Department of Orthopaedic Surgery, Clinical Hospital Centre Zagreb, University of Zagreb Medical School

Introduction: Patellar luxation comprises 2-3% of all knee injuries. After patellar dislocation in more than 90% of cases there is a damage to the medial patellofemoral ligament (MPFL). MPFL injury disrupts a complex of passive medial patellar stabilizers and subsequently comes to instability of the patella in a number of patients. Patellar instability causes much discomfort, and it is necessary to do a reconstruction of the MPFL. Reconstructive techniques utilizing gracilis tendon graft are mostly used. Gracilis tendon is harvested from structures that have important role in biomechanics of the knee. Physiological role of the plantaris tendon in the knee is not of high relevance. We believe that the plantaris muscle tendon is suitable as a graft for MPFL reconstruction.

Materials and methods: Gracilis and plantaris tendons will be procured from 15 cadavers in a way as already described in the literature. Each tendon will be double-folded and grafts will be made, not less than 9 cm long. Double-folded tendon grafts will be looped over fixed part at one end and then caught in specially designed tendon clamp at the other end. Clamp will be placed in tensile testing machine and strength and tension parameters will be measured. Biomechanical properties of the plantaris tendon graft will be compared with biomechanical properties of the gracilis tendon graft, which is currently commonly used for MPFL reconstruction. Depending on type of distribution data will be analyzed using parametric or non-parametric statistical tests.

Results: The study is currently in the phase of collecting gracilis and plantaris tendons from cadavers. Experiment formation and the force cracking results for plantaris tendon graft in three samples amounts 186 N, 199 N and 209 N respectively, which approximately corresponds to the strength of native MPFL. For a moment our results show that the plantaris tendon graft has comparable biomechanical properties with MPFL, but because of small sample we cannot predict end results and more samples are needed.

Discussion: The aim of this study is to compare the biomechanical properties of the graft made up of double-folded plantaris tendon, to be used for substitute a damaged MPFL, with biomechanical properties of double-folded gracilis tendon graft whose biomechanical properties are adequate for the MPFL reconstruction. Our preliminary results so far are in favor of our expectations, which supports original hypothesis.

Acknowledgments: Authors would like to thank following institutions and their staff: Department of Orthopedic Surgery University Hospital Centre Zagreb, Department of Forensic Medicine School of Medicine University of Zagreb, Department of Pathology and Cytology University Hospital Centre Zagreb, Faculty of Mechanical Engineering and Naval Architecture University of Zagreb.

MeSH/Keywords: medial patellofemoral ligament reconstruction, plantaris tendon graft

Poster code: R-B-20-98

Poster Title: TISSUE ANALYSIS OF KNEE FOLLOWING CARTILAGE RECONSTRUCTION WITH AUTOLOGOUS OSTEOCHONDRAL GRAFT ENGINEERED IN PERFUSION BIOREACTOR

PhD candidate: Tadija Petrović, MD

Part of the thesis: Autologous osteochondral grafts cultured in a perfusion bioreactor generate less inflammatory response in the synovium and underlying subchondral bone when compared to the cell-free scaffolds.

Mentor/s: Davor Ježek, MD, PhD and Alan Ivković MD, PhD

Affiliation: Department of Histology and Embryology, School of Medicine University of Zagreb, Croatia, Department of Surgery, Orthopedics and Ophthalmology, Faculty of Veterinary Medicine, University of Zagreb, Croatia

Introduction: Due to the lack of a quality treatment, articular cartilage focal defects represent great socioeconomic problem of modern society. Due to their specific structure, focal defects of the articular cartilage have little ability to regenerate. Although current treatment options can provide substantial improvement of clinical symptoms, the search for optimal modality is still ongoing. Autologous three-dimensional osteochondral grafts produced in perfusion bioreactors represent one of the most promising ways to treat these defects. It is known that implantation of these grafts, along with the surgical procedure itself may induce local inflammatory response within the joint. It is also known that inflammation is detrimental to the formation of new cartilage. The purpose of this study is to evaluate which part of the joint is affected with inflammatory reaction and whether the bioengineered graft is responsible for the observed inflammatory response.

Materials and methods: 24 sheep were divided into four groups of six sheep. Osteochondral defects were created on both condyles of the right posterior leg of all sheep. After six weeks first group get articular cartilage graft, second group get nasal cartilage graft, third group get only scaffold without cells and fourth group get only empty defects. 2 animals of each group were sacrificed after 6 weeks, next 2 after 3 months and the rest after 12 months post-

operatively. Collected samples of subchondral bone and synovium will be analyzed with qRT-PCR, histologically and immunohistochemically for the presence of inflammatory markers IL-1B, IL-6, TNF α

Results: Preliminary results obtained by immunohistochemical methods show that there is no significant difference in the concentration of the analyzed inflammatory markers between the operated knee and the non-operated knee.

Discussion: Preliminary immunohistochemical results show that scaffold or graft after the 6th week, 3 months and 12 months after the implantation don't cause increased inflammatory reaction of the synovium and subchondral bone in the operated knee in 24 sheep compared to the non-operated knees. However, the final conclusion is that it is necessary to wait and analyze the results obtained by the qRT-PCR method.

Acknowledgments: The research leading to these results has received funding from the European Union's Seventh Framework Programme (FP7/2007-2013) under grant agreement n°278807 – Bioreactor based, clinically oriented manufacturing of engineered tissues (BIO-COMET)

MeSH/Keywords: articular cartilage, perfusion bioreactor, subchondral bone, inflammation, synovium

Poster code: R-B-20-125

Poster Title: ASSOCIATION OF TGF β 1 29C/T AND IL6 -572G/C POLYMORPHISMS WITH DEVELOPMENTAL HIP DYSPLASIA (DDH): A CASE-CONTROL STUDY IN ADULTS WITH SEVERE OSTEOARTHRITIS WITH AND WITHOUT DDH

PhD candidate: Tomislav Čengić

Part of the thesis: Association of vitamin D binding protein (VDBP), vitamin D receptor (VDR), transforming growth factor β 1 (TGF- β 1) and interleukin 6 (IL-6), gene single nucleotide polymorphisms with developmental dysplasia of the hip

Mentor/s: Prof. Vladimir Trkulja, Prof. Robert Kolundžić

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

Introduction: Developmental dysplasia of the hip (DDH) increases the risk of severe adult hip osteoarthritis (OA). Transforming growth factor- β 1 (TGF- β 1) and interleukin-6 (IL-6) are included in pathogenesis of OA, as well as in development of the musculoskeletal system. We investigated the association of single nucleotide polymorphisms (SNPs) known to reflect on the circulating levels of the two cytokines, specifically, 29T \rightarrow C transition in the TGF β 1 signal sequence (rs1800470) and -572G \rightarrow C transversion in the IL6 promoter (rs1800796), with DDH.

Materials and methods: We conducted a case-control study in consecutive unrelated adults with severe hip OA scheduled for total hip arthroplasty. Cases, patients with OA secondary to DDH (n=68) and controls, patients with OA unrelated to DDH (n=152), were genotyped at the two loci.

Results: With adjustment for age, sex and genotype at the concurrent locus, cases were more likely (OR=2.42, 95%CI

1.08-5.43, p=0.032) to be transition homozygous at TGF β 1 locus 29, and also more likely (OR=6.36, 95%CI 2.57-15.7, p<0.001) to be transversion homozygous at IL6 locus -572 than controls. Cases were also more likely (OR=11.3, 95%CI 4.25-29.8, p<0.001) than controls to carry one of the three genotypes combining transition/transversion homozygosity at both loci, or transition/transversion homozygosity at one and heterozygosity at the concurrent locus.

Discussion: Data suggest association between TGF β 1 29T \rightarrow C transition (rs1800470) and IL6 -572G \rightarrow C transversion (rs1800796) with DDH, and also a possibility of TGF- β 1 and IL-6 interaction in DDH pathogenesis.

Acknowledgments:

MeSH/Keywords: developmental dysplasia of the hip, hip osteoarthritis, TGF β 1, IL6, single nucleotide polymorphisms

Poster code: R-B-20-160

Poster Title: ARE THERE BENEFITS OF TOURNIQUET USE IN ANTERIOR ANKLE ARTHROSCOPY?

PhD candidate: Damjan Dimnjaković

Part of the thesis: Koristi li bližnja staza u artroskopskim zahvatima u prednjem dijelu gležnja?

Mentor/s: Associate Professor, Ivan Bojanić, MD, PhD

Affiliation: Department of orthopedic surgery, University hospital center Zagreb, University of Zagreb School of medicine

Introduction: Arthroscopic surgery of the ankle is nowadays an irreplaceable technique for the treatment of ankle injuries and disorders. Use of the tourniquet in all arthroscopic surgeries is taken for granted worldwide, with the main goal to improve intraoperative visualization and, hopefully, shorten the duration of the surgery. Although rare, complications after arthroscopic surgery can probably be related to the tourniquet time, with the infection and the deep vein thrombosis being the most severe of complications. During the last decade researches have been published which did not confirm the advantages of tourniquet use in knee arthroscopy. Aim of this research is to define the benefits of tourniquet use in anterior ankle arthroscopy.

Materials and methods: 16 patients (7 male and 9 female), which required anterior ankle arthroscopy, were randomly assessed into two groups. AOFAS, FADI and Tegner score were used preoperatively and 3 and 6 months postoperatively to determine the function of the operated ankle. Surgery log was filled out by the surgeon. Postoperative pain diary was filled out by patients.

Results: The mean age of patients was 29,7 years (range 16-45). Patients were treated

for anterior ankle impingement in 10 cases, OCD of the talus in 4 cases and loose bodies in 2 cases. The tourniquet was used in 7 patients, while 9 patients were treated without the tourniquet. The mean preoperative AOFAS score was 69,2 (42-92) points, FADI score was 70 (29-102) points and the mean Tegner activity level was 2. The mean postoperative results showed improvement at both 3 and 6 months after the operation in AOFAS, FADI and Tegner score, which was noticed regardless the tourniquet use. The perioperative period was uneventful in both groups. Similar early postoperative blood loss was noticed in both groups. There was no difference regarding the early postoperative pain noted in the pain diary.

Discussion: Anterior ankle arthroscopy shows good clinical outcome and similar postoperative blood loss in the patients in which the tourniquet was not used when compared to patients in which the tourniquet was used.

Acknowledgments:

MeSH/Keywords: arthroscopy, ankle, tourniquet

Poster code: R-B-20-173

Poster Title: ROLE OF PGE2/EP4 RECEPTOR SIGNALING ON THE EFFECTS OF HYPEROXIA ON AIRWAY SMOOTH MUSCLE

PhD candidate: Qëndresa Beqiraj, MD

Part of the thesis: Role of Rho/Rho-kinase signaling pathways in development of bronchopulmonary dysplasia in the experimental rat model

Mentor/s: Prof. Dr. Muharrem Jakupi-aj PhD Prof.dr.sc. Zdenko Kovač

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

Introduction: Bronchopulmonary dysplasia (BPD) is a chronic lung disorder that is most common among children born prematurely. Hyperoxic exposure is widely believed to contribute to the development of BPD. Preterm infants especially those with BPD are predisposed to airway hyperactivity. Hyperoxia has been shown to induce airway hyperactivity in newborn rat pups. Hyperoxia reduces relaxation of airway smooth muscle (ASM) by impairing Prostaglandin E2 (PGE2) release from ASM. There are 4 different receptors of PGE2. Therefore, the aim of this study was to investigate the role of PGE2-EP4 signaling on ASM rat pups under hyperoxic conditions.

Materials and methods: On day 5th of the life, Sprague Dawley rat pups were exposed to hyperoxia ($\geq 95\%$ O₂) or room air for seven days. Then, animals were euthanized by asphyxiation in CO₂ at day 12 of post-natal life. A cylindrical airway segment of 3-mm length was isolated from mid-portion of the tracheas of each animal, and placed in Krebs – Henseleit (KH) solution. The preparations were used to study contractile and relaxant responses. The contractile were induced by Bethanechol in presence or absence of PGE2 or EP4 agonist, and the force was expressed in gram (g). Relaxant responses were induced by Electrical Field Stimulation (EFS) or PGE2 or EP4 agonist on pre-contracted tissues. The results are expressed as mean \pm SEM. Statistical significance was determined by two-way ANOVA with repeated measurements. In all cases, $p < 0.05$ was considered statistically significant.

Results: 1. Contraction (g) Hyperoxia
-log [Bethanechol] (M)

	MEAN	SE
8	0,02	0,01
7,5	0,10	0,04
7	0,21	0,11
6,5	0,34	0,14
6	0,74	0,16
5,5	1,75	0,25
5	2,37	0,31
4,5	2,94	0,40
4	3,11	0,41
3,5	3,25	0,45
3	3,24	0,44

Discussion: 1. Effect of hyperoxia on contraction of ASM in response to bethanechol demonstrate that hyperoxia enhances the contractile responses of ASM as compared to responses of ASM obtained from tissues of animals exposed to room air ($P < 0.01$ $n = 7$). Role of PGE2 and EP4 agonist (AE1-329) demonstrate that enhanced contractile responses to bethanechol in hyperoxia-exposed tissues were attenuated by PGE2 (1 μ M) and/or AE1-329 (10 μ M). ($P < 0.001$ $n = 7$). Hyperoxia enhances contractile responses and reduces relaxant responses of ASM of rat pups.

Acknowledgments: I wish to express my sincere thanks to my mentors, my family and prof. Ramadan Sopi for providing me with necessary facilities for this research.

MeSH/Keywords: Bronchopulmonary dysplasia, hyperoxia, Prostaglandine E2.

Poster code: R-B-22-114

Poster Title: MEASUREMENT STANDARDISATION AND DETERMINATION OF NORMAL GLOMERULAR BASEMENT MEMBRANE THICKNESS AT DEPARTMENT OF PATHOLOGY AND CYTOLOGY, DUBRAVA UNIVERSITY HOSPITAL, ZAGREB

PhD candidate: Petar Šenjug, MD

Part of the thesis: Characteristics of glomerular basement membrane in Alport's syndrome and thin basement membrane nephropathy

Mentor/s: Danica Galešić Ljubanović, MD, PhD

Affiliation: Department of Pathology and Cytology, Dubrava University Hospital, Zagreb

Introduction: Electron microscopy (EM), along with light microscopy and immunofluorescent analysis, represents key method in renal biopsy specimen analysis. EM is crucial for diagnosing disorders that directly influence structure of glomerular basement membrane (GBM) such as Alport's syndrome (AS), thin glomerular basement membrane nephropathy (TBMN) and diabetic nephropathy. Thickness of GBM depends on multiple factors (age, sex, tissue preparation and processing). Many authors emphasize need for referential span of normal GBM thickness for each laboratory. Orthogonal intercept/mean harmonic thickness measurement is considered the most precise method of measurement but due to its complexity, the most frequently used method is direct measurement of GBM thickness.

Materials and methods: We have applied modification of the direct measurement/arithmetic mean method to measure GBM thickness in our laboratory. Digital EM photographs with magnification of x4000 – x8000 were selected from our database of EM pictures of kidney biopsy samples. Pictures were taken on multiple capillaries from 1-3 glomeruli. A total of 30 GBM measurements were taken on 10 randomly selected capillaries to determine an average GBM thickness for each biopsy. Position of measurements in capillary loops was determined similarly as described by Haas (Arch Pathol Lab Med, 2009). Direct measurements were

made using iTEM software (Olympus Soft Imaging Solutions GmbH), with digital zoom of 150-400% to measure the distance between the endothelial and podocyte plasma membranes.

Results: Using this method we obtained mean \pm SD values for the normal GBM thickness of adult males and females of 340 ± 36 nm and 301 ± 44 nm. These values were based on average GBM thickness for each of 23 males and 22 females, aged from 19 to 84 years, with minimal change disease, acute interstitial nephritis, normal renal parenchyma or acute tubular injury. Exclusion criteria were hematuria and diabetes mellitus. We defined normal ranges for each gender (268-412 nm for males, 213-389 for females), as being within 2 SD of these means.

Discussion: With this research we have standardized method for GBM thickness measurement for Laboratory for Nephropathology and Electron Microscopy at Dubrava University Hospital and defined referential span of normal GBM thickness for our laboratory. Our research results are crucial for more accurate diagnosis of disorders characterized with structural changes of GBM such as AS and TBMN.

Acknowledgments:

MeSH/Keywords: Kidney, Electron Microscopy, Glomerular Basement Membrane

Poster code: R-B-23-66

Poster Title: IMMUNOHISTOCHEMICAL EXPRESSION OF E-CADHERIN IN METASTATIC AND NONMETASTATIC COLORECTAL CANCER

PhD candidate: Petra Jurčić, MD

Part of the thesis: Immunohistochemical expression of NEDD9 and E-cadherin in Metastatic and Nonmetastatic Colorectal Cancer

Mentor/s: Professor of Pathology Božo Krušlin, MD, PhD

Affiliation: Department of Radiation Therapy and Internal Oncology, Tumor Clinic, Sestre milosrdnice University Hospital

Introduction: Colorectal cancer is a major health problem. In Eastern Europe incidence and mortality rates are still rising. E-cadherin is a transmembrane cellular adhesion glycoprotein molecule present in most tissues and involved in forming intercellular junctions. Loss of E-cadherin is responsible for abnormal cell structure, breach of basement membrane, local invasion and metastasis.

Materials and methods: In a retrospective study we analysed 50 samples of metastatic colorectal cancer and 26 samples of nonmetastatic colorectal cancer from surgically treated patients who had not previously received chemotherapy and/or radiation therapy. In tissue microarray technique, tissue cylinders from regions of interest in paraffin-embedded tissues were inserted in a recipient paraffin block in a precisely spaced, array pattern. Sections from this block were cut using a microtome, mounted on a microscope slide and then analysed by method of standard histological analysis. We used mouse monoclonal primary antibody E-cadherin (diluted 1:50, Abcam, UK). Immunohistochemical analysis was performed following indirect ABC Technique, LSAB Method as a visualization system, using the MSIP protocol.

Results: In a pilot study, 50 samples of metastatic colorectal cancer and 26 samples of

nonmetastatic cancer were analysed. 38 (76%) samples of metastatic colorectal cancer were E-cadherin-negative. 12 (46,2%) samples of nonmetastatic colorectal cancers were E-cadherin-negative. The most common intensity of membrane staining in metastatic colorectal cancers was 1 (72%), whereas in nonmetastatic it was 2 (53,8%). There was high expression (3) of E-cadherin in tumor cells in 34 (68%) samples of metastatic colorectal carcinomas, and in 20 (77%) samples of nonmetastatic.

Discussion: Based on the analysis results of a small number of samples, we conclude that metastatic colorectal cancers were more often E-cadherin negative. It is necessary to analyse a large number of samples of metastatic and nonmetastatic colorectal cancer in order to confirm these preliminary results.

Acknowledgments: I'd like to thank Professor Božo Krušlin for his support and help, Dr Petra Radulović for her help with the immunostaining evaluation, as well as the staff of Ljudevit Jurak University Department of Pathology for their assistance.

MeSH/Keywords: colorectal cancer, metastasis, E-cadherin

Poster code: R-B-23-168

Poster Title: SINGLE NUCLEOTIDE POLYMORPHISMS (SNP) OF TOLL LIKE RECEPTOR(TLR) 2 AND 4 IN MULTIPLEX JUVENILE IDIOPATHIC ARTHRITIS (JIA) FAMILIES

PhD candidate: Marija Perica

Part of the thesis: Role Of Innate Immune System In Pathophysiology Of Juvenile Idiopathic Arthritis In Multiplex JIA Families

Mentor/s: Professor Miroslav Harjaček, MD, PhD

Affiliation: Children's Hospital Srebrnjak

Introduction: Juvenile idiopathic arthritis (JIA) represents a group of heterogenic, multifactorial and multigenic diseases affecting children under 16 years of age with undefined role of innate and adaptive immune system in the disease development. Multiplex families represent rare entity, defined by two or more children diagnosed with JIA, in contrast with simplex families, with only one child diagnosed with JIA. Pathophysiology underlying disease development in multiple members of the same family has not been clarified.

Materials and methods: Clinical database of Children's Hospital Srebrnjak was searched for patients diagnosed with JIA according to ILAR criteria. Among identified patients, brothers and sisters diagnosed with JIA were selected as multiplex family group. Control group was formed of JIA patients correlating with multiplex group according to age, gender, but without sibling diagnosed with JIA. Real-time PCR-SNP analysis of TLR4 (Asp299Gly, Thr399Ile) and TLR2 (Arg753Gln) was performed in 3 multiplex family group members and 5 simplex family group members, using an ABI PRISM 7300 SDS and TaqMan SNP genotyping assays.

Results: There were 670 patients fulfilling ILAR criteria in 5 year interval, 67% were male, 33% were female with median age of 13.1 years. We have identified 34 members of 17 multiplex families, 38% male and 62% female members. Six members of multiplex

families were diagnosed with juvenile spondyloarthritis (jSpA), 13 with oligoarticular JIA, 6 with poliarticular JIA and 9 with reactive arthritis.

SNP analysis for TLR4 (Asp299Gly, Thr399Ile) and TLR2 (Arg753Gln) SNP revealed wild type allele homozygous carriers for all three SNP among control group. On the contrary, there were 2 heterozygote carriers of TLR4 (Asp299Gly) and one heterozygous TLR4 (Thr399Ile) SNP carrier among multiplex family members. Multiplex family members were wild type allele homozygous carriers for TLR2 SNP. The difference in genotype frequency of TLR4 SNP was not statistically significant.

Discussion: There was no difference among participants from both groups regarding TLR2 (Arg753Gln) SNP presence. Although the genotype frequency for TLR4 (Asp299Gly and Thr399Ile) variants was not statistically significant in multiplex group due to small sample, a larger study on all multiplex and simplex members will be done to elucidate whether these polymorphisms, influence susceptibility to JIA development in multiple members of the same family.

Acknowledgments:

MeSH/Keywords: juvenile idiopathic arthritis, toll like receptor, single nucleotide polymorphism

Poster code: R-B-24-75

Poster Title: CORRELATION OF MORPHOLOGICAL AND KINETIC FEATURES AT MAGNETIC RESONANCE IMAGING AND PATHOHISTOLOGICAL PROGNOSTIC FACTORS IN INVASIVE DUCTAL BREAST CANCER

PhD candidate: Ana Marija Alduk, MD

Part of the thesis: Correlation of morphological and kinetic features at magnetic resonance imaging and pathohistological prognostic factors in invasive ductal breast cancer

Mentor/s: Assistant Professor Maja Prutki, MD, PhD

Affiliation: University Hospital Centre Zagreb

Introduction: Breast magnetic resonance imaging (MRI) is a highly sensitive modality for imaging of breast cancer. Tumor size, axillary lymph node status, histological grade, expression of estrogen (ER) and progesterone receptors (PR), HER2 and Ki-67 are well-established prognostic factors for breast cancer. The kinetic of contrast enhancement is related to tumor vascularization, which shows strong correlation with biological and clinical aggressiveness. It would be valuable if an association could be found between MRI features and pathohistological prognostic factors used in breast cancer because it could be useful in the preoperative assessment of breast cancer.

Materials and methods: 114 women with invasive ductal carcinomas who underwent preoperative MRI were included in this retrospective study. MRI features were interpreted with a multifactorial classification system (Göttingen score) that included morphological (shape, margins and pattern of enhancement) and kinetic characteristics (initial signal increase and post-initial behaviour). Each parameter was scored with 0, 1 or 2 points and the total score was estimated. Histological specimens were analyzed for tumor size, axillary lymph node status, histological grade, ER, PR, HER2, and Ki-67. Statistical analysis was performed to correlate MRI features and pathohistological findings using Kruskal-Wallis test, X² test, and logistic regression analysis.

Results: By multivariate analysis, a spiculated or irregular margin was a significant, independent predictor of a smaller tumor size ($p < 0.041$), and a higher expression of ER ($p = 0.022$). High Göttingen score was significant, independent predictor of a higher histological grade ($p < 0.022$).

Discussion: In this study, a spiculated or irregular margin of breast cancer on high spatial resolution dynamic MR was able to predict a smaller tumor size and higher expression of ER. Less aggressive cancers show a spiculated margin probably because of their low cellularity, rich collagen matrix and desmoplastic host reaction. Another important result of this study was that high Göttingen score was a significant, independent predictor of a higher histological grade ($p < 0.022$). A multivariate interpretation model for breast MRI that includes morphological and kinetic characteristics may have prognostic value for breast cancer and could be correlated with pathohistological characteristics indicating biological behavior of breast cancer.

Acknowledgments:

MeSH/Keywords: breast neoplasm, magnetic resonance imaging, prognostic factors, kinetic characteristics

Poster code: R-B-25-20

Poster Title: ESTIMATION AND COMPARISON OF PATIENT DOSES IN CAROTID ARTERIAL STENTING WITH OR WITHOUT CEREBRAL PROTECTION

PhD candidate: Marko Slavica, MD

Part of the thesis: Values of dose should be positioned below the dose recommended by the relevant European and Croatian professional and legal institutions.

Mentor/s: Ass.Prof. Vinko Vidjak, MD PhD

Affiliation: interventional radiology, radiobiology,

Introduction: Interventional radiology (IR) procedures are developing faster than bio-medicine dosimetry research during those procedures. Interventional radiology (IR) considerable participate in cumulative lifetime dose which population receive from medically indicated irradiation and percentage of IR procedures is growing by day. The total number of complex procedures like carotid arterial stenting (CAS) is also growing and there is few relevant research in skin and cumulative patient doses for these procedures or dosimetry comparison in different approach to carotid arterial stenting (CAS) with or without cerebral protection. Data given in this study reveal new knowledge in patient dosimetry and create foundations for further dosimetry and biomedical research helping understanding total cumulative lifetime population doses.

Materials and methods: A five year long, multicenter dosimetry study, conducted and in progress in clinical centers where stenting of the carotid artery- CAS procedures are performing. On a statistically relevant number of patients, we try to verify the hypothesis presented. Indication must be confirmed by at least two medical specialists, one of which must be a sub-specialist in interventional radiology.

Results: For all patients these will be recorded: height, weight, BMI, degree of stenosis, duration of fluoroscopy, electrical and Conditions (kV, mAs) etc. We will promote the dosimetry phantom (Rando-Aldersonov fantom – humanoid phantom, an average high person-to 25mm / layer). Dosimetry will be made respecting the anthropometric characteristics of the patients. Doses will be measured at locations radio-sensitive organs and tissues (lens, thyroid gland) using thermoluminescent dosimeters (TLD LiF).

Discussion: Based on the results we should confirmed the hypotheses about the safety of interventional procedures stenting of the carotid arteries regarding radiation doses received by patients. Values of dose should be positioned below the dose recommended by the relevant European and Croatian professional and legal institutions.

The hypothesis should confirm that there is no statistical difference in the dose for patients between treatments with and without cerebral protection..

Acknowledgments:

MeSH/Keywords: CAS, interventional radiology, carotid stenting, referent doses levels

Poster code: R-B-25-82

Poster Title: HIPPOCAMPAL SCLEROSIS: MAGNETIC RESONANCE IMAGING AND HISTOPATHOLOGY CORRELATION

PhD candidate: Natasa Katavic, MD

Part of the thesis: Hippocampal sclerosis: magnetic resonance imaging (MRI) and histopathology correlation

Mentor/s: Ass.Prof. Dijana Zadavec, PhD

Affiliation: Clinical Hospital Center Sisters of Mercy, Clinical Department of Diagnostic and Interventional Radiology, Zagreb / Health Center Osijek, Department of Radiology

Introduction: Hippocampal sclerosis (HS) is considered one of the major pathogenic factors of refractory temporal lobe epilepsy (TLE), a status which is treated surgically. Magnetic resonance imaging (MRI) is important in the preoperative detection of HS. The aim of this study is to evaluate MRI accuracy in preoperative assessment of HS grade in patients with refractory TLE.

Materials and methods: This retrospective study will include 30 patients with a diagnosis of refractory TLE due to HS who underwent selective amygdalohippocampectomy and 5 healthy controls. Preoperative and postoperative MRI scans were performed on a 1,5T Avanto Magnetom MRI system. Qualitative visual MR image assessments for the increased signal intensity of the hippocampus were performed on T2WI and FLAIR 3mm slices. Signal intensity changes of the hippocampal head, body and tail were assessed in three grades by two neuroradiologists. Histopathological (HP) examination of the resected hippocampus will be performed by neuropathologists using immunohistochemistry (IHC) to distinguish the three subtypes of HS according to the most recent HP classification. Statistical analyses will test the correlation of hippocampus qualitative MR assessments and HP findings on the removed hippocampus.

Results: Until now, 16 patients (9 female, 7 male mean age 36 years) and 5 controls

(mean age 36 years) have been enrolled. Two independent neuroradiologists visually evaluated MRI signal intensity changes of each hippocampal slice as high, mild and low. Ten slices were analyzed per patient. High signal intensity was easily assessed but it was difficult to differentiate mild and low signal intensity. IHC analyses will be conducted. Although there was not enough data for statistical analysis, the difference in signal intensity between slices was observed.

Discussion: More precise MR imaging can provide more sensitive detection and localization of lesions.

Better understanding of the correlation between hippocampal changes on MRI and HP findings should improve management of patients with refractory TLE. A positive correlation between MRI changes and HS grade may provide better determination for minimally invasive surgical procedures to achieve the best postoperative outcome for patients with refractory TLE and to identify patients who will benefit most from hippocampal surgery.

Acknowledgments: /

MeSH/Keywords: hippocampal sclerosis, magnetic resonance, histopathological findings

Poster code: R-B-25-123

Poster Title: VALIDATION OF COLOR DOPPLER IN DIAGNOSING ACUTE SACROILIITIS IN PATIENTS WITH ENTHESITIS-RELATED ARTRITIS

PhD candidate: Dubravko Bajramović, MD

Part of the thesis: Value of Color Doppler of Sacroiliac Joints in Patients with Juvenile Idiopathic Arthritis

Mentor/s: Prof. Kristina Potočki, MD, PhD

Affiliation: University of Zagreb School of Medicine, University Hospital Centre Zagreb, Clinical Department of Diagnostic and Interventional Radiology

Introduction: Value of ultrasound and magnetic resonance imaging in detection of acute joint inflammatory changes has been confirmed by many studies but data which compare the use of Color Doppler and magnetic resonance imaging (MRI) in detection and monitoring of sacroiliitis are rare.

