

Sveučilište u Zagrebu, Medicinski fakultet/University of Zagreb, School of Medicine
Doktorski studij Biomedicina i zdravstvo/PhD Programme Biomedicine and Health Sciences
Dan doktorata 2014/PhD Day 2014
Knjiga sažetaka/Abstract book

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A CIP catalogue record for this book is
available from the National and University
Library in Zagreb under ??????.
ISBN 978-953-176-???-?

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**Doktorski studij
Biomedicina i zdravstvo
PhD Programme
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Abstract book



MEDICINSKA NAKLADA
ZAGREB, 2014.

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PREFACE

PHD DAY 2014 PROGRAMME

1. RESEARCH ABSTRACTS

1.1. BASIC MEDICAL SCIENCES – RESEARCH ABSTRACTS

POSTER TITLE: EXPRESSION OF PLAKOPHILIN 3 IN DIFFUSE MALIGNANT PLEURAL MESOTHELIOMA

PhD candidate: Silvija Mašić, MD

Part of the thesis: Expression of plakophilin 3 in diffuse malignant pleural mesothelioma

Mentor/s: Professor Sven Seiwert, MD, PhD

Affiliation: Institute of Pathology, University of Zagreb, School of Medicine, Šalata 10, Zagreb
Institute of Emergency Medicine, City of Zagreb, Heinzelova 88, Zagreb

Introduction: Diffuse malignant pleural mesothelioma is the most common primary malignant neoplasm of pleura. It represents diagnostic and also clinical challenge due to its histological heterogeneity and clinical outcome. There are 3 main histological types: epithelioid, sarcomatoid and biphasic. Epithelioid type is the most common and has the most favourable prognosis, while sarcomatoid is related to the worst prognosis. Plakophilins are structural proteins important for stability, adhesion of cells, intercellular interactions and cellular signaling, but there are little data about their role in tumorigenesis and tumor progression. Research on various types of tumor demonstrated that the change of plakophilin 3 expression is related to biological characteristics of tumor and patients survival.

Materials and methods: Archival tissue samples of 97 patients with established diagnosis of diffuse malignant pleural mesothelioma and 5 samples of normal pleural tissue were used. Samples were classified into 3 main histological types of diffuse malignant pleural mesothelioma and subtypes of epithelioid mesothelioma based on the prevalent histological component of the tumor. After immunohistochemical staining, levels of plakophilin 3 expression in cytoplasm and membranes of immunoposi-

tive tumor cells were evaluated. Expression of plakophilin 3 with consideration to histologically estimated aggression in tumor growth and its prognostic value in diffuse malignant pleural mesothelioma was studied.

Results: Plakophilin 3 expression was significantly increased in membrane and cytoplasm in samples with more aggressive tumor growth, when all of them considered. In subtypes of epithelioid mesothelioma, significantly increased expression was seen in the cytoplasm of trabecular and tubular type with more aggressive growth and in the membrane of histologically more aggressive trabecular and tubulopapular type. There was no significant association between plakophilin 3 expression and patients survival.

Discussion: Based on our results, expression of plakophilin 3 in both cytoplasm and membrane was increased in samples with more aggressive tumor growth, so increased plakophilin 3 expression may indicate a histologically invasive phenotype.

Acknowledgments:

MeSH/Keywords: Plakophilin 3, diffuse malignant pleural mesothelioma, prognostic value, immunohistochemistry

Poster code: A-3-50

POSTER TITLE: BPC 157 HEALS COLOVESICAL FISTULAS IN RATS

PhD candidate: Tihomir Grgić MD

Part of the thesis: BPC 157 has beneficial activity on the special healing circumstances in the colovesical fistulas healing. Thus, we studied gastric pentadecapeptide BPC 157 parental and peroral therapy in rats with colovesical fistulas.

Mentor/s: prof. dr. sci. Predrag Sikirić

Affiliation: University of Zagreb, School of Medicine

Introduction: We created model of internal fistula- enterovesical fistula in rat. The pentadecapeptide BPC 157 has already shown the effectiveness in healing gastrocutaneous and colocutaneous fistulas as a model of external fistulas, so we suggest it as a possible therapy of colovesical fistulas as a model of internal fistulas. In our study we showed effectiveness of BPC 157 in healing of colovesical fistulas.

Materials and methods: 75 male Wistar albino rats were randomly assigned into five groups. Colovesical fistulas were created at 5 cm from anocutaneous borderline, with diameter of 3 mm. Control groups were received drinking water, saline i.p (5 mL/kg). Therapy groups were received pentadecapeptide BPC 157 i.p. (10 µg/kg, 10 ng /kg) and perorally (10 µg/kg). First application at 30 min following surgery, last 24 h before sacrifice (at postoperative days 7, 14, 28).

Results: We showed that BPC 157 heals enterovesical fistulas caused healing process on

the colon, vesical and on the fistula canal at the same time. BPC 157 has healing effect at the different ways of its application(perorally, intraperitoneally) and at the different doses of BPC.

Discussion: As we described before, BPC 157 improve healing of external fistulas, and this healing may be related to the NO – system. We proposed that the NO- system has a particular significance in this multiple wound healing system: maintaining an undisturbed and non- blunted NO- generation would sustain the normal healing course of the colovesical fistula, bladder and colon wounds and these findings were also supported biomechanically and functionally.

Acknowledgments: According to this, results could present a new possible pathway in therapy of colovesical fistulas.

MeSH/Keywords: fistula, rat, BPC 157

Poster code: A-4-10

POSTER TITLE: PENTADECAPEPTIDE BPC 157 ANTIARRHYTHMIC EFFECT IN RATS TREATED WITH BUPIVACAINE TOXIC DOSES

PhD candidate: Gordana Živanović-Posilović, MD, MSc

Part of the thesis: Pentadecapeptide BPC 157 Antiarrhythmic Effect in Rats Treated With Bupivacaine Toxic Doses

Mentor/s: Professor Predrag Sikirić, MD, PhD

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

Introduction: Bupivacaine, still drug of choice in all the techniques of regional anaesthesia, acts mainly through blockade of Na⁺ channels, K⁺ and Ca²⁺ channels as well, changing the way heart conduction system works with very serious and mostly lethal cardiac rhythm disturbances in a case of inadvertent i.v. application because we still don't have an antidote that could be applied. Pentadecapeptide BPC 157 antiarrhythmic effects were already established in previous studies of digoxin toxicity, hyper- and hypokalemia. These effects were realized through the interaction with NO-system. The aim of the study is to establish BPC 157 antiarrhythmic effect when cardiac rhythm disturbances are caused by bupivacaine toxic dose and to explore whether this effect is dose-dependent and related with NO-system.

Materials and methods: The study was conducted on female Wistar albino rats, divided into groups of 6. We had two protocols with 4 experimental groups each, treated with BPC 157 i.p. (50 µg/kg, 10 µg/kg, 10 ng/kg, 10 pg/kg) and the control group treated with saline 5ml/kg i.p. either 30 minutes before (preventive) or 1 minute after bupivacaine 100 mg/kg i.p. (therapeutic). Three standard leads ECG was recorded for 90 minutes. The wave amplitudes P, R, S and T, the duration of waves and intervals P, PR, QRS and

RR, the presence of ventricular ectopies, tachycardia, AV block and asystolia were analyzed.

Results: Bupivacaine caused bradycardia, PQ prolongation, all degrees of AV block, QRS widening, ST-T wave changes, multiform ventricular ectopies (VES), ventricular tachycardia (VT) and asystolia, as well as the decrease of wave amplitudes. BPC 157 treated animals had in both protocols and in all the applied doses less prolongation of P wave in particular ($p < 0.001$), of QRS complex and PR, QT and RR intervals as well ($p < 0.05$). The decrease of the wave amplitudes was also counteracted, with lower mortality in the experimental groups (16.7% vs. 50%). All the animals who did not survive had T wave elevation.

Discussion: BPC 157 has shown cardio protective effect in both protocols and in all the applied doses. The T wave elevation present in all the non survivors is a sign of impending cardio toxicity and inevitable death, so we can confirm the conclusion of Mauch and all. and propose it to use in clinical practice as an early sign of threatening catastrophe.

Acknowledgments:

MeSH/Keywords: cardiac arrhythmias, bupivacaine, pentadecapeptide BPC 157

Poster code: A-4-36

POSTER TITLE: THE EFFECT OF PENTADECAPEPTIDE BPC 157 ON HEALING OF RECTOVAGINAL FISTULAS IN RATS

PhD candidate: Marko Barić, MD1,2

Part of the thesis: The Effect of Pentadecapeptide BPC 157 on Healing of Rectovaginal Fistulas in Rats

Mentor/s: Professor Predrag Sikirić, MD, PhD1

Affiliation: 1Department of Farmacology and Pathology, University of Zagreb School of Medicine, 2Department of Surgery, University Hospital "Sveti Duh", Zagreb

Introduction: It is known that rectovaginal fistulas are great medical therapeutic problem because in many cases they require the formation of bipolar anus praeter or Hartmann operation and the establishment of intestine continuity in the second act. Given that pentadecapeptide BPC 157 helps healing of gastrocutaneous (Skorjanec et al, *Dig Dis Sci* (2009) 54:46–56), duodenocutaneous (Skorjanec et al, *DDW* 2010) and colcutaneous fistulas (Klicek et al, *J Pharmacol Sci* 108, 7 – 17 (2008). Momentary there is no adequate pharmacological therapy for rectovaginal fistula. In this study we investigated the effect of pentadecapeptide BPC 157 on the rectovaginal fistula healing.

Materials and methods: For the model of rectovaginal fistula, we used female Wistar rats. In deep anesthesia on the rats, we made a longitudinal incision on the rear wall of the vagina and anterior rectal wall in the length of 5 mm and formed rectovaginal fistula using single-layer extension suture technique. Pentadecapeptide BPC157 (Diagen d.o.o., Ljubljana, Slovenia) dissolved in saline solution was applied in daily doses of 10 µg/kg / ng/kg i.p. during the entire duration of the experiment (1, 3, 5, 10, 14 and 21 days). The control group animals got daily equivalent amount of 0.9% NaCl-solution i.p. (5 mL/kg). During the sacrifice we measured the volume required for leakage of fluid through fis-

tula (mL H₂O), evaluated the macroscopic differences in rectovaginal fistula healing (diameter of the fistula (mm, rectal and vaginal side). Microscopical evaluation was also performed.