Materials and methods: Radiological imaging (Ultrasound/Color Doppler and MRI of sacroiliac joints) was performed on 28 patients with low back pain and suspected acute sacroiliitis who fulfill the ILAR criteria for ERA. Out of 28 patients 16 were male and 12 female with average age being 14. Ultrasound examination was performed on a high-quality device with high-frequency linear array using B-mode and Color Doppler. Results were recorded using two semi-quantitative methods. MRI of SI joints was performed on 1.5T machine in standard series of sequences. Presence of synovitis, joint effusion, subchondral bone marrow edema, erosions and marginal appositions was noted and inflammatory changes quantified using SPARCC method.

Results: Active disease or acute sacroiliitis was noted using ultrasound/Color Doppler examination in 8 patients, 20 showed no signs of synovitis. MRI detected 9 patients with active disease. Only two patients had ultrasound signs of disease activity confirmed on MRI. Based on preliminary results sensitivity of ultrasound/Color Doppler examination in detecting acute sacroiliitis in ERA patients is 22.2% and specificity is 68.4%. Positive predictive value is 0.25 while negative predictive value is 0.65. Preliminary

results show high number of ERA patients (15 of 29) who developed sacroiliitis relatively early in the course of the disease. Analysis of MRI sequences shows that the active lesions are seen on STIR sequences and that administration of contrast agent is not necessary.

Discussion: Preliminary results show low sensitivity and relatively low specificity of ultrasound/Color Doppler examination in detecting acute sacroiliitis in ERA patients. These results demand serious re-thinking of the diagnostic procedure considering that this examination is frequently indicated by the clinicians due to the long waiting lists for the MRI. Results also show high number of patients who developed sacroiliitis early in the course of the disease which is in contrast with previously published data. Analysis of the MRI sequences used support recently published guidelines for the MRI of the sacroiliac joints imaging protocol which state that the use of contrast medium is not required in order to show signs of active disease.

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

MeSH/Keywords: juvenile idiopathic arthritis, enthesitis-related arthritis, acute sacroiliitis, Color Doppler, Magnetic Resonance Imaging

Poster code: R-B-25-166

Poster Title: OSTEOMETRIC SEX DETERMINATION BASED ON DIMENSION OF ACETABULUM AURICULAR AND RETROAURICULAR SURFACE OF PELVIC BONE IN VICTIM OF INDEPENDENCE WAR IN CROATIA

PhD candidate: Pero Bubalo MD

Part of the thesis: Osteometric parameters obtained by measuring the auricular and retroauricular surface and acetabulum of pelvis will differ significantly between males and females

Mentor/s: Davor Mayer MD PhD

Affiliation: Institute of Forensic Medicine and Criminalistics School of Medicine University in Zagreb

Introduction: Pelvis is the most sexually dimorphic area of the adult human skeleton which makes it one of the fundamental bases of forensic identification. Over time, confirming sexual divergence by osteometric analysis of the bones became increasingly recognized. Creating the discriminant function formulas from osteometric data is the most common method. It is widely argued in the literature that these formulas are population specific. Acetabulum features are recognized as being useful for sex determination. At the same time, characteristics of auricular and retroauricular surface are not systematically investigated.

Materials and methods: The material consists of skeletal remains of the victims of Croatian Homeland War. The skeletal remains used in this study have been identified and the sex has already been determined. One hundred female and one hundred male individuals will be included in the study. Using flexible meter and sliding caliper, we will measure seven parameters on auricular and retroauricular surface and two parameters on acetabulum. The measurements will be taken from both sides of pelvis. Data will be subjected to statistical analysis using SPSS program.

Results: Preliminary statistical analysis was performed at 20 male and 10 female pelvic bones. The results demonstrate statistically significant differences between male and female pelvis for eight measured parameters. The results are shown in the table 1.

Discussion: The results confirm significant difference between male and female pelvis. Surprisingly, differences in transversal auricular surface diameter did not prove to be statistically significant. This is in contrast with previously published results which state that male auricular surface is longer and wider than female. The most dimorphic measurements were central auricular surface distance and ischiatic notch auricular retroauricular distance. We expect that discriminant function based on these parameters will show accuracy above 85%.

Acknowledgments: The author would like to thank to Ministry of Veterans for their support in this research.

MeSH/Keywords: acetabulum, sex determination, analysis, pelvic bones

Poster code: R-B-27-81

Poster Title: TWO DIFFERENT PROSTATE BIOPSY PROTOCOLS AND CANCER DETECTION RATES

PhD candidate: Branimir Lodeta

Part of the thesis: Comparison of two prostate biopsy schemes and selection of optimal protocol regarding PSA blood levels and localisation of positive cores in prostate cancer diagnostics

Mentor/s: Professor Vladimir Trkulja, MD, PhD

Affiliation: General hospital Varazdin

Introduction: Transrectal ultrasound (TRUS) guided prostate biopsy is a routine diagnostic method for detection of prostate carcinoma. Since the first description of a TRUS guided prostate biopsy the technique has been modified many times. We aimed to compare cancer detection rates of two 12-core prostate biopsy schemes targeting the peripheral zone and to evaluate a potential impact of patient characteristics on their performance.

Materials and methods: This single-center retrospective analysis embraced TRUS-guided prostate biopsies performed in 897 consecutive patients employing two different 12-core sampling schemes. 269 patients underwent a biopsy directed towards the far lateral areas of the peripheral zone (S1) and 628 patients underwent a biopsy with six parasagittal and six laterally targeted samples covering the base, the mid zone and the apex of prostate (S2).

Results: Cancer detection rates with both schemes were similar (39.0% and 38.9%). Abnormal digital rectal exam, lower prostate volume and higher prostate specific antigen (PSA) levels were independently associated with higher odds of cancer detection. Regarding the first biopsies (n=747), there

was a significant interaction between the biopsy scheme and PSA ($p < 0.001$). Overall, adjusted odds of cancer detection were higher with S1 (S1/S2 OR=2.54, 95%CI 1.12-5.74), but the S1-S2 relationship was conditional on PSA: ORs progressively increased with increasing PSA from 0.64 (95%CI 0.40-1.02) at PSA 5 ng/mL to 39.1 (95%CI 2.71-566) at 75 ng/mL.

Discussion: The main finding of the present study is that the relative efficiency of the two protocols is conditional on the PSA concentration. Data suggest that, considering first biopsies, the sampling scheme focused on the far lateral parts (S1) appears somewhat less effective at PSA levels < 10 ng/mL and (progressively) more effective at higher PSA than the sextant biopsy scheme with additional peripheral cores (S2). This could be explained by the patterns of spread of the prostatic adenocarcinoma. The present study suggests that PSA levels should be taken into account when choosing the sampling scheme.

Acknowledgments:

MeSH/Keywords: Prostatic Neoplasms, Prostate-Specific Antigen, Biopsy

Poster code: R-B-28-27

Poster Title: THE EFFECT OF DIALYSIS MODALITY ON THE OUTCOME OF RENAL TRANSPLANTATION

PhD candidate: Ivan Neretljak, MD

Part of the thesis: Dialysis modality and renal transplantation

Mentor/s: Associate Professor Mladen Knotek, MD, PhD

Affiliation: University of Zagreb School of Medicine, Clinical Hospital Merkur, Zagreb

Introduction: Kidney transplantation is the best and ultimately the cheapest form of renal replacement therapy, which increases the overall survival of the patients. Although studies have shown that peritoneal dialysis is more economical than haemodialysis there is shortage of studies that compared the complications, outcome and cost of transplantation related to dialysis modality before transplantation. Infection is one of the most common complications after renal transplantation. Routine early removal of peritoneal catheter is advised but the optimal time remains controversial.

Materials and methods: Kidney and simultaneous pancreas and kidney recipients, transplanted 2007–2013 in Merkur Clinical Hospital, Zagreb have been included in this retrospective study. Incidence of infection was studied for the first three months after transplantation. In peritoneal dialysis patients the peritoneal catheter was removed during transplantation. Patients received triple or quadruple immunosuppressive therapy. Urinary tract infection was defined according to clinical symptoms, laboratory findings and positive microbiological results. Sepsis was defined according to Surviving Sepsis Campaign guidelines. Wound infection was defined according to the clinical manifestation and positive wound microbiological result. An intra-abdominal infection was defined as the existence of peritonitis, abdominal abscess, together with positive

microbiological results. Infections were assessed according to the cause of the infection

Results: At current date we collected data for 226 patients. 49 patient was on peritoneal dialysis and 170 patient on haemodialysis before transplantation. 7 patients were not on dialysis before transplantation. There was no statistically significant difference in analyzed data when compared to dialysis modality before transplantation. Incidence of urinary tract infections ($p=0.781$), wound infections ($p=0.392$), intraabdominal infections ($p=0.381$) and sepsis ($p=0.891$) in the first three months after transplantation, kidney function 6 ($p=0.683$) and 12 ($p=0.225$) month after transplantation, the cost of transplantation (0.693) and duration of the first hospitalization ($p=0.771$), patient ($p=0.903$) and graft survival ($p=0.823$)

Discussion: So far this study showed that there was not statistically significant difference in analyzed data. The rest of the data should be analyzed before one can assume that the results are valid.

Acknowledgments:

MeSH/Keywords: peritoneal dialysis, haemodialysis, kidney transplantation, infection, surgical wound infection

Poster code: R-B-28-78

Poster Title: CORRELATION BETWEEN ATTACHMENT STYLE AND CLINICAL DIAGNOSIS OF CONDUCT DISORDER IN ADOLESCENCE

PhD candidate: Ivana Maček, prof.reh.

Part of the thesis: Correlation between attachment style and clinical diagnosis of conduct disorder in adolescence

Mentor/s: Professor Vlasta Rudan, MD, PhD, psychiatrist and psychotherapist

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

Introduction: Attachment is a strong emotional connection with the object of attachment, in order to achieve security through maintaining proximity with the object of affection, especially in stressful situations. When this strong connection disrupted some traumatic event that can have a strong influence on the further development of the child. Such traumatic experiences and delay in the normal mental development leading to pathological patterns. Conduct disorder refers to a group of behavioural and emotional problems of children and youth. Therefore, conduct disorder as a diagnostic entity can be classified only when the symptoms persisted lasting and repeated over a period of one year.

Materials and methods: A sample of 100 adolescents 14-18 years of age who were examined in the Department of Psychological Medicine and diagnosed with conduct disorder. The control group will be 100 high school students. They will fulfilling self-report questionnaires. The assessment tools included: Questionnaire of general data, Clinical psychiatric interview, according to ICD-10 guidelines, The inventory of experiences in close relationships, Rosenberg

self-esteem scale (RSES), Child behaviour checklist -CBCL /6-18, Parental Acceptance/Rejection Questionnaire. Up to date, 10 adolescent participated in research.

Results: The study is currently in the phase of data collection and preliminary result processing. Currently is collected 10 % of the sample, out of the planed 100, 10 patient (8 females and 2 males) have completed study protocol testing and their samples are being analyzed.

Discussion: Preliminary results on small sample support the hypothesis that adolescents with conduct disorder have disorganised attachment style. For more detailed analysis and conclusions is required a larger number of patients.

Acknowledgments: Thanks to Prof.dr.sc Vlasta Rudan which supported this research, as well as all employees of the Department of Child and Adolescent Psychiatry and Psychotherapy, KBC Zagreb

MeSH/Keywords: attachment, conduct disorder, adolescence

Poster code: R-B-29-4

Poster Title: ATTACHMENT STYLE AND EMOTIONAL REGULATION IN PATIENTS WITH BULIMIA NERVOSA – PRELIMINARY RESULTS

PhD candidate: Trpimir Jakovina, MA

Part of the thesis: Attachment style and emotional regulation in patients with bulimia nervosa

Mentor/s: Ivan Begovac, MD, PhD

Affiliation: Department of Psychological Medicine, University Hospital Centre Zagreb, Zagreb, Croatia

Introduction: Bulimia Nervosa (BN) was first described by Russell in 1979, as a variant of anorexia nervosa. There are two subtypes of BN: purging and the non-purging. Both types are characterised by binge eating episodes. The purging type involves compensatory behaviours, the non-purging type may not include these purging behaviours although it may involve compensatory behaviours. Theoretical models associate BN with insecure attachment style and dysfunctional emotional regulation. Studies on BN are rare, with limited scientific evidence to support such a perspective. The aim of the study is to examine the relationship between attachment styles and emotional regulation with symptoms of BN.

Materials and methods: The Questionnaire of general data, Eating Disorders Inventory (EDI-2), Difficulties in Emotion Regulation Scale (DERS) and Experience in close relationship-revised (ECR-R) will be administered to 100 female participants 15-25 yoa. Clinical group will include 50 participants with BN, and control group will include 50 healthy matched participants. Statistical comparison and logistic regression will determine whether there are differences in factors of attachment styles and emotional regulation, as well as determine whether insecure attachment style and dysfunctional emotional regulation are positively associated with the presence of BN symptoms.

Results: By now we collected in total 28 female participants suffering from BN. The

mean age was 16.88 ± 2.16 years. Overall mean BMI was 20.14, $SD=1.65$. The preliminary results of EDI-2 subscales: Drive for thinness (DT) $M=16.87$, $SD=4.58$, Bulimia (B) $M=11.87$, $SD=6.64$, Body dissatisfaction (BD) $M=13.87$, $SD=6.57$, Ineffectiveness (I) $M=8.62$, $SD=8.71$, Perfectionism (P) $M=8.57$, $SD=4.07$, Interpersonal distrust (ID) $M=7.62$, $SD=3.37$, Interoceptive awareness (IA) $M=18$, $SD=7.85$, Maturity fears (MF) $M=13.37$, $SD=7.67$, Asceticism (A) $M=8.75$, $SD=5.89$, Impulse Regulation (IR) $M=13.28$, $SD=6.72$, and Social Insecurity (SI) $M=8.37$, $SD=6.06$.

Discussion: Since the collected data is limited and collecting of the control group data is not yet started, it is not possible to conduct the methods of comparison or logistic regression analysis. Calculated BMI is in the range expected for the bulimia sample ($BMI > 17.5 \text{ kg/m}^2$). So far, we analysed data for EDI-2. Initial results of all EDI-2 subscales are higher than the typical profile for healthy subjects. The results were consistent with expectations for the group of patients with BN, except subscales IA and IR, which are higher than expected.

Acknowledgments: I would like to express my gratitude to my mentor Ivan Begovac, MD, PhD

MeSH/Keywords: Bulimia nervosa, attachment style, emotional regulation.

Poster code: R-B-29-53

Poster Title: PSYCHOSOCIAL DETERMINANTS OF SATISFACTION WITH HOSPITAL CARE IN ADULT PATIENTS WITH ADVANCED CANCER

PhD candidate: Maja Boban, MS psychologist

Part of the thesis: Thesis is part of project "Palliative care in Croatia"

Mentor/s: Marijana Braš, MD, PhD

Affiliation: Agency for quality and accreditation in health care and social welfare

Introduction: Patients' satisfaction in hospital is considered to be important element in quality improvement work in hospitals and also as indicator of quality of healthcare, especially in the oncology setting. According to tentative model the way that a person appraises and copes with a situation causally contributes to his or her emotional reaction. In turn, the appraisal process is shaped by interacting person-related conditions and actual, external, conditions. Sociodemographic characteristics, the individual's health condition and personality interact with external, objective, conditions. The appraisal and coping process follow the perception of actual care received and give an emotional reaction called patient satisfaction.

Materials and methods: The sample consisted of N = 75 patients. Inclusion criteria: advanced cancer (stage IV.), treatment without curative intent, ECOG = 0 or 1. Exclusion criteria: proven metastatic disease of the CNS, acute psychosis, delirium, dementia or psychoorganic syndrome, < 26 scores on MoCA. Instruments: General questionnaire, MoCA, EORTC IN-PATSAT32, mini-MAC, HADS. A cross-sectional study

Results: Age is significantly correlated only with 1 item of the satisfaction questionnaire: satisfaction with „comfort/cleanness“ ($r=0.266$, $p>0.05$). Duration of the disease is not significantly correlated with satisfaction with hospital care, HADS or mini-MAC ($p<0.05$). HADS scales and mini-MAC scales/factors are significantly correlated

($p<0.05$). Mini-MAC factor 1 (anxious-depressive preoccupation) is significantly negative correlated with some scales of EORTC INPATSAT32 ($p<0.05$). HADS and EORTC INPATSAT32 are significantly negative correlated ($p<0.05$).

Age is significant moderator variable between anxiety, depression and satisfaction with comfort/cleanness (I. block $R=0.355$, $R^2=0.126$, $p<0.05$, II. block $R=0.456$, $R^2=0.208$, $p<0.05$). Moderator and/or mediator effects of mental adaptation to cancer on the correlation between symptoms of depression and anxiety and satisfaction with care is not significant ($p>0.05$).

Discussion: Results are not completely consistent with the results of previous studies maybe due to different ways of measuring the concept of quality of care, the combination and number of conditions included in the studies, or different statistical analyses.

Acknowledgments: I would like to express my sincere gratitude to those who have made the work presented here possible and supported me throughout it. In particular, I am specially grateful to all the patients who have participated in this thesis, to all the personnel of the oncology wards at Clinical Hospital Center Zagreb and Clinical Hospital Center „Sisters of Mercy“ and to all my supervisors.

MeSH/Keywords: advanced cancer, satisfaction with hospital care, coping with stress, depression, anxiety

Poster code: R-B-29-91

Poster Title: CORRELATIONS BETWEEN TRICHOTILLOMANIA AND ATTENTION DEFICIT/HYPERACTIVITY DISORDER (ADHD) IN CHILDREN AND ADOLESCENTS

PhD candidate: Aleksandra Klobučar, MD

Part of the thesis: In children and adolescents with TTM there is a notable incidence of ADHD symptoms that make sufficient criteria for the diagnosis of one of this disorder subtypes

Mentor/s: Professor Vera Folnegović-Šmalc, MD, PhD

Affiliation: Department of child and adolescent psychiatry, Children's Hospital Zagreb

Introduction: Trichotillomania (TTM) is a relatively rare disorder. In recent editions of the Diagnostic and Statistical Manual of Mental Disorders (DSM-V, 2013), TTM is classified in the group including obsessive-compulsive and related disorders. The clinical picture in children and adolescents is often complicated by the presence of comorbidity. In children and adolescents, the most common comorbidity is in the domain of affect, specifically depression and anxiety. Attention Deficit/Hyperactivity Disorder (ADHD) is a rarely described comorbidity.

Materials and methods: It is being planned to examine a total of 120 children and adolescents in three diagnosed groups TTM (40), ADHD (40), OCD (40). The diagnosis is led by the criteria of the Diagnostic and Statistical Manual of Mental Disorders (DSM-V, 2013). The subtypes of ADHD are diagnosed by using Attention Deficit/Hyperactivity Disorder Test (ADHDT). Other instruments used in the research are Achenbach Child Behaviour Check List (CBCL), Scale of confrontation with stress for children and adolescents (SUO) and questionnaires designed for this research related to predictors and modulators of disorders (prenatal, postnatal, age, gender, family structure, occurrence of the first symptoms, stressful events).

Results: The study is still in progress, the samples are collecting. Up to now we have completed data for total of 63 patients and another 20 are in process. According to the

preliminary results, it has been shown that there is a notable incidence of ADHD (mostly attention deficit symptoms) in patients with TTM and links between these two disorders and OCD that are related to frequency, predictors and modulators. The most of processed patients are those with TTM and ADHD, but the number of patients is still not sufficient for statistical data analysis.

Discussion: The objectives of testing have been focused on analyzing each particular disorder together with the disorder subtypes and links in relation to frequency, predictors and modulators. Specific objectives are focused on determination whether there is significant incidence of certain subtypes of ADHD in children and adolescents with TTM and establishing a possible higher risk for the occurrence of TTM in children and adolescents with ADHD. The choice of psychotherapeutic techniques and broader approach to the treatment in these disorders very often depended on the comorbidity. We have to complete data collection for further statistical analysis.

Acknowledgments: I would like to thank my mentor for advices and support during this investigation.

MeSH/Keywords: Trichotillomania, Attention Deficit/Hyperactivity Disorder – ADHD, children and adolescents, comorbidity, risk factors.

Poster code: R-B-29-143

Poster Title: PREVALENCE OF PATHOLOGICAL RESPONSE TO ORTHOSTATIC PROVOCATION IN PATIENTS WITH CLINICALLY ISOLATED SYNDROME (CIS)

PhD candidate: Iva Milivojević

Part of the thesis: Prevalence of pathological response to orthostatic provocation in patients with clinically isolated syndrome (CIS)

Mentor/s: Assist. Prof. Mario Habek, MD, PhD

Affiliation: Special Hospital for Physical Medicine and Rehabilitation Krapinske Toplice

Introduction: The aim of this study was to determine the prevalence of pathologic response to orthostatic challenge in patients with clinically isolated syndrome (CIS) suggestive of multiple sclerosis (MS) and to correlate autonomic dysfunction with clinical and MRI findings and EDSS (expanded disability status scale) score.

Materials and methods: We included 133 CIS patients, 45 males and 88 females. The pain-provoked head up tilt table test (PP-HUTT) was used to provoke an orthostatic reaction. After 15-min rest in the supine position, patients were tilted at 70° during 10 min or until symptoms occurred. If there were no symptoms after initial 10 min, a painful stimulus with the insertion of 0.7 mm needle into the dorsum of hand subcutaneously for 30 s was performed with the patient in the tilted for further 5 min. Blood pressure and cardiac rhythm were continuously monitored. The tilt table was lowered when the subject developed a positive response (syncope or presyncope), or when the test ended according to the protocol.

Results: Altogether 68 patients (51.1%) had one or more pathological responses: orthostatic hypotension (OH) (N=16), vasovagal syncope (N=38) and postural orthostatic tachycardia (POTS) (N=26). Although there was no significant difference ($p=0.059$) between EDSS and pathological

response, patients with low EDSS tend to have fewer pathological response. We found there was significant correlation ($p=0.009$) between syncope and EDSS. Patients without syncope on PP-HUT more often had lower or normal EDSS. There was no significant difference ($p=0.126$) between type of CIS and type of pathological response to orthostatic provocation. There was no significant difference ($p=0.425$) between BS-EDSS (brainstem EDSS) and pathological response.

Discussion: Preliminary results of this study have shown that orthostatic intolerance is frequent in the initial phase of MS. As autonomic dysfunction is not routinely assessed in CIS patients this data stresses the importance of tilt table testing in work-up of patients with a disseminated disease of the central nervous system. Furthermore, these results could have a significant impact on the management of CIS patients since a number of them present with nonspecific symptoms characteristic of autonomic dysfunction such as dizziness, fatigue, vision blurring.

Acknowledgments:

MeSH/Keywords: clinically isolated syndrome, head up tilt table test, autonomic dysfunction

Poster code: R-B-30-126

1.3.

Public Health and Health Care – Research Abstracts

Poster Title: MARKOV MODEL FOR PREDICTING PREVALENCE OF SKIN MELANOMA IN CROATIA

PhD candidate: Goran Benčina

Part of the thesis: Epidemiological models of therapy, diagnostics and prevention of melanoma

Mentor/s: Ranko Stevanović

Affiliation: GlaxoSmithKline

Introduction: Basal cell carcinoma, squamous cell carcinoma and melanoma are three most common types of skin cancer. Malignant melanoma (MM) is cancer of melanocytes, which is very aggressive and with high metastatic potential. Unless treatment is received very early – before the melanoma reach 4 mm depth, prognosis is very poor. MMs are below 2 % from total skin cancer diagnosed, but they account for about 80% of skin cancer deaths. Objective of this study is to estimate prevalence of melanoma in Croatia in year 2013.

Materials and methods: This study develops forecasts of the number of people with diagnosed melanoma in Croatia in year 2013. A Markov modeling framework was used to generate forecasts by melanoma staging. The model forecasts the number of individuals in each of four stages (diagnosed with local disease, regional disease - melanoma with lymph node involvement, distant disease – metastatic melanoma and unknown stage) in 2013. The source of data is Croatian Cancer data registry which provides national data on melanoma incidence and mortality. Data for period from 2008. – 2012. is recorded by stages, sex and age. Model is calculating prevalence by multiplying the incidence with overall survival taking

into account the different survival data per staging.

Results: The projected number of people with diagnosed melanoma in Croatia in 2013. is 2236. Local disease accounts for about 72,6 %, regional disease 20,7% and metastatic melanoma around 6,7%. When diagnosed 66% patients have local disease, 22% regional disease and 12% metastatic disease.

Discussion: Compared to Western European countries in Croatia melanoma is still diagnosed in late stages and with poor survival rates. Despite many public health campaigns and education melanoma health burden is still increasing and close monitoring will be needed. The diagnosis of melanoma at an early stage can save lives, reduce treatment costs and generates significant savings directly and indirectly, furthermore the funds could be redirected towards programs of prevention and early detection of melanoma or be invested in drugs for the treatment of advanced-stage patients.

Acknowledgments:

MeSH/Keywords: melanoma, epidemiology, Markov model

Poster code: R-C-1-10

Poster Title: ASSOCIATIONS OF CYTOKINE GENE POLYMORPHISMS WITH ATOPIC RESPIRATORY DISEASES

PhD candidate: Željka Babić

Part of the thesis: Association of cytokine gene polymorphisms TNF α -308G>A and -238G>A, IL1 α -889C>T and IL10 -1082G>A with atopic respiratory diseases

Mentor/s: Jelena Macan

Affiliation: Institute for Medical Research and Occupational Health

Introduction: Since cytokine genetic polymorphisms influence protein expression and inflammation, genetic polymorphisms of TNF α , IL1 α and IL10 could influence the odds of having atopic asthma and/or rhinitis.

Materials and methods: Participants (N=356) were part of a larger study concerning atopic diseases in Croatian young adult population (median age 19 years, range 18-29). Diagnosis of atopic asthma (AA) and atopic rhinitis (AR) was based on symptoms reported by modified "International Study of Asthma and Allergies in Childhood" questionnaire and positive skin prick test to at least one common inhalatory allergen (SPT). Atopic respiratory disease was defined as having AR and/or AA. Genetic polymorphisms TNF α -308G>A and -238G>A, IL1 α -889C>T and IL10 -1082G>A were genotyped from buccal swab samples using polymerase chain reaction-based technique. Univariate and multivariate data analysis controlled for personal characteristics (gender, body mass index), lifestyle factors (smoking, pet ownership), environmental factors (urban/rural residency, residency in continental /Mediterranean region) and history of atopic disease in parents was performed.

Results: There were 26 (7%) subject with AA, 63 (18%) with AR and 72 (20%) with AA and/or AR (i.e. atopic respiratory disease). Among subjects with AA, 1 (4%) was TNF α -308G>A carrier, which was significantly

lower than 76 (24%) carriers in non-AA subjects (Fisher's exact = 0.022), but this association was not confirmed in multivariate analysis. Among subjects with atopic respiratory disease, 23 (35%) were IL1 α -889C>T carriers, significantly less than 133 (50%) carriers among subject without atopic respiratory disease (Pearson chi² = 4.647, p=0.031), and this result was confirmed in multivariate model for atopic respiratory disease (P model =0.000, pseudo R² =0.26, OR=0.38, 95% CI 0.19-0.78, p =0.008) and AR alone (P model =0.000, pseudo R² =0.38, OR=0.35, 95% CI 0.17-0.86, p =0.020). There were no other significant associations of atopic respiratory diseases with studied polymorphisms.

Discussion: The most consistent result indicate that AR is significantly less common among carriers of IL1 α -889C>T polymorphism. We addressed the confounding factors by recruiting only young adults, using objective criteria for diagnosis, and controlling for the effect of environmental and lifestyle factors.

Acknowledgments: Study was performed under the Grant 022-0222411-2410, Croatian Ministry of Science, Education and Sports and with support of the COST Action BM0903.

MeSH/Keywords: atopy, asthma, rhinitis, cytokine, polymorphism

Poster code: R-C-1-157

Poster Title: THE ROLE OF SOCIAL SUPPORT IN THE RELATIONSHIP BETWEEN FAMILY CHARACTERISTICS AND HEALTH-RISK BEHAVIORS

PhD candidate: Lidija Čilić Burušić

Part of the thesis: The role of social support in the relationship between family characteristics and health-risk behaviors

Mentor/s: Professor Dubravka Kocijan Hercigonja, PhD

Affiliation: Croatian National Institute of Public Health, SUVAG Polyclinic

Introduction: Researches in the field of adolescent health-risk behaviors have pointed to a number of determinants of health and have indicated the need in recognizing mediators in the expression of certain health behaviors. The central interest of this paper is to empirically verify and explain the role of social support as a possible mediator in the expression of health-risk behaviors among adolescents who come from families with different socioeconomic conditions.

Materials and methods: The data are collected during 2010 within the international project Health Behaviour in School-Aged Children with the participation of the Croatian representative sample of adolescents (3244 girls and 3018 boys). The project in Croatia leads and coordinates the Croatian National Institute of Public Health. Indicators of social support will be used as moderator measures and it will be expressed through: the source and strength of social support, peers social support, a sense of acceptance in the peers group, the amount of time that adolescents spend with their peers.

Family characteristics will be used as predictor measures and they are: family structure and family socioeconomic status.

Adolescent health-risk behaviors are the criterion measure and it will be expressed through: food habits, physical activity, alcohol, tobacco and cannabis use, being bullied and bullying others.

Results: Preliminary statistical analysis of the part of data showed that adolescents who easily communicate with their parents, consume less alcohol than their peers who communicate with parents with more difficulty.