Results: In all pentadecapeptide BPC 157 treated rats, we noticed throughout the experiment a significant increase in volume required for leakage of fluid through fistula compared to control animals (14th day - 5,3 ± 0,3 mL H₂O vrs 1,1 ± 0,4 ml H₂O) (Chart 1). We also noted a significant reduction in diameter of the fistulas after the third postoperative day in BPC 157 groups, which spreads throughout the experiment (complete closure of fistulas during 14 days), while the diameter of fistulas in the control group showed less tendency of closing and are also present even after 21th postoperative day (21th day – 0 ± 0 (BPC157 – rectal side), 0 ± 0 (BPC 157 – vaginal side) vrs 3,1 ± 0,6 (con. rectal side), 3,3 ± 0,8 (con. vaginal side) (Chart 2).

Discussion: Considering the results obtained, we suggest that pentadecapeptide BPC 157 could be an adequate pharmacological solution to the problem of rectovaginal fistulas healing.

Acknowledgments:

MeSH/Keywords: pentadecapeptide BPC 157, rectovaginal fistula

Poster code: A-4-48

POSTER TITLE: PENTADECAPEPTIDE BPC 157 IN INTERACTION WITH NO-AGENS IN AN EXPERIMENTAL MODEL OF PSYCHOSIS IN RATS

PhD candidate: Andrea Zemba Čilić

Part of the thesis: Pentadecapeptide BPC 157 in Interaction with NO-agens in an Experimental Model of Psychosis in Rats

Mentor/s: Professor Predrag Sikirić, MD, PhD

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

Introduction: Stable gastric pentadecapeptide BPC 157 counteracted acute and chronic disturbances caused by amphetamine in rats. BPC 157 was evaluated in animal models in condition of inhibition and/or stimulation of NO-system.

Materials and methods: Antipsychotic-like effects were tested by the ability to reduce amphetamine-, apomorphine- and MK-801 induced hyperactivity and to prevent locomotor sensitization, catalepsy was assessed by measuring step-down latency.

Results: BPC 157 reduced amphetamine, apomorphine and MK-801 induced hyperactivity, and prevented the induction and the progression of locomotor sensitization caused by methamphetamine. BPC 157 antagonized both catalepsy produced by haloperidol and potentiated with L-NAME. L-arginine active alone or together with BPC 157, couldn't interfere with compounds in combination with L-NAME. By subchronic ad-

ministration, BPC 157 counteracted locomotor sensitization, L-arginine and L-NAME alone were ineffective, but interfered with BPC 157, and counteracted its effect.

Discussion: According to our results we could conclude that BPC 157 being resistant to L-NAME and NOS-blockade, was active by itself and counteracted the effects of tested compounds while L-arginine did not. These data indicate that BPC 157 has a behavioral profile consistent with antipsychotic-like efficacy and shows liability for counteraction of extrapyramidal symptoms.

Acknowledgments: I would like to thank my mentor professor Predrag Sikirić for support and guidance.

MeSH/Keywords: antipsychotic, nitric oxide, schizophrenia

Poster code: A-4-74

POSTER TITLE: DISTRIBUTION OF CYP2C9 AND CYP2C19 ALLELIC VARIANTS IN KOSOVO'S HEALTHY POPULATION

PhD candidate: Valon Krasniqi, MD, Clinical Pharmacologist

Part of the thesis: Genetic Polymorphism of CYP2C19, CYP2C9 and VKORC1 in Kosovo's Population

Mentor/s: Associate Prof. Nada Božina (Zagreb), Full Prof. Aleksandar Dimovski (Skopje)

Affiliation: University of Prishtina, Faculty of Medicine, University Clinical Centre of Kosova and University "Ss Cyril and Methodius", Faculty of Pharmacy, Center for Biomolecular Pharmaceutical Analyses, Skopje

Introduction: Recently, as a major focus of a large number of pharmacogenomic researches realized in several countries of the world was determination of polymorphisms' frequencies in drug detoxification genes among different ethnic groups, as well as the influence of these variant alleles on clinical drug response.

Materials and methods: Distribution of allelic variants of CYP2C9 (*2*3) and CYP2C19*2 in Kosovo's population was analyzed selecting a population sample of 31 healthy volunteers. In this research have participated unrelated healthy persons, representing a mixed population from all parts of Kosovo. 10 males and 21 females (age range 32 to 63 years) were included in the study. Genomic DNA was isolated for each participants from 2.5 ml peripheral blood, collected in EDTA vacutainers by standard procedure. Genotyping was performed using ABI TaqMan® assays on Stratagene Real-time PCR instrument.

Results: The prevalence of genotypes and variant allele frequencies obtained in this research are as follows: CYP2C9*1/*1 (18 individuals or 58,06%), CYP2C9*1/*2 (5 individuals or 16,13%), CYP2C9*1/*3 (6 individuals or 19,35%), CYP2C9*2/*2 (1 individual or 3,22%), CYP2C9*2/*3 (0 individuals or 0%) and CYP2C9*3/*3 (1 indi-

vidual or 3,22%). The frequency of CYP2C19*2 allelic variant was 9,7% (6 subjects).

Discussion: The preliminary study results present similarities as well as differences regarding the frequency of most important allelic variants of Cytochrome CYP2C9 between Kosovars and other populations. As evidence of this, the prevalence of CYP2C9*2 among Kosovars (11,29%) was found to be nearly similar to the frequency of Caucasians (specifically Slovenians 10,8.%) but was significantly lower comparing to the frequency of this variant allele observed among Argentineans (25,73%), and Southern Iranians (25,3%).

Acknowledgments: I'm very grateful to the Ministry of Education, Science and Technology of Kosova for supporting financially this scientific research. In addition, I would like to express my utmost gratitude to Professor Nada Božina and Professor Aleksandar Dimovski for their continuous support, advice and encouragement with regard to my research.

MeSH/Keywords: CYP2C9, CYP2C19, VKORC1, Kosovo Healthy Population, Pharmacogenetics, Allelic Variant, Real-Time PCR assay.

Poster code: A-4-125

POSTER TITLE: INFLUENCE OF PENTADECAPEPTIDE BPC 157 AND ESTROGEN ON UROGENITAL ATROPHY IN OVARIECTOMIZED RATS

PhD candidate: Karlo Tomičić, MD

Part of the thesis: Influence of pentadecapeptide BPC 157 and estrogen on urogenital organs in ovariectomized rats

Mentor/s: Associate Professor Hrvoje Vrčić, MD, PhD

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

Introduction: Ovariectomy in rats causes a deficiency of estrogen which leads to changes similar to those in postmenopausal women like urogenital atrophy, osteopenia, changes in lipid and carbohydrate metabolism. Previous research of the application of BPC 157 in animal models of other diseases found that BPC 157 has a positive effect on genital atrophy but those findings were not systematically investigated.

Materials and methods: Female albino rats' weight 200-220 g will be randomized into 10 groups. Both ovaries will be ligated with resorbable sutures and removed. The control group will receive 1 ml NaCl solution, while the treated group 1 and 2 will receive dose of BPC 157 (10 µg/kg and 10ng/kg). Group 3 will receive estradiol (0.5 mg/kg). Groups 4 and 5 will be treated with a combination of both drugs in earlier mentioned doses. Animals in groups 6 and 7 will drink BPC 157 (12 ml/rat/day at 10 µg/kg and 10ng/kg). Groups 8 and 9 will drink BPC 157 in combination with estrogen. The animals will be treated for 8 weeks and then sacrificed. Urogenital organs are going to be removed, measured and histologically analysed. Kruskal-Wallis and Mann-Whitney U test will be used for the statistical analysis.

Results: Preliminary results include values of glucose, triglycerides, cholesterol, HDL, LDL and liver enzymes tests in the serum of the 3 groups - control group, the group that received BPC 157

(10 µg/kg) and estradiol (0.5 mg/kg) group. Statistical analysis was performed by the Kruskal Wallis test. Differences in glucose, cholesterol and liver enzymes tests were not significant. Statistically significant were lower triglyceride levels in the group of rats treated with estrogen compared to ones treated with BPC. Also significantly higher were the levels of HDL in BPC group compared to the control group, and a lower LDL values in the estrogen group as compared to the control.

Discussion: Menopause brings to women an increase of triglycerides, cholesterol and LDL, while HDL levels decline. Result in ovariectomized rats show no statistically significant differences in levels of glucose and cholesterol in all three groups. BPC group has higher levels of HDL compared to the control, but also higher levels of triglycerides compared to estrogen. The estrogen group had lower LDL compared to control. Treatment with estrogen has favorable effects on lipid metabolism in ovariectomized rats compared to BPC.

Acknowledgments: I would like to thank Professors Vrčić and Sikirić for their help and guidance that made this study possible.

MeSH/Keywords: BPC 157, estradiol, ovariectomized rat, urogenital atrophy

Poster code: A-4-135

POSTER TITLE: PENTADECAPEPTIDE BPC 157 PREVENTS MONOCROTALINE INDUCED COR PULMONALE IN RATS - PRELIMINARY RESULTS

PhD candidate: Mario Udovičić

Part of the thesis: Effect of Pentadecapeptide BPC 157 on Monocrotaline Induced Cor Pulmonale in Rats

Mentor/s: Prof. Sven Seiwerth, MD, PhD and Prof. Predrag Sikirić, MD, PhD

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

Introduction: Pentadecapeptide BPC 157 has proven angiogenic effect, protective effect on endothelium and it modulates synthesis of NO. It furthermore reduces the duration of arrhythmias induced by ischemic-reperfusion injury in isolated pig heart, and also has antihypertensive effect in the model of L-NAME induced hypertension. Monocrotaline (MCT) is a pyrrolizidine alkaloid, which given subcutaneously in the rat model of pulmonary hypertension on day 1 selectively injures the vascular endothelium of the lung and induces pulmonary vasculitis and induces muscularization and hypertrophy of media in pulmonary arteries, that lead to increased vascular resistance, increased pulmonary arterial pressure and the development of compensated RV hypertrophy, which progresses to failure within weeks.

Materials and methods: This study included 6 groups by 6 rats (male, body weight 150-200 grams). After initial application of monocrotaline on day 1 (80 mg/kg body weight, subcutaneously) the animals were randomized into 2 control groups and 4 experimental groups. BPC was given daily from day 1 till day 29, either orally in drinking water or intraperitoneally, in two different dosages (10 µg/kg i 10 ng/kg), while one control group received saline intra-

peritoneally also from daily from day 1 till day 29 and the other just drinking water. On day 30 animals were killed and the lungs were fixed for histology. After staining by van Gieson, the remodeling of pulmonary arteries was assessed by measuring muscularization of arterioles with diameters 25-200 µm using computerized morphometric system ISSA. Hearts were dissected, and the ratio of the right ventricle to left ventricle plus septum weight was calculated as index of right ventricular hypertrophy

Results: BPC 157 inhibited the development of muscularization and hypertrophy of media in pulmonary arteries and prevented right heart hypertrophy. A corresponding efficacy profile was also noted for long-term peroral administration of BPC 157 in drinking water. Moreover, the death rate significantly decreased in those animals treated with BPC 157.

Discussion: We conclude that BPC157 prevents development of MCT-induced pulmonary hypertension and cor pulmonale in rats.

Acknowledgments:

MeSH/Keywords: BPC 157, monocrotaline, cor pulmonale, pulmonary hypertension, rats

Poster code: A-4-146

POSTER TITLE: THE EFFECT OF PENTADECAPEPTIDE BPC 157, L-ARGININE AND L-NAME IN CYCLOPHOSPHAMIDE-INDUCED HEMORRHAGIC CYSTITIS IN RATS

PhD candidate: Mario Sučić, MD

Part of the thesis: The Effect Of Pentadecapeptide BPC 157, L-arginine And L-NAME In Cyclophosphamide-induced Hemorrhagic Cystitis In Rats

Mentor/s: Professor Predrag Sikirić, MD, PhD

Affiliation: University of Zagreb School of Medicine, Department of Pharmacology and Pathology University Hospital " Sveti Duh", Zagreb, Department of Urology

Introduction: Cyclophosphamide (CYP) is an alkylating agent in malignant and non-malignant diseases, and organ transplantation. Hemorrhagic cystitis is the most common complication of treatment, depends on the dose, caused by acrolein, a metabolite of CYP excreted in the urine. Given pentadecapeptide BPC 157 beneficial effect in the different models, we investigated the effect of BPC 157 on hemorrhagic cystitis induced by repeated high doses of cyclophosphamide. This effect is related with NO-system.

Materials and methods: Study was conducted on female Wistar albino rats. Hemorrhagic cystitis model was established according to the methods described by Botta et al 1973. CYF (150 mg/kg) applied intraperitoneally and pentadecapeptide BPC157 (10 ng/kg and 10 µg/kg) intraperitoneally or perorally for 3 days. Samples of the bladder were evaluated macro/microscopically. Vesical edem was quantified by wet bladder weight, (mg/ 100 g body). The gross appearance (Gross edema and Gross hemorrhage) and histologic section of the bladders was graded by a bladder damage score: 0-3 (normal, mild, moderate, severe) using previously described methods (Gray et al, 1986). To determine relation with NO-system animals were exposed with or without the administration of L-arginine (100 mg/kg) and/or nitric oxide synthase inhibitor (L-NAME), 5 mg/kg. Finally, we measured the leak point pressure of one group of rats.

Results: PRELIMINARY RESULTS: In the control group wet bladder weight was 102,1 (±5,5) g/100 mg body weight. Pentadecapeptide BPC 157 treated group (µg and ng) WBW was 61,9 and 63,6 g/100 mg body weight. The damage score (median values) of edema in the positive control (CYP) group was 3 vs 1 in the BPC 157 (µm or ng) treated rats. The score hemorrhage was 3 in cyclophosphamide group, 0,5 and 1 in BPC 157 treated group, (µg or ng). Values were confirmed by histological analysis. Leak point pressure in positive control (CYP) was 36 mm Hg (±9,1). BPC 157 treated group 25mm Hg (±7,2) µg or 26 mm Hg (±7,4) ng. Relation with NO-system was confirmed in the results of animals that were exposed with or without the administration of L-arginine and/or nitric oxide synthase inhibitor (L-NAME).

Discussion: In this study, we postulated that pentadecapeptide BPC 157 could slow acrolein absorption in the bladder resulting in reduced tissue edema, hemorrhage, inflammation, and ulceration.

Acknowledgments:

MeSH/Keywords: hemorrhagic cystitis, cyclophosphamide, pentadecapeptide BPC 157, urinary bladder.

Poster code: A-4-166

POSTER TITLE: EFFICACY OF BONE MORPHOGENETIC PROTEIN(BMP)1-3 IN THE PROCESS OF BONE HEALING

PhD candidate: Dragan Đurđević, prim., MS, MD

Part of the thesis: It has been recently discovered that BMP1-3 circulates in human and rat blood and accelerates maturation of the extracellular matrix. The aim of this research is to determine the role of the BMP1-3 molecule in bone healing process.

Mentor/s: Prof Slobodan Vukičević, PHD, MD

Affiliation: Laboratory for Mineralized Tissues, Center for Translational and Clinical Research and Orthopaedic Surgery, University of Zagreb, Zagreb, Croatia, University Truma Hospital, CHC

Introduction: BMP1 regulates maturing of the extracellular matrix(ECM) proteins and several growth factors. Recent knowledge is that BMP1-3 is present in the human plasma and in acute bone fracture it's level is increased significantly. We presume that circulating BMP1-3 may play an important role in bone healing process.

Materials and methods: Bone nodule formation assay. Bone marrow cells, harvested from four 8-weeks-old mice, were pooled and plated on 6 well plates and treated with medium containing either BMP1-3 or BMP1-3 antibody. At day 21 the von Kossa stain was used to determine the mineralised matrix formation. Rat femoral fracture model. In male Sprague-Dawley rats osteotomy of the femur was performed. The fracture was than intramedullary fixed with Kirschner wire. The rats were randomly divided into four groups (n=8): control, IgG, rhBMP1-3 and BMP1-3 antibody. The effects were periodically analysed by radiographs. Critical size defect of rabbit ulna. A critical size defect of ulna was produced in adult male New Zealand White rabbits. The defect was filled with whole blood containing device (WBCD) and rhBMP1-3 (20µg) with or without BMP7 (100 µg). The animals were divided into four groups (n=8): control, rhBMP1-3, BMP7 and rhBMP1-3 plus BMP7. Trabecular bone and new bone formation were analysed using microCT (SkyScan).

Results: Circulating BMP1-3 enhances fracture repair in rats. Intravenous administration of a neutralizing BMP1-3 antibodies resulted in significantly delayed bone union. Systemic administration of BMP1-3 increased bone volume and accelerated fracture healing. Locally administered BMP1-3 accelerates and bone regeneration. In the model of critical size defect individual therapy with BMP1-3 or BMP7 did not achieve rebridgement of the ulnar defect .The combination of BMP1-3 and BMP7 produced rebridgement and trabecular bone remodeling.

Discussion: Rat femur fracture model and osteoblast differentiation culture demonstrate that inhibition of BMP1-3 leads to a significant delay in the fracture healing process and that BMP1-3 plays a role in the osteoblast differentiation and bone formation. BMP1-3 enhanced the bone formation when implanted locally together with BMP7. Systemic administration of the specific BMP1-3 antibody delayed the bone healing confirming that the circulating level of BMP1-3 is relevant for bone repair.

Acknowledgments: prof Slobodan Vukičević, PhD,MD, prof Lovorka Grgurević, PhD, MD

MeSH/Keywords: BMP1-3, BMP7, bone fracture, differentiation

Poster code: A-5-71

POSTER TITLE: WNT AND SONIC HEDGEHOG SIGNALING PATHWAYS IN PRIMARY AND SECONDARY MYELOFIBROSIS

PhD candidate: Marko Lucijanić

Part of the thesis: Analysis of genes and proteins of Wnt and Sonic Hedgehog signaling pathways in primary and secondary myelofibrosis

Mentor/s: Rajko Kušec

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

Introduction: Wnt and SonicHedgehog signaling pathways play important role during fetal histogenesis, in homeostasis and morphogenesis of adult tissues, self-renewal, proliferation and differentiation of stem cells/tissue progenitor cells. They are part of larger molecular network. Target genes activated by Wnt and SonicHedgehog signaling are involved in oncogenesis, fibrosis and neoangiogenesis. Primary genetic lesion responsible for primary myelofibrosis is unknown at the time. Current findings suggest possible role of Wnt and Sonic Hedgehog signaling pathways in pathogenesis of this disease.

Materials and methods: Bone marrow samples of primary myelofibrosis patients obtained by trephine biopsy and fine needle aspiration are used for analysis. Total of 30 patients with primary myelofibrosis are analyzed and compared to control groups of 10 patients with secondary myelofibrosis and 10 subjects with healthy bone marrow (patients with aggressive NHL without bone marrow infiltration). Patient included have been evaluated in time period from 1st January 2005 to 31st December 2013. RT-PCR methods is used to analyze gene expression on fine needle aspiration samples. Immunohistochemistry is used to analyze protein expression on paraffine embedded trephine biopsy samples and level of expression is expressed semiquantitatively by one pathologist (0 – no positivity, 1 – less than

25% of positive cells, 2 – more than 25% of positive cells). Non-parametric statistics will be used to analyze obtained clinical and laboratory data.