Discussion: The obtained results are in accordance with the established hypothesis that should be then checked in their entirety by moderated regression analysis.

Acknowledgments:

MeSH/Keywords: social support, health-risk behaviors, family characteristics

Poster code: R-C-2-40

Poster Title: OUTPATIENT UTILIZATION OF CARDIOVASCULAR DRUGS

PhD candidate: Maja Marić Bajs, MD

Part of the thesis: The Quality of Prescribing and Rational Outpatient Utilization of Cardiovascular Drugs in the City of Zagreb

Mentor/s: Associate Professor Danijela Štimac Grbić, MD, PhD

Affiliation: Andrija Stampar Teaching Institute of Public Health

Introduction: With a limited funding and the continuous increase in drug utilization rational drug utilization is the basis of each national health policy. Searching the literature in the field of drug utilization indicated a dominant share of utilization cardiovascular drugs both in Croatia and the European and global levels. Cardiovascular diseases are a significant public health problem and burden of the health system as a cause of mortality, morbidity and disability for work. For the purposes of standardization and comparability with other communities 70s of 20th century SZO started to develop appropriate methods for monitoring drug utilization.

Materials and methods: Based on data obtained from Zagreb Pharmacy on the number of packages for all prescription drugs indicators of DDD and number DDD/1000/day will be calculated. The distribution of utilization within the main ATC group C for each particular drug by the generic name included in the CIHI Lists of Drugs during the twelve-year period, from 2001 till 2012, in the City of Zagreb will be analyzed. The quality and rationality of prescribing will be evaluated using WHO "Drug utilization 90%" (DU90%) method and the DU90% segment step adherence to guidelines for prescribing cardiovascular drugs in accordance with current professional guidelines.

Results: Total utilization of cardiovascular drugs decreased in the 2001-2012 period from 391.5 to 325.3 DDD/1000/day. All classes of cardiovascular drugs showed a decline in consumption. The renin-angiotensin system agents showed highest share in the utilization of group C drugs, followed by hypolipemics. Total cost per DDD as well as cost per DDD within DU90% segment decreased, while Cost per DDD beyond DU90% segment and Ratio Cost per DDD beyond and within DU90% segment increased. The number of drugs within DU90% segment decreased between 2001 and 2012, although the total number of drugs increased.

Discussion: Studies of drug utilization based on the ATC/DDD methodology in the field of public health and pharmacoepidemiology are not represented or routinely used in Croatia when assessing the quality of outpatient drug consumption within certain subgroups of the ATC system. Due to the high cost of unsustainability, the economic, rational use of drugs is essential to limit further growth.

Acknowledgments: None

MeSH/Keywords: outpatient, utilization, cardiovascular drugs, ATC/DDD methodology, Zagreb

Poster code: R-C-2-58

Poster Title: PREDICTIVE VALUE OF OVERWEIGHT IN EARLY DETECTION OF METABOLIC SYNDROME IN SCHOOLCHILDREN

PhD candidate: Marjeta Majer, MD, research fellow/assistant

Part of the thesis: Predictive Value of Overweight in Early Detection of Metabolic Syndrome in Schoolchildren

Mentor/s: Professor Vesna Jureša, MD, PhD

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

Introduction: Development and presence of metabolic syndrome in children are still discussed topics with an opened question whether there is a tracking phenomenon. The aim of this thesis is to determine ability to identify risks at an early school age for development of metabolic syndrome in adolescence.

Materials and methods: Longitudinal study included 481 students (mean age 17.93 y) which is 49.64% proportional sample of the initial cohort (N=969) from a representative sample of first-grade students of elementary school year 2003/2004. Respondents completed questionnaire, and anthropometric measurements and laboratory analysis of blood were carried out. The CDC BMI criteria were used to define overweight and obesity. Data were processed by appropriate statistical and analytical procedures.

Results: Out of 481 students (243 girls), 18 y old, abdominal obesity had 6.3% boys and 14.8% girls. According to the BMI overweight were 20.2% boys and 10.7% girls and obese 5.0% boys and 4.5% girls, respectively. IDF criteria for metabolic syndrome at

age 18 y met 2.52% boys (N=6) and 3.70% girls (N=9). Out of that number at age 18y one of nine girls was normal weight, one of six boys and one of nine girls were overweight, and five of six boys and seven of nine girls were obese, while at age 7y two of six boys and one of nine girls were normal weight, one of six boys and two of nine girls were overweight and three of six boys and six of nine girls were obese.

Discussion: Preliminary results showed prevalence of metabolic syndrome in 18 y adolescents of 3.11% without significant difference between genders. In other studies prevalence of metabolic syndrome in children and adolescents ranges from 3-11%, depending on the applied criteria, and is higher among population of overweight and obese children, in boys and in adolescents compared to younger children.

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

MeSH/Keywords: children, adolescent, overweight, obesity, metabolic syndrome x

Poster code: R-C-2-65

Poster Title: RELATIONSHIP BETWEEN ANTHROPOMETRIC CHARACTERISTICS, MOTOR ABILITIES AND PHYSICAL ACTIVITY AMONG MEDICAL STUDENTS

PhD candidate: Tonći Mašina

Part of the thesis: Relationship between anthropometric characteristics, motor abilities, healthy habits and self-esteem among medical students

Mentor/s: Milan Milošević MD, PhD

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

Introduction: Physical activity plays an important role in the prevention of chronic non-communicable diseases. Specific working conditions and shift work which are an integral part of working environment for future physicians can have a negative impact on the habits of practicing additional physical activity and adopting healthy lifestyle.

Materials and methods: Study included 450 students from first two years of the School of Medicine, University of Zagreb. Subjects completed a questionnaire about healthy lifestyle (HPLP II), international physical activity questionnaire (IPAQ), Rosenberg self-esteem scale and were tested in some anthropometric characteristics and motor abilities.

Results: Results showed equal total physical activity in both genders on the first and second year of the study. However, male students are more physically active in the category of sport and leisure (1607.25 vs. 767.50 minutes, $P=0,02$) during the second year. By contrast, female students recorded higher values in physical activity in the category of „Domestic work“ (480.0 vs. 240.00 minutes, $P=0,02$), also in the second year of the study. At the first year, female students spend more time in the sitting position in relation to men (420.00 vs. 360.00 minutes, $P=0,01$). Significant correlations were found between physical activity (PA) and body composition (percentage of mus-

cle mass in women and biceps brachi skin folds in men), both at the second year. In the area of motor abilities, positive correlations with PA were recorded in the first year between variables that evaluated isometric muscle endurance by trunk flexors and extensors and repetitive strength of the legs, but only among female students. As opposed to that, at the second year, the significant correlations were found between PA and repetitive strength of trunk and legs and isometric muscle endurance of trunk flexors for both genders while the correlation between PA and isometric muscle endurance of trunk extensors was recorded only among female students.

Discussion: Results of a preliminary study confirm findings of previous studies in the field of physical activity among the population of students. Men often take part in various sport activities, while women are more active in carrying out domestic work. One of the important benefits of continuous physical activity is an increase in the active muscle mass that will help students as future physicians to secure good posture and movement functionality.

Acknowledgments:

MeSH/Keywords: Healthy habits, physical activity, psycho-social well-being

Poster code: R-C-2-105

2. RESEARCH PROPOSALS

2.1. Basic Medical Sciences – Research Proposals

Poster Title: EFFECTS OF BONE MORPHOGENETIC PROTEIN 2 AND 7 ON BONE METABOLISM IN RATS WITH REMOVED THYROID AND PARATHYROID GLANDS

PhD candidate: Ivo Dumić-Čule, MD

Part of the thesis: Effects of bone morphogenetic protein 2 and 7 on bone metabolism in rats with removed thyroid and parathyroid glands

Mentor/s: Professor Lovorka Grgurević, MD, PhD

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

Introduction: Bone morphogenetic proteins (BMPs) play an important role in the bone and joint regeneration. BMP2 and 7 with the bovine collagen carrier were approved for the treatment of spinal fusions, long bone non-unions and acute fractures after randomized, controlled and blinded clinical trials. The osteoinductive ability of BMP2 and 7 distinguishes them from other available bone grafts and eliminates the donor-site morbidity in contrast to autologous bone grafting. Recently, they were confronted with side-effects and unresolved clinical issues. Specifically, vertebral implant migration and subsidence as a result of early osteolysis, heterotopic ossification and retrograde ejaculation were among registered complications. Additionally, it is unknown whether their systemic release following a local implantation might impact the bone metabolism. Furthermore, it is unknown whether systemic BMP effects on bone are direct or mediated by calciotropic hormones. To answer these questions we examined effects of systemically administered BMP2 and 7 on bone in a newly developed rat model with a low level of calciotropic hormones.

Hypothesis: Systemically released BMP2 and 7 after local implantation will affect bone volume.

Aims: The general aim is to demonstrate the effect of systemically administered BMP2 and 7 on bone volume in rats. Specifically, it

will be distinguished whether BMP influence bone directly or indirectly via calciotropic hormones. Moreover, in vitro confirmation of BMP mechanism of action will be performed.

Materials and methods: Removal of thyroid and parathyroid glands (TPTx) in rats resulted in the decreased level of thyroid hormones, PTH, calcitonin and 1,25(OH)₂D₃ and a subsequent bone loss assessed by microCT and measurement of serum bone formation and resorption markers, including osteocalcin, C-telopeptide, osteoprotegerin and receptor activator of nuclear factor kappa-B ligand. Additionally, BMP2 and 7 will be tested in vitro to estimate their influence on osteoblast and osteoclast activity. The administered doses have been calculated according to published bioavailability data from pre-clinical BMP2 and 7 studies.

Expected scientific contribution: This thesis will define systemic effects of BMP2 and 7 which will enable their safe clinical use, without side-effects on bone volume. Additionally, it will scrutinize mechanism of action of commercially available BMP based bone healing devices.

Acknowledgments: -

MeSH/Keywords: bone morphogenetic protein 2, bone morphogenetic protein 7, microCT, bone volume

Poster code: T-A-2-94

Poster Title: TOXIC DOSE OF LITHIUM ON RATS AND EFFECT OF PENTADECAPEPTIDE 157

PhD candidate: Sanja Štrbe

Part of the thesis: The effect of pentadecapeptide 157 on the toxic dose of lithium on rats

Mentor/s: Professor Predrag Sikirić, MD, PHD, Assistant Professor Igor Filipčić MD, PHD

Affiliation: University of Zagreb School of Medicine, Department of pharmacology, Psychiatry hospital "Sveti Ivan"

Introduction: Lithium has been used to treat bipolar affective disorder, but for numerous side effects so far there is no antidote.

Hypothesis: Toxic dose of lithium will lead to muscle weakness, brain damage and cardiotoxicity. We believe that BPC 157 could have a positive effect on lithium side effects.

Aims: Aim is to demonstrate a positive effect of pentadecapeptide BPC 157 on muscle, heart and brain tissue during acute lithium intoxication

Materials and methods: Five rats will be randomly selected per experimental group and interval. Acute and subacute toxicity in rats will be induced by lithium intraperitoneal application at a dose of 500 mg/kg. Lithium thus will be administered once daily, at the same time in the period through one, two and three days. We will also explore the independent effect of L-NAME and

L-arginine as well as their combination with BPC 157. Muscle weakness will be considered after the administration of substance and each rat will be observed and recorded at the vertical grids during the period of 8 minutes. In inhalation anesthetized rats EKG will be recorded in all three main derivations stainless electrodes on all four limbs using EKG monitor Medtronic programmer. For pathological analysis, brain and striated muscle will be microscopically examined by a pathologist.

Expected scientific contribution: To demonstrate protective action of pentadecapeptide BPC 157 on skeletal muscle tissue, brain and heart in acute intoxication caused by toxic doses of lithium

Acknowledgments:

MeSH/Keywords: BPC 157, L-NAME, lithium toxicity

Poster code: T-A-4-24

Poster Title: THE EFFECT OF BPC 157 ON TRACHEOCUTANEOUS FISTULA HEALING IN RAT

PhD candidate: Goran Madžarac, MD

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

Mentor/s: Professor Dinko Stančić- Rokotov, MD, PhD Professor Predrag Sikirić, MD, PhD

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

Introduction: A tracheotomy is a surgical procedure that creates a temporary passage to the trachea. One of the common late complications of tracheotomy is tracheocutaneous fistula. Surgical procedure is needed to close such fistulas while pharmacotherapy is not yet established. BPC 157 is an original anti-ulcer peptide (GEPPPGKPADDAGLV, M.W. 1419) successful in trials for inflammatory bowel disease, wound treatment, effective alone without carrier. BPC 157 interfere with effects of nitric oxide system in vitro and in vivo on different models and different animal species. Previous studies which demonstrate the impact of BPC 157 and NO-system on gastrocutaneous, colcutaneous and oesophagocutaneous fistulas healing process indicate potential effect of BPC 157 through NO- system in tracheocutaneous fistulas healing process, which has not yet been investigated.

Hypothesis: Pentadecapeptide BPC 157 accelerates healing process in tracheocutaneous fistula in rat.

Aims: Aim of this study is to determine the effect of BPC 157 on tracheocutaneous healing process related to nitric oxide system blockade (L-NAME) and stimulation (L-arginine), respectively.

Materials and methods: Albino Wistar male rats are used in this experiment,

250-280 g. Tracheocutaneous fistula, 4 mm trachea and skin defect, is surgically made under anaesthesia (Thyopental 3,75 mg/100 g and Apaurin 0,375/100 g). Animals are treated according to the experiment protocol: a) saline 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 i.p., e) BPC 157 (10 µg/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 and L- arginine i.p., j) L- NAME and BPC 157 (µg) i.p., k) L- arginine and BPC 157 (µg) i.p., l) L-NAME and BPC 157 (µg) i.p., m) L-NAME and BPC 157 (ng) i.p., n) L- arginine and BPC 157 (ng) i.p., o) L-NAME and L- arginine and BPC 157 (ng) i.p.. Third, fifth and seventh postoperative day animals are euthanized with high dose of Thyopental. Trachea specimens are harvested and macroscopic and microscopic analysis is made.

Expected scientific contribution: To determine pharmacologic, nonsurgical way in treatment of tracheocutaneous fistula.

Acknowledgments:

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

Poster code: T-A-4-69

Poster Title: THE EFFECT OF PENTADECAPEPTIDE BPC 157 ON THE OPENING OF PRESENT COLLATERAL BLOOD VESSELS AFTER LIGATION OF ANTERIOR PANCREATICODUODENAL VEIN

PhD candidate: Fedor Amić, dr.med.

Part of the thesis: The effect of pentadecapeptide BPC 157 on the opening of present collateral blood vessels after ligation of anterior pancreaticoduodenal vein

Mentor/s: prof.dr.sc. Ante Tvrdeić, doc.dr.sc. Mario Zovak

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

Introduction: We theorize that in various tissues, in physiological conditions, there is a certain number of inactive blood vessels, which do not participate actively in blood distribution and are activated in case of blood stasis or ischemia. These blood vessels do not form de novo but are present in physiological conditions in organism and are activated only in pathological conditions. We also theorize that the previously mentioned effect is a precursor to the formation of new blood vessels and that BPC 157 will have special effect in activation of those blood vessels, their number and the speed of their activation, which is not shown in previous models.

Hypothesis: The ligation of anterior pancreaticoduodenal vein will cause duodenal stasis and congestion which, if left uncountered, will cause duodenal lesions. We theorize that BPC 157 will enhance healing causing the opening of greater number of already present collateral blood vessels, opposed to control groups in which the number of opened blood vessels will be significantly lesser in the same period of time.

Aims: The goal is to show the healing effect of pentadecapeptide BPC 157 on healing of duodenal lesions by fast opening of present collateral blood vessels after ligation of anterior pancreaticoduodenal vein.

Materials and methods: The experiment is conducted on female Wistar Albino rats. Af-

ter the application of anesthetic, medial laparotomy will be preformed. After the preparation of anterior pancreaticoduodenal vein, ligation is performed in both animals simultaneously. Pentadecapeptide BPC 157 will be applied in dose of 10 μ g/kg and will be applied locally on duodenum. Duodenum will then be observed with micro camera. We will observe the speed of opening and number of collateral blood vessels 5 minutes, 24 hours and 48 hours after ligation. Length of observed duodenal segment is determined from the pylorus to the last congested blood vessel. Animals will be sacrificed after 5 minutes, 24 and 48 hours and duodenum will then be extirpated from the animal and sent to patohystologycal analysis. Between the congested blood vessels blood vessels will be counted in control and treated animals and the number of those vessels will then be compared.

Expected scientific contribution: To show the effect of BPC 157 of the number and speed of oppening of collateral blood vessels as well as the application of the observed phenomenon in treatment of conditions induced by venal congestion.

Acknowledgments: I would like to thank my supervisor at the Department of Pharmacology, University of Zagreb

MeSH/Keywords: BPC 157, collateral blood vessels

Poster code: T-A-4-110

2.2. Clinical Medical Sciences – Research Proposals

Poster Title: ESTIMATING RISK FACTORS ASSOCIATED WITH ADVERSE CARDIOVASCULAR EVENTS IN PATIENTS WITH LIVER TRANSPLANTATION

PhD candidate: Nataša Višković Filipčić, MD

Part of the thesis: Estimating risk factors associated with adverse cardiovascular events in patients with liver transplantation

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

Affiliation: University Hospital Merkur, Zagreb, Croatia

Introduction: Liver transplantation is a curative method for end-stage liver disease. This demanding procedure carries great risk for perioperative cardiovascular complications. These complications can vary from arrhythmias, through heart failure, myocardial infarction, pulmonary embolism and in worst case- death. High-risk patients undergoing transplantation, with their accompanying comorbidities, together with organs of different donor characteristics might aggravate this risk even more. There are a very few studies that link cardiovascular complications during and after liver transplantation to donor and recipient's characteristics.

Hypothesis: Despite the high risk of transplantation procedure and liver transplant recipients that usually present with several comorbidities that further increase the risk of adverse cardiovascular events following transplantation, the incidence of these events is still rather low in our population. In patients where these events occur, there might be a connection between donor and recipient's characteristics.

Aims: To estimate the incidence of new adverse cardiovascular incidents during the transplantation and in the early period following liver transplantation. In this subgroup of patients we will try to establish possible relationship between donor and recipient's characteristics.

Materials and methods: The study will be conducted at the University Hospital Merkur

in Zagreb, Croatia, in liver transplantation recipients between January 2013 and December 2015. Patients that underwent living-donor, split liver, combined and re-transplantation, those having acute hepatic insufficiency and <18 years will be excluded from the study. Medical records will be reviewed and significant data collected from pretransplantation workout, Eurotransplant donor reports, list of anaesthesia and intensive care documentation and sheets. Use of vasopressors and haemodialysis in period prior, during and after transplantation will also be noted as well as total duration of mechanical ventilation support after transplantation and ICU length of stay. Multivariable statistical analysis will be performed.

Expected scientific contribution: This study should show the level of cardiovascular complications during and following liver transplantation. If there are common patterns linking donor and recipient in regards to these complications, they might be acknowledged prior to transplantation. In such cases we might consider avoiding matching recipients and donors with susceptible traits.

Acknowledgments:

MeSH/Keywords: liver transplantation, donors, transplant recipients, risk factors, cardiovascular complications

Poster code: T-B-1-72

Poster Title: OXIDATIVE STRESS IN CHILDREN WITH HYDRONEPHROSIS. COMPARISON BETWEEN BALANCED ANESTHESIA AND TARGET CONTROLLED INFUSION

PhD candidate: Sandra Alavuk, MD

Part of the thesis: Oxidative stress in children with hydronephrosis. Comparison between balanced anesthesia and Target Controlled Infusion

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

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 (TCI/TIVA, balanced anesthesia) using BIS (Bispectral Index) and INVOS (In Vivo Optical Spectroscopy) in children subjected to Anderson - Hynes operation.

Hypothesis: Anesthesia with Target Controlled Infusion in children with hydronephrosis subjected to Anderson-Hynes operation, causes smaller degree of oxidative stress than balanced anesthesia.

Aims: To investigate which anesthesiologic technique (balanced, TCI/TIVA) causes smaller degree of oxidative stress in children with hydronephrosis subjected to Anderson-Hynes operation. We would also like to determine dynamics of oxidative markers in perioperative period.

Materials and methods: The study includes 60 patients aged 3-16. It will be carried out in children with hydronephrosis subjected to Anderson-Hynes operation because of ureteropelvic junction stenosis. All patients will

be randomized into two groups, Group 1-balanced anesthesia and Group 2-TCI/TIVA. Everybody will have the standard monitoring, INVOS (In Vivo Optical Spectroscopy) and BIS (Bispectral Index). 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.

Expected scientific contribution: Confirming the hypothesis will be the first time affirmed the value of determining oxidative stress markers in the assessment of the best anesthetic techniques between balanced anesthesia and TCI/TIVA in children with hydronephrosis undergone surgery per Anderson-Hynes method for ureteropelvic junction stenosis.

Acknowledgments:

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

Poster code: T-B-1-86

Poster Title: CORRELATION OF HISTOLOGICAL AND IMMUNOHISTOCHEMICAL PROPERTIES OF T-CELL SKIN LYMPHOMA (MYCOSIS FUNGOIDES) WITH THE CLINICAL PICTURE, STAGE AND PATIENT OUTCOME IN TEN-YEAR PERIOD

PhD candidate: Sandra Jerković Gulin, MD

Part of the thesis: correlation of histological and immunohistochemical properties of T-cell skin lymphoma (*Mycosis fungoides*) with the clinical picture, stage and patient outcome in ten-year period

Mentor/s: Assist. Prof. Romana Ceovic, MD, PhD

Affiliation: Department of Dermatology and Venereology, University Hospital Center Zagreb and School of medicine Zagreb, Department of Pathology and Cytology, University Hospital Center Zagreb and School of Medici

Introduction: Mycosis fungoides (MF) is the most common cutaneous T-cell lymphoma (CTCL). Diagnosis is based on clinical presentation and course of disease and histological and immunohistochemical analysis of bioptic samples of skin lesions. MF has many forms of clinical presentations.

Hypothesis: Patients who were diagnosed with MF in the early stage (IA, IB i IIA) and who have dense lichenoid infiltrate of lymphocytes in the dermis, big Pautrier's microabscesses and loss of CD2 surface marker in the initial biopsy will have more aggressive course of disease and worse prognosis.

Aims: The goal of this study is to determine the relationship between initial histological, immunohistochemical and clinical characteristics with disease course in patients with primary CTCL – MF in a ten-year period. Specific goals are: to determine morphological properties in the initial biopsy that correlate with disease course, to determine demographic (age and sex) and clinical properties of patients that correlate with disease course, to determine the frequency of patients with MF who were initially diagnosed with parapsoriasis, to determine duration of premitotic stage in patients with MF who were initially diagnosed with another histological diagnosis such as psoriasis, atopic dermatitis etc.

Materials and methods: Patients will be included in this retrospective study if they

were diagnosed with MF at the Department of Dermatology and Venerology and Department of Pathology and Cytology, UHC Zagreb between January 2003 and December 2012, have complete clinical data and enough stored samples for further histological and immunohistochemical studies. From existing medical documents we will anal the age, sex, clinical picture, duration of premitotic stage, response to therapy, recurrence and disease progression. Following histological and immunohistochemical characteristics will be analysed 1) lichenoid dermal infiltrate of lymphocytes, 2) Pautrier's microabscess, 3) lymphocytes keepers, 4) atypical lymphocytes and 5) loss of surface markers of T lymphocytes CD2, CD3, CD5 and / or CD7. We will determine the morphological features in the initial biopsy that correlate with the course of the disease.

Expected scientific contribution: The scientific contribution of the dissertation is reflected in the definition of initial features, demographic, clinical, morphological and immunohistochemical, which are of prognostic significance and on the basis of which it is possible to predict the course of disease more accurately.

Acknowledgments:

MeSH/Keywords: mycosis fungoides, cutaneous t cell lymphoma, prognostic factors, early diagnosis

Poster code: T-B-2-19

Poster Title: RISK FACTORS FOR DEVELOPMENT OF SKIN CANCER AFTER RENAL TRANSPLANTATION

PhD candidate: Tajana Borlinić, MD

Part of the thesis: Risk factors for development of skin cancer after renal transplantation

Mentor/s: assistant professor Zrinka Bukvić-Mokos, MD, PhD, professor Nikolina Bašić-Jukić, MD, PhD

Affiliation: Department of Dermatology and Venereology, Zagreb University Hospital Center and School of Medicine, Zagreb, Croatia, Department of Nephrology, Arterial Hypertension, Dialysis and Transplantation, Uni

Introduction: Non-melanoma skin cancers are the most frequent cancers in organ transplant recipients. Renal transplant recipients (RTRs) develop more aggressive types of skin cancers. Scientific studies imply that squamous cell carcinoma (SCC), being the more aggressive type of non-melanoma skin cancer, is more frequent than basal cell carcinoma (BCC) in renal transplant recipients. Development of skin cancers is mostly influenced by chronic UV exposure, but with RTRs age at transplantation, type, extent and duration of immunosuppression seem to be of great importance.

Hypothesis: Incidence of squamous cell carcinoma among renal transplant recipients (RTRs) is higher than the incidence of basal cell carcinoma. Stronger and longer period of immunosuppression, older age at transplantation and longer dialysis period before transplantation are independent risk factors for skin cancer development after renal transplantation

Aims: General aim: To identify independent risk factors for skin cancer development in renal transplant recipients. Specific aims: To determine incidence, type and time of development of skin cancers in renal transplant recipients. To identify population of immunosuppressed patients with high risk of skin cancer formation

Materials and methods: Patient database of the Department for Nephrology, Arterial

Hypertension, Dialysis and Transplantation, University Hospital Center, School of Medicine, University of Zagreb will be searched to identify renal transplant recipients. We will extract data of patients who developed skin cancer after renal transplantation, and determine the incidence of SCC and BCC. Data of interest will be age, total sun burden, type and duration of dialysis before transplantation, age at transplantation, time between transplantation and occurrence of first non-melanoma skin cancer, type of cancer, type of immunosuppression, duration of immunosuppression. Using the statistical methods, independent risk factors will be calculated.

Expected scientific contribution: Being able to identify and recognize specific risk factors for non-melanoma skin cancers in renal transplant recipients will help implementing early and continued dermatological surveillance regimens after renal transplantation.

Acknowledgments: I would like to thank assist. prof Bukvić Mokos and prof. Bašić Jukić for scientific guidance and Hrvoje Barić, MD for helping me with statistical methods

MeSH/Keywords: renal transplant recipient, squamous cell carcinoma, basal cell carcinoma

Poster code: T-B-2-49

Poster Title: ASSOCIATION OF SERUM CONCENTRATIONS OF INTERLEUKINS IL-18, IL-19, IL-21 AND IL-22 WITH THE ETIOPATHOGENESIS AND ASSESSMENT OF CLINICAL ACTIVITY OF NONSEGMENTAL FORM OF VITILIGO

PhD candidate: Maja Kovačević, MD

Part of the thesis: Association of serum concentrations of interleukins IL-18, IL-19, IL-21 and IL-22 with the etiopathogenesis and assessment of clinical activity of nonsegmental form of vitiligo

Mentor/s: 1. Assistant professor Vesna Lukinović Škudar 1, MD, PhD 2. Professor Andrija Stanimirović, MD, PhD 2

Affiliation: 1 Department of Physiology and Immunology, Zagreb School of Medicine, Šalata 3, Zagreb, Croatia, 2 Naftalan Special Hospital for Medical Rehabilitation, Omladinska 23a, Ivanić Grad, Croatia

Introduction: Vitiligo is pigmentary disorder characterized by appearance of depigmentation macules on skin and mucosa. The autoimmune factors have an important role in disease development. Present studies about the role of IL-18, IL-19, IL-21 and IL-22 in etiopathogenesis of vitiligo and clinical activity are limited, but those cytokines in autoimmune diseases related to vitiligo provoke inflammation and aggravate the disease.

Hypothesis: In patients with nonsegmental vitiligo (NSV), serum concentrations of IL-18, IL-19, IL-21 and IL-22 are increased in comparison to serum concentrations of these interleukins in healthy volunteers, and serum concentrations of mentioned interleukins correlate with clinical findings, disease duration and activity.

Aims: To determine a correlation between the serum concentrations of IL-18, IL-19, IL-21 and IL-22 with clinical findings (VASI score), activity of the disease (VIDA score) and disease duration in patients with NSV.

Materials and methods: 75 participants aged 18-65 (50 patients with NSV aged 18-65 and 25 age- and sex-adjusted healthy volunteers as controls) will be included in the cross-sectional study. A detailed patient history will be taken, in addition with specially designed questionnaire. Clinical examination of the patient under the visible and

UV light will be performed as well as determination of VASI and VIDA score. Skin lesions will be photographed with Canon Eos 5D MkII camera. Peripheral venous blood samples (5 mL) will be collected and serum concentrations of IL-18, IL-19, IL-21 and IL-22 in patients with NSV and control group will be determined with ELISA method, using commercial kits (MBLI for IL-18 and R and D Systems, Minneapolis, USA, for IL-19, IL-21 and IL-22). The differences in the indicated parameters between patients with NSV and the control group will be observed as well as the differences in the indicated parameters between patients with NSV depending on clinical findings (VASI score), activity of the disease (VIDA score) and disease duration. Statistical significance will be considered to be achieved when $P < 0,05$.

Expected scientific contribution: We expect that our results would expand the lacking knowledge about the role of cytokines IL-18, IL-19, IL-21, IL-22 in the complex pathogenesis of vitiligo. The obtained new data could be used for the assessment of clinical activity and prognosis of the disease and may be useful for the development of targeted biologic therapy of NSV.