Results: Adequate number of samples from patients with primary myelofibrosis has been collected and stored, we are currently expanding the group of subjects. Clinical data is being regularly updated. We are in the process of purchase of antibodies needed for immunohistochemistry and primers needed for PCR reactions due to administrative and organization difficulties.

Discussion: Wnt and SonicHedgehog pathways play significant role in processes of tissue fibrosis and neoangiogenesis and their involvement in primary and secondary myelofibrosis is very likely. We are hoping that our research will give us answer is there a detectable difference in expression of proteins of these two pathways between primary and secondary myelofibrosis, two similar diseases but with different pathogenesis. New emerging therapeutic options, such as suppressors of SonicHedgehog pathway, could possibly find a role in this disease entity.

Acknowledgments:

MeSH/Keywords: Primary myelofibrosis, Wnt, Sonic Hedgehog, β -catenin

Poster code: A-6-157

POSTER TITLE: ANTI-TNF THERAPY ONLY TRANSIENTLY AFFECTS OSTEOCLAST PROGENITORS IN RHEUMATOID ARTHRITIS

PhD candidate: Alan Šučur, M.D.

Part of the thesis: Phenotypic and Functional Characterization of Osteoclast Progenitors in Patients with 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 the most severe chronic joint disease marked by the persistent inflammation and osteodestruction. The mechanisms leading to joint destruction involve differentiation and activation of osteoclasts. Human osteoclast progenitors (OCPs) represent a subpopulation of peripheral blood monocytes and are present at low frequency in healthy subjects. Tumor necrosis factor- α (TNF α) increases peripheral blood OCP numbers in arthritic patients, implying that circulating OCPs may have an important role in the pathogenesis of RA. The aim of our study was to analyze the phenotype, frequency and osteoclastogenic potential of OCPs in the peripheral blood and synovial fluid of RA patients in relation to anti-TNF therapy.

Materials and methods: Monocytes were isolated from peripheral blood of healthy controls and RA patients. A subset of blood and synovial fluid samples were collected from RA patients prior and in the follow-up of anti-TNF treatment. The phenotype of isolated monocytes was determined within peripheral blood mononuclear cells using flow cytometry for the markers: CD3, CD11b, CD11c, CD14, CD16, CD19, CD56, CD115 and CCR2. Lymphoid lineage negative (CD3-CD19-CD56-) population was then sorted and cultured in osteoclast differentiation medium for two weeks. Osteoclasts were detected by the staining for tartrate-resistant acid phosphatase.

Results: We have verified human peripheral blood OCPs as an osteoclastogenic population

bearing the phenotype CD3-CD19-CD56-CD11b-CD115⁺. This monocyte subpopulation is increased in RA patients, comprising 2.5-5.5% of circulating monocytes compared to 1.5% in healthy controls. The same population was found to comprise approximately 1% of synovial fluid monocytes. Cultures of sorted lymphoid lineage negative population from RA patients revealed that both circulatory and synovial monocyte progenitors exhibit in vitro osteoclastogenic potential. Anti TNF-treatment only transiently suppressed OCP differentiation in cultures.

Discussion: Peripheral blood monocyte subpopulations, including OCPs, are heterogeneous by surface marker expression, size, and function, and could be specifically induced during chronic inflammatory diseases. Our study revealed that anti-TNF treatment only transiently suppressed osteoclastogenic potential of peripheral OCPs, indicating that additional therapeutic modalities, besides TNF-blocking agents, should be considered for sustained antiresorptive effect.

Acknowledgments: I would like to thank my mentor, prof. 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, osteodestruction

Poster code: A-7-4

POSTER TITLE: WHOLE GENOME SEQUENCING ANALYSIS OF HUMAN LIVER SINUSOIDAL ENDOTHELIAL CELLS REVEALS EVIDENCE FOR ANTI-INFLAMMATORY ROLE DURING HCV INFECTION

PhD candidate: Neven Papić

Part of the thesis: The role of liver sinusoidal endothelial cells in HCV infection

Mentor/s: Professor Adriana Vince, MD, PhD, Professor Curt Hagedorn, MD, PhD

Affiliation: University Hospital for Infectious Diseases Zagreb, Croatia

Introduction: Liver sinusoidal endothelial cells (LSEC) due to their extraordinary scavenger activity are playing a pivotal role in blood-borne virus clearance. LSEC account for the 20% of hepatic cells and are unique organ-resident cell population with diverse functions, including degradation of bacterial by-products, antigen presentation and induction of tolerance. While these processes are particularly relevant to HCV infection, the role of LSEC in chronic hepatitis C is not defined.

Materials and methods: Aim of this study was to apply systems biology approaches to evaluate the role of LSEC in HCV infection. Poly(A) RNAs from HCV, MOCK or LPS treated primary LSEC cultures were analyzed by RNA-sequencing (Illumina) to identify differentially expressed genes (DEG) and biological pathways. Cell transcriptomes were compared to similar analysis with mild (no fibrosis) and severe (cirrhosis) hepatitis C livers, hepatoma and Kupffer cells.

Results: Following exposure LSEC internalized HCV, but failed to support HCV replication. LSEC overall displayed 754, 245 and 2543 DEG at 8, 24 and 48h after HCV exposure, respectively. While LPS stimulation triggered exceptionally potent activation, HCV in general induced a down-regulation of inflammatory signals. This involve changes in network of transcriptional regulators (>100 DEG), such as MAFB (4x) and NURP1 (7x)

that antagonize antiviral inflammatory responses, a decrease in transcription of cytokines and increase in inhibitors of their biological functions (ACP5 9x, A2M 6x, SERPING1 7x), an unaffected IFNs and ISGs expression. Gene pathway analysis highlighted changes associated with angiogenesis (40), adhesion (142), ECM-organization (107), signaling (153), apoptosis (109) and regulation of immune responses (104). Interestingly, most of these pathways showed significant overlap with HCV infected livers, in contrast to HCV infected hepatoma and Kupffer cells that presented with distinct gene expression profiles.

Discussion: This is the first comprehensive gene expression analysis of LSEC that provided insight into the broad portrait of genomic changes associated with HCV infection. These genes are critical components of host immune and inflammatory pathways and provide new evidence that LSEC downregulate inflammation during HCV infection.

Acknowledgments: This study was financially supported by Croatian Ministry of Science (143-000000-0117) and Division of Gastroenterology, Hepatology and Nutrition at University of Utah.

MeSH/Keywords: HCV, chronic hepatitis C, liver sinusoidal endothelial cells, next-generation RNA sequencing, gene expression

Poster code: A-7-24

POSTER TITLE: 5-AMINOIMIDAZOLE-4-CARBOXAMIDE RIBONUCLEOSIDE ENHANCES DIFFERENTIATION OF ACUTE MYELOID LEUKEMIA CELL LINES

PhD candidate: Hrvoje Lalić, MD

Part of the thesis: The role of AMPK/mTOR signaling pathway in differentiation of leukemia cells

Mentor/s: Professor Dora Višnjić, MD, PhD

Affiliation: Department of Physiology and Croatian Institute for Brain Research, School of Medicine, University of Zagreb, Salata 3, 10 000 Zagreb, Croatia

Introduction: The most successful differentiation therapy with all-trans-retinoic acid (ATRA) has been restricted to acute promyelocytic leukemia (APL) carrying typical t(15:17) translocation. Pharmacological modulators of AMP-activated protein kinase (AMPK)/mammalian target of rapamycin (mTOR) pathway have been reported to exert antiproliferative effects in leukemia, but their role in differentiation is less explored. The aim of this study was to test for the effects of AMPK modulators on proliferation and differentiation of APL and non-APL acute myeloid leukemia (AML) cell lines.

Materials and methods: Monocytic U937, promyelocytic NB4 and myeloblastic HL-60 were incubated in the presence of AMPK/mTOR-modulators: 5-aminoimidazole-4-carboxamide ribonucleoside (AICAR), metformin, rapamycin and compound C. The number of viable cells was determined by hemocytometer. The expression of differentiation markers, cell cycle analysis and apoptosis were determined and analyzed by FACSCalibur, Cell Quest and ModFit software (Becton Dickinson). Total cell lysates were analyzed for the level of total and phosphorylated p70 S6K, AMPK α and mitogen-activated protein kinase (MAPK) by Western blot. siRNA transfection of AMPK α 1/2 and controls was performed using NeonTM transfection system (Invitrogen). The data are shown as means \pm S.E.M. and analyzed using Student t-test or ANOVA.

Results: AMPK activators, AICAR and metformin, significantly reduce the number of viable cells. Morphologic and FACS analyses show the significant increase in apoptosis in cells treated with AICAR. AICAR enhances ATRA-mediated differentiation of NB4 and HL-60 cells. In U937 cells,

AICAR alone induces the expression of cell surface markers associated with mature monocytes and macrophages and siRNA data show that these effects occur independently of AMPK expression. In both U937 and NB4 cell lines, AICAR increases the activity of MAPK, and the increase in the expression of CD64 and CD14 is inhibited in the presence of MAPK inhibitors.

Discussion: AICAR inhibits proliferation, increases apoptosis and induces expression of differentiation markers in monocytic U937 cells. This is, to our knowledge, the first report showing that AICAR has some differentiating properties in leukemia cells. These results suggest that a strategy using drugs targeting metabolism may improve differentiation therapy for non-APL AML.