Acknowledgments:

MeSH/Keywords: vitiligo, autoimmunity, IL-18, IL-19, IL-21, IL-22

Poster code: T-B-2-146

Poster Title: PREDICTING RISK OF HIGH HEALTHCARE COSTS IN ALZHEIMER PATIENTS – PROSPECTIVE COHORT STUDY

PhD candidate: Jelena Sušac, MD, psychiatrist

Part of the thesis: Predicting risk of high healthcare costs in Alzheimer patients - prospective cohort study

Mentor/s: Professor Ninoslav Mimica, MD, PhD, psychiatrist, Professor Dinko Vitezić, MD, PhD, clinical pharmacologist

Affiliation: Health Center Zagreb Zapad, University Psychiatric Hospital Vrapče

Introduction: A total of 44% of all health care resources are spent on the care of patients affected with Alzheimer's disease. Published predictive models on highest expenses are based on univariate analyses of singular factors and on cross-sectional studies. Such studies feature a high risk of systematic errors. The objective of this research is to design and internally validated multivariate predictive model which will simultaneously include all seven proven modifiable risk factors for Alzheimer's disease, the patients' sociodemographic and socioeconomic characteristics, other chronic comorbidities and the severity of dementia, the ability to perform activities of daily living and behavioral symptoms, with the aim of predicting highest costs of formal and informal care and treatment.

Hypothesis: Multivariate model including diabetes, hypertension, obesity, depression, physical and cognitive inactivity, smoking and the result of the scale "Activities of Daily Living" (ADL) has greater predictive validity for highest costs of care and treatment of Alzheimer's disease than ADL scale alone.

Aims: General aim is to establish statistical multivariate predictive model of the highest costs of formal care, informal care and treatment of patients diagnosed with Alzheimer's disease. Specific aims are: 1) determine the annual cost of informal care 2) determine the annual costs of formal care and

treatment 3) compare the informal and formal costs 4) create a model for prediction of the high cost of health care 5) internal validation of predictive models.

Materials and methods: This is unicentric, observational, applied research (prospective cohort, prognostic study). The research will be conducted at the Health Center Zagreb Zapad for a period of six months. Target population are patients diagnosed with Alzheimer's disease who live in private households at the time of inclusion in the study. Estimated sample size is 205 patients (by two-stage, stratified random sampling). The main outcome is the upper quartile of the total cost of treatment for formal and informal care. It will be measured by calculating the cost of formal medical and social care and treatment at average prices and with Resource Utilization in Dementia (RUD) questionnaire.

Expected scientific contribution: This research may contribute to understanding interrelationship of risk factors for the high cost of health care of patients with Alzheimer's disease. Such model can be valuable for better allocation of healthcare resources.

Acknowledgments:

MeSH/Keywords: Alzheimer disease, costs, predictive model

Poster code: T-B-4-36

Poster Title: THE COMPARISON BETWEEN GnRH AGONIST VERSUS hCG AS OVULATION TRIGGERS IN THE NATURAL MODIFIED IVF CYCLES

PhD candidate: Fatos Muhaxhiri MD Gynecologist/Obstetrician

Part of the thesis: The first IVF baby in the world was born as a result of fertilized egg from the natural cycle.

Mentor/s: Prof.dr.sc. Dinka Pavičić Baldani, Prof.Assoc. Zeqir Dervishi

Affiliation: University of Zagreb, School of Medicine, Clinic of Gynecology and Obstetrics-UCC of Prishtina

Introduction: The first IVF baby in the world, Louise Brown born from the in vitro fertilization in 1978 was conceived following an natural cycle IVF. Early stimulation protocols involved minimal dosage of fertility medication to retrieve more than one oocyte fearing of achieving supra physiologic levels of hormones that could probably interfere with implantation. Natural Cycle IVF compared to controlled ovarian stimulation is safer and avoids the risks associated with stimulated IVF treatments. The International Society for Mild Approaches in Assisted Reproduction (ISMAAR) has described a mode of the natural cycle IVF so called modified natural cycle IVF where the low dose medications are involved too, in terms to sustain the follicular growth by gonadotrophines aiming that more than one egg to be collected. There is now increasing emphasis on methods that make IVF safer and more patient-friendly like modified natural cycle-IVF. The cumulative success rates is higher comparing the natural IVF as the risk of spontaneous ovulation is reduced. Treatment can be repeated in consecutive cycles with lower costs than conventional cycles with no risk of ovarian hyper stimulation syndrome, and lower risk for multiple gestation.

Hypothesis: Ovulation triggering by GnRH-analogues compared to hCG provides better final oocyte maturation and the pregnancy rate in the modified natural cycle IVF.

Aims: To evaluate the effect of the natural LH in the oocyte final maturation and pregnancy outcomes in modified natural cycle IVF.

Materials and methods: Hypothesis will be tested in 150 cases of modified natural IVF. Patients will be randomized in one of the two groups by electronically generated list. Inclusive criteria will be the age of 18-38 years divided in the groups aged from 18-25, 26-34 and 35-38 years, BMI 19-30kg/m², MC d2-4: LH and FSH < 10 mIU/ml, E₂≥100, PRL=4.5-23 and TSH=0.5-2.5, AFC>6 to<12 follicles. The study will be approved by the ethical comity of the Faculty of Medicine of Prishtina, and by the comity of the Special Hospital FATI IM where the study will be conducted. Patients priory will sign an informed consent.

Expected scientific contribution: We will gain more knowledge on the impact of natural LH on the final oocyte maturation and the pregnancy rate in the modified natural IVF cycles compared to hCG.

Acknowledgments: University of Zagreb, School of Medicine, Centre for Excellence for Reproductive and Regenerative Medicine / Medical Institute FATI IM.

MeSH/Keywords: Ovulation triggering, GnRHa, hCG, modified natural cycle.

Poster code: T-B-5-52

Poster Title: MODIFICATIONS OF ANTIRETROVIRAL THERAPY IN CROATIA

PhD candidate: Šime Zekan

Part of the thesis: Factors related to antiretroviral drug modifications in individuals starting therapy in Croatia between 1998 and 2013

Mentor/s: Professor Josip Begovac, MD, PhD

Affiliation: University Hospital for Infectious Diseases „Dr Fran Mihaljević“, Zagreb/University of Zagreb School of Medicine

Introduction: Infection with the human immunodeficiency virus (HIV) is a chronic, progressive disease which starts when HIV enters the human body. If not treated this condition leads to collapse of immunologic system, opportunistic infections and death. Introduction of antiretroviral therapy (ART) dramatically changed the prognosis of these patients. Modifications to ART regimens can occur for a number of reasons.

Hypothesis: Among HIV infected patients in Croatia there is a significant difference in the number and reasons for ART modifications during the first 3 years after initiation of ART if we compare patients who started ART between 1998 and 2005 and those who started ART between 2006 and 2013.

Aims: To investigate the frequency of and reasons for ART modifications during the first 3 years after initiation of ART in a cohort of adult patients in Croatia who started treatment in the period 1998-2013. We will divide the patients in two groups: those who started ART between 1998 and 2005 and those who started ART between 2006 and 2013. To establish factors associated with ART modifications (age, sex, time from start of ART, starting ART regimen, naïve CD4 lymphocyte count, level of HIV in serum, diagnosis of AIDS, distance from HIV center, route of transmission of HIV).

Materials and methods: This is an observational longitudinal cohort study. We will use the data from the electronic database avail-

able at our HIV center and compare the number and reasons for treatment modifications. Patients treated between 1998 and 2015 will be included. Detailed demographic, clinical and treatment data will be extracted for analysis from all patients who meet the inclusion criteria. They have to be over 18 years of age, previously treatment naïve and received ART for at least one month. The time of follow up will be stopped after 3 years. The main outcome will be the change of ART. The outcome will be classified as modification due to toxicity including intolerance, virological failure or other reasons. Basic characteristics of the population will be presented and possible factors associated to drug modifications will be analyzed.

Expected scientific contribution: This research would provide insight into number and changes of drug modifications in the population of HIV infected patients in Croatia. It has not been studied on such large number of patients and in such long time period. Previous studies of ART modifications analyzed only the first change of therapy. We plan to analyze all changes in the first 3 years of treatment.

Acknowledgments:

MeSH/Keywords: HIV, Highly Active Antiretroviral Therapy, Croatia

Poster code: T-B-7-85

Poster Title: PREVALENCE AND RISK FACTORS FOR UROLITHIASIS IN PATIENTS WITH HEMOPHILIA

PhD candidate: Marijo Vodanović

Part of the thesis: Prevalence and risk factors for urolithiasis in patients with hemophilia

Mentor/s: prof.dr.sc. Silva Zupančić Šalek

Affiliation: Hematology/Haemophilia

Introduction: Haemophilia is an inherited coagulation disorder which is manifested by increased bleeding tendency due to lack of FVIII (haemophilia A) or FIX (haemophilia B) activity. Due to improved treatment patients with haemophilia nowadays have more age-related disorders such as hypertension, diabetes, thromboembolic incidents, renal diseases, urolithiasis. It is divided according to the factor activity: mild (5-40%), moderate (1-5%), severe hemophilia (<1%). Urolithiasis is the appearance of stones in the urinary tract with the incidence of 4.5 / 10,000 in the group younger than 40 years, while the prevalence varies from 1-20%. There is a correlation of recurrent hematuria and the occurrence of urinary stones. Hypercalciuria is important for the formation of stones, while the presence of stones does not depend on the severity of hemophilia.

Hypothesis: 1. Patients with haemophilia have a higher incidence of urolithiasis than the general male population. 2. Hematuria and hypercalciuria contribute urinary tract stones formation in patients with haemophilia.

Aims: 1. The first aim is to show that PWH have a higher incidence of urolithiasis in relation to the general male population. 2. Determination of risk factors for urolithiasis in PWH. 3. Influence of treatment modality (recombinant vs. plasma derived factor) on the incidence of urolithiasis.

Materials and methods: In prospective study is planned to include about 120 patients with haemophilia A and B, 60 patients with severe and 60 with mild haemophilia. Data will be collected using standard laboratory (full blood count, biochemistry (glucose, creatinine, urea, liver tests, etc), coagulation tests, urine, urinalysis 24-hour collected urine, PTH, vitamin D). Primary diagnostic radiology tool is ultrasound. Non-contrast enhanced CT will be performed if it is indicated. Results will be analyzed using standard statistical tests. All data will be entered into a database and prepared for statistical analysis that will be performed using appropriate statistical program. Depending on the distribution of data, and on whether a qualitative or quantitative data, we will use parametric or non-parametric statistical tests.

Expected scientific contribution: This results should contribute to the successful monitoring and treatment of patients with haemophilia, providing more data about the incidence and risk factors for urolithiasis.

Acknowledgments: University Hospital Center Zagreb, Department of Internal Medicine, Division of Hematology

MeSH/Keywords: haemophilia, coagulation factor, renal stone, urolithiasis

Poster code: T-B-9-13

Poster Title: GLUCOCORTICOID RECEPTOR GENE POLYMORPHISMS AND RISK OF METABOLIC SYNDROME IN PATIENTS WITH ADRENAL INCIDENTALOMA

PhD candidate: Bojana Gardijan, MD

Part of the thesis: Glucocorticoid receptor gene polymorphisms and risk of metabolic syndrome in patients with adrenal incidentaloma

Mentor/s: Associate Professor Darko Kaštelan, MD, PHD

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

Introduction: The effect of glucocorticoids is mediated through binding on the glucocorticoid receptor (GR). Various gene polymorphisms of the GR are associated with modified glucocorticoid sensitivity. Certain single nucleotide polymorphisms (SNP) are associated with increased glucocorticoid sensitivity (BclI, N363S). The ER22/23EK polymorphism is associated to a resistance to glucocorticoid action.

Hypothesis: GR gene polymorphisms ER22/23EK, BclI and N363S are associated to cortisol value in overnight dexamethasone suppression test and the risk of metabolic syndrome in patients with adrenal incidentaloma.

Aims: We aim to analyse the association of SNP of GR and the phenotype of the patient. Through analysis of the parameters of the metabolic syndrome and the sensitivity to glucocorticoid action, measured by overnight dexamethasone suppression test (DST), we aim to evaluate the association of SNP to dyslipidemia, hypertension, diabetes, insulin resistance and obesity. We plan to show the frequency of SNPs in the specific population with adrenal incidentaloma (AI), and to show the possible effect of GR polymorphisms in the development of AI.

Materials and methods: We plan to enrol 100 patients with AI verified by MSCT or MRI (based on G power analysis, X^{**2} test, 100 patients, $\alpha = 0.05$, $1-\beta = 0.95$, $\rho = 0.5$). Exclusion criteria include pheochromocytoma, primary hyperaldosteronism, adrenocortical carcinoma, Cushing syndrome, adrenal me-

tastates, use of exogenous glucocorticoids and inability to consent to the trial. Data on tumor size, hypertension, dyslipidemia, diabetes and previous cardiovascular events will be collected. Body height, weight, waist circumference and blood pressure will be measured. Complete laboratory work-up, including plasma ACTH, free urinary cortisol and overnight DST will be performed. GR polymorphisms will be determined using PCR and pyrosequencing. Statistical analysis (descriptive and analytical) using Statistica v12.0, Dell, with $p < 0.05$ to determine the association of SNPs to hormonal status or clinical phenotype.

Expected scientific contribution: To show the frequency of GR polymorphisms in the specific population with AI, and the genetic background of different response to glucocorticoid action. We expect to provide more information on the possible cause of adrenal incidentaloma. We hope to evaluate the association of GR polymorphisms and metabolic syndrome including obesity, diabetes, hypertension, depending on the hormonal analysis and glucocorticoid sensitivity

Acknowledgments: would like to thank Professor Daniela Giachino from the Department of Medical Genetics, University of Torino, Italy for the collaboration and DNA sequencing

MeSH/Keywords: glucocorticoid gene receptor polymorphism, adrenal incidentaloma, metabolic syndrome

Poster code: T-B-9-17

Poster Title: Wnt SIGNALING IN DIFFUSE GASTRIC CANCER

PhD candidate: Maja Sremac

Part of the thesis: The expression of Wnt-signaling pathway components in diffuse gastric cancer

Mentor/s: Professor Nadan Rustemović, MD, PhD², Assistant Professor Tamara Nikuševa Martić²

Affiliation: ¹University Hospital Center Zagreb, Department of Internal Medicine, Division of Gastroenterology and Hepatology, ²University of Zagreb, School of Medicine, Department of Medical Biology

Introduction: Although the overall incidence of gastric cancer has declined rapidly over the recent few decades, increase in the incidence of the diffuse subtype is concerning since it is more likely to occur in younger patients, is characterized by rapid disease progression and poor prognosis. Despite some recent advances, gastric cancer remains the third leading cause of cancer-associated death worldwide. This indicates the absence of therapeutic options, stemming from the limited understanding of the molecular mechanisms involved in carcinogenesis.

Hypothesis: Components of the Wnt - signaling pathway Dishevelled (DVL), Secreted frizzled-related protein (SFRP) and transcription factor T-cell factor-1 (TCF-1) are involved in the development and progression of diffuse gastric cancer.

Aims: The aim of our study is to assess the expression of SFRP1, SFRP3, DVL-2, DVL-3 and TCF-1 in diffuse gastric cancer and healthy gastric tissue samples to gain a better understanding of biological signaling pathways responsible for the epidemiological and clinical parameters of diffuse gastric cancer.

Materials and methods: The study will be performed on 65 diffuse gastric cancer tissues from patients who underwent total gastrectomy and 65 healthy gastric mucosa samples gained during routine endoscopy. Tissue samples will be retrieved from the ar-

chives of the Department of Pathology and Cytology at the Clinical Hospital Center Zagreb. Clinicopathological information and survival data will be collected from hospital records of patients. The expression pattern of SFRP1, SFRP3, DVL-2, DVL-3 and TCF-1 in diffuse gastric cancer and healthy gastric tissue samples will be assessed using immunohistochemical staining. The immunomarking will be classified according to location (membrane, nucleus, or cytoplasm) and intensity (absent, poor, moderate, intense). The correlation between the expression of SFRP1, SFRP3, DVL-2, DVL-3 and TCF-1 in cancer and healthy tissues and clinicopathological features will be analysed for statistical significance.

Expected scientific contribution: Although the pathogenesis of gastric adenocarcinoma is the subject of numerous studies, the molecular profile of diffuse gastric cancer is still a big mystery. Detection of the roles of genes and proteins responsible for the onset and progression of these tumors gives us potential new biomarkers and targets for the development of specific treatments.

Acknowledgments:

MeSH/Keywords: diffuse gastric cancer, Wnt-signaling pathway, Dishevelled (DVL), Secreted frizzled-related protein (SFRP), T-cell factor-1(TCF-1)

Poster code: T-B-9-23

Poster Title: USE OF DRUG-ELUTING BALLOON IN THE SIDE BRANCH OF BIFURCATION CORONARY ARTERY LESIONS

PhD candidate: Dario Gulin

Part of the thesis: Use of drug-eluting balloon in the side branch of bifurcation coronary artery lesions

Mentor/s: Jozica Šikić, MD, PhD, Professor Roman Urek, MD, PhD.

Affiliation: University Hospital Sveti Duh, Department for Cardiovascular diseases, Internal Clinic of Zagreb School of Medicine, Sveti Duh 64, 10 000 Zagreb

Introduction: Interventions on bifurcation lesions (BL) of coronary arteries belong to the most complex procedures in interventional cardiology. BL is located where the side branch (SB) separates from the major blood vessel. In recent years, with a bare metal stent (BMS) and drug-eluting stent (DES), drug-eluting balloon (DEB) was introduced. It is commonly used to treat restenosis in BMS. Based on several well-defined studies, DEB was introduced in the guidelines for percutaneous coronary interventions of the European Society of Cardiology, but for now only for treatment of in-stent restenosis (ISR) in the BMS. Recently, indications for DEB are the subject of numerous studies and include ISR in the drug-eluting stent, BL, and "de novo" lesions of large and small coronary arteries.

Hypothesis: The use of DEB into the SB of BL simplifies the complexity of treating the BL which reduces the duration of the procedure with equally good angiographic result as the application of the DES (non-inferiority).

Aims: To compare angiographic result of DEB with DES in the SB of BL comparing ISR and late lumen loss six months after the intervention. Specific goals are: to determine in the test group reduced level of target vessel failure that includes cardiac death, myocardial infarction and repeated revascularization caused by the treated lesion, to determine the association between known car-

diovascular risk factors (age, gender, family history of early coronary artery disease (diagnosis of family coronary artery disease - before 55 years in father and 65 years in mother), smoking, hyperlipidemia, diabetes mellitus, arterial hypertension, physical activity) and adverse events in the study groups.

Materials and methods: This prospective research will include 60 patients with bifurcation lesions (Medina 1,1,1, 1,0,1, 0,1,1). In investigated group it is planned to use DES in main branch and DEB in SB whereas in the control group two DES will be used. After six months coronary angiography will be performed in both groups. Angiographic status of side branch will be determined measuring ISR in control group and late lumen loss in investigated group.

Expected scientific contribution: The scientific contribution of the dissertation is reflected in the possibility of treating BL using DEB that leads to simplifying the complexity of the procedure and reducing the amount of metals in the blood vessels which can reduce the most common adverse effect, restenosis and stent thrombosis.

Acknowledgments:

MeSH/Keywords: coronary artery disease, percutaneous coronary intervention, drug-eluting stents, coronary balloon

Poster code: T- B-9-29

Poster Title: PREDICTORS OF BIOLOGICAL BEHAVIOUR OF PITUITARY TUMORS

PhD candidate: Mirsala Solak, MD

Part of the thesis: Predictors of biological behavior of pituitary tumors

Mentor/s: Associate Professor Tina Dušek, MD, PhD

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

Introduction: Pituitary tumors are benign intracranial tumors, however, from clinical point of view they can vary in terms of aggressiveness. Most of them are well defined adenomas that can be successfully removed, however, significant proportion of them are locally aggressive. Ki-67, transcriptive factor p53 and mitotic activity in pituitary tumors are considered as markers of proliferative activity.

Hypothesis: Expression of Ki-67, p53 and mitotic activity in pituitary tumors is related to proliferative activity and potential aggressive behavior.

Aims: Aim is analyze the expression of Ki-67, p53 and mitotic activity in pituitary tumors and to determine their connection to proliferative activity. We will analyze clinical course of patients with pituitary tumors during 5 years of follow up, compare Ki-67, p53 and mitotic activity to secretory type of tumors, analyze relapse rate depending on the secretory activity of tumors, investigate correlation between Ki-67, p53 and mitotic activity to progression of tumor residue, investigate correlation between these markers and 5-year survival rate and investigate correlation between Ki-67, p53 and mitotic activity and treatment response after the surgery.

Materials and methods: Proposed research is retrospective, and it will be conducted in the Department of Endocrinology, University Hospital Center Zagreb. All patients between

18 and 85 years of age referred to surgery to the Department of Neurosurgery, University Hospital Center Zagreb due to pituitary tumor since 2004 to 2011 will be included in the study. Invasiveness, relapse and progression of the tumor will be assessed by MR imaging. Detailed hormonal assessment is performed in all patients prior and after the surgery. Immunohistochemical staining and expression of Ki-67 was determined in all patients, however p53 and mitotic activity were not, so in this research we will determine their expression. We will assess response to treatment and complications, relapse and progression of the disease during 5 years of follow up. Data will be analyzed using descriptive statistic.

Expected scientific contribution: Due to unreliable prognostic indicators of pituitary tumors we are not able to select patients with unfavorable course. The proposed research will allow us to better understand specific histologic markers and their role in etiopathogenesis of pituitary tumors. Should they prove to have prognostic and predictive value they could have potential role in selecting patients with unfavorable course and applying optimal treatment.

Acknowledgments:

MeSH/Keywords: pituitary tumors, proliferation, tumor markers, invasiveness, Ki-67, p53, mitotic activity

Poster code: T-B-9-34

Poster Title: CORRELATION OF GHRELIN AND GHRELIN RECEPTOR WITH THE GRADE OF DYSPLASIA IN COLONIC ADENOMAS

PhD candidate: Sanja Stojsavljević, MD

Part of the thesis: Correlation of ghrelin and ghrelin receptor with the grade of dysplasia in colonic adenomas

Mentor/s: Professor Marko Duvnjak, MD, PhD, Docent Davor Tomas, MD, PhD

Affiliation: University Hospital Centre "Sestre milosrdnice", Zagreb, Croatia

Introduction: Obesity, as well as malignant diseases have become epidemics of the modern age. Obesity can change the relationship of concentrations of circulating ghrelin levels, lead to a relative surplus of acyl-ghrelin and deficit of des-acyl ghrelin, which could account to insulin resistance in metabolic syndrome. Prevalence of colonic adenomas, considered as precancerous lesions, accompanies the prevalence of colonic adenocarcinomas. Consummation of food with high percentage of unsaturated fat, alcohol, obesity, smoking and poor physical activity are considered as risk factors for developing colonic carcinoma.

Hypothesis: The concentration of des-acyl ghrelin is lower in patients with metabolic syndrome, and the expression of ghrelin and ghrelin receptor is higher in colonic adenomas with a higher grade of dysplasia.

Aims: With this study we will determine if and in what way does the concentration of acyl-ghrelin and des-acyl ghrelin in serum, expression of ghrelin and ghrelin receptor in colonic polyp tissue, patient anthropometric measures and other components of metabolic syndrome correlate with the type and grade of dysplasia of colonic adenoma.

Materials and methods: This is a prospective study that will include 90 patients of both genders, aged 18 to 75, with endoscopically proven colonic adenomas. If the patients agree to participate in the study, a complete medical history will be obtained,

blood tests and physical examinations connected with the presence of metabolic syndrome will be performed, as well as serum acyl-ghrelin and des-acyl ghrelin concentration will be determined with ELISA method. Pathohistological analysis of the colonic adenoma and a part of the healthy tissue will be performed, as well as immunohistochemical staining using polyclonal antibodies for ghrelin receptor and ghrelin. Patients will be divided in groups with low and high grade dysplasia of colonic adenomas, relationship between the expression of ghrelin and ghrelin receptor in colonic adenoma tissue and healthy tissue, concentrations of acyl-ghrelin and des-acyl ghrelin in serum, anthropometric measures and the components of the metabolic syndrome will be evaluated.

Expected scientific contribution: With this study a correlation between the serum concentration of ghrelin and colon adenoma dysplasia could be defined, and in that way patients with an increased risk for high grade dysplasia and colon carcinoma development easily recognized

Acknowledgments:

MeSH/Keywords: acyl-ghrelin, des-acyl ghrelin, ghrelin receptor, obesity, metabolic syndrome, colonic adenomas, dysplasia in colonic adenoma

Poster code: T-B-9-37

Poster Title: PROSPECTIVE EVALUATION OF METABOLIC FEATURES AND HYPOTHALAMIC-PITUITARY-ADRENAL FUNCTION IN PATIENTS WITH SUBCLINICAL CUSHING'S SYNDROME: RANDOMIZED STUDY

PhD candidate: Arita Haxhiu, MD, PhD Candidate

Part of the thesis: Thesis proposal

Mentor/s: Darko Kaštelan, Prof.dr.sc.

Affiliation: University of Zagreb, School of Medicine

Introduction: Adrenal incidentaloma is a mass lesion greater than 1 cm in diameter, incidentally discovered by radiological examinations, being performed for other reasons. A substantial percentage of these incidentalomas are hormonally active, with 5% to 20% of the tumors producing glucocorticoids. Autonomous glucocorticoid production without specific signs and symptoms of Cushing's syndrome is termed subclinical Cushing's syndrome (SCS). Although these patients lack many of the classical stigmata of overt Cushing's syndrome, they have a high prevalence of metabolic complications such as central obesity, hypertension, impaired glucose tolerance or type 2 diabetes mellitus and dyslipidemia, resulting from chronic exposure to slight cortisol excess. The most appropriate management of SCS is controversial, either adrenalectomy or close follow-up being recommended for their treatment.

Hypothesis: Remission of subclinical Cushing's syndrome leads to improvement of the components of metabolic syndrome.

Aims: The aim of the study is to investigate improvement of metabolic profile following remission of SCS and to find out endogenous cortisol secretion in response to stress, after unilateral adrenalectomy being performed for adrenal tumors.

Materials and methods: The prospective randomized study will include 24 patients

with SCS, 15 with pheochromocytoma and 20 with nonfunctional adrenal adenoma admitted to the division of endocrinology at Clinical University Zagreb. Patients with SCS will be randomised in 1:1 ratio in two different medical approaches: one group will undergo laparoscopic unilateral adrenalectomy while another one conservative treatment. Patients with pheochromocytoma and nonfunctional adrenal adenoma following surgery would serve as a control group. Clinical, biochemical (body mass index, waist circumference, blood pressure, fasting plasma glucose, insulin and lipid profile) and evaluation of hypothalamic pituitary adrenal (HPA) axis: (late-night serum cortisol level, 24-hour UFC, plasma ACTH level at 8 AM, serum cortisol after 1 mg overnight DST, as well as ACTH stimulation test) will be performed during first hospitalisation as well as during the follow up period.

Expected scientific contribution: The study will evaluate the benefits of surgery versus conservative treatment in patients with SCS in order to determine the best medical approach. The study also will define the need for hormonal replacement therapy in patients with adrenal tumors following unilateral adrenalectomy.

Acknowledgments:

MeSH/Keywords:

Poster code: T-B-9-43

Poster Title: CIRCULATING NEUREGULIN-1 β LEVELS AS A PREDICTOR OF PATHOLOGICAL VENTRICULAR REMODELING IN PATIENTS WITH ACUTE ST ELEVATION MYOCARDIAL INFARCTION

PhD candidate: Ozren Vinter

Part of the thesis: Circulating Neuregulin-1 β levels as a predictor of pathological ventricular remodeling in patients with acute ST elevation myocardial infarction

Mentor/s: Matias Trbušić, MD, PhD, research associate

Affiliation: University Hospital Center Sestre Milosrdnice, University of Zagreb School of Medicine

Introduction: The signalling complex consisting of the growth factor neuregulin-1 (NRG1) and its tyrosine kinase receptors ErbB2 and ErbB4 has a critical role in cardiac development and homeostasis of the structure and function of the adult heart. Research has so far shown a correlation between circulating neuregulin 1 β and prognosis in patients with ischemic cardiomyopathy and in patients with congestive heart failure with NYHA III/IV functional stadium. In other study inverse correlation between circulating neuregulin 1 β levels and severity of CAD was shown.

Hypothesis: Higher plasma circulating levels of neuregulin 1 β in patients with acute ST elevated myocardial infarction correlates with higher probability of development of pathological ventricular remodelling

Aims: The aim of the research is to determine whether there is a correlation between neuregulin 1 β plasma circulating levels in acute MI and development of pathological ventricular remodeling and whether neuregulin 1 β can be used as an independent predictor of development of ischemic cardiomyopathy.

Materials and methods: In this prospective, observational study on patients with acute

STEMI levels of circulating plasma neuregulin 1 β in acute phase will be determined using an ELISA method. Cardiac remodeling is defined with echocardiography parameters and will be assessed 6 months after the MI. In every patient the concentration of NT-proBNP as a marker of congestive heart failure will be determined.

Expected scientific contribution: Mechanism of NRG-1 β /ErbB regulatory axis and its role in heart is not completely understood. Research to date have discovered conflicting results regarding NRG-1 β levels in ischemic heart disease (lowered in coronary artery disease, elevated in stress induced ischaemia and in ischemic cardiomyopathy). The clinical relevance of this study is possible use of NRG-1 β as a biomarker that would help us identify patients at high risk for developing ischemic cardiomyopathy and therefore in need of a more intensive therapy and follow up.

Acknowledgments:

MeSH/Keywords: STEMI, neuregulin 1 β , ischemic cardiomyopathy, pathological ventricular remodeling

Poster code: T-B-9-48

Poster Title: CORRELATION OF ESTROGEN RECEPTOR ALFA AND INTERLEUKIN 6 POLYMORPHISM WITH ENDOTHELIAL FUNCTION IN ASYMTOMATIC DESCENDANTS OF PATIENTS WITH EARLY CORONARY DISEASE AND ACUTE CORONARY SYNDROME

PhD candidate: Zoran Miovski, MD

Part of the thesis: Correlation of estrogen receptor alfa and interleukin 6 polymorphism with endothelial function in asymptomatic descendants of patients with early coronary disease and acute coronary syndrome

Mentor/s: Ass. Prof. Ljiljana Banfić, MD. PhD

Affiliation: University Hospital Centre Zagreb, Department of cardiovascular diseases

Introduction: Coronary artery disease (CAD) is the leading cause of death in developed countries. The key moment in the development of coronary artery disease is endothelial dysfunction. According to large studies 40% of patients with acute coronary syndromes had three or more classical risk factors, and 60% of patients had only few classical risk factors. In those patients it is believed that hereditary factors have a strong influence. Described hereditary factors for coronary heart disease are estrogen receptor alfa polymorphism (ER α) and polymorphism of interleukin 6 (IL6). Studies showed strong correlation between endothelial dysfunction and coronary disease.

Hypothesis: Asymptomatic descendants of patient with early CAD and acute coronary syndrome (ACS) who inherit ER α and/or IL6 polymorphism will have significantly greater endothelial dysfunction than descendant without ER α and IL6 polymorphism

Aims: Main aim is to analyse correlation between ER α /IL 6 polymorphism and endothelial (dis)function using FMD method

Materials and methods: Prospective study will be performed in University Hospital Centre Zagreb. First phase will include at least 50 patients (M \leq 45 y., F \leq 55 y.) with CAD who will develop ACS. Diagnosis of ACS is based on symptoms, ECG and levels of troponine (ESC guidelines). Levels of troponine T, CK, LDH, cholesterol, LDL, HDL, triglycerides, apoA, apoB, hsCRP, IL6, will be measured to

the CAD patients. Coronary angiography (or percutaneous coronary intervention) will be performed to patient with ACS using transfemoral or transradial approach. Using PCR method, TA length of estrogen receptor alfa will be analysed. According to the length of TA sequence, patient will be divided to those who have short length TA polymorphisms (<18 „S“) and those who have long length TA polymorphisms (\geq 18 „L“). Subjects can have this allelic form: SS, LL, SL. Allelic forms that are connected to CAD are LL and SL. IL6 -174 G>C genotyping will be done using PCR method. According to the polymorphism and allelic forms subject will be grouped: GG, CC, and GC. Allelic forms that are connected to CAD are CC and CG. Second phase will include asymptomatic descendants of patients with early CAD and ACS who have ER α /IL6 polymorphism. FMD will be performed on right brachial artery using Aloka alfa 10 and 2002. FMD guidelines.

Expected scientific contribution: Early detection of young healthy individuals with endothelial dysfunction and hereditary risk factors for cardiovascular disease can result in earlier medical intervention and finally reducing coronary artery disease mortality

Acknowledgments:

MeSH/Keywords: Coronary artery disease, estrogen receptor alpha, IL6, FMD, endothelial dysfunction

Poster code: T-B-9-55

Poster Title: EFFECTIVENESS OF LONG TERM DOPAMINE AGONISTS THERAPY IN PATIENTS WITH PROLACTINOMA

PhD candidate: Arta Haxhiu, MD, PhD candidate

Part of the thesis: Thesis proposal

Mentor/s: Doc. Tina Dusek MD, PhD

Affiliation: University of Zagreb, School of Medicine

Introduction: Prolactinomas are the most common hormone-secreting pituitary tumours. The diagnosis of prolactinomas has been simplified in recent years, and only prolactin (PRL) assay and MRI of the sella are required. Given the remarkable success of dopamine agonist (DA) therapy in lowering prolactin levels, decreasing tumour size, and restoring gonadal function, medical therapy has become the mainstay of treatment for both micro and macro-prolactinoma. In general, transsphenoidal surgery is restricted to: patients with pituitary apoplexy, patients who have persistent chiasmal compression with visual loss despite DA therapy and to patients unresponsive to DA therapy. This group represents only a small percentage of patients. Current challenges related to the management of prolactinoma remain in the: recurrence of the disease after withdrawal of DA, the potential of increased risk of cardiac valvulopathy which is observed in patients treated with high-dose cabergoline for Parkinson's disease and treatment of prolactinoma in pregnancy. Although most prolactinomas are biochemically well controlled by pharmacological treatment, long-term follow-up is required

Hypothesis: In prolactinoma cessation of long term DA therapy in majority of patients leads to recurrence of symptoms and hyperprolactinaemia.

Aims: The study is planned to assess the efficacy of long term DA therapy as well as to

investigate whether the withdrawal of DA treatment is safe and effective.

Materials and methods: The retrospective study will include 100 patients with prolactinoma admitted in Division of Endocrinology at Clinical University Zagreb from 2008-2014. Several important outcomes (improvement of clinical symptoms, prolactin normalization, tumour shrinkage and restoration of pituitary function), following treatment (2,3 and 4 years) with DA therapy will be evaluated. Clinical, biochemical and radiological evaluation also will be performed in patients following DA therapy withdrawal in order to detect remission or refractory disease.

Expected scientific contribution: To determine: 1. Potential predictors for maintaining prolonged remission after the discontinuation of DA therapy. 2. The maximum effective and safe doses, for symptomatic patients with macroprolactinoma not responsive to standard doses of DA therapy, that will lead to significant tumor volume reduction before considering transsphenoidal surgery. 3. After what period of time will the satisfactory responses of DA therapy in tumor size reduction no longer be expected.

Acknowledgments:

MeSH/Keywords:

Poster code: T-B-9-62

Poster Title: KETOSIS AND DIABETIC KETOACIDOSIS IN TYPE 2 DIABETES MELLITUS

PhD candidate: Ivan Kruljac

Part of the thesis: Hyperglycemic crises in patients with diabetes mellitus in Republic of Croatia

Mentor/s: Milan Vrkljan MD, PhD, Professor of medicine

Affiliation: University Hospital Center "Sestre milosrdnice", Zagreb, Croatia

Introduction: Diabetic ketoacidosis (DKA) is a common acute complication of type 1 diabetes mellitus (T1DM). Ketosis precedes the onset of DKA in these patients. Increasing evidence exists that DKA can occur in patients with type 2 diabetes mellitus (T2DM). Studies have shown that up to 50% of patients with DKA have T2DM. However, these studies have included patients of afro-american, hispano-american or asian ethnicity and they did not determine the incidence of DKA in patients with T2DM. On the other hand, clinical implications and the incidence of diabetic ketosis is unknown for patients with T2DM. **HYPOTHESIS:** Ketosis and DKA are common complications of T2DM and their overall incidence is higher in T2DM. Patients with ketosis and DKA have similar characteristics. Hence, ketosis precedes the onset of DKA in T2DM.

Hypothesis: Ketosis and DKA are common complications of T2DM and their overall incidence is higher in T2DM. Patients with ketosis and DKA have similar characteristics. Hence, ketosis precedes the onset of DKA in T2DM.

Aims: The aim of this study is to determine the incidence of ketosis and DKA in well defined Croatian population and to detect clinical and laboratory parameters that can serve as predictors of DKA and ketosis.

Materials and methods: Search for patients with diabetes mellitus in electronic database of all patients examined in emergency de-

partment of University Hospital Center "Sestre milosrdnice" in the period between January 1st 2010 and January 1st 2015 will be carried out. Prevalence of diabetes mellitus will be compared to standard European population. Standardized prevalence ratio will be calculated in order to assess the quality of the sample. Standardized incidence of ketosis and DKA will be calculated in patients with plasma glucose >13.9 mmol/L. Multivariate models will be used to detect clinical and laboratory parameters which can serve as prognostic factors for DKA or ketosis.

Expected scientific contribution: This study is first to determine the incidence of ketosis and DKA in T2DM. We will be able to compare the characteristics of DKA in patients with T1DM and T2DM. Prognostic factors for DKA and ketosis will be detected, which could potentially change the strategies in treatment and follow-up of patients with T2DM.

Acknowledgments: I wish to thank Vedran Ostojić MD and Mario Štefanović MD PhD for the development of patient database and Mario Šekerija MD, PhD for the epidemiological data on prevalence of diabetes mellitus.

MeSH/Keywords: ketosis-prone diabetes mellitus, type 2 diabetes mellitus, diabetic ketosis, diabetic ketoacidosis, incidence

Poster code: T-B-9-67

Poster Title: ASSOCIATION BETWEEN ACE GENE POLYMORPHISMS AND SEVERITY OF SYSTEMIC SCLEROSIS

PhD candidate: Boris Karanović, MD

Part of the thesis: Association between ACE gene polymorphisms and severity of systemic sclerosis

Mentor/s: Professor Branimir Anić, MD, PhD

Affiliation: School of Medicine University of Zagreb, Department of Clinical Immunology and Rheumatology, University Hospital Center Zagreb

Introduction: Angiotensin converting enzyme (ACE) is a widely distributed enzyme, with roles in various pathophysiological conditions. It is controlled by an ACE gene on chromosome 17 (17q3). More than 160 polymorphisms of ACE gene were found, with one polymorphism, including insertion (I) or deletion (D) of 287-bp DNA sequence on introne 16 of the ACE-gene that distinguishes subjects with greater activity of ACE (DD) compared to other subjects (II). Systemic sclerosis is characterised by micro and macrovascular changes. It is possible that ACE has a role in susceptibility, as well as severity of clinical presentation of systemic sclerosis. Researches in this field are contradictory and inconclusive.

Hypothesis: ACE gene polymorphisms correlate with severity of phenotypic manifestations of systemic sclerosis.

Aims: Main aim is to correlate ACE gene polymorphisms and phenotype of systemic sclerosis, including correlation between ACE gene polymorphisms and age of onset of the disease, differences between distal and proximal sclerosis, severity of clinical manifestations in other autoimmune diseases and the correlation between disease severity and use of ACE inhibitors.

Materials and methods: With the approval of medical ethics committee, 82 patients (with possible extra addition of patients) fulfilling the strict ACR inclusion criteria and

under the care of Department of Clinical Immunology and Rheumatology, University Hospital Center Zagreb, enrolled in EULAR Scleroderma Trials and Research group (EUSTAR) project, will be investigated. Every patient will undergo blood sampling for ACE gene analysis performed in laboratory in our Institution. Other data will be obtained from patients' medical history, and clinical evaluation. Data from the initial patient visit, as well as one visit annually through 3-4 years, will be analysed. Severity of lung interstitial fibrosis will be assessed by HRCT, spirometry and CO diffusion, pulmonary hypertension by echocardiography, severity of Raynaud phenomenon and peripheral vasculopathy by Rodnan score and ankle brachial index (ABI) and renal insufficiency by laboratory findings.

Expected scientific contribution: This research may contribute to better understanding of systemic sclerosis. The results could be implemented in everyday medical practice by using ACE genotype as a marker for assessment of severity of the disease, thus distinguishing patients in need for more aggressive treatment and more frequent evaluations.

Acknowledgments:

MeSH/Keywords: systemic sclerosis, ACE, gene polymorphism

Poster code: T-B-9-95

Poster Title: THE ROLE OF MARKERS OF ENDOTHELIAL DYFUNCTION: ASYMMETRIC DIMETHYLARGININE AND NITRIC OXIDE IN THE ASSESSMENT OF CARDIOVASCULAR RISK AFTER LIVER TRANSPLANTATION

PhD candidate: Maro Dragičević, dr. med.

Part of the thesis: The role of markers of endothelial dysfunction: asymmetric dimethylarginine and nitric oxide in the assessment of cardiovascular risk after liver transplantation

Mentor/s: doc.dr.sc. Anna Mrzljak, dr.med., dr.sc. Marijana Vučić Lovrenčić, spec. med. biokemije

Affiliation: University hospital "Merkur"

Introduction: Cardiovascular (CV) diseases are the leading cause of mortality in patients with stable liver graft function. Assessment of CV risk based on traditional risk factors in this population is insufficient. Endothelial dysfunction is the first step in the development of atherosclerosis, which is the main feature of CV diseases. Asymmetric dimethylarginine (ADMA) and nitric oxide (NO) have an important role in the development of endothelial dysfunction and they can be seen as indicators of early CV risk, as shown by numerous studies on general population. The aim of this prospective study is to investigate the dynamics and the role of markers of endothelial dysfunction (ADMA/NO) in a population of patients one year after liver transplantation and explore their correlation with known CV risk factors in order to more adequately assess the risk and consequently reduce CV mortality and morbidity in transplanted patients.

Hypothesis: After liver transplantation, increasing levels of ADMA and decreasing levels of NO, in patients with stable liver transplant function, correlate with an increased CV risk.

Aims: The main objective is to investigate the dynamics and the role of markers of endothelial dysfunction (ADMA/NO) in a population of patients one year after liver transplantation and explore their correlation with known CV risk factors.

Materials and methods: The study will include about 160 patients who are candidates for liver transplantation. Predefined parameters will be determined before and after LT. Most of these parameters are used for the evaluation of the classic CV risk factors. Levels of ADMA and NO will be determined at the time of allocation of the liver graft as well as 6 and 12 months after LT.

Expected scientific contribution: This study would help to determine the prevalence of CV diseases before LT and the incidence of CV risk factors after LT. It would also determine the dynamics and the role of markers of endothelial dysfunction (ADMA/NO) in a population of patients one year after liver transplantation and explore their correlation with known CV risk factors in order to more adequately assess the risk and consequently reduce CV mortality and morbidity in transplanted patients. Furthermore, the results of this study could open a pathway towards other intervention which goal would be to restore the homeostasis of NO in the liver transplant recipient.

Acknowledgments:

MeSH/Keywords: cardiovascular diseases, liver transplantation, endothelial dysfunction, atherosclerosis, asymmetric dimethylarginine (ADMA), nitric oxide (NO)

Poster code: T-B-9-130

Poster Title: N-GLYCOSYLATION OF IMMUNOGLOBULIN G IN CHRONIC GRAFT-VERSUS-HOST DISEASE AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

PhD candidate: Ema Prenc, M. biol.

Part of the thesis: N-glycosylation of immunoglobulin G in chronic Graft-versus-Host disease after allogeneic hematopoietic stem cell transplantation

Mentor/s: Steven Z. Pavletic, Drazen Pulanic

Affiliation: Affiliation: University of Zagreb School of Medicine, Šalata 3, HR-10000 Zagreb, Croatia/ Research Institution: Clinical Hospital Center Zagreb, Kišpatičeva 12, HR-10000 Zagreb, Croatia

Introduction: Chronic graft-versus-host disease (cGVHD) is a systemic alloimmune and autoimmune disorder and major late complication after allogeneic hematopoietic stem cell transplantation (alloHSCT). However, pathogenesis of cGVHD is still poorly understood. Among other, the disease is characterized by an altered homeostasis of the humoral immune response and the production of allo- and autoantibodies. Immunoglobulin G (IgG) is the most abundant glycoprotein in human plasma and the main effector molecule of the humoral immune response. Changes in IgG glycosylation are associated with a number of autoimmune diseases. This research will be the first to analyze the IgG glycosylation in cGVHD patients and to determine associations of different glycoforms with clinical manifestations of cGVHD.

Hypothesis: We hypothesize that N-glycosylation of plasma IgG of cGVHD patients will be associated with clinical manifestations of cGVHD, and could lead to development of potential diagnostic or prognostic biomarkers of cGVHD.

Aims: Aims of this study are to determine association of IgG N-glycosylation with: 1) severity and activity of cGVHD, 2) demographic characteristics of cGVHD patients and clinical manifestations of cGVHD and 3) laboratory markers of inflammation in patients with cGVHD.

Materials and methods: Plasma samples were collected as part of the cross-sectional study "Natural History Study of Clinical and Biological Factors Determining Outcomes

and Chronic Graft-Versus-Host Disease" (04-C-0281, clinicaltrials.gov identifier: NCT00331968) led by Prof. Steven Z. Pavletic (National Cancer Institute, National Institutes of Health, Bethesda, USA) from 2004 to 2014. The study collected 250 plasma samples of cGVHD patients and 10 control plasma samples (patients after alloHSCT, without cGVHD). Included patients have been diagnosed with cGVHD according to the established NIH criteria. Glycan composition will be analyzed by high-resolution biochemical methods (liquid chromatography and mass spectrometry). Additional 35 plasma samples (30 cGVHD patients and 5 non-cGVHD controls) are being collected through UKF project of the University of Zagreb School Of Medicine at Clinical Hospital Centre Zagreb and will be analyzed following the same protocol.

Expected scientific contribution: It is expected that N-glycosylation analysis of plasma IgG will contribute to understanding of the disease biology and could lead to development of potential biomarkers of cGVHD.

Acknowledgments: This research is supported by Unity through Knowledge Fund (UKF) project entitled "Clinical and biological factors determining severity and activity of chronic graft-versus-host disease after allogeneic hematopoietic stem cell transplantation".

MeSH/Keywords: allogeneic hematopoietic stem cell transplantation, chronic Graft versus Host Disease, immunoglobulin G, N-glycosylation

Poster code: T-B-9-149

Poster Title: IMMUNOHISTOCHEMICAL EXPRESSION OF CONNEXIN 43 AND NEDD9 IN GASTRIC CANCER

PhD candidate: Ivan Lerotić

Part of the thesis: Immunohistochemical expression of connexin 43 and NEDD9 in gastric cancer

Mentor/s: Davor Hrabar, MD, PhD

Affiliation: Sestre milosrdnice University Hospital Center (Ljudevit Jurak University Department of Pathology, Department of gastroenterology and hepatology)

Introduction: Gastric cancer (GC) is the second most common cause of cancer-related death worldwide and factors promoting metastasis are still unknown. Gap junctions and connexins are downregulated in various cancers suggesting their tumor-suppressive effect. However, some recent studies suggest that connexins may play a positive role in the process of metastasis. Connexin 43 (Cx43) is major connexin homolog expressed in gastric tissue. Another possible control point in GC metastasis could be the protein NEDD9, a scaffolding protein identified as a key protein in tumor cell proliferation and migration. Increased expression of NEDD9 results in increased metastatic potential in several tumors, and some recent studies suggested that same role also in GC.

Hypothesis: Differences in expression of proteins NEDD9 and Cx43 reflect the metastatic potential of GC tumor cells, which should thus demonstrate concurrently reduced immunohistochemical expression of Cx and increased expression of NEDD9 in metastatic as compared with non-metastatic GC.

Aims: The aim of this study is to determine and compare the immunohistological expression of Cx43 and NEDD9 in primary gastric tumors with and without lymph node or distant metastases, and to explore the clinical and pathological correlations of expression of these proteins.

Materials and methods: This retrospective study will analyze immunohistochemical expression of Cx43 and NEDD9 in 50 cases of GC without metastases and 50 cases of GC with lymph node and/or distant metastases. Expression of Cx43 and NEDD9 will be analyzed by measuring the intensity of immunohistochemical staining as well as the percentage of positive tumor cells in tissue samples. Immunohistochemistry will be performed using formalin-fixed, paraffin-embedded tissue sections (thickness 5 μ m). Deparaffinization and immunohistochemical staining are carried out following microwave streptavidin immunoperoxidase (MSIP) protocol and by the use of labeled streptavidin-biotin (LSAB) method on DAKO TechMateTM Horizon automated immunostainer. Polyclonal rabbit antibodies against NEDD9 (dilution 1:400, Abcam, Cambridge, UK) and Cx43 (dilution 1:300, Santa Cruz Biotechnology, Santa Cruz, California) will be used.

Expected scientific contribution: This study will contribute to the understanding of the role of Cx43 and NEDD9 in gastric cancer metastatic process, and potentially to the development of new therapeutic targets.

Acknowledgments:

MeSH/Keywords: gastric cancer, connexin 43, NEDD9

Poster code: T-B-9-151

Poster Title: PATHOGENETIC MECHANISMS AND PREDICTORS OF ELEVATED PULMONARY VASCULAR RESISTANCE REVERSIBILITY AND PULMONARY HYPERTENSION IN PATIENTS WITH CHRONIC SYSTOLIC HEART FAILURE

PhD candidate: Marijan Pašalić

Part of the thesis: Pathogenetic mechanisms and predictors of elevated pulmonary vascular resistance reversibility and pulmonary hypertension in patients with chronic systolic heart failure

Mentor/s: Academician Davor Miličić

Affiliation: Department for Cardiovascular Diseases, Zagreb University Hospital Centre, University of Zagreb, School of medicine

Introduction: Chronic heart failure (CHF) is one of the most significant medical issues of the modern society. Although a heterogeneous etiological entity, it has a common pathogenetic and pathophysiological sequence. Pulmonary circulation regulation and CHF induced high pulmonary venous pressure play an essential role in the development of the pulmonary hypertension (PH) and pulmonary vascular resistance (PVR). Finding the most important factors in this process and defining the predictors of patient outcomes is crucial in implementing the optimal therapy.

Hypothesis: The right ventricle systolic function is an important predictor of PH and PVR severity, patient outcomes and response to the optimal therapy. Pulse pressure in the pulmonary blood vessels predicts the level and reversibility of the PVR. Increased platelet aggregation is associated with higher levels of PH and PVR. Women with CHF tend to have higher values of PVR than men. Chronic renal failure correlates to the degree of PH and PVR. NT-proBNP and troponin T are biomarkers of PH and PVR.

Aims: The aim of this study is to shed light on certain pathogenetic mechanisms of PH and PVR in patients with CHF. Furthermore, the aim is to recognize the optimal predictors of outcome and response to different approaches in therapy of CHF (drugs, mechanical cardiac support-MCS and heart transplantation-HTx).

Materials and methods: 250 patients diagnosed with CHF (NYHA III/IV class) and pulmo-

nary hypertension will be included. Initial diagnostics will comprise of the patient history, standard laboratory (with platelet aggregometry), echocardiography and right heart catheterization. Follow-up hospitalizations will be conducted on a 3 to 6 month basis and will include standard laboratory, echocardiography and the evaluation of the functional status. Patient outcomes will include the overall survival, patient functional status, changes in PH, PVR and cardiac function parameters.

Expected scientific contribution: Detection of new mechanisms of PVR reversibility in patients with severe CHF. Identification of predictors of outcome and response to different therapy approaches. Evaluation of the right ventricle and pulmonary circulation interaction in determining the response to therapy of CHF. Assessment of the importance that pulsatile blood flow and platelet aggregation have on pulmonary circulation, especially today in the era of continuous blood flow pumps and antiplatelet drugs.

Acknowledgments: I would like to thank my mentor and the Department of cardiovascular diseases at Zagreb University Hospital Centre, for their scientific and professional advice. I would also like to thank my family for their support.

MeSH/Keywords: chronic heart failure, pulmonary vascular resistance, right ventricle, pulse pressure, platelet aggregation, sex-differences

Poster code: T-B-9-155

Poster Title: BORIS AND MAGE-A10 EXPRESSION IN METASTATIC AND NONMETASTATIC COLORECTAL CARCINOMA

PhD candidate: Vedran Tomašić, MD

Part of the thesis: BORIS and MAGE-A10 expression in metastatic and nonmetastatic colorectal carcinoma

Mentor/s: Monika Ulamec, MD, PhD

Affiliation: Sestre milosrdnice University Hospital Center (Ljudevit Jurak University Department of Pathology, Department of gastroenterology and hepatology)

Introduction: Despite a better understanding of the tumor biology, the introduction of a national screening program and recent advances made in the field of surgical/oncologic treatment, colorectal carcinoma (CRC) is still associated with the increasing trends of the incidence and mortality in Croatia. It is of utmost importance to identify regulatory factors which lead to malignant alternation and increase metastatic potential of CRC. We plan to investigate the role of two cancer/testis antigens BORIS and MAGE-A10 in CRC progression and invasion.

Hypothesis: Immunohistochemical expression of BORIS and MAGE-A10 reflects the metastatic potential of CRC.

Aims: We aim to investigate immunohistochemical expression of BORIS and MAGE-A10 in nonmetastatic and metastatic forms of CRC, to evaluate possible causative connection of BORIS and MAGE-A10 and their potential effect on the development of liver metastases. Also we will try to establish whether there is a connection between the expression of BORIS and/or MAGE-A10 and other observed clinical-pathological features and to determine which of the two investigated markers has greater prognostic value in patients with CRC.

Materials and methods: In this retrospective study, the immunohistochemical expression of BORIS and MAGE-A10 will be analyzed in patients with CRC who have been

treated in our institution in the period 2010-2014. Randomly chosen 50 patients with primary tumors located in the colon or rectum and 50 CRC patients with liver metastasis are included in the study. Expression of BORIS and MAGE-A10 will be analyzed by measuring the intensity of immunohistochemical staining as well as the percentage of positive tumor cells in tissue samples. Immunohistochemistry will be performed by using formalin-fixed, paraffinembedded tissue sections (thickness 5 μ m). Deparaffinization and immunohistochemical staining will be carried out following microwave streptavidin immunoperoxidase (MSIP) protocol and by use of labeled streptavidin-biotin (LSAB) method on DAKO TechMateTM Horizon automated immunostainer. Monoclonal antibodies against BORIS (1:50, Santa Cruz biotechnology, Texas, USA) and MAGE-A10 (University of Basel, Switzerland) will be used.

Expected scientific contribution: Obtained results could further clarify CRC pathophysiology and serve as a development tool for new prognostic biomarkers and targeted immunotherapy.

Acknowledgments: Thanks to my mentor, my co-workers and to my family.

MeSH/Keywords: colorectal carcinoma, liver metastases, cancer/testis antigen, BORIS, MAGE-A10

Poster code: T-B-9-163

Poster Title: A MECHANISM-BASED APPROACH TO HEART FAILURE WITH PRESERVED EJECTION FRACTION

PhD candidate: Dora Fabijanović

Part of the thesis: A Mechanism-Based Approach to Heart Failure with Preserved Ejection Fraction

Mentor/s: Doc.dr.sc. Maja Čikeš

Affiliation: Department for Cardiovascular Diseases, School of Medicine, University of Zagreb

Introduction: Heart failure with preserved ejection fraction (HFpEF) is observed in nearly half of the chronic heart failure population, comprising etiologically very heterogeneous patients. The diagnosis is based on several complimentary methods, and research on novel treatment options expected to reduce morbidity and mortality is underway.

Hypothesis: HFpEF is a heterogeneous syndrome, with various underlying etiologic and pathophysiologic factors and a more comprehensive approach is needed to understand disease onset and progression: an integration of data on left ventricular (LV) diastolic dysfunction and systolic function measured as longitudinal and circumferential function, as well as LV torsion can predict the onset of disease, while the occurrence of post-systolic shortening is a predictor of arrhythmias in HFpEF. Furthermore, increased left atrial pressure leads to a gradual loss of various components of its function (conductive, tank and pump function). Furthermore, pulmonary hypertension due to elevated LV filling pressures can in some patients be induced only in exertion, while pulmonary hypertension ultimately leads to right ventricular (RV) dysfunction as measured by RV strain which is a sensitive predictor of outcomes in HFpEF.

Aims: The aim of the study is to further define etiologic subgroups of HFpEF patients, establish a link between etiology, morphology and regional LV function, to demonstrate an association between post-systolic shortening and arrhythmias in HFpEF, define the sequence of pathophysiological events in LA function reduction, define the subgroup of patients with pulmonary hypertension under exertion and prove a direct effect of RV deformation on outcomes in patients with HFpEF.

Materials and methods: The proposed study will include 150 HFpEF patients, subject to a full echocardiographic study including 2D-strain, 6-minute walk test and right heart catheterization.

Expected scientific contribution: The thesis will define the pathophysiological mechanisms and the relation between morphology and heart function in HFpEF, particularly the diagnostic parameters focused on identification of certain subpopulations of "at risk" patients with HFpEF as well as predictors of outcome in HFpEF.

Acknowledgments: -

MeSH/Keywords: HFpEF, 2-D strain, right heart catheterization

Poster code: T-B-9-170

Poster Title: PARVOVIRUS B19 INFECTION IN RENAL TRANSPLANT PATIENTS

PhD candidate: Mihaela Gunjača

Part of the thesis: Parvovirus B19 infection in renal transplant patients

Mentor/s: Professor of Medicine Slobodanka Ostojic Koloic, MD PHD

Affiliation: Division of Internal Medicine, Department of Nefrology, Clinical Hospital Merkur, Zagreb, Croatia

Introduction: Parvovirus B19 infection in kidney transplant recipients is underestimated, although in these patients may develop viral load as a result of a dysfunctional immune response. According to current recommendations require further research on the connection between B19 infection and kidney disease.

Hypothesis: In renal transplant patients parvovirus B19 infection during the first 6 months after transplantation is common. Immunosuppression in patients with transplanted kidney exacerbates existing infection by parvovirus B19 and contributes to the development of complications of viral infection.

Aims: To determine the incidence and prevalence of parvovirus B19 (PVB19) infection in kidney transplant recipients and to determine association between viremia and clinically significant anemia early after transplantation. To determine risk factors for PVB19 infection.

Materials and methods: The study will be conducted at the Department of Nephrology, University Hospital Merkur, Zagreb, Croatia. This prospective, observational study will enroll 100 de novo kidney transplant recipients, who will be prospectively followed for 6 months. PVB19 serostatus will be determined pretransplant and six months post-transplant, while plasma PVB19 DNA will be determined at beginning, one month, three months and six months posttransplant, as well as in case of unexplained worsening anemia (decrease in Hb of >15 g/L, or of >10% from baseline). Immunosuppression

will consist of basiliximab, or ATG induction, with tacrolimus and mycophenolate \pm steroid maintenance. Protocol biopsies will be performed at transplant, as well as three and six months post transplant. Primary endpoint will consist of the cumulative incidence of PVB19 viremia during first six months post transplant. Univariate and multivariate analyses will be performed in order to assess the relationship between PVB19 viremia and putative risk factors such as acute rejection episodes, tacrolimus and mycophenolate exposure, type of induction, recipient PVB19 serostatus pretransplant. Similarly, univariate and multivariate analyses will be used to evaluate relationship between PVB19 viremia and clinical outcomes (graft function, acute rejection incidence, six-month histology and graft loss).

Expected scientific contribution: The scientific contribution of this thesis will be to prove the connection between B19 infection with immunosuppression in transplantation of kidney disease, estimating its frequency and importance.