Acknowledgments: We thank Ms Dunja Tankovic for valuable technical help and assistance. This study was supported in part by the Ministry of Science, Education and Sport of the Republic of Croatia, grant No. 108-1081347-1448 (to Dora Višnjić). Presented results have already been published (Lalic H, Lukinovic-Skudar V, Banfic H, Visnjic D. Rapamycin enhances dimethyl sulfoxide-mediated growth arrest in human myelogenous leukemia cells. *Leuk Lymphoma* 2012; 53:2253-2261. Lalic H, Dembitz V, Lukinovic-Skudar V, Banfic H, Visnjic D. 5-Aminoimidazole-4-carboxamide ribonucleoside induces differentiation of acute myeloid leukemia cells. *Leuk Lymphoma* 2014 Feb 24.[Epub ahead of print] DOI:10.3109/10428194.2013.876633

MeSH/Keywords: AICAR, Leukemia, Differentiation Markers, AMP-Activated Kinase

Poster code: A-7-70

POSTER TITLE: REGIONAL DIFFERENCES IN DENDRITIC MORPHOLOGY OF MEDIUM SPINY STRIATAL NEURONS IN FOXP2 MICE ARE INFLUENCED BY SUBSTITUTION AT POSITION T302N

PhD candidate: Ivana Bičanić MD

Part of the thesis: Changes in morphology of projection striatal neurons in mice with humanized versions of Foxp2 gene

Mentor/s: Zdravko Petanjek MD, PhD

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

Introduction: The transcription factor FOXP2 (Forkhead-box-protein-P2), involved in speech and language development, carries two amino acid substitutions (T303N, N325S) on the hominine lineage which were likely positively selected during human evolution. When the human variant of the FOXP2 protein is expressed in mice (Enard et al, Cell 137:861, 2009), these animals show an increased dendritic complexity of neurons that are a part of the basal ganglia circuitry and highly express FOXP2, e.g. striatal medium spiny neurons (MSN) (Reimers-Kipping et al, Neuroscience 175:75, 2011).

Materials and methods: Here we analysed regional differences in dendritic morphology and spine density of Golgi-Cox impregnated MSNs in mice homozygous for the human Foxp2 variant (Foxp2^{hum/hum}) and in a strain which carries only the substitution (uniquely found in humans) at position 302 (T302N).

Results: Differences in dendritic morphology and spine density were present in the same pattern in both mouse lines. Data in the caudal region suggest a slight outgrowth of new segments. In other regions changes might be considered as “functional”: in DMS/DLS slight increase in segment length, spine density and slight decrease in diameter whereas in the rostral striatum we found a decrease in segment length and an increase in thickness.

Discussion: Our findings suggest a region specific circuitry reorganization in the striatum and that the human specific substitution at position T302N seems to be required.

Acknowledgments:

MeSH/Keywords: Foxp2, speech development, cortico-striatal circuitry, dopamine

Poster code: A-9-109

1.2.
CLINICAL MEDICAL SCIENCES
– RESEARCH ABSTRACTS

POSTER TITLE: INFLUENCE OF DEXAMETHASONE ADMINISTRATION IN SPINAL ANESTHESIA FOR FEMUR FRACTURE

PhD candidate: Livija Šakić

Part of the thesis: INFLUENCE OF DEXAMETHASONE ADMINISTRATION IN SPINAL ANESTHESIA FOR FEMUR FRACTURE

Mentor/s: Associate Professor Dinko Tonković, MD, PhD

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

Introduction: Spinal anesthesia blocks acute pain in older patients with femur fracture. Delirium is a common complication seen after femur fracture, affecting approximately 10-16% of patients. It is associated with increased mortality at 1st year, delayed rehabilitation efforts, prolonged length of hospital stay, poorer functional outcomes, and increased risk of nursing home placement.

Materials and methods: The study is planned as a prospective, interventional, randomized clinical trial. A total of 60 patients ASA2 and ASA3 status, scheduled for surgical procedures will be sorted into two groups and undergo surgery in spinal anesthesia with levobupivacaine (SA) and with or without dexamethasone (DSA). The primary outcome measure is the occurrence of postoperative disturbance of consciousness and plasma cortisol levels. As a secondary outcome measure, we are following pain intensity, blood glucose levels and recovery. Cortisol and glucose are analyzed in five measurements. Peripheral venous blood samples are collected before anesthesia, one hour after surgery, third, fifth and on the tenth day after surgery. Postoperative delirium is defined by using Confusion Assessment Method (CAM) criteria. Visual analogue scale (VAS) is used to record pain severity among patients.

Results: We collected data for 6 patients so far. As expected, cortisol plasma levels are signifi-

cantly lower in all patients having spinal anesthesia with levobupivacaine and dexamethasone in comparison to patients in spinal anesthesia with only local anesthetic. Glucose levels taken on the admission to the hospital are above the referent interval due to pain and stress of the injury, and in between the referent interval after SA in both groups. Sensory block lasts much longer and opioid requirements are decreased in all patients in DSA. Cognitive disturbances are seen in 2 patients after spinal anesthesia with only local anesthetic.

Discussion: The addition of dexamethasone to the local anesthetic significantly prolongs the duration of sensory block and decreases opioid requirements in postoperative management. The effective pain management may reduce postoperative cognitive disturbances. Therefore effective analgesia and the impact on the hypothalamic-pituitary-adrenal axis may reduce postoperative delirium in patients with femur fracture.

Acknowledgments: This work was supported by grants from the Croatian Ministry of Science (projects: 108-0000000-3433)

MeSH/Keywords: spinal anesthesia, dexamethasone, cortisol, POCD

Poster code: B-1-72

POSTER TITLE: ULTRASOUND GUIDED SUPRACLAVICULAR BLOCK IN ELDERLY PATIENTS – DO THEY NEED LESS LOCAL ANAESTHETIC?

PhD candidate: Tamara Lupis, MD, MSc

Part of the thesis: Influence Of Age On Time Of Onset And Duration Of Sensory Blockade For Ultrasound Guided Supraclavicular Brachial Plexus Block

Mentor/s: Mladen Knotek, MD, PhD

Affiliation: Department of Anaesthesiology and Intensive care, Clinical Hospital

Introduction: Minimum effective anaesthetic volume required for ultrasound guided supraclavicular brachial plexus block (US SCB) is reduced in elderly patients due to structural changes of brachial plexus as well as increased sensitivity to local anaesthetics. The content of adipose and connective tissue compartment involutes with age, which markedly contributes to altered characteristics of regional blocks. The influence of ageing on the time of onset and duration of effective sensory blockade in elderly is unknown.

Materials and methods: Middle-aged (<45y) and elderly (>65y) patients undergoing upper limb surgery received an ultrasound guided supraclavicular brachial plexus block. We measured the cross-sectional area of the brachial plexus in supraclavicular region for each patient. The prospective, observer-blinded study method is a previously validated step-up/step-down sequence model where the local anaesthetic volume for the next patient is determined by the outcome of the previous block. The starting volume was 30 ml 50:50 mixture (0.5%wt/vol levobupivacaine, 2%wt/vol lidocaine). We analysed the time of onset and duration (minutes) of complete sensory blockade in distal nerve territory of brachial plexus (ulnar, median, radial, musculocutaneous nerve). We exclude patients

in whom an adequate block did not develop.

Results: Minimal effective local anaesthetic volume significantly differed between middle-aged and elderly in ED50 [23.0 ml, 95% confidence interval (CI) 13.7–32.3 vs. 11.9 ml, 95% CI 9.3–14.6). 95% CI of the difference 1.6–20.6, $P = 0.027$] as well as in ED95 [44.52 ml, 95% CI 19.05 – 69.99 mL vs 16.49 ml, 95% CI 12.23 – 20.75 mL. 95% CI of the difference 0.7- 55.3 mL, $P=0.044$]. The cross sectional area of brachial plexus was 0.95 ± 0.15 in middle-aged and 0.51 ± 0.06 cm² in elderly patients ($P < 0.001$).

Discussion: In the present study we found a reduced minimal effective anaesthetic volume for ultrasound-guided supraclavicular block was necessary for elderly patients. Additionally, we observed a smaller cross-sectional surface area of brachial plexus in the supraclavicular region for this group of subjects.

Acknowledgments: I would like to thank Jadranka Pavičić Šarić, MD PhD and Jelena Zenko, MD.

MeSH/Keywords: regional anaesthesia, supraclavicular block, ultrasound, levobupivacaine, lidocaine, elderly patients

Poster code: B-1-165

POSTER TITLE: QUALITY OF LIFE IN FAMILIES WITH CHILDREN SUFFERING FROM ATOPIC DERMATITIS

PhD candidate: Nives Pustišek, MD

Part of the thesis: The Pediatric Atopic Eczema: The Impact of Structured Education

Mentor/s: Professor Mirna Šitum, MD, PhD, Associate Professor Maja Vurnek Živković, PhD

Affiliation: Children's Hospital Zagreb, Medical School, University of Zagreb, Zagreb, Croatia

Introduction: Atopic dermatitis is a common childhood disease of increasing prevalence that not only changes the life of the affected child but also affects the social and emotional functioning of their parents and families. Restriction of normal family life, difficulties with complicated treatment regimens and increased caring for a child with eczema lead to parental exhaustion and feeling of hopelessness, guilt, anger and depression. The hidden costs involved in eczema management can be significant and have particular impact on lower income families.

Materials and methods: The aim of our study was to assess the quality of life of parents of children with atopic dermatitis and its predictors. The parents were asked to complete the Croatian version of Family Dermatology Life Quality Index (FDLQI), Patient Oriented (PO) Scoring Atopic Dermatitis (SCORAD), Perceived Stress Scale (PSS) and a general questionnaire during one of the regular follow ups. In FDLQI, the items concern the impact of a patient's skin disease on different aspects of the family caregivers' quality of life (emotional and physical wellbeing, relationships, social life, leisure activities, burden of care, impact on job/study, housework and expenditure). The severity of atopic dermatitis was

evaluated by using SCORAD index (performed by dermatologist) and PO SCORAD index (performed by parent). Subjective symptoms, PO itch and PO sleeplessness were measured.

Results: Data on 147 family caregivers were collected, mean age was 31,48 years. Results from this study show that family quality of life is significantly correlated with: SCORAD ($R=0,605$), PO SCORAD (0,526), PO itch (0,526), PO sleeplessness (0,611) and PSS (0,431). When these factors were entered in a regression analysis, they predicted as much as 67% of the variance of quality of life (FDLQI), with significant predictors being PO SCORAD, PO sleeplessness and PSS, and they remained significant even after controlling for a number of general and medical factors.

Discussion: Patient oriented scored and perceived stress are the most important predictors of quality of life of parents caring for children with atopic dermatitis.