Acknowledgments: I would like to thank to my mentor and Head of Department of Internal Medicine Professor Ostojic as well as to Head of Department of Nefrology Professor Kontek for their support and assistance in the making of this thesis. Also would like to thank my family for their patience and support.

MeSH/Keywords: Parvovirus B19, infection, immunosuppression, renal transplant

Poster code: T-B-9-174

Poster Title: INFLAMMATORY CELLS REACTION IN THE ABDOMINAL AORTIC ANEURYSM WALL

PhD candidate: Vedran Pažur MD

Part of the thesis: Inflammatory cells reaction in the abdominal aortic aneurysm wall and atherosclerotic aorta

Mentor/s: Ana Borovečki MD, PhD

Affiliation: University hospital Merkur Zagreb

Introduction: Previous studies have shown that inflammation is a key regulatory process that connects numerous factors for atherosclerosis. Although the inflammatory response is defined as a key regulatory process in atherosclerosis yet there is little previous research available on the type of cellular reactions, equilibrium of specific cytokines and determining the outcome of changes - healing, creating atherosclerotic plaque or development of aneurysms.

Hypothesis: Abundant cellular inflammatory reaction in the wall of abdominal aortic aneurysm compared to atherosclerotic abdominal aorta without aneurysm has been associated with abdominal aortic aneurysm. The increased number of regulatory CD4 Foxp3 T lymphocytes and B lymphocytes is associated with scarce cellular inflammatory response, stabilization of atherosclerotic plaque and lower frequency of intraluminal thrombus.

Aims: To prove that the inflammatory reaction in atherosclerotic changed aortic wall leads to weakening of the wall and creates a preference of development of aneurysms and that the inflammatory process in the wall of the aneurysm aorta is more intensified than in atherosclerotic aorta only.

Materials and methods: Tissue samples (front abdominal aortic wall) of patients with abdominal aortic aneurysm (at least 40 respondents) and second control group with non aneurismatic atherosclerotic aorta (minimum of 20 participants) will be analyzed with histology and immunohistochemistry. Blood findings, anamnestic data and MSCT will be used to determine characteristic of respondents.

Expected scientific contribution: The connection of increased number of inflammatory cells in the wall of aortic aneurysm and an increased number of regulatory lymphocytes with a lower incidence of intraluminal thrombosis will improve understanding of the role of inflammatory cells in the formation of aneurysms abdominal aorta and thrombotic complications. This opens and confirms the possibility of preventing or treating atherosclerosis or aneurysmatically changed aorta.

Acknowledgments:

MeSH/Keywords: abdominal aortic aneurysm, inflammation, thrombosis

Poster code: T-B-10-54

Poster Title: PROGNOSTIC SIGNIFICANCE OF THE PREOPERATIVE HEMOGLOBIN LEVEL ON TUMOR RECURRENCE, LATER METASTASES OCCURRENCE AND SURVIVAL RATE IN THE PATIENTS WITH EARLY STAGE OF THE ORAL SQUAMOUS CELL CARCINOMA

PhD candidate: Enis Gllareva

Part of the thesis: Prognostic significance of the preoperative hemoglobin level on tumor recurrence, later metastases occurrence and survival rate in the patients with early stage of the oral squamous cell carcinoma

Mentor/s: Doc. dr. sc. Ivica Lukšić MD, Prof. asoc. dr. Sami Salihu DMD

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

Introduction: Squamous cell carcinoma of the oral cavity(SCCOC) is the most common type of oral cancer. The etiology is tobacco usage, alcohol consumption, infective agents, etc. In addition, patients' presented with anemia are also at higher risk of occult metastasis(due to low response of hipoxic cell to radiotherapy) and worse survival.

Hypothesis: Patients with early stage of SCCOC presented with preoperative low hemoglobin(Hb) level are associated with higher risk of tumor recurrence, later metastases occurrence and lower survival rate in surgical treated patients, independently of other risk factors. There is not any difference in patients' outcome according to type of anemia (microcytic, macrocytic or normocytic).

Aims: The aim of this project is to assess the effect of preoperative hemoglobin level and also other specific measures including type of anemia on tumor recurrence, later metastases occurrence and survival rate in patients with early stage of SCCOC.

Materials and methods: We will retrospectively collect records of 150 patients with T1-T2N0M0 SCCOC (such as: preoperative hemoglobin level, mean cell volume, hematocrit level and white blood cell count) using preoperative hemogram. Patients' records will be collected in a 10-year period (January 2000-January 2010). Patients will be divided into three groups based on he-

moglobin level (with normal hemoglobin, mild anemia and severe anemia), same for mean cell volume (MCV): with low MCV (microcytic anemia), normal MCV (normocytic anemia) and high MCV(macrocytic anemia). Data which are taken during the follow-up for tumor recurrence, later metastases occurrence and survival rate (using clinical examination, MRI, CT, death protocol, etc) will be used. Kaplan-Meyer analysis and COX Regression analysis will be used for statistical analysis.

Expected scientific contribution: Our study will strengthen the known effect of preoperative hemoglobin level in outcome and in addition we will define if this association will be retained after adjusting for other risk factors. Also, we will define the influence of different types of anemia in patients' outcome. Confirmation of these finding will affect the treatments strategy of these patients, including preoperative blood transfusion or transfusion of erythropoietin. Also treatment of anemia based on its etiology could be of importance for patients outcome.

Acknowledgments: University Clinical Center fo Kosova, Professional Dent (Dental Clinic)

MeSH/Keywords: Squamous cell carcinoma of the oral cavity(SCCOC), hemoglobin level, prognostic factor, survival rate

Poster code: T-B-10-120

Poster Title: CLINICAL TRIAL OF THE EFFICACY OF TOPICAL 2% LIDOCAINE FOR THE TREATMENT OF SYMPTOMATIC HEMORRHOIDS

PhD candidate: Tihomir Kekez, MD

Part of the thesis: Double blind randomized clinical trial of the efficacy of topical 2% lidocaine for the treatment of symptomatic hemorrhoids

Mentor/s: Mate Majerović, MD, PhD

Affiliation: Division of Gastrointestinal Surgery, University Hospital Centre, Zagreb

Introduction: There are no published studies supporting the use of pharmacological agents for the treatment of hemorrhoids or the symptoms related to hemorrhoid disease. Despite the lack of evidence supporting their use, there are a plethora of agents available to the general population. Topical lidocaine can not penetrate the skin. Small amount could be absorbed through the anorectal mucosa but plasma peak concentrations of lidocaine remained below the minimal effective therapeutic plasma concentration.

Hypothesis: We set the hypothesis that lidocaine does not have anesthetic effect on the perianal skin and could not alleviate haemorrhoidal symptoms

Aims: The primary objective of this study is to evaluate the efficacy in the therapy of symptomatic hemorrhoids. Efficacy will be determined by: a) the change from baseline in pain, itching, bleeding, swelling, discomfort, general wellbeing and improvement since the beginning of treatment as separate components of CORRECTS scale; b) the change in overall CORRECTS values from baseline, c) the change in degree of hemorrhoids from baseline, d) Secondary objective is to assess the safety and tolerability of by determining percentage of adverse events (complications) and percentage of treatment discontinuations due to adverse events

Materials and methods: Patients with symptomatic hemorrhoids not eligible for surgical or interventional treatment within 30 days from the screening day will be considered. Calculated sample size is 70 patients per arm, based on expected improvement of pain and healing by 30% at $p < 0.05$ and power goal of 95%. Patients will be randomly assigned into 2 arms ([TREATMENT] and [CONTROL]). Treatment arm – Topical application of 2% lidocaine in vaseline base repeated three times per day, Control arm – Topical application of pure vaseline base three times per day. Currently we have 103 patients enrolled: 71% female and 31% men. Median age 46y (range 25-75). Haemorrhoids grade: I 22%, II 68% and III 12%. No statistical difference in symptom reduction was shown between treatment and control arm.

Expected scientific contribution: To provide data should lidocaine be the active component in the topical ointment and cream for relieving haemorrhoidal symptoms

Acknowledgments:

MeSH/Keywords: Haemorrhoids, topical treatment, lidocaine

Poster code: T-B-10-148

Poster Title: EFFECT OF RESVERATROL ON OXIDATIVE STRESS PARAMETERS AND SYSTEMIC INFLAMMATORY RESPONSE IN PATIENTS UNDERGOING CARDIOPULMONARY BYPASS DURING CARDIAC SURGERY

PhD candidate: Mislav Planinc, MD

Part of the thesis: Effect of resveratrol on oxidative stress parameters and systemic inflammatory response in patients undergoing cardiopulmonary bypass during cardiac surgery

Mentor/s: Željko Sutlić, MD, PhD, Ivana Novak Jovanović PhD

Affiliation: University Hospital Dubrava, Zagreb, Institute for Medical Research and Occupational Health, Zagreb

Introduction: There is a well-established connection between cardiopulmonary bypass (CPB), oxidative stress and systemic inflammatory response syndrome (SIRS) in cardiac surgery. Reactive oxygen species are thought to be responsible for such effects. They are produced during surgical trauma, contact of blood with non-biological surfaces and due to ischemic – reperfusion injury which can lead to SIRS. Previous researches have shown that intake of antioxidants in preoperative period can markedly reduce the incidence of SIRS and lower the negative effects of CPB. Scientific interest for resveratrol, a member of stilben family, started with observation of “French paradox” – lower incidence of cardiovascular diseases in people who regularly ingest moderate amounts of red wine. There has not been a research yet about a resveratrol as an antioxidant in cardiac surgery.

Hypothesis: Antioxidant resveratrol given orally to patients undergoing CPB during elective cardiac surgery lowers the serum level of oxidative stress markers and incidence of SIRS.

Aims: To investigate the effect of resveratrol on level of oxidative stress and incidence of SIRS in patients undergoing cardiac surgery with usage of CPB.

Materials and methods: This research is going to be undertaken at the Department of Cardiac and Transplant Surgery at Univer-

sity Hospital Dubrava and at Institute for Medical Research and Occupational Health, Zagreb. In this placebo controlled double blind randomized clinical experiment 30 elective valve patients that meet inclusion criteria will be included and administrated with resveratrol or placebo. Inclusion criteria are elective cardiac valve repair or replacement procedure, male gender, age 18 – 80 and signed informed consent. Capsulated resveratrol or placebo capsules same size and shape will be given to the patients 48 hours before surgery. In five time points during and after the procedure the level of biomarkers of oxidative stress will be measured. We will analyze total antioxidative capacity of plasma and then each biomarker. Laboratory parameters of systemic inflammatory response and postoperative complications will be observed.

Expected scientific contribution: Resveratrol is potent antioxidant. Its effect on oxidative stress and systemic inflammatory response syndrome has not been investigated yet. Proposed research will confirm or deny the effect of resveratrol in this group of patients. Also, it will be seen if there is a clinical potential of this compound.

Acknowledgments:

MeSH/Keywords: Cardiac surgery, resveratrol, oxidative stress, systemic inflammatory response

Poster code: T-B-10-164

Poster Title: COMBINED FUNCTIONAL, ELECTROPHYSIOLOGICAL AND STRUCTURAL OPHTHALMOLOGICAL INVESTIGATION IN EARLY DIAGNOSIS OF OPTIC NEURITIS IN MULTIPLE SCLEROSIS

PhD candidate: Danijela Mrazovac, MD

Part of the thesis: Combined functional, electrophysiological and structural ophthalmological investigation in early diagnosis of optic neuritis in multiple sclerosis

Mentor/s: Professor Branimir Cerovski, MD, PhD

Affiliation: Department of Ophthalmology, University Hospital Centre Zagreb and University of Zagreb, School of Medicine

Introduction: Multiple sclerosis is one of the most frequent causes of neurological and ophthalmological disabilities in younger adults. Inabilities it causes, like visual dysfunction, are a great burden for an individual, as well as for society and healthcare system, since they reduce work ability and lead to permanent disability. Patients with clinically isolated syndrome, such as optic neuritis, are now recognized to have higher risk of developing multiple sclerosis. Recognizing these isolated syndromes is an important aspect in early treatment of multiple sclerosis, because there are strong arguments for an early administration of therapy that can slow down the pathological process. Previous studies have shown a high possibility of unrecognized, subclinical and chronic visual impairments, that are greater than the acute ones, and which should be taken into consideration.

Hypothesis: Visual function impairment in patients with optic neuritis and multiple sclerosis can be better assessed by combined functional, electrophysiological and structural diagnostic procedures than by individual ophthalmological methods.

Aims: To determine a combination of ophthalmological diagnostic procedures which most accurately diagnose visual impairments in patients with optic neuritis and multiple sclerosis. To determine which diag-

nostic procedure best reveals asymptomatic visual function impairment. To determine which combination of diagnostic procedures most accurately predicts the extent of damage after 1 year of follow-up.

Materials and methods: Study will include 140 patients (age 18-55 years) divided in 4 groups – patients with acute optic neuritis, multiple sclerosis patients with and without chronic symptomatic optic neuritis and a healthy control group. All patients will undergo extended complete ophthalmological examination, optical coherence tomography, visual field assessment and visual evoked potentials. Follow-up will be performed 1 year after the initial examination.

Expected scientific contribution: This research will enable an objective evaluation of ophthalmic impairments in optic neuritis and multiple sclerosis, as well as their value for timely diagnostics, treatment and tracking the dynamic of ophthalmological disease in multiple sclerosis.

Acknowledgments:

MeSH/Keywords: optic neuritis, optical coherence tomography, automatic static perimetry, visual evoked potentials, multiple sclerosis

Poster code: T-B-18-96

Poster Title: DIRECT TEAR FILM SURFACE VISUALISATION METHOD FOR NON-INVASIVE TEAR BREAK-UP TIME (NIBUT) MEASUREMENT

PhD candidate: Sania Vidas, MD

Part of the thesis: Non-invasive tear break-up time (NIBUT) measurement using hand held instrument for lipid layer examination

Mentor/s: Tomislav Jukić, MD, PhD

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

Introduction: Basic indicator of tear film function (TFF) is tear film stability. Standard method for tear film stability assessment is tear film break-up time (TBUT), an invasive method that requires instillation of fluorescein solution in eye, resulting in changes of tear film physiology. Compatible to TBUT, non-invasive tear break-up time (NIBUT), provides tear film stability assessment with no need for eye drops instillation, enabling native TFF evaluation. NIBUT is usually performed by sophisticated and expensive instruments (Tearscope, Keratograf), what makes them unsuitable for routine practice. In literature, in general population TBUT values are significantly shorter than the NIBUT, but almost equal or very similar in patients with dry eye. On the other hand, visualization of the tear film surface and appearance of its irregularities at the time of its destabilization, theoretically, could allow NIBUT assessment. It can be performed by Tearscope or by using more practical and accessible instrument, hand held instrument for lipid layer examination. At this moment Tearscope is the only standardized instrument for NIBUT measurement. Since hand held instrument for lipid layer examination works on the same physical principle, it might also be used for NIBUT assessment.

Hypothesis: NIBUT can be assessed by using hand held instrument for lipid layer examination.

Aims: To determine the possibility of NIBUT assessment by visualization of tear film sur-

face using hand held instrument for lipid layer examination, and to compare the values with those obtained by standard test, TBUT, in order to introduce this method in everyday clinical practice.

Materials and methods: Every adult patient attending the standard ophthalmic examination, who will, after being introduced to the aim of the research, sign the informed consent and give written consent to participate in research. Patients with ocular trauma, inflammation and other surface diseases would not be included. First a standardized Schein questionnaire, modified for issues relevant to this research, will be used in order to determine the symptoms of dry eye. After that the standard examination, including NIBUT, will be performed, using slit lamp and handheld instrument.

Expected scientific contribution: To determine comparability between NIBUT values, measured using hand held instrument, and standard test values in diagnostics of dry eye. To examine the clinical applicability of this method, enabling native tear film function evaluation on more simple and accessible way

Acknowledgments:

MeSH/Keywords: Cornea, Dry eye syndrome, TBUT, NIBUT

Poster code: T-B-18-99

Poster Title: HISTOPATHOLOGY OF INVOLUTIONAL LOWER EYELID ENTROPION

PhD candidate: Daliborka Miletić

Part of the thesis: Histopathological characteristics of involutional lower lid entropion

Mentor/s: Professor Biljana Kuzmanović Elabjer, MD, PhD

Affiliation: School of Medicine Osijek, University Josip Juraj Strossmayer Osijek, University Hospital Sveti Duh, University Eye Clinic

Introduction: Involutional lower eyelid entropion is inward rotation of an eyelid margin associated with important visual morbidity. Although involutional entropion is one of the most common pathology in oculoplastic surgery, its etiopathology is still not entirely clarified. Generally accepted mechanisms of its development involve increased vertical and horizontal eyelid laxity with atrophy and shrinkage of tarsal plate, as well as hyperactivity of m. orbicularis. However, reports of histopathological evaluation of this condition are surprisingly scarce

Hypothesis: Our hypothesis is that thickening of the tarsal plate – m. orbicularis complex, in conjunction with impaired lower eyelid retractor attachments are responsible for involutional entropion.

Aims: The aim of this research is to show that patients with involutional lower lid entropion have thickened tarsal plate – m. orbicularis complex with changed retractor attachments, in comparison with the control group without involutional entropion. The specific goals are to histopathologically analyze tarsal thickness and height, structure and thickness of pretarsal m. orbicularis, as well as diameter of individual muscle fiber

and to define lower eyelid retractor attachments.

Materials and methods: Case-control study include surgically treated 20 consecutive patients older than 60 years with involutional lower eyelid entropion and 20 matching control patients with lateral lower eyelid basal cell carcinoma. Histopathological analysis of surgically obtained full-thickness eyelid specimens includes measurements of tarsal plate and m. orbicularis dimensions, as well as definition of lower eyelid retractor attachments. Collected data will be processed and presented using appropriate statistical methods.

Expected scientific contribution: Contrary to the present knowledge, the dynamic of involutional lower eyelid entropion development is related to thickening of the tarsal plate – m. orbicularis complex.

Acknowledgments: : I would like to express my gratitude to pathologist Z. Petrović and my mentor Prof. B. Kuzmanović Elabjer.

MeSH/Keywords: involutional entropion, m. orbicularis, retractor, tarsal plate

Poster code: T-B-18-129

Poster Title: PARABENS EFFECT ON THE DEVELOPMENT OF HUMAN BREAST CANCER

PhD candidate: Željka Roje

Part of the thesis: Changes in parabens concentration in breast upper lateral quadrant in women with breast cancer

Mentor/s: prof. Zdenko Stanec, MD, PhD

Affiliation: Department for Plastic, Reconstructive and Aesthetic Surgery, University Hospital 'Dubrava', Zagreb

Introduction: The general population is exposed to numerous exogenous hormonally active substances. These substances are called xenoestrogens. Scientific based evidences confirm the impact of xenoestrogens on carcinogenesis. Currently there are about 160 xenoestrogens that may be involved in the development of breast cancer. Parabens, synthetic manufactured xenoestrogens, are used in cosmetics products as preservatives. Women mostly use cosmetic products, which can thus be a significant source of xenoestrogens. Since only 5% of breast cancer is in relation to genetic predisposition, still remains a much larger part of which the exact ethology is still an open scientific question.

Hypothesis: The paraben concentration is increased in malignant breast tissue in relation to healthy breast tissue. There is statistically significant correlation between the paraben concentrations in breast tissue and urine.

Aims: To analyse the concentration of parabens from breast tissue, adipose tissue around the metastatic axillary lymph nodes and from urine samples. The results will determine the statistical associations between paraben concentrations and the frequency

of application of cosmetic products with the developing of breast cancer.

Materials and methods: This research will include 170 patients in a period time of 1,5 years, 60 healthy women to whom the tissue will be taken from the upper lateral breast quadrant (the most common location of tumor). From other 110 women with cancer subjected to radical mastectomy the tissue will be taken from all 4 breast quadrants, from malignant breast tumor itself if it is equal or over 1ccm of size, and from fat tissue around metastatically caught lymphatic nodes of axillae region. The extraction of paraben from tissue and urine and its analysis by gas chromatography method and mass spectrometry (CG-MS) method will be done by Govindaraj method.

Expected scientific contribution: Data will determine whether there is an increased concentration of parabens in malignant breast tissue and whether ever day cosmetics and their chemicals can contribute to breast cancer development.

Acknowledgments:

MeSH/Keywords: paraben, oestrogen

Poster code: T-B-19-47

Poster Title: IL-17 IN EARLY INVASIVE BREAST CANCER

PhD candidate: Marina Barić, MD

Part of the thesis: IL-17 in early invasive breast cancer

Mentor/s: Professor Damir Vrbaneć, MD, PhD, Senior Research Associate Ana Kulić, PhD

Affiliation: Department of Medical Oncology, University Hospital Centre Zagreb

Introduction: There is a growing body of evidence supporting the role of immunity and inflammatory responses at different stages of tumor development, including initiation, promotion, malignant conversion, invasion, and metastasis. Recent studies have shown that there is an increased expression of IL-17 in breast cancer tissue compared to healthy breast tissue. The role of inflammatory response mediated by IL-17 in the development and progression of breast cancer has not yet been clarified. The results of previous studies are inconclusive. Some studies suggest antitumor activity of IL-17, and others speak in favor of its association with tumor aggressiveness and poorer prognosis.

Hypothesis: The serum concentration of IL-17 is elevated in women with an early invasive breast cancer and positively correlated with the expression of IL-17 in tumor tissue.

Aims: The aim of this study is to determine and compare the concentration of IL-17 in the serum of women with an early invasive breast cancer and healthy women, to determine the expression of IL-17 in the tumor tissue of women with an early invasive breast cancer, to examine the correlation between serum concentrations and the expression of IL-17 in tumor tissue, to analyze the association of serum concentration and tissue expression of IL-17 with other clinical

and pathohistological characteristics and surrogate biological subtypes, and to compare the concentration of IL-17 in the serum of women with an early invasive breast cancer preoperative and after 3 cycles of adjuvant chemotherapy or 3 months of hormone therapy.

Materials and methods: Blood samples and tumor tissue specimens from 120 patients with an early invasive breast cancer, diagnosed and operated in the Clinical Hospital Centre Zagreb, and the serum of 60 healthy women who will serve as the control group, will be analyzed accordingly. The serum IL-17 levels will be measured by the enzyme-linked immunoadsorbent assay (ELISA), using the Human IL-17A Platinum ELISA antibody, eBioscience San Diego, CA, USA. The IL-17 tissue expression will be determined immunohistochemically using the Rabbit polyclonal anti-IL17 antibody, ab 9565/Abcam.

Expected scientific contribution: The results will be used to further investigate the role of IL-17 in human breast cancer and the development of new diagnostic and therapeutic possibilities.

Acknowledgments:

MeSH/Keywords: Breast cancer, interleukin 17, IL-17

Poster code: T-B-19-50

Poster Title: SLEEP DISORDERS IN CHILDREN WITH EPILEPTIC ENCEPHALOPATHIES

PhD candidate: Nataša Nenadić Baranašić, MD

Part of the thesis: Evaluation of sleep structure and organization and assessment of sleep-disordered breathing in children with epileptic encephalopathies using all-night video-polysomnography

Mentor/s: Prof. Nina Barišić, MD, PhD, Associate Prof. Romana Gjergja Juraški, MD, PhD

Affiliation: Srebrnjak Children's Hospital Zagreb, University Hospital Centre Zagreb

Introduction: Epileptic encephalopathies (EE) are age-dependent electroclinical syndromes that cause disorder of cognitive functioning, behavior and psychomotor regression as a result of recurrent uncontrolled seizures and diffuse bihemispherical epileptogenic EEG changes. They are usually refractory to standard antiepileptic therapy. Studies on the sleep structure and sleep-disordered breathing in children with EE are deficient and inconsistent. There is paucity of prospective studies on a larger number of children.

Hypothesis: Children with EE have disorders of sleep structure, organization and sleep-disordered breathing. Disrupted sleep structure and sleep-disordered breathing in children with EE are significantly associated with younger age of disease onset and comorbidities.

Aims: GENERAL AIM: 1) to determine the type and frequency of sleep structure and organization disorders and sleep-disordered breathing, in relation to the age of disease onset and comorbidities, compared to the control group of healthy children. SPECIFIC AIM: 1) to investigate the association among polysomnographic parameters and different types of sleep disorders in children with EE, 2) to investigate the relationship among polysomnographic parameters and epilepsy activity, 3) to determine the combination of polysomnographic parameters that would serve as predictors of poorer disease control.

Materials and methods: In total 50 children from birth to 18 years will be included in this prospective study: Group 1: 25 children with EE, Group 2(control group): 25 healthy children, In both groups age, gender, percentile curves will be evaluated. In Group 1 also comorbidities, psychological testing, age of disease onset, ictal and interictal EEG findings, antiepileptic therapy and brain MRI findings will be additionally evaluated. Parameters of two all-night video-polysomnography studies in time interval of 6 months for each patient will be analyzed. Following polysomnographic parameters will be analysed: continuous EEG, video and audio recording, hipnogram, sleep latency, REM sleep latency, total sleep time, total time of awakeness, number of microarousals, saturation of hemoglobin with oxygen, respiratory events, EMG, sensor snoring, pulse, ECG

Expected scientific contribution: This research will contribute to better understanding of sleep structure, organization and sleep-disordered breathing in children with EE. The results will give us further insight into the pathophysiology and epileptogenesis of EE.

Acknowledgments: I would like to thank my mentors and EEG technicians in the Srebrnjak Children's Hospital.

MeSH/Keywords: children, all-night video-polysomnography, sleep, epileptic encephalopathy

Poster code: T-B-24-74

Poster Title: OXIDATIVE STRESS IN CHILDREN WITH CROHN'S DISEASE

PhD candidate: Andro Gliha, MD

Part of the thesis: Oxidative stress in children with Crohn's disease

Mentor/s: Associate Professor Stjepan Višnjić, MD, PhD / Professor Tihomir Balog, MPharm, PhD

Affiliation: University of Zagreb School of Medicine, Children's Hospital Zagreb / University of Rijeka, Ruđer Bošković Institute

Introduction: Crohn's disease is one of the most common chronic diseases in children, characterized by severe inflammation of the mucosa, causing an increased production of free radicals and oxidative stress. The etiology of Crohn's disease is multifactorial, including genetic, environmental and host factors with aberrant immune response to triggering event.

Hypothesis: Oxidative stress in children with Crohn's disease is much higher than in healthy children. Enteral nutrition lowers oxidative stress in the children with Crohn's disease.

Aims: The aim of this study is to demonstrate oxidative stress in children with newly diagnosed and relapsed Crohn's disease and to evaluate the effects of enteral nutrition (the most effective treatment for induction of remission) on oxidative / antioxidative status.

Materials and methods: The research is based on longitudinal and prospective study of the children with Crohn's disease treated in Children's Hospital Zagreb. The study will include 30 children with newly diagnosed Crohn's disease, 30 children with relapse of Crohn's disease treated exclusively with enteral nutrition and 30 healthy children as control group. We will analyse complete blood count, sedimentation rate, CRP and fecal calprotectin (except control group) and

nutritive status by measuring body mass, height and body mass index. The inflammatory response will be analysed by measuring pro - and anti - inflammatory cytokines (IL-1, IL-6, TNF alpha, IL-1R antagonist, IL-4, IL-10) in plasma while oxidative stress will be analysed by measuring antioxidative enzymes in plasma and in tissue specimens of intestinal biopsies (superoxide-dismutase (SOD), catalase (Kat) and glutathione-peroxidase (Gpx)). The markers of oxidative stress and damage of the free radical to the lipids and proteins (lipid peroxidation and protein carbonyl groups) will be measured from tissue specimens of intestinal biopsies of the children with Crohn's disease. Data will be statistically analysed using Kolmogorov Smirnov Test, χ^2 test, t-test and Mann-Whitney test with statistical significance of the P value lesser than 0,05.

Expected scientific contribution: Following the patients through active phase and remission of the Crohn's disease will give us better insight and knowledge of oxidative stress and the roll of free radicals in pathogenesis of the disease and influence of enteral nutrition on oxidative stress markers.

Acknowledgments:

MeSH/Keywords: Oxidative stress, enteral nutrition, Crohn disease

Poster code: T-B-24-102

Poster Title: GENETIC AND ENVIROMENTAL FACTORS IN CONGENITAL HEART DEFECT DEVELOPMENT

PhD candidate: Maša Davidović, MD

Part of the thesis: The effect of genetic and enviromental factors on congenital heart defect development

Mentor/s: Ingeborg Barišić, MD, PhD/ Ivan Malčić, MD, PhD

Affiliation: Department of Pediatrics, University of Zagreb School of Medicine/Department of Pediatrics, Children's Hospital Zagreb, Unversity of Zagreb School of Medicine

Introduction: Congenital heart defects (CHD) are amongst the most common congenital defects in humans. The etiology of CHD is multifactory, but genetic factors are considered to have a crucial role. Mutations of 55 genes, mostly involved in cardiac development, have been found to cause CHD. Chromosomic abberations are a common cause of CHD, while monogenetic disorders are rare. Gene copy number variants, CNVs, are also considered to have a role in the development of CHD.

Hypothesis: By integrating clinical information with results of molecular and genetic testing we will gather valuable information about the etiology and pathogenesis of CHD. This information will be appliable in primary and secondary prevention, and possibly in inovative treatment of these disorders in the future.

Aims: The aim of our study is to find out more about the etiology of CHD and to improve primary and secondary prevention as

well as the management of CHD by integrating clinical information with genome analysis results.

Materials and methods: Clinical and medical history data as well as blood samples will be collected from 300 patients with CHD. Blood samples will be genetically analyzed, including genome sequencing in selected patients. Collected data will be analyzed statistically.

Expected scientific contribution: We believe that the results of our study will contribute in better understanding of the etiology and pathogenesis of CHD.

Acknowledgments:

MeSH/Keywords: Congenital heart disease CHD, Cardiac development, Chromosomal and single gene disorders, Copy number variants CNVs, exome sequencing

Poster code: T-B-24-128

Poster Title: HEPATIC COMPLICATIONS IN TYPE 1 DIABETES MELLITUS

PhD candidate: Mirna Aničić, MD

Part of the thesis: Hepatic complications are insufficiently recognized in patients with type 1 diabetes mellitus

Mentor/s: Professor Jurica Vuković, MD, PhD

Affiliation: Department of Gastroenterology, hepatology and nutrition, University Department of Pediatrics, University Hospital Center Zagreb, Croatia

Introduction: Diabetes mellitus type 1 (DM1) is a metabolic disease characterized by insulin deficiency and dependence on the application of exogenous insulin. Poor metabolic control leads to development of both acute and chronic complications. Recently, liver became subject of great interest in such patients, due to hepatic consequences of DM1 related metabolic complications. Two new entities that affect the liver emerged in patients with poorly controlled DM1: glycogen hepatopathy (GH) and nonalcoholic steatohepatitis (NASH). GH is characterized by elevated transaminases, hepatomegaly and accumulation of glycogen in hepatocytes. Wide fluctuations in glucose and insulin concentrations are essential for its pathogenesis. It is observed that after a few weeks of good metabolic control clinical symptoms disappear and transaminases levels normalize. GH cannot be distinguished from NASH by physical examination, laboratory tests or by liver ultrasound. Therefore liver biopsy is essential for diagnosis. It is very important to distinguish these two entities since NASH can progress to cirrhosis, while GH seems to be reversible with adequate glycemic control.

Hypothesis: Patients with poorly regulated DM1 can develop hepatic complications.

Aims: To determine prevalence of hepatic complications in patients with DM1 and compare their frequency considering the degree of metabolic control and duration of DM1, to investigate the connection between

chronic complications of DM1 and hepatic complications.

Materials and methods: 250 patients (125 males and 125 females) aged 1-25 years, suffering from DM1 for at least 1 year will be examined for presence of liver disease. They will be subjected to the following: medical history, physical examination, liver function tests, lipid profile, HbA1c, liver ultrasound (US) and screening for coeliac disease, autoimmune thyroiditis, nephropathy and retinopathy. Patients with abnormal liver function tests will be further investigated to exclude infectious, autoimmune and metabolic liver disease (alpha 1 AT deficiency, Wilson disease, hemochromatosis). MRI of the liver will be performed in those with abnormal laboratory and/or US findings. Percutaneous liver biopsy will be done in patients with US and MRI verified liver disease.

Expected scientific contribution: No studies enable insight into the frequency, duration and optimal methods of diagnosis of hepatic complications in patients with DM1. This research will determine the incidence of hepatic complications in children and adolescents with DM1 and examine the factors that contribute the most.

Acknowledgments:

MeSH/Keywords: diabetes mellitus type 1, poor glycemic control, hepatic complications, glycogen hepatopathy, NASH

Poster code: T-B-24-167

Poster Title: SHEAR-WAVE ELASTOGRAPHY STIFFNESS OF BENIGN AND MALIGNANT BREAST LESIONS

PhD candidate: Maja Crnogorac, MD

Part of the thesis: Shear-wave elastography stiffness of benign and malignant breast lesions

Mentor/s: Professor Brkljačić Boris, MD, PhD

Affiliation: University Department of Diagnostic and Interventional Radiology, University Hospital Dubrava

Introduction: Breast cancer is the most common cancer in women and the second cause of death related to cancers. In 2012 incidence in Croatia was 24%. In order to improve early diagnosis, which increases survival rate, new methods are investigated. Tissue stiffness can be measured by ultrasound elastography, and best described by Young's modulus ($E=\sigma/\epsilon$), which shows the ratio of the applied pressure and the resulting tissue deformation. Shear-wave elastography (SWE) uses the repeated, focused pulses (push pulse) to induce low intensity shear waves in the tissue. Young's modulus is then calculated from the mean velocity of shear waves. Tissue stiffness is displayed as a color-coded image (red color shows hard tissues, soft are shown in blue) and measured in m/s or in kilopascals. Many studies have shown value of elastography in measuring breast tissue stiffness (fat values are less than 7 kPa, glandular parenchyma stiffness is 30 to 50 kPa). Benign breast lesions are generally softer than malignancies.

Hypothesis: It is possible to differentiate benign from malignant breast lesions, as well as their subtypes, by measuring their stiffness with shear-wave elastography (SWE).

Aims: Investigation of quantitative SWE values of various benign and malignant lesions, specially recurrent lesions, and connection of elasticity values with patient data related to breast cancer.

Materials and methods: This cross-sectional study will include patients scheduled for breast core-biopsy, regardless of age. Information about: age, menstrual status, parital status, family and personal history of breast cancer, hormonal agents intake will be collected by questionnaire or from the hospital information system. All patients with adequately labeled and archived sonoelastographic findings in the three-year period will be included. Patients who underwent reconstructive breast surgery or radiation therapy of the breast, chest wall and thoracic spine will be excluded. After the classic breast examination in B-mode by one researcher SWE in real time is performed. Measured parameters are: lesion size, medium, minimum and maximum elasticity value and E-ratio (lesion/fat ratio).

Expected scientific contribution: This research will determine the quantitative values of various breast lesions, including recurrent cancer, taking into account the details of patient history. This will enable better use of this non-invasive method in breast cancer diagnostics.

Acknowledgments:

MeSH/Keywords: breast ultrasound, sonoelastography

Poster code: T-B-25-31

Poster Title: IMAGING FEATURES AND CLINICAL PRESENTATION OF BREAST CANCER PATIENTS IN KOSOVO

PhD candidate: Ardian Biçaku, MD

Part of the thesis: Imaging features and clinical presentation of breast cancer patients in Kosovo – Analysis of patients at University Clinical Center of Kosovo - Pristina

Mentor/s: Professor Boris Brkljačić, MD, PhD

Affiliation: University of Zagreb School of Medicine, UH "Dubrava", University Clinical Center of Kosovo, Pristina, Clinic of Radiology

Introduction: Breast cancer (BC) is a major source of disease burden among women in developed countries, and in many developing countries the incidence and mortality rates are increasing. It is the second most common cancer in the world and, by far, the most frequent cancer among women with an estimated 1.67 million new cancer cases diagnosed in 2012 (25% of all cancers) and ranks as the fifth cause of death from cancer overall (522,000 deaths). Kosovo is a country with no BC screening program and a country with many different features compared to European countries with regard to health care system, population age and attitude of women and public towards BC. So far, there are no studies that demonstrate imaging features and clinic-pathologic presentation of BC in Kosovo.

Hypothesis: It is expected that much larger and more advanced BC are diagnosed in Kosovo compared to other countries in the region and in Europe. BC will be diagnosed by other means than screening mammography. Time from onset of clinical complaints to time of seeking treatment is more than 1 month. The proportion of DCIS is lower than in developed European countries that have organized programs for breast cancer screening. The ratio of invasive ductal to invasive lobular cancer is not different compared to other countries.

Aims: The aim of this study is to evaluate imaging features and clinical-pathological presentation of BC currently detected in Kosovo. Correlation of BC tumor size in mammography, ultrasound and histopathology will be studied.

Materials and methods: Prospective study of all BC diagnosed at University Clinical Center of Kosovo – Clinic of Radiology - Department of Breast Imaging during period 2015-2016. The sample size will be 250 patients. Demographic data, clinical characteristics, imaging features (mammography, ultrasound), histopathologic findings and data for surgery procedure (if possible) will be prospectively analyzed for all patients diagnosed with BC.

Expected scientific contribution: Results from this study will contribute in obtaining data regarding the types of cancer, their size, imaging findings and clinical presentation of BC detected in Kosovo.

Results might induce changes in public health care policy regarding BC imaging, and organizing screening program for BC.

Acknowledgments:

MeSH/Keywords: breast cancer, mammography, morpohology, Kosovo

Poster code: T-B-25-56

Poster Title: THE ROLE OF MAGNETIC RESONANCE IMAGING IN EARLY DETECTION OF PATHOLOGICAL CHANGES OF THE CERVICAL SPINE IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

PhD candidate: Ana Tripalo Batoš

Part of the thesis: The role of magnetic resonance imaging in early detection of pathological changes of the cervical spine in patients with juvenile idiopathic arthritis

Mentor/s: Professor Kristina Potočki, MD, PhD, Assistant professor Alenka Gagro, MD, PhD

Affiliation: Children's hospital Zagreb

Introduction: Juvenile idiopathic arthritis (JIA) is an autoimmune disease of unknown etiology that begins before the age of 16 and lasts for at least six weeks. The current criteria for the diagnosis of the disease do not consider inflammatory changes of the spine as a criterion for distinguishing between types of JIA, prognosis and treatment modifications. Cervical spine changes have been studied in a small number of studies, mainly by conventional X-rays. Studies using magnetic resonance imaging (MRI) as the most sensitive method in the analysis of changes in the cervical spine children with JIA are scarce and a small number of patients with different types of JIA was described to date.

Hypothesis: Comparing X-rays of the cervical spine and MRI of the cervical spine, with the administration of contrast media, in patients with pJIA and enthesitis associated arthritis (ERA) who have symptoms, changes are visible to a greater extent and earlier with MRI.

Aims: The aim of this study is to examine changes in the cervical spine MRI before changes are visible on a conventional X-ray radiograph in children with pJIA and ERA in children whose spine symptoms last less than five years from diagnosis of JIA.

Materials and methods: In the study 60 patients with spine symptoms treated at Children's hospital Zagreb with a confirmed diagnosis of pJIA and ERA according to ILAR

criteria will be included. X-ray images of the cervical spine with a minimum dose of irradiation will be performed, following by MRI of the spine with gadolinium contrast application in the MRI machine with field strength 1.5T. Two control groups comparable with the test group by age and gender distribution will be included: first that include patients with brain and/or cervical tumors and second, that include patients with possible head and neck trauma Parents / foster parents of patients younger than 12 years, and parents / foster parents and patients older than 12 years will be given informed consent and approval for participation in research as well as a standardized form for radiological examination.

Expected scientific contribution: Detection of changes in cervical MRI would confirm the pathological changes of the cervical spine before development of irreparable changes in children with JIA. This would offer the possibility of more efficient, faster and better therapeutic outcome and would improve the quality of life, prevent the occurrence of disability and need of assistance. This would allow that children with JIA to live a life as their peers.

Acknowledgments:

MeSH/Keywords: juvenile idiopathic arthritis, magnetic resonance, cervical X-ray

Poster code: T-B-25-84

Poster Title: INFLUENCE OF RADIOTHERAPY ON APPARENT DIFFUSION COEFFICIENT VALUE OF NORMAL BREAST TISSUE AND LESIONS AT MRI

PhD candidate: Niko Radović, MD

Part of the thesis: Influence of radiotherapy on apparent diffusion coefficient value of normal breast tissue and lesions at MRI

Mentor/s: Asst. Prof. Gordana Ivanac, MD, PhD

Affiliation: University of Zagreb School of Medicine, University Hospital Dubrava, Clinical Department for Diagnostic and Interventional Radiology

Introduction: Magnetic resonance (MR) imaging is garnering an increasingly important role in diagnostic evaluation of breast cancer, with diffusion weighted imaging (DWI) making a special contribution. DWI accompanied by measurement of apparent diffusion coefficient (ADC) values and combined with dynamic contrast enhanced MR (DCE MR) shows 95.7% sensitivity and 89.2% specificity for breast cancer detection, yielding 13.5% increased specificity compared to DCE MR alone. In the context of residual and recurrent tumor detection at DWI following breast conserving surgery (BCS) with radiotherapy the influence of radiation-induced decrease of tissue cellularity should be considered, and consequently higher average ADC values of normal tissue and „non mass“ lesions should be expected.

Hypothesis: Histologic changes induced by radiotherapy following BCS result in higher average ADC values of normal breast tissue and lesions when compared to values in untreated breast.

Aims: General aim is to compare ADC values of breast tissues exposed to radiotherapy following BCS with values in untreated breast in order to determine whether a significant difference between the two groups exists, with possible influence on clinical interpretation of diffusion sequences. Specific aims are to compare values specifically for

each type of normal breast tissue and different benign and malignant lesions as well as to evaluate the influence of other factors.

Materials and methods: The study will include 100 female patients referred at our department for breast MR imaging with various, generally acceptable indications. Exams consisting of conventional non-contrast sequences as well as DWI and DCE MR will be performed using a 1.5T machine with dedicated breast coils. ADC measurements will be recorded for a given region by drawing regions of interest (ROIs) on the parametric map using b-values of 0, 800 and 1000. All detected lesions will be diagnosed according to the ACR-BIRADS lexicon and patients with suspicious lesions will subsequently undergo biopsy.

Expected scientific contribution: Reduction in number of false negative MR findings in patients with residual or recurrent breast cancer, which would positively influence outcome in patients with malignant disease and lower the frequency of unnecessary biopsies and follow-up exams.

Acknowledgments:

MeSH/Keywords: breast cancer, MR, DWI, ADC, breast conserving surgery, radiotherapy

Poster code: T-B-25-136

Poster Title: ASL IN EARLY DIAGNOSIS OF DEMENTIA

PhD candidate: Marko Batinica, MD

Part of the thesis: Arterial Spin Labeling MR Imaging in Early Diagnosis of Dementia

Mentor/s: Associate Professor Fran Borovečki, MD, PhD, Assistant Professor Milan Radoš, MD, PhD

Affiliation: Croatian Institute for Brain Research, Polyclinic Aviva

Introduction: Dementia is a clinical syndrome marked by an acquired loss of cognitive functions leading to impaired functioning and reduced quality of life. Approximately 80.000 people in Croatia suffer from dementia. Early and accurate diagnosis of dementia, such as Alzheimer's disease (AD) or vascular dementia (VaD), is of paramount importance for appropriate patient management. Dementia is diagnosed according to clinical, neuropsychological, radiological and laboratory criteria. Early diagnosis of dementia can sometimes be problematic, and the NINCDS-ADRDA criteria only have a sensitivity of 50-90% for probable AD. More accurate diagnosis can be achieved by including functional brain imaging, such as single-photon emission computed tomography (SPECT). Arterial spin labeling (ASL) is a non-invasive functional MR imaging technique, with clear advantages over SPECT, such as absence of radio ligand application and wider availability of MR.

Hypothesis: ASL can be used in early diagnosis of dementia by detecting brain perfusion changes indicative of AD and VaD.

Aims: To analyze patients with AD and VaD compared to controls using ASL. To assess

the sensitivity and specificity of ASL compared to SPECT. To detect specific patterns of perfusion changes indicative of AD and VaD. To establish possible automated algorithms for AD and VaD detection.

Materials and methods: Twenty patients with AD and twenty patients with VaD will be analyzed compared to controls using ASL performed on the 3T MR scanner, as well as using SPECT. The brain perfusion patterns will be compared and specific changes identified capable of differentiating between the two states. Automated detection protocols will be developed capable of detecting specific changes.

Expected scientific contribution: The study will help establish specific patterns of brain perfusion perturbations indicative of AD and VaD, with an emphasis of differentiating between the two diseases and providing automated protocols for image analysis.

Acknowledgments:

MeSH/Keywords: MR imaging, SPECT, ASL, Alzheimer's disease, vascular dementia

Poster code: T-B-25-138

Poster Title: THE RELATIONSHIP BETWEEN NEUROCOGNITIVE STATUS AND PSYCHOPATHOLOGY, TREATMENT RESPONSE AND VARIANTS OF GENES MTHFR AND ZNF804A IN PATIENTS WITH THE FIRST PSYCHOTIC EPISODE

PhD candidate: Ivana Kekin

Part of the thesis: The relationship between neurocognitive status and psychopathology, treatment response and variants of genes MTHFR and ZNF804A in patients with the first psychotic episode

Mentor/s: Assist. Prof. Martina Rojnić Kuzman, MD, PhD

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

Introduction: Schizophrenia is one of the most disabling psychiatric illnesses, affecting about 1% of population worldwide. In majority of cases, schizophrenia is a chronic illness with a recurrent course, characterized by alternating periods of acute psychotic illness and its remission. Clinical presentation includes cognitive symptoms from the beginning of the disease. Cognitive symptoms in schizophrenia have strong biological basis that is defined from the genetic level.

Hypothesis: Untreated FEP patients show a lower level of cognitive functioning when compared to a healthy control group and results received after 18 months of antipsychotic treatment and remission achievement. The level of cognitive damage will be in correlation with gene variants.

Aims: The general aim is to investigate changes in cognitive functioning and correlated factors in patients with FEP and in comparison to a healthy control group and results received after remission achievement.

Materials and methods: In this study we will include one hundred of up to that moment untreated patients with FEP, and one hundred of healthy controls. The first test will be conducted in the first two weeks of hospitalization and it will include: a detailed psychiatric interview, taking sociodemographic data, and a variety of clinical ques-

tionnaires aiming at assessing the psychiatric and neurological data. During the conduction of the test blood samples will be taken with the aim of genotyping. Also, using the Transcranial Doppler Ultrasonography Method (TCD) we will cerebral blood vessels we will examine the changes in the speed of cerebral blood flow in the medium and anterior cerebral artery while conducting a neurocognitive paradigm consisting of three cognitive tasks, lasting 25 minutes. The second test will be conducted after 12 to 18 months, that is after achieving the full remission and it will again include assessment of psychiatric and neurocognitive status and TCD.

Expected scientific contribution: We expect the results of this study to show the changes in the neurocognitive functioning during FEP and a consequential remission in comparison to a healthy control group. Also, we expect to find correlation between the therapeutic response/progression of illness measured by neurocognitive symptoms and variants of MTHFR and ZNF904A genes.

Acknowledgments:

MeSH/Keywords: schizophrenia, neurocognitive, MTHFR, ZNF804A

Poster code: T-B-29-6

Poster Title: ANTIPSYHOTICS AND DRY EYE SINDROME

PhD candidate: Ivana Bakija, MD.

Part of the thesis: Quality of tear film in chronic schizophrenic patients on long term antipsychotic therapy

Mentor/s: Associate Profesor Igor Filipčić, MD, PhD and Associate Profesor Snjezana Kastelan, MD, PhD

Affiliation: Psychiatric Hospital Sveti Ivan, Zagreb, Croatia, Clinical Hospital Dubrava, Zagreb, Croatia

Introduction: The quality of life of schizophrenic patients is markedly reduced as compared with the general population, in part due to the nature of disease but also the continuous long-term use of antipsychotics. Among the problems that are not often documented are ophthalmic or ocular problems. However there is limited research into the incidence and intensity of these symptoms and there is little known about the reasons for the development of these problems. We believe that the population of schizophrenic patients taking antipsychotics is at risk of developing dysfunction of the tear film and dry eye symptoms.

Hypothesis: Prolonged antipsychotics use causes damage to the tear film in schizophrenic patients resulting in tear film dysfunction and disorders of visual function.

Aims: The primary objective is to compare subjective and objective measures of tear film dysfunction between those taking long-term antipsychotics and healthy controls. The secondary objectives are to establish whether there is a connection between taking antipsychotic drugs and tear film dysfunction and to establish whether there is a need for initial ophthalmic examinations and therapeutic interventions in patients where long-term use of antipsychotics is expected.

Materials and methods: This observational case-control study plans to recruit 200 par-

ticipants, 100 patients treated for schizophrenia with antipsychotic medication for five years or more and 100 healthy subjects who would form the control group. The groups will be matched for relevant parameters where possible (age, sex, smoking, etc). Outcome measures will include evaluation of subjective symptoms of dry eye measured by means of the OSDI questionnaire (Ocular Surface Disease Index). Objective outcome measures will include a Schirmer test to estimate the amount of tear secretion, TBUT (Tear break-up time test) for testing the stability precorneal tear film and Fluorescein test to assess the integrity of the corneal and conjunctival epithelium.

Expected scientific contribution: The expected scientific contribution of this research is to establish whether long-term antipsychotic use reduces the quality of tear film and causes tear film dysfunction. This could improve the health and quality of life of psychiatric patients so that when long-term antipsychotic use is planned, attention will be paid to their ophthalmologic status, which may previously have been ignored due to the nature of their underlying psychiatric condition.

Acknowledgments:

MeSH/Keywords: schizophrenia, antipsychotics, tear film

Poster code: T-B-29-25

Poster Title: GROUP SUPPORTIVE PSYCHOTHERAPY EFFICACY IN TREATMENT OF SCHIZOPHRENIA

PhD candidate: Nataša Đuran, MD, psychiatrist

Part of the thesis: Group supportive psychotherapy (GSP) efficacy in treatment of schizophrenia, a randomized control trial

Mentor/s: Professor Vlado Jukić, MD, PhD, psychiatrist

Affiliation: University Psychiatric Hospital Vrapče

Introduction: Schizophrenia is a set of symptoms that affects thinking, mood, perception and behavior. Despite the new antipsychotics the illness is not well controlled in about 40% of patients. Many clinical trials has tested the effectiveness of different types of psychotherapy but the group supportive psychotherapy was most often used as a comparator, not as the objective itself. In this randomized controlled trial efficacy of group psychotherapy by Kanas model will be compared to the standard therapy.

Hypothesis: Patients suffering from schizophrenia treated with GSP and pharmacotherapy are less in hospital during the first 12 months after discharge, than patients suffering from schizophrenia treated only with pharmacotherapy

Aims: GENERAL To investigate the possible existence of additional performance GSP with the effects of pharmacotherapy in the treatment of schizophrenia. SPECIFIC To explore the differences between patients with schizophrenia treated with pharmacotherapy and GSP and patients with schizophrenia treated with pharmacotherapy in number of rehospitalization, achieving remission, change in quality of life.

Materials and methods: It is planned unicentric, prospective, interventional, randomized, controlled study. The research will be conducted at a hospital Vrapče in Zagreb. The target population makes the

general population of patients diagnosed with schizophrenia (MBK-10, F20), the hospital treated by maintenance therapy with new atypical antipsychotics. It will be used stratified block randomization, the ratio of the experimental and control groups 1: 1. Investigator will do the screening and enrolling patients, and each participant assigned a code number. Randomization will do an independent IT company. Measurement of the main outcomes will not be blinded because the risk of systematic errors in determining the number of rehospitalization is negligible. Measurement of secondary outcome (remission defined PANSS and CGI-) will be blind. Initial measurement and measurement after 12 months will spend a psychiatrist who did not participate in the intervention.

Expected scientific contribution: Any confirmation of hypotheses about the effectiveness of the GSP would present new knowledge about the psychosocial supportive treatment of schizophrenia and thereby contribute to further understanding and shaping the bio-psycho-social model of treatment.

Acknowledgments:

MeSH/Keywords: schizophrenia, group psychotherapy, supportive psychotherapy, rehospitalization

Poster code: T-B-29-35

Poster Title: SUICIDALITY AND AGGRESSION OF ALCOHOL ADDICTS AND OPIATE ADDICTS IN RELATION TO INTERNET DEPENDENCE COMORBIDITY, APPLICATION OF THESIS

PhD candidate: Irena Rojnić Palavra

Part of the thesis: Suicidality and aggression of alcohol addicts and opiate addicts in relation to Internet dependence comorbidity

Mentor/s: professor Vlado Jukić, MD, PhD, psychiatry specialist, assistant professor Ante Bagarić, MD, PhD, psychiatry specialist

Affiliation: Clinic for Psychiatry Vrapče, Croatian National Institute of Public Health

Introduction: Internet dependence is a concept discussed and debated among experts for many years now. The very term implies excessive computer activities which lead to bio-psycho-social changes and problems in an individual. Although entity, diagnostic criteria and guidelines for treatment are not fully defined, it is undisputable that the number of those seeking help increases. The symptoms which are the main reason for searching psychiatric help usually meet the criteria of addiction.

Hypothesis: Research hypotheses are: The prevalence of Internet dependence is higher among hospitalized opiate addicts than among hospitalized alcohol addicts. Suicidality and aggression are higher among hospitalized alcohol addicts with comorbid Internet dependence than among hospitalized alcohol addicts without comorbid Internet dependence. Suicidality and aggression are higher among hospitalized opiate addicts with comorbid Internet dependence than among hospitalized opiate addicts without comorbid Internet dependence.

Aims: The general aim of the research is: To identify differences in the prevalence of Internet dependence among the population of alcohol addicts and the population of opiate addicts and to determine differences in suicidality and aggression among alcohol and opiate addicts in relation to comorbid Internet dependence.

Materials and methods: The sample is made of 548 people - 274 alcoholics and 274 opiate addicts, aged 18-50 years, hospitalized in the Department for Addictions Treatment of the Clinic for Psychiatry Vrapče, Zagreb. We are planning to conduct control of confounders: socio-demographic characteristics, socioeconomic characteristics, personality traits, other psychiatric comorbidities, psychiatric therapy. Statistical analysis will be performed in SPSS 17.0 program, with the level of statistical significance $p < 0.05$ and confidence interval CI 95%. Tool for conducting research is a questionnaire with several parts. The result of 80 or more at Internet addiction test will be considered cut-off score for determining Internet dependence. We are planning to conduct a pilot study on 50 patients before the main study.

Expected scientific contribution: Expected scientific contribution is to identify frequency of Internet dependence with comorbid alcohol and opiate addiction and determining the differences in suicidality and aggression of persons suffering from alcoholism or opiate addiction with comorbid Internet dependence.

Acknowledgments: I thank my mentors for guidance and devoted help.

MeSH/Keywords: MeSH key words: internet

Poster code: T-B-29-39

Poster Title: COMPLEMENTARY AND ALTERNATIVE MEDICINE METHODS FOR THE TREATMENT OF GENERALIZED ANXIETY DISORDER: SYSTEMATIC REVIEW AND META-ANALYSIS

PhD candidate: Hrvoje Barić

Part of the thesis: Complementary and Alternative medicine methods for the treatment of Generalized Anxiety Disorder: Systematic review and Meta-analysis

Mentor/s: Professor Vladimir Trkulja, MD, PhD/ Professor Veljko Đorđević, MD, PhD

Affiliation: Department of Pharmacology, Zagreb University School of Medicine/ Center for Palliative Medicine, Medical Ethics and Communication Skills, University of Zagreb School of Medicine

Introduction: Anxious individuals are a group prone to use of complementary and alternative remedies and it is estimated that half of them uses one of the treatments from the domain of complementary and alternative medicine (CAM) and nearly half of them uses conventional and complementary modalities simultaneously. Number of research confirming efficiency of interventions of alternative and complementary medicine is in rise, as is the number of modalities of CAM interventions.

Hypothesis: Some of the methods of the complementary and alternative medicine are valid in the treatment of generalized anxiety disorder.

Aims: GENERAL AIM: To identify, appraise and summarize "evidence" on efficacy/safety of 5 major groups of modalities used in the past 15 years in the treatment of the generalized anxiety disorder. SPECIFIC AIMS: 1. To identify existing randomized controlled trials (RCT) which assess efficiency and/or safety of CAM methods in treatment of GAD. 2. To appraise quality of individual trials. 3. To quantitatively estimate efficiency and harmfulness of individual CAM modalities. 4. To estimate trends of appearance of randomized clinical trials of individual CAM modalities during past 15 years.

Materials and methods: GENERAL DESCRIPTION Systematic review and meta-analysis. To quantify trends of appearance of

RCTs which investigate CAM methods in the treatment of GAD during last 15 years. QUALITY ASSESMENT, OUTCOMES OF INTEREST and DATA EXTRACTION "Cochrane collaboration risk of bias" will be used for quality assessment. There are two defined groups of outcomes of interest: efficacy and safety/tolerability. For quantitative synthesis of data standard meta-analytical methods will be employed. Individual modalities will be appraised directly, or, where appropriate, indirectly via establishing comparison networks. A final evaluation of the quality of total body of evidence will be made using the GRADE system.

Expected scientific contribution: Detailed identification, systematization, qualitative evaluation and quantitative characterisation of effects of CAM methods in treatment of GAD will provide a synthesis of individual fragmentary elements of „evidence“ in a unified estimate which can have impact on daily practice, as well as point to directions of further primary research. Identification of trends in number and quality of primary studies of evaluated CAM methods defines candidates for further procedures of knowledge synthesis.

Acknowledgments: I would like to thank both mentors for guidance and support.

MeSH/Keywords: complementary therapies, meta-analysis, generalized anxiety disorder

Poster code: T-B-29-60

Poster Title: THE CONCENTRATION OF TRACE ELEMENTS IN THE HAIR OF PEOPLE WITH SCHIZOPHRENIA

PhD candidate: Ivana Todorić Laidlaw, MD

Part of the thesis: The concentration of trace elements in the hair of people with schizophrenia

Mentor/s: Professor Ninoslav Mimica, MD, PhD, Professor Berislav Momčilović, MD, PhD

Affiliation: Psychiatric Hospital Sveti Ivan, Zagreb

Introduction: Differences in the concentration of BE can play an important part in the pathogenesis of schizophrenia. Oxidative stress and thought disorders, often frequent with individuals with schizophrenia, can be the consequence of an alteration in the level of certain metals. Most studies have confirmed the hypothesis that there are differences between the concentration of BE. Nevertheless, the results have mainly been contradictory. Discrepancies could be partly due to insufficiently sensitive analytical procedures, the lack of information on most BE in one sample of biological matrix, or the impossibility of controlling the potentially confusing effects of the nutritive and socioeconomic status, which is lower among individuals with schizophrenia.

Hypothesis: There are differences in the concentration of BE and in the main BE samples between individuals with schizophrenia and healthy individuals.

Aims: The main aim is to establish the differences in the concentration of 43 BE between the target and the control group comparable by age, sex and permanent residence. The specific aims are to establish the differences in the concentration of each one of 43 BE between healthy population and individuals with schizophrenia, describe the main samples of BE.