Acknowledgments: I would like to thank to my mentors.

MeSH/Keywords: childhood atopic eczema, atopic dermatitis, family quality of life

Poster code: B-2-92

POSTER TITLE: PROPRIOCEPTIVE THERAPEUTIC TRAINING PROGRAM IN PATIENTS WITH KNEE OSTEOARTHRITIS

PhD candidate: Lana Bobić Lucić, MD

Part of the thesis: Effects Of A Proprioceptive Therapeutic Training Program On Pain And Functional Ability Compared With Standard Therapeutic Training Program In Patients With Knee Osteoarthritis: Single-Blind Controlled Study

Mentor/s: Professor Simeon Grazio, MD, PhD

Affiliation: Special Hospital for Medical Rehabilitation Lipik, Lipik

Introduction: Compared with a healthy population, people with knee OA have reduced proprioceptive function of the affected joint. Many of clinical trials are researching training programs that are unspecific in relation to the nature of the damage. The efficacy of proprioceptive training in prevention, rehabilitation and improvement of a number of motor characteristics is proven. Leading body in situations which could induce activation of proprioceptors, the optimal response in emergency situations that could cause injury is enabled, which is the basic meaning of proprioceptive training. This research aims to evaluate the effectiveness of proprioceptive training, in addition to standard training, and these effects will be compared with the effects of standard therapeutic training program.

Materials and methods: The study included a total of 20 subjects both men and women, 50 to 80 years of age in whom OA have been diagnosed according to the criteria of The American College of Rheumatology. They were randomly assigned to 1 of 2 groups that performed exercises for 12 days under the supervision: a standard-exercise group (SEG) and a proprioceptive-exercise group (PEG). The outcome measures included a visual analog scale (VAS) for pain, the Western Ontario and McMaster Universities Osteoarthritis Indeks (WOMAC) and joint position test (JPT) (15°,45°,75°). Measurements are recorded by a blinded researcher at baseline, after 12 days, and 3 months after initiating the intervention.

Results: The participants in both groups SEG (total-10, male 1, female 9, mean age 65,7 /-9,61) and PEG (total-10, male 3, female 7, mean age 69,7 /-5,80) had a reduction in pain but only participants in PEG group had a significant reduction (P=0,02 between initial and medial and initial and final measurements). Additionally, participants in both groups had a significantly better results in WOMAC index between initial and medial measurements (P<0,05). Participants in both groups had a improvement in JPT but no statistically significant differences were noted.

Discussion: Prior to training, both the experimental and the control groups of participants demonstrated similar performance on the JPT and in all measured variables. Following a different training type, VAS for pain significantly improved in the training group compared to the control group. Although proprioceptive training improve sense of position of the knee joint the exact evidence of these phenomena can not yet be explained.

Acknowledgments: I would like to thank Mr.D.Kelemen, a director of the hospital, for financial support and my mentor Prof.S.Grazio, MD, for his guidance, encouragement and corrections.

MeSH/Keywords: osteoarthritis, knee, proprioception, exercise

Poster code: B-3-58

POSTER TITLE: CORRELATION BETWEEN THE GRIP FORCE AND DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS

PhD candidate: Ines Doko, MD

Part of the thesis: Evaluation of the Hand Function using a New Electronic Dynamometer in Patients with Rheumatoid Arthritis

Mentor/s: Professor Simeon Grazio, MD, PhD

Affiliation: University of Zagreb School of Medicine, 'Sestre Milosrdnice' University Hospital Centre

Introduction: Rheumatoid arthritis (RA) is the commonest inflammatory rheumatic disease which at an early stage already can lead to substantial functional limitations in individuals affected by this disease. The measurement of the hand grip strength is a common method of evaluation and is recommended for assessing the functional ability in RA. New parameters of the functional hand potential measured by a modern dynamic electronic dynamometer represent a unique concept in evaluating the functional status and monitoring the rehabilitation process.

Materials and methods: Twenty-five out of previously planned forty consecutive patients with established RA were evaluated. Demographic data, anthropometric data, medical history and physical examination findings (including number of tender joints and number of swollen joints) were recorded. Disease activity score-28 (DAS28) was calculated using serum C-reactive protein (CRP). In the evaluation of motor hand function a new measurement expert system for dynamic acquisition of hand grip force developed at the "Ruđer Bošković" Institute was used.

Results: The median age (23 women and 2 men) was 56.04 ± 5.87 years and duration of disease 102.76 months. Values for DAS 28 ranged from 2.21 to 6.44 (median 4.47). Mean maximum grip

force of the dominant hand was 99.54 N (ranged from 25.80 to 119.10), and agility of grip 16.79 N/s (ranged from 11.15 to 103.60). Spearman's correlation test did not reveal any significant correlation between DAS28 scores and dynamometric parameters. Correlation significance was set at 0.05.

Discussion: Preliminary results have shown no correlation between maximal grip force and DAS28 score or between grip agility and DAS28 score in this group of patients with rheumatoid arthritis. The reason might be insufficient sample of respondents. In further research more patients will be included and measurements for non-dominant hand will be also evaluated. In addition, anthropometric measurements: length and circumference of the forearm, length and circumference of the hand, will be evaluated as possible covariate.

Acknowledgments: I would like to thank the engineer Amir Dubravić, PhD from the "Ruđer Bošković" Institute for great help in working with a dynamometric system.

MeSH/Keywords: dynamometer, disease activity, grip strength, rheumatoid arthritis

Poster code: B-3-63

POSTER TITLE: QUALITY OF LIFE AND FUNCTIONAL PROSTHETICS REHABILITATION OUTCOME

PhD candidate: Tamara Vukić, MD

Part of the thesis: Evaluation of quality of life and functional prosthetics rehabilitation outcome in patients with unilateral lower limb amputation

Mentor/s: Assistant Professor: Ida Kovač, MD, PhD

Affiliation: Institute For Rehabilitation And Orthopaedic Devices, University Hospital Centre – Zagreb

Introduction: In this study we will analyze the functional outcome of prosthetic rehabilitation of patients with unilateral lower limb amputation and its interaction with their quality of life and its interaction with ICF classification

Materials and methods: Research will be conducted on a group of 140 patients. Expected duration of this study is 12 months. Participants will complete three questionnaires. The first questionnaire Prosthetic Profile of the Amputee is a questionnaire specific to patients with amputation. This questionnaire will determine the functional outcome of prosthetic rehabilitation and the success of prosthetic supply. The second questionnaire the Short Form 36 will be used to analyze the quality of life of patients with the prosthesis. We will also use the ICF classification to describe the main characteristics of patients with lower limb amputation. Data will be analyzed by descriptive statistics. To test the normality of data distribution Kolmogorov - Smirnov test will be used. Differences between groups will be assessed by independent t-test or Mann-Whitney U test. P values below 0.05 will be considered statistically significant

Results: One of the aims of this study was to make a scientifically based proposal of ICF core set in people with lower limb amputation. We took ICF classification and ICF checklist to

choose specific categories that will meet the criteria for people with lower limb amputation. We have made a list of 82 categories that were chosen between three main domains of ICF classification (body structures and body functions, activity and participation and environmental factors). We still haven't finished our research but our preliminary results show that not all of 82 categories will be included in our proposed ICF core set for people with lower limb amputation

Discussion: ICF core set for people with lower limb amputation is derived from the ICF classification, many health conditions have already defined their ICF core sets but it is yet not defined for people with lower limb amputation. This research will also contribute to the analysis of functional outcome of prosthetic rehabilitation and to the analysis of quality of life of patients with prosthesis. Data analysis of all three methods will determine a significant predictors for more successful prosthetic rehabilitation of patients with lower limb amputation. To our knowledge this kind of research was not yet conducted or published

Acknowledgments:

MeSH/Keywords: prostheses, rehabilitation, quality of life, questionnaires, ICF classification

Poster code: B-3-79

POSTER TITLE: ASSOCIATION OF DISEASE ACTIVITY MEASURED BY RAPID3 WITH PHYSICAL FUNCTION OF THE HAND AND QUALITY OF LIFE IN PATIENTS WITH RHEUMATOID ARTHRITIS

PhD candidate: Merita Martinaj, Master of Science in Physiotherapy

Part of the thesis: Association of disease activity measured by RAPID3 with physical function of the hand and quality of life in patients with rheumatoid arthritis

Mentor/s: Professor Simeon Grazio MD, PhD, Professor Hajrije Hundozi-Hysenaj MD, PhD

Affiliation: Rheumatology Clinic, Univesity Clinical Center of Kosova

Introduction: In rheumatoid arthritis (RA), joint damage and disability increase with progression of the disease, affecting the quality of life. The aim of this study is to evaluate the correlation of RAPID3, the simple test for disease activity in RA, with functional ability of the hand and quality of life in patients with RA.

Materials and methods: The research was performed on 32 consecutive ambulatory RA patients, following previously established inclusion and exclusion criteria. The demographics and disease history data, anthropometric data, level of pain, disease activity, hand function, grip strength, fingertip-palm distance, overall function Health Assessment Questionnaire, quality of life, level of deformities and structural changes, were obtained.

Results: In our sample of patients there were 5 men and 17 women (mean age 54.2 years, range 21 to 71 years), mean body height 166.2 cm, weight 75.1 kg, disease duration of 8.9 years. Mean value of morning stiffness was 45 min, pain (VAS scale) 53.3 mm. Thirty-one patients were right-handed, and one patient was left-handed. Mean value of length of the forearm (r-l) was 24.4-24.4 cm, circumference of the forearm (r-l) 24.3-24.3 cm, length of the hand (r-

l) was 17.7-17.8 cm, circumference of the hand (r-l) 20.4-20.6 cm, fingertip-palm distance 1.76 cm, grip strength (r-l) 15.6-14.7 kg. The mean value of RAPID 3 was 5.02, while of HAQ DI-1.76. High disease activity (DAS 28> 5.1) was found in 24 patients. Regarding the JAM scale, 3 patients had score 0, 11 patients score 1, 12 patients score 2, 4 patients score 3 and 2 patients score 4. Four patients had stage IV, 3 patients stage III, 6 patients stage II and 19 patients stage I, according to Steinbrocker classification.

Discussion: Our study is still ongoing. We will compare results of our research to other studies (i.e. Eberhardt K 2008, Pincus T 2009, Fraser A 1999, Tyrber I 2005).

Acknowledgments: I thank Matej Mustapić, MD, specialist in radiology, subspecialist in skeletal radiology for scoring hands X-rays according to Steinbrocker's classification (Department of Radiology, University Clinical Center Sestre milosrdnice in Zagreb), Rheumatology Clinic, University Clinical Center of Kosova.

MeSH/Keywords: Arthritis, rheumatoid • function • hand • quality of life

Poster code: B-3-144

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

PhD candidate: Vesna Sokol, MD

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 thrombophilic 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 thrombophilic 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 thrombophilic 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: B-5-22

POSTER TITLE: IMPAIRED TROPHOBLAST DIFFERENTIATION IN PATHOLOGICAL PREGNANCIES

PhD candidate: Jasenka Zmijanac Partl MD

Part of the thesis: Differentiation of Human Trophoblast Cells in Normal and Pathological Pregnancy

Mentor/s: Associate Professor Ljiljana Šerman MD PhD

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

Introduction: Trophoblast cells undergo epithelial-mesenchymal transition in order to acquire mesenchymal phenotype. Differentiation of trophoblast cells is achieved by factors that activate or inhibit signalling pathways. SFRP1 acts as Wnt antagonist and plays a role in development by maintaining epithelial cell characteristics. Transcription factor Elf5 mediates early specification of blastocyst cell lines and acts as a regulatory protein in order to ensure epithelial characteristics of trophoblast cells. The aim of the present study was to analyse the distribution of SFRP1 as well as Elf5 in normal and pathological human placentas (IUGR, high blood pressure with HELLP, diabetes).

Materials and methods: Placentas were delivered in the third trimester from uncomplicated pregnancies (control group, $n = 24$) and those complicated by intrauterine growth restriction (IUGR) ($n = 18$), high blood pressure (RR) and HELLP ($n=15$) and gestational diabetes (GD) ($n =14$). IUGR was defined as birth weight less than 10th percentile for gestational age, parity and sex of the newborn. High blood pressure was defined according to ACOG, and GD according to HAPO study. SFRP1 and Elf5 antigen distribution was analysed by immunohistochemistry. Antigen expressions were scored using quantitative stereological analysis of volume density (Vv). Statistical significance was set at $p < 0.05$.

Results: SFRP1 positive staining was found in cytoplasm of syncytiotrophoblast, decidua, extravillous intermediate trophoblasts, and cytotrophoblasts of terminal villi. Expression of Elf5 proteins was detected in cytoplasm of decidual cells and nuclear signal was found in trophoblast cells in the basal layer of placenta. A statistically significant difference ($p < 0,05$) was found between SFRP1 expression in placental tissues of IUGR group, RR-HELLP group, and GD group in comparison to control group. Elf 5 expression was also significantly different ($p < 0.05$) in placental tissues of IUGR group and GD group in comparison to control group. There was no statistical difference regarding SFRP1 and Elf5 expression among groups from pathological pregnancies.

Discussion: Statistically higher expression ($p < 0.05$) of SFRP1 and Elf5 antigens in human placentas from pathological pregnancies in comparison to normal placentas may indicate a role in pathogenesis of placental dysfunction. We can assume that placentas obtained from pathological pregnancies show overexpression of epithelial phenotype markers (SFRP 1 and Elf5) due to impaired epithelial-mesenchymal transition.

Acknowledgments:

MeSH/Keywords: trophoblast, Wnt, Elf5, SFRP1

Poster code: B-5-35

POSTER TITLE: QUALITY OF LIFE AFTER “SLING” OPERATION

PhD candidate: Damir Hodžić, MD, MSc

Part of the thesis: Quality of Life in Female Patients After “Sling” Operation for Stress Urinary Incontinence

Mentor/s: Professor Slavko Orešković, MD, PhD

Affiliation: Department of Obstetrics and Gynecology, School of Medicine, University of Zagreb Department of Obstetrics and Gynecology, Clinical Hospital “Merkur”, Zagreb

Introduction: Stress urinary incontinence (SUI) is involuntary discharge of urine caused by the congenital or acquired defect of pelvic organs static with loss of vesicourethral anatomic support. The diagnosis of SUI can be set by the history, because patients referred incontinence in sneezing, coughing, running or similar physical straining, which significantly reduces their quality of life and ability to work.

Materials and methods: The research will include a minimum of 50 patients treated by “sling” method, and an equal number of patients operated by conventional anterior vaginal wall repair. All patients will preoperatively make assessment of defect anterior vaginal wall by POP-Q system and fill in two customized questionnaires (PFDI-20 and PFIQ-7) which includes questions about the quality of life until the past 3 months before operation. The collection of clinical data and the responses from the questionnaire will continue to be 3, 6 and 12 months after surgery, and will also record any perioperative or late complications.

Results: According to preliminary data of “sling” method correction of SUI there was no significant difference in the mean age, parity and hormonal state between the “sling” operation and traditional anterior colporrhaphy group. The mean operating time for SPARC and MiniArc procedure was <20 and <10 minutes, respectively.

Average duration of hospitalization was <3 days. No major intraoperative or immediate postoperative complications were observed. None of the patients required releasing of sling tension because of urinary retention and no significant voiding difficulties or strain to void occurred on routine check-up controls. Other milder complications like transitory episodes of pain, urinary urgency, polakisuria and nocturia were infrequent and not statistically significant. Patient’s satisfaction and the imposing short-time surgical outcome were achieved in all cases including sex life improvement.

Discussion: We consider the “sling” procedure as highly efficacious and safe minimally invasive and body integrity preserving method with impressively low rate of complications. In patients with SUI, especially without preceding vaginal operations, “sling” methods promising successful long-term results and high patient satisfaction. Our experience strongly supports initial favorable impressions of recent published studies, so we intend to evaluate wider aspects and perspectives of this procedure.

Acknowledgments:

MeSH/Keywords: stress urinary incontinence, sling, quality of life

Poster code: B-5-77

POSTER TITLE: THE SIGNIFICANCE OF TOTAL AND FETAL CELL FREE DNA FROM MATERNAL BLOOD IN NONINVASIVE DETECTION OF FETAL ANEUPLOIDIES

PhD candidate: Ivanka Bekavac Vlatković

Part of the thesis: The significance of total and fetal cell free DNA from maternal blood in noninvasive detection of fetal aneuploidies

Mentor/s: Assisted professor Feodora Stipoljev, MSC, PhD

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

Introduction: Prenatal screening for fetal chromosomopathies is an important part of obstetric care. Currently, the most cost effective prenatal screening tests for aneuploidies combine maternal age with a sonographic measurement of nuchal translucency in the first trimester and measurement of several maternal serum markers. This approach detects up to 90% of all cases of Down syndrome with the, false positive rate of 3-5%. In the current prenatal programs, definitive diagnosis of fetal chromosomal conditions is conducted through fetal sampling by amniocentesis or chorionic villus sampling associated with an abortion risk of 0.5-1%. To obviate the risk that is associated with invasive procedures, noninvasive diagnostic tests based on total and fetal cell free DNA in maternal circulation are investigated in the course of improvement of current screening protocols.

Materials and methods: Total and fetal cell free DNA pre corious villous sampling was extracted from maternal plasma from 60 pregnancies with aneuploid fetuses, between 11-13 6 weeks of gestation. Indication for CVS was based upon

abnormal ultrasonography finding and/or first trimester screening. Furthermore 60 samples in the same gestational age were obtained from women with normal first trimester ultrasonography and/or screening and were confirmed by birth a chromosomally normal group.

Results: Analysis of total and fetal cell free DNA levels showed correlation with crown-rump length in both groups. No correlation was found with nuchal translucency measurements. Additionally, analysis of cell free fetal DNA revealed differences between chromosomally normal and aneuploid fetuses.

Discussion: Our results showed that fetal and total cell DNA might be an prognostic marker of chromosomal abberations in first trimester pregnancy, and might be incooperated in screening procedures.

Acknowledgments:

MeSH/Keywords: screening, total and fetal cell free DNA, aneuploidies

Poster code: B-5-80

POSTER TITLE: CYSTEAMINE DAMAGE OF UTERUS AND BENEFICIAL EFFECT OF PENTADECAPEPTIDE BPC 157

PhD candidate: Tatjana Pavelić Turudić

Part of the thesis: The effect of pentadecapeptide BPC 157 and the role of NO systeme on uterus damaged by cysteamine

Mentor/s: Associate Professor Predrag Sikiric, MD, PhD

Affiliation: University of Zagreb School of Medicine, University Hospital "Sveti Duh" Zagreb

Introduction: Cysteamine has an ulcerogenic effect on doudenum and colon while it's effects on uterus is unknown. Pentadecapeptide BPC 157 inhibits doudenum and colon lesions, thus we hypothesized it's beneficial effect on uterus.

Materials and methods: We examined the effect of BPC 157 on cysteamine lesions of uterus in Wistar Albino rats. Cysteamine was applied in uterus horns as 10% solution and its effects were determined by macroscopic and by microscopic evaluation after 2h, 3d and 7 days. Medication given after cysteamine, either immediately, or later, at 2h, included pentadecapeptide BPC 157 10µg/kg or 10ng/kg per day, intraperitoneally or per-orally . Controls received saline (5ml/kg) i.p. and p.o.

Results: Cysteamine caused damage to uterus, and BPC 157 administrated intraperitoneally and orally inhibited the formation of the lesions.

Discussion: Our hypothesis was about damaging effect of cysteamine, and a beneficial effect of BPC 157 on cysteamine damages of endometrium. Penatadecapeptide BPC 157 counteracts doudenum and colon lesions while its effect on uterus, up to date, is not known. Our results revealed that BPC 157 inhibited uterus lesions and accelerated the healing of existing ones.