Materials and methods: The target population will include individuals diagnosed with schizophrenia of both sexes, between 25 and 35 years of age, permanently resident in

the area of the City of Zagreb, hospitalized in both hospitals. The control group will be made of employees, not affected by psychiatric illnesses, and homogeneous by age, sex and residence. Samples of hair will be taken between the scalp and the occipital region, cut off and prepared for analysis according to scientific standards. The samples will be analyzed using Inductively Coupled Plasma Mass Spectrometry at the Centre of Medical Research in Zagreb. The multielement profile will be expressed in micrograms of elements per gram of sample tissue ($\mu\text{g/g}$). Data about demographic, social, nutritive and clinical parameters will be gathered with the help of a questionnaire.

Expected scientific contribution: Possible findings on different concentrations and main concentration components of BE would contribute to the better understanding of the pathogenesis of schizophrenia. More sensitive analytical procedures, and data about a higher number of BE in the same biological matrix sample may contribute to understand the contradictory results of former studies.

Acknowledgments: I would like to thank my mentors Professor N.Mimica and Professor B.Momčilović for their support, teachings and guidance.

MeSH/Keywords: Schizophrenia, Trace elements, Multielement profile, ICP-MS, hair

Poster code: T-B-29-68

Poster Title: FIGHTING HOPELESSNESS

PhD candidate: Goran Jurcan, MD

Part of the thesis: The effect of short group dynamic psychotherapy on a sense of hopelessness in patient with depression and anxiety disorders: randomized controlled trial

Mentor/s: Professor Vlado Jukić, MD, PhD

Affiliation: University of Zagreb School of Medicine, University Psychiatric Hospital Vrapče

Introduction: Hopelessness is one of the key predictors of all three forms of suicidality: suicidal thoughts, attempts and committed suicide, regardless of the primary diagnosis. In this randomized controlled trial we will examine the effect of short group dynamic psychotherapy on a sense of hopelessness in patients who are hospitalized and treated for depression and anxiety disorders.

Hypothesis: A brief group dynamic psychotherapy will have a positive impact on reducing feelings of hopelessness in patients suffering from depression and/or anxiety disorders.

Aims: Main objective is to determine whether there is a statistically significant change in the results on the Beck Hopelessness scale before, during and after a short group dynamic psychotherapy.

Specific objectives are to compare changes on Hamilton anxiety rating scale, Hamilton depression rating scale, Rosenberg self esteem scale, Columbia suicidality rating scale, to determine whether there is a correlation between the reduction of hopelessness with other observed parameters and to determine predictive factors for reducing feelings of hopelessness.

Materials and methods: It is planned a unicentric, prospective, interventional, ran-

domized, single-blinded, controlled study. The target population makes the population of patients with depression (ICD-10: F32, F33), neurotic and somatoform disorders and disorders caused by stress (ICD 10: F40-F48) treated at the Department for treatment and rehabilitation of University Hospital Vrapče. Subjects will be randomized into two groups. The first group will be treated with short group dynamic psychotherapy for four weeks, four times a week, ninety minutes per session. The second will be the control group. Assessments will be carried out before, after two weeks and at the end of the trial.

Expected scientific contribution: The effect of short group dynamic psychotherapy on a sense of hopelessness has not yet been investigated. This research may help in better scientific and clinical positioning of short group dynamic psychotherapy and in the evaluation and compilation of future treatment algorithms for depressive and anxiety disorders and suicidality.

Acknowledgments:

MeSH/Keywords: hopelessness, suicidality, short group dynamic psychotherapy, depression, anxiety

Poster code: T-B-29-73

Poster Title: EXAGGERATED PLATELET ACTIVITY IN BLOOD AND SALIVA AS AN INDICATOR OF INCREASED CARDIOVASCULAR RISK IN PATIENTS WITH PTSD

PhD candidate: Iva Rakoš

Part of the thesis: Platelet reactivity can be an indicator of cardiovascular risk in people with PTSD.

Mentor/s: Anđelko Vidović, PhD, MD

Affiliation: University Hospital Dubrava, Department of Psychiatry

Introduction: In addition to traditional risk factors, stress is recognized as an important risk factor for cardiovascular disease. The biological mechanisms responsible for this association have not been adequately investigated thus we have not yet found the potentially useful measures for the prevention of cardiovascular disease in people with PTSD. Although it is known that people with PTSD have increased adrenaline secretion, it is not known whether their platelets are activated more strongly in stress reactions in relation to persons without PTSD. It is also not known whether the indicators of platelet activation can be reliably measured in saliva, which would allow non-invasive determination of indicators of cardiovascular risk.

Hypothesis: Exaggerated platelet activity can be a non-invasive indicator of cardiovascular risk in patients with PTSD.

Aims: The general objective of the proposed research is a better understanding of the pathophysiological mechanisms linking PTSD and cardiovascular disease and finding biomarkers of that connection in saliva in order to improve prevention and treatment of cardiovascular disease in people with PTSD. Specific objectives of the proposed research are: 1. determination of platelet reactivity as an indicator of cardiovascular risk in people with PTSD and comparison with healthy subjects 2. determining the indicator of platelet activation in saliva.

Materials and methods: Recruitment of participants will be carried out according to pre-defined criteria for inclusion in the study. The following psychiatric instruments for the diagnosis and assessment of symptoms will be applied: MINI, HAMD, HAMA, CAPS, STAI. The health of the oral cavity will be checked with clinical oral examination. CPITN will be used for the assessment of periodontal health. For the assessment of excretory function of the salivary glands we will measure the total volume of unstimulated saliva in a unit of time. We will use standardized test for induction of acute stress in laboratory conditions. We will determine the expression of CD62P on platelets and shares of the platelet-leukocyte aggregates.

Expected scientific contribution: By achieving clearly defined specific objectives, the proposed research will contribute to a better understanding of the pathophysiological mechanisms linking stress and cardiovascular disease. Analysis of saliva will contribute to the development of new, non-invasive method of detection and monitoring of cardiovascular risk.

Acknowledgments:

MeSH/Keywords: Blood Platelet Disorders/complications, Platelet Activation/physiology, Stress Disorders, Post-Traumatic/complications

Poster code: T-B-29-87

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

PhD candidate: Andrea Ražić Pavičić, MD

Part of the 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 Centar 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.

Hypothesis: 1. Primary infertile women in the procedure of IVF, compared with women with natural conception have more pronounced insecure style of attachment, temperament dimension of harm avoidance and more maladaptive ways of coping with stress. 2. Primary infertile women with negative outcome of IVF, compared with primary infertile women with positive outcome of IVF have more pronounced insecure style of attachment, temperament dimension of harm avoidance and more maladaptive ways of coping with stress.

Aims: Main aim: To examine the correlation between attachment styles, personality dimensions and ways of coping with stress, and the outcome of IVF. Specific aims: 1. To determine whether there are differences in attachment styles, personality dimensions and ways of coping with stress, between infertile women in the procedure of IVF and the healthy control group. 2. To determine whether there are differences in attachment styles, personality dimensions and ways of coping with stress, between infertile women

with positive outcome of IVF and infertile women with negative outcome of IVF.

Materials and methods: The research will include a total of 100 women divided into three groups. Clinical group (N 50): women diagnosed with primary infertility entering for the first time IVF treatment. There will be two points of investigation: T1: before the start of treatment, T2: at 6-8 weeks' gestation. Regarding the outcome, group will be divided to primary infertile women with positive IVF outcome and primary infertile women with negative IVF outcome. Control group (N50): women with natural conception. Instruments: psychological questionnaires: General data questionnaire, Experiences in close relationships inventory, TCI-R, Cope inventory.

Expected scientific contribution: This study will contribute to better understanding of specific psychological concepts- attachment styles, personality traits- and their role in the way of coping of infertile couples in the process of IVF with stress. If the hypothesis will be confirmed we will support the existing theoretical models, and the results could be used in psychotherapeutic interventions during IVF treatment.

Acknowledgments:

MeSH/Keywords: attachment, temperament, infertility, in vitro fertilization

Poster code: T-B-29-140

Poster Title: IMPACT OF OBSTRUCTIVE SLEEP APNEA SYNDROME ON MACROSTRUCTURE AND MICROSTRUCTURE OF SLEEP AND FUNCTION OF CARDIOVASCULAR AUTONOMIC NERVOUS SYSTEM

PhD candidate: Marina Mioč

Part of the thesis: Impact of Obstructive Sleep Apnea Syndrome on Macrostructure and Microstructure of Sleep and Function of Cardiovascular Autonomic Nervous System

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

Affiliation: Barbara Barun, MD, PhD

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

Hypothesis: Sleep disorders are a growing problem and they can be associated with many other diseases. In recent years a growing number of studies suggest the influence of macro- and microstructure of sleep on the functioning of the autonomic nervous system. In patients with obstructive sleep apnea syndrome (OSA) the upper airways tend to collapse during sleep and this leads to intermittent hypoxia and sleep fragmentation which can cause structural damage of the brain. This is a possible cause of the autonomic system damage, particularly cardiovascular autonomic function.

Aims: Damage of cardiovascular autonomic function in patients with sleep apnea syndrome is associated with changes in micro and macrostructure of sleep.

Materials and methods: The main goal of this study is to determine the frequency of autonomic dysfunction and characteristics of sleep macro and microstructure in patients with the OSA syndrome and patients with other sleep disorders and differences between those two groups.

Expected scientific contribution: In the study will be included 100 people, 50 pa-

tients with OSA syndrome and 50 patients with other sleep disorders. All participants in the study will sign an approved informed consent. They will visit the clinic three times during the research. On their first visit they will be introduced with the methods and the objectives of the research and will sign an informed consent. All patients will have to meet the following criteria: they will need to have a diagnosis of sleep disorders according to the international classification of sleep disorders of the American Academy of Sleep Medicine, they should not have any cognitive or psychiatric disorders that could prevent understanding of the research or have any contraindication for Tilt-table testing. Subjects who meet the criteria will be re-invited to the hospital and will fill out questionnaires for evaluation of sleep quality and then will spend the night at the clinic in order to do full night polysomnography and Tilt table test the next day.

Acknowledgments: I would like to thank my mentors Barbara and Mario.

MeSH/Keywords: sleep disorders, sleep microstructure, autonomic nerve function.

Poster code: T-B-30-8

Poster Title: THE IMPACT OF STATINS ON COGNITIVE STATUS IN PATIENTS WITH MILD COGNITIVE IMPAIRMENT

PhD candidate: Irena Kovačić, MD

Part of the thesis: The impact of statins on cognitive status in patients with mild cognitive impairment

Mentor/s: Professor Goran Šimić, MD, PhD, Professor Silvio Bašić, MD, PhD

Affiliation: Clinical Hospital Dubrava – Zagreb, Clinical Hospital Merkur – Zagreb

Introduction: Mild cognitive impairment (MCI) is a syndrome at the boundary of normal aging and dementia that includes deficits in cognitive abilities not expected in regard to age and level of education. Studies have shown that people with MCI have an increased risk for developing dementia, especially Alzheimer's disease. Some studies have shown that plasma cholesterol can influence the metabolism of amyloid precursor protein. In addition to their cholesterol-lowering effects, statins also inhibit isoprenylation of amyloid precursor protein, which reduces amyloid beta production and amyloid plaque formation.

Hypothesis: Liposoluble statins (which lower cholesterol levels, reduce the deposition of amyloid, and inhibit isoprenylation of amyloid precursor protein) may decelerate changes in cognitive status in patients with hypercholesterolemia and mild cognitive impairment.

Aims: 1. To determine cognitive status of patients initiating treatment, after 6 months and after one year. 2. To determine levels of total cholesterol, LDL, HDL, and triglycerides at treatment onset and then every three months for a duration of one year. 3. To determine the impact of changes in total cholesterol, LDL, HDL and triglyceride levels and changes in cognitive status in both groups of patients at baseline, after six months, and after a one year period.

Materials and methods: Using recommendations from the National Institute on

Aging-Alzheimer's Association workgroups, Mini Mental State Examination (MMSE) and ADAS/ADAScog, we will assess 100 MCI patients with hypercholesterolemia, 50 of whom will be given statins, while the other 50 will not receive a statin. All respondents will be advised to change their diet to a Mediterranean diet. At initiating treatment we will determine complete blood tests including electrolytes, thyroid function, albumin, levels of vitamin B12, VDRL, ECG and MRI of the brain. The level of total cholesterol, LDL, HDL and triglyceride we will determine when initiating treatment and then every three months for a period of one year. Mini-mental status and ADAS/ADAScog will be determined at baseline, after 6 months, and after one year.

Expected scientific contribution: The research results will contribute to answering the question about the use of statins in the treatment of dementia: any demonstrated positive effect of statins on cognitive abilities will contribute to the consideration of a possibility of their preventive use in individuals with MCI and AD.

Acknowledgments:

MeSH/Keywords: cognitive status, statins, hypercholesterolemia, mild cognitive impairment (MCI)

Poster code: T-B-30-64

Poster Title: THE SIGNIFICANCE OF THE POSTPROCESSING BRAIN MRI (MAGNETIC RESONANCE IMAGING) IN THE PREOPERATIVE DIAGNOSIS OF PATIENTS WITH PHARMACORESISTANT EPILEPSY

PhD candidate: Andreja Bujan Kovač

Part of the thesis: The significance of the postprocessing brain MRI (magnetic resonance imaging) in the preoperative diagnosis of patients with pharmaco-resistant epilepsy

Mentor/s: Professor Sanja Hajnšek, MD, PhD and Assistant professor Milan Radoš, MD, PhD

Affiliation: University Hospital Centre Zagreb and School of Medicine, University of Zagreb, Department of Neurology, Referral Centre for Epilepsy of the Ministry of Health of the Republic of Croatia

Introduction: Epilepsy is a chronic disease of the central nervous system that affects 1% of the population. The large number of patients with the proper selection of AEDs (antiepileptic drug), can achieve satisfactory seizure control, while the remaining 25-35% have pharmaco-resistant epilepsy and are considered for neurosurgical treatment. The most significant neuroradiological procedure in proper selection of candidates suitable for neurosurgery is MRI 3T (magnetic resonance imaging). Post-processing of brain MRI with MAP07 software (Morphometric Analysis Program) is a new sophisticated diagnostic procedure that offers a number of graphical post-processing maps which facilitates detection of subtle cortical malformations.

Hypothesis: MAP07 software facilitates detection and localization of structural epileptogenic lesions.

Aims: The aim of proposed study is to assess the impact of application MAP07 in more accurate detection of structural epileptogenic lesions that are CVA (conventional visual analysis) and MRI negative.

Materials and methods: 100 patients with pharmaco-resistant epilepsy will be recruited in the research and processed according to algorithm which includes Phase I procedures, and in the case of pharmaco-resistance Phase II of preoperative assessment.

In all patients 3 T MRI will be acquired according to the protocol for epilepsy. MRI will be analysed by neuroradiologist specially trained in MAP07 software and classified as MRI positive or MRI negative. Then, post-processing of brain MRI with MAP07 will be performed by using three statistical maps -"extension image", "junction image" and "thickness image" and the method of "curvilinear reformatting". Finding will be marked as MAP07 positive or negative. Neuroradiologist in collaboration with two neurologists and electrical engineer will re-examine all MRI sequences marked by MAP07 and conclude findings as MAP07 positive/MRI positive or MAP07 positive/MRI negative.

Expected scientific contribution: MAP07 is a highly sophisticated non-invasive software that uses standard 3T MRI sequences. Implementation of MAP07 in routine preoperative assessment of patients with refractory epilepsy may help in detection of subtle epileptogenic lesions and lead to early decision of resective neurosurgical treatment.

Acknowledgments: Prof. Sanja Hajnšek, MD, PhD and Assist. Prof. Milan Radoš, MD, PhD

MeSH/Keywords: epilepsy, post-processing, malformation of cortical development, hippocampal sclerosis

Poster code: T-B-30-162

2.3.

Public Health and Health Care – Research Proposals

Poster Title: RISK ASSESMENT ON WEST NILE VIRUS INFECTION IN CROATIA

PhD candidate: Iva Pem Novosel, MD

Part of the thesis: Risk assesment on West Nile virus infection in Croatia

Mentor/s: Tatjana Vilibić-Čavlek, MD, PhD, Ljubo Barbić, VMD, PhD, Professor

Affiliation: Croatian Institute of Public Health (CIPH), Faculty of Veterinary Medicine University of Zagreb

Introduction: West Nile virus (WNV) is a mosquito-borne virus that belongs to the family Flaviviridae, genus Flavivirus. Its natural cycle involves birds as the amplifying hosts and mosquitoes (mainly of the genus *Culex*) as vectors, whereas humans and horses are considered incidental hosts. Suitable climatic conditions are essential to maintain the natural cycle of WNV.

Hypothesis: There is a correlation between the prevalence of WNV infection in humans/horses and climatic, geomorphological and demographic parameters.

Aims: 1. Analyze epidemiological characteristics of WNV infection in Croatia in humans and sentinel horses during 2011-2014 transmission seasons. 2. Analyze correlation of climatic, geomorphological, spatial and demographic parameters with WNV infection in humans/horses and develop a multivariate model to predict WNV infection.

Materials and methods: Study design: Cross-sectional study. Material: Human (patients with WNV neuroinvasive disease and asymptomatic subjects) and horse serum samples from counties with reported human clinical cases (200 human/horse samples/county). Stratified convenience sample. Human samples will be tested for WNV IgM/IgG antibodies by ELISA (Euroimmun, Lübeck, Germany) and confirmed by neutralization test. Horse samples will be tested for WNV IgG antibodies by ELISA. Reactive samples will be tested for IgM antibodies (ID.VET, Montpellier, France). Climatological parame-

ters: temperature/temperature changes in the month prior to the occurrence of cases, relative humidity, rainfall. Geomorphological and spatial features: geographical position, distance from the rivers, marshes, lakes and estuaries, flood area, forests, population density, level of urbanization, altitude, vector control measures. Demographic and clinical characteristics of patients: age, gender, date of disease onset, clinical diagnosis, comorbidities, place of residence. Statistical analysis: $P < 0.05$ will be considered statistically significant. Two-tailed tests of statistical significance will be used. Univariate association of independent variables with WNV prevalence will be analyzed by binary logistic regression. All variables with statistically significant univariate association with WNV ($P < 0.25$) will be included into the multivariate logistic regression model.

Expected scientific contribution: Potential successful modeling with satisfactory predictive values of WNV infection would allow develop algorithm of early warning system and improve targeted vector control measures.

Acknowledgments: Author thanks Marica Glamočanin, Ljiljana Milašinčić, Snježana Artl, and Snježana Kovač for technical assistance.

MeSH/Keywords: West Nile virus, epidemiology, Croatia

Poster code: T-C-1-150

Poster Title: INTEGRATED METHOD IN CULTURAL ADAPTATION AND TRANSLATION OF INSTRUMENTS MEASURING MASCULINITY AND INJURIES

PhD candidate: Natko Gereš

Part of the thesis: Methodology

Mentor/s: Aida Mujkić Klarić, Pamela Loretto Orpinas

Affiliation: A. Štampar School of Public Health, School of Medicine, University of Zagreb

Introduction: College of Public Health, University of Georgia, USA

Hypothesis: Assessment of health is main component of health care. In order to measure or assess aspects of physical, mental or social health of people in diverse settings, and the societal influences on it, measures need to undergo a process of cultural adaptation and translation, to accurately capture conditions related to health. In this article, we discuss the usage and further development of an integrated method for cultural adaptation and translation of measures before they are to be used in the local context.

Aims: The measure should secure etic (relevant across cultures) and emic (specific to culture) perspectives, identifying similarities and differences in the indicators of the measure.

Materials and methods: Article presents phase of development of methodology for measuring impact of masculine norms on the incidence of accidents and injuries among male adolescents in Croatia, by using the suggested integrated method, concluding with additional steps to challenge limitations of the original proposed method. Author suggests five phases in using the integrated method that involve two groups of authorities: the researchers that will turn to representatives of the target community (community experts) in cultural and lingu-

istic issues. In using this integrated methodology, we included, as suggested by the author, bilingual and bicultural community members to strengthen the task performance. We included community experts fluent in both the source and target language and who expressed belonging to both the source and target culture.

Expected scientific contribution: Described integrated method is grounded in the logical frame which consists of joined collaboration between researchers and community members in development of a research project in conceptualizing and operationalizing health concepts, in this case also adding concepts related to masculinity, suggested to influence health. Method depends upon determining if the concept entrenched in the measure in the source language, is explained and embodied in a complementary way in the target culture.

Acknowledgments: Souraya Sidani SG, Joyal Miranda, Marilyn Ford-Gilboe, Colleen Varcoe. Cultural Adaptation and Translation of Measures: An Integrated Method. RESEARCH IN NURSING

MeSH/Keywords: injuries, accidents, integrated method, translation, masculinity, adolescents

Poster code: T-C-2-5

Poster Title: CONCEPTUAL MODELING OF THE HOSPITAL UNITS BASED ON ENVIRONMENTAL AND ECONOMIC SUSTAINABILITY

PhD candidate: Vitaliy Sarancha

Part of the thesis: Application of LCA, FA, S-LCA to the Healthcare System Unit to become sustainable

Mentor/s: Prof. Stjepan Orešković, PhD, Prof. Ksenija Vitale, PhD, MPH

Affiliation: Department of Medical Biochemistry – General Hospital of Zabok

Introduction: New designed methodologies emphasize the importance of a “holistic” systems understanding. The Life Cycle Assessment could be applied to processes in a Healthcare. The method offers 4 stages, step – by - step assessment process. A combination of LCA together with financial analysis could be proposed in relation to a particular HCS unit.

Hypothesis: The optimization of Input parameters of a given HCS unit according to sustainability principles leads to higher socioeconomic efficiency.

Aims: General aim: to prove that optimization of input parameters leads to higher socioeconomic efficiency with possibility to transpose results for development of a strategy for a Healthcare system as a whole to become more sustainable. Specific aims: - To define and analyse input and output parameters, - To perform modeling while changing the inputs into more environmentally friendly and cost – efficient, - To define possible parameters that would lead to optimization.

Materials and methods: As methods of evaluation the financial analysis, statistics, modeling and life cycle assessment have been proposed. All given inputs, such as chemical reagents, solutions, materials produced of glass, plastic, paper, water, energy resources – gas, fuels, electricity and expenses have been analysed. The outputs, such as air, water pollution, waste products elimination or reuse and needed costs, have

been performed through the unit’s life cycle. The changes and substitution of the material and non - material (e.g. human resources qualification) components have been proposed in order to optimize the productivity and efficiency. More environmentally friendly and cost – effective materials and processes have been advised, while those non – environmentally friendly and economically ineffective have been excluded. The quantitative data will be presented according to international standards ISO 14040–14043, ISO 26000.

Expected scientific contribution: A complex pattern - matching score system for obtained results formalization will be designed. An efficient application of the life cycle assessment methodology to the Healthcare system unit’s life cycle as one leading to sustainable use of limited resources and materials will be proved. Consequently, more financial means will be remained in a Healthcare system and could be used for purposes of research, primary medical and better patients care.

Acknowledgments: Prof. Stjepan Orešković, PhD, Prof. Ksenija Vitale, PhD, MPH, Prof. Vadym Sulyma MD, PHD, Gromada Zlata d.o.o

MeSH/Keywords: Life cycle assessment, environmental health, healthcare management, public health, sustainability

Poster code: T-C-2-42

Poster Title: IMPLICATIONS OF A SIMPLISTIC APPROACH TO AR DRG IMPLEMENTATION IN CROATIA

PhD candidate: Karolina Kalanj, MD

Part of the thesis: Impact of AR DRG payment model on hospital efficiency in Croatia

Mentor/s: Stipe Orešković, PhD, Professor

Affiliation: Karol consulting d.o.o

Introduction: AR DRG is an Australian inpatient classification system and it has been used as a method for hospital activity measurement and payment in many countries. Croatia embarked on AR DRG implementation ver.5.2 in 2007 expecting to increase hospital efficiency and transparency, and contain costs.

Hypothesis: Introduction of the Australian Diagnosis Related Groups Classification System (AR DRG) did not result in improved efficiency of Croatian acute hospitals. Monitoring of hospital performance based on grouping patients in AR DRG groups and data transparency did not have an effect on hospital organizational network. Impact on improved quality of healthcare services in hospitals as a result of introduction of the prospective payment model cannot be demonstrated.

Aims: The objective of research is to analyse the implementation of AR DRG model in the hospital health care system and its impacts on hospital efficiency, transparency and quality of care.

Materials and methods: Croatian Health Insurance Fund data, that are specific to AR DRG reporting will be used for evaluation of hospital performance: a) Number of episodes of care per annum, b) Casemix (average patient complexity in the context of severity of clinical features for each hospital), c) Number of same day cases, d) PCCL index (PCCLs are a measure of the cumulative effect of a patient's complications and co-

morbidities, and are calculated for each episode.), e) Frequency analyses for Error DRGs, f) Number of bed days per hospital, f) Hospitals annual financial reports. All data are publicly available for the period from 2010 to 2014. Evaluation of the effects of introduction of AR DRG model on hospital efficiency will be conducted using data envelope analyses and stochastic frontier analyses.

Expected scientific contribution: Introduction of a prospective payment model for hospital services is a complex process, requiring extensive technological, managerial and political willingness. This thesis will serve as a technical know-how model and identify the corrective actions that would contribute to the improvement of the efficiency of the Croatian hospital system and the quality of healthcare services. Considering that the AR DRG model is in use in all former Yugoslav countries, the topic of this thesis will be applicable regionally.

Acknowledgments: I would like to thank to my mentor prof. Stipe Orešković, who thought me how to find answers and not to be afraid to ask why, He was always there for me. I dedicate this thesis to my family for their constant care and unconditional love.

MeSH/Keywords: Health reform, AR DRG, hospital payment formula, efficiency, quality of care

Poster code: T-C-2-61

Poster Title: 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

Part of the 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.Arjana Tambic Andrasevic, Prof.Gjylle Mulliqi Osmani

Affiliation: University of Zagreb Hospital for Infectious Diseases, Department of Microbiology Institute of Public Health Kosova, University of Prishtina, Faculty of Medicine

Introduction: Urinary tract infections are the most frequent bacterial infections. E.coli is the most common urinary tract pathogen. Resistance to antibiotics is a growing problem worldwide, and rates of bacterial resistance vary depending on local antibiotic usage habits.

Hypothesis: Antibiotic resistance rates in Kosovo are high particularly in enterobacteriaceae. Resistance rates greatly affect treatment options for urinary tract infections.

Aims: Aim was to investigate the level and mechanisms of resistance in major urinary tract pathogens and to evaluate treatment options for urinary tract infections (UTI).

Materials and methods: We will collect bacterial isolates that are non-copy isolates and are present in urine in pure culture in

the amount $\geq 10^5$ cfu/mL in the period for six months. Antibiotic sensitivity testing will be done by disk diffusion according to EUCAST standards. Isolates with important resistant phenotypes will be analysed further for presence of resistance mechanisms by phenotypic and molecular techniques.

Expected scientific contribution: Antibiotic resistance is a global problem so analysing resistance patterns locally is extremely important for understanding global spread of resistant organisms. The results of the study will also help to develop evidence based guidelines for treatment of urinary tract infections.

Acknowledgments:

MeSH/Keywords: UTI, ESBL

Poster code: T-C-2-79

Poster Title: RELATION OF METEOROLOGICAL PARAMETERS, ATMOSPHERIC PARTICULATE MATTER CONCENTRATION AND NUMBER OF PATIENTS WITH CARDIOVASCULAR CONDITIONS IN AN EMERGENCY DEPARTMENT

PhD candidate: Vedrana Ereš, MD

Part of the thesis: Relation of meteorological parameters, atmospheric particulate matter concentration and number of patients with cardiovascular conditions in an emergency department

Mentor/s: Professor Jadranka Mustajbegović, MD, PhD, Professor Hrvoje Pintarić, MD, PhD

Affiliation: University of Zagreb, School of Medicine, Andrija Štampar School of Public Health, Zagreb, Emergency Department of University Hospital Center Sestre milosrdnice, Zagreb

Introduction: The Emergency Department (ED) of University Hospital Center (UHC) Sestre milosrdnice currently integrates four medical specialties: internal medicine, surgery, neurology and psychiatry. Medical staff of the ED noted different frequency in medical diagnosis from day to day. Some days prevailing medical conditions in the ED include cardiovascular (CV) problems, other days various types of gastrointestinal bleeding or epileptic seizures or suicidal attempts. It is known that meteorological conditions (temperature, atmospheric pressure, air humidity) and, more recently, particulate matter (PM particles) atmospheric concentration can affect human health. PM particles are aerosols composed of a number of components, including acids, metals, organic chemicals, soil, dust. Their size is directly connected to their negative effect on human health – the smaller the diameter of PM particles the more dangerous is the effect on health. Of our concern are particles smaller than $10\ \mu\text{m}$ in diameter, especially those below $2.5\ \mu\text{m}$. Inhaled from the air, they can dissolve in blood and be transported via blood to other body organs.

Hypothesis: Meteorological conditions and the atmospheric PM particles concentration are related to the number of patients presenting with CV symptoms in the ED.

Aims: To explore the relation of the occurrence of CV emergencies and meteorological condi-

tions (data from 1st July 2008 to 30th June 2015). Our objectives would be: A) to investigate the number of patients presenting with CV symptoms in the ED of UHC Sestre milosrdnice, B) to examine the prevalence of CV conditions by diagnosis (ICD 10), C) to present meteorological parameters and the atmospheric PM particles concentration in the part of Zagreb that administratively belongs under the ED of UHC Sestre milosrdnice.

Materials and methods: The IT database of the ED of UHC Sestre milosrdnice and data regularly measured (on an hourly and daily basis) by the Meteorological and hydrological institute of Croatia will be used. The statistical analysis of the normal distribution of the data obtained will be performed (Kolmogorov – Smirnov test). Depending on the results appropriate parametric and/or non-parametric test will be used.

Expected scientific contribution: We expect that our study will contribute to the routine use of meteorological data in the risk assessment of possible CV incidents and expected number of patients with CV symptoms in EDs and consequently improve the organization of this department, particularly in appropriate staffing.

Acknowledgments:

MeSH/Keywords: particulate matter, emergency.

Poster code: T-C-6-144

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