Acknowledgments:

MeSH/Keywords: MeSH/Keywords: cysteamine, uterus, BPC 157

Poster code: B-5-83

POSTER TITLE: A COMPARISON OF PLACENTAL HISTOLOGY AND PLACENTAL ELASTICITY MEASURED BY SHEAR WAVE ELASTOGRAPHY. PRELIMINARY RESULTS.

PhD candidate: Maryna Kharchenko, MD

Part of the thesis: Evaluation of the Elastic Properties of Placental Tissue in Fetal Growth Restriction

Mentor/s: Docent Berivoj Miskovic, MD, PhD

Affiliation: Department of Obstetrics and Gynecology, Medical School University of Zagreb, Sveti Duh Clinical Hospital, Zagreb. Health center Ozalj, Ozalj

Introduction: Elasticity (stiffness) is a mechanical properties of placental tissue which depends on the tissue micro- i macrostructure. Elasticity can be expressed quantitatively by Young's modulus. This is a first study to investigate how placental stiffness depends on histological microstructure of placental tissue. The aim of this study was to evaluate the correlation between placental histological patterns and the Young's elasticity modulus of placental tissue obtained by ultrasound shear wave elastography mode.

Materials and methods: The 26 placentas of full term normal singleton pregnancies were investigated in vitro immediately after birth, using the ultrasound machine with the shear-wave elastography mode and a 5-12 MHz linear probe. We analysed the average values of Young's modulus. Thereafter, investigated placental area was fixed in formalin and hematoxylin and eosin, Van Gieson, Mc Manus and Picro-Mallori stainings were performed on placental slides. The following variables were analysed: the density of collagen fibers in terminal villi, the density of terminal villi, the amount of syncytial knots, intervillous fibrin deposition and perivillous fibrin deposition.

Results: A strong positive correlation ($r = 0,788$) was between Young's elasticity modulus and intervillous fibrin deposition, $p < 0,001$. A weak positive correlation ($r = 0,283$) was between Young's elasticity modulus and the density of collagen fibers in terminal villi, $p = 0,161$. A moderate negative correlation ($r = -0,48$) was between Young's elasticity modulus and the density of terminal villi, $p = 0,840$. There was not correlation ($r = 0,116$) between Young's elasticity modulus and the amount of syncytial knots, $p = 0,364$. There was not correlation ($r = -0,124$) between Young's elasticity modulus and perivillous fibrin deposition, $p = 0,545$.

Discussion: We found strong and significant correlation only between the values of the Young's elasticity modulus and intervillous fibrin deposition. More samples are needed for definitive conclusions.

Acknowledgments:

MeSH/Keywords: elastography, placental elasticity

Poster code: B-5-98

POSTER TITLE: IMPACT OF OBESITY ON THE OVARIAN RESERVE

PhD candidate: Albert Lila, M.D

Part of the thesis: The ovarian reserve markers are disturbed more frequently in overweight and obesity group of infertile women than in infertile women with normal BMI and the standards and procedures for estimation of ovarian reserve in infertile women will be simplified

Mentor/s: Prof. Dr Velimir Simunic and Prof. Dr Shefqet Lulaj

Affiliation: Kosovo Occupational Health Institute in Gjakova

Introduction: Through this prospective study, it will be comparison and evaluation of the impact of overweight and obesity of women's in the reproductive age (23y-38y), in ovarian reserve and their reproductive functions, making comparison between the two observed groups with (BMI 25-29.9 kg/m² and BMI ≥30 kg/m²), with control group BMI 18-24.9 kg/m²,

Materials and methods: Enrollment group: 150 female, aged 23-38 years, Observed Outcome Measures: Serum levels of FSH, LH, Estradiol, Testosterone, SHBG, AMH, TSH, HbA1C in third day of menstrual cycle and ultrasound measurement of AFC and ovarian volume. Explanatory factors: BMI and Abdominal circumference. Confounding factors: Age, Metabolic syndrome, Stress and Life style, Statistical analysis: Statistical analysis will be performed by using statistical package SPSS 17.0. Data will report as mean ± standard deviation and through Odds Ratio with confidence interval 95% (95% CI).

Results: 1. Patient Management Information (PMS) - Has been designed and developed the Software Application for registration of patient data, their management and protection system which secure confidentiality. Databases are designed in MySQL and the programming is done in PHP scripting language. Then the software team has designed the Software, which is Web based, making possible access from the LAN and

remote sites, using the Internet connections. 2. First 15 patients have attended the procedure of taking blood analyses for measurements of values for each hormone-marker unit proposed in research. It will be their final results confirmed by end of May 2014. 3. Have been developed a system of procedures from invitation of patients about research, consent form, examinations, data registration and their evaluation. 4. Have been established the personal management system involved in the implementation of the research.

Discussion: Several studies have suggested a negative effect of obesity on parameters of ovarian reserve. Other investigators reported lower levels of AMH in obese women compared with normal weight women in the late reproductive age. Some studies showed that ovarian volume decreases with an increase in the BMI, indicating the possible decrease in fertility with an increase in a woman's weight. There might be, however, an adverse effect associated with increasing obesity leading to a loss of ovarian function.

Acknowledgments: BMI (Body Mass Index), AMH (Antimüllerian Hormone), AFC (Antral Follicle Count)

MeSH/Keywords: Obesity, overweight, ovarian reserve

Poster code: B-5-147

POSTER TITLE: LYMPH NODE MAPPING AND SENTINEL NODE DETECTION IN PATIENTS WITH EARLY CERVICAL CANCER (FIGO IA2-IIA1)

PhD candidate: Pavao Planinić, MD

Part of the thesis: We report our preliminary results on lymphatic mapping of SLNs using blue dye as well as the value of detected SLNs in prediction of the pelvic lymph node status in patients with early cervical cancer (FIGO IA2- IIA1).

Mentor/s: Professor, Ante Ćorušić MD, PhD

Affiliation: Division of Gynecological Oncology, Department of Obstetrics and Gynecology, University Hospital Center Zagreb, University of Zagreb Medical School, Zagreb Croatia

Introduction: Colorimetric and radioactive tracer mapping are currently mostly used mapping methods for the detection of sentinel lymph nodes (SLNs) in prediction of the pelvic lymph node status in cervical carcinoma. When used separately both methods are equally successful in detecting SLNs. In contrast to blue dye, radioisotopes are costly and require more time, logistic efforts and preparation.

Materials and methods: Diluted methylene blue is injected intracervically in the operating room prior to surgery, at 4 quadrants of the exocervix and at 4 quadrants on the level of transition of the cervix to vaginal fornices. Following detection and excision of SLNs, systematic bilateral pelvic lymphadenectomy and radical hysterectomy (or trachelectomy) is performed in all patients.

Results: From December 2011 to April 2013, 22 patients diagnosed with FIGO stage IA2 – IIA1 cervical cancer were enrolled in the study. The median age was 45 years. Sixty eight percent of the patients had squamous cell carcinoma, 23% had adenocarcinoma and 9% had adeno-squamous cervical carcinoma. A total number of excised lymph nodes was 621 (28.2 per patient) and we detected the total of 100 SLNs. Intraop-

erative SLN detection rate was 100%, and in all patients SLNs were detected bilaterally. We detected 4.5 SLNs per patient (2.27 SLNs per pelvic side). Metastatic sentinel nodes were found in 2 patients (9%). There was no case with positive non-SLNs in the presence of a negative sentinel node.

Discussion: The standard treatment option for cervical cancer involves complete pelvic lymphadenectomy which increases operating time, and may increase postoperative morbidity and length of hospital stays. Our results are concurrent with the data in the literature that the SNL detection is a feasible procedure in cervical cancer patients and increases detection rate of lymph node metastases compared to systemic pelvic lymphadenectomy, thus improving nodal staging. Our preliminary results demonstrate that SLN detection rate is high with the use of blue dye. The advantage of this mapping method is that it is fast, easy and cheap.

Acknowledgments:

MeSH/Keywords: sentinel lymph node, cervical cancer

Poster code: B-5-170

POSTER TITLE: RESEARCH OF EXTRACORPOREAL MAGNETIC STIMULATION IN TREATMENT OF NON-INFLAMMATORY TYPE CHRONIC PELVIC PAIN SYNDROME IN MEN

PhD candidate: Miram Pasini, MD

Part of the thesis: Extracorporeal magnetic stimulation in treatment of chronic pelvic pain syndrome

Mentor/s: Professor Višnja Škerk, MD, PhD

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

Introduction: Chronic pelvic pain syndrome (CPPS) is one form of prostatitis and is used to designate unexplained chronic pelvic pain in men. The National Institutes of Health (NIH) describes 4 categories of prostatitis: type III - chronic abacterial prostatitis, ie, categorized as either type IIIa (inflammatory CPPS) or type IIIb (noninflammatory CPPS). The most common type of prostatitis syndrome is chronic pelvic pain syndrome, whose aetiology is uncertain and treatment is often unsatisfactory. We will investigate the effect of extracorporeal magnetic stimulation on symptoms of chronic pelvic pain syndrome in men

Materials and methods: We're conducting a monocentric, prospective, double-blind, placebo controlled and randomized trial. Inclusion criteria: symptomatic men over 18 years old, whose previous treatment was inefficient. From all patients medical history will be taken and physical and digitorectal examinations performed. Infection will be excluded by taking urine, urine culture, urethra smears, expressed prostatic excretion and ejaculate analysis for microbiology, ureaplasma, mycoplasma, chlamydia and vaginal trichomonas. Inclusion criteria will be normal PSA values and urotract ultrasound. Exclusion criteria: patients with previous radiotherapy, electrostimulators, heart arrhythmia, and metal implants. Informed consent and questionnaire from NIH Chronic Prostatitis Symptom Index (CPSI) will be fulfilled (this index is calculated using a series of 9 questions that con-

tain 21 items used to assess patient history in a standardized and quantifiable format). Patients will be divided into active and placebo group. In active group there will be a total of 16 treatments conducted twice a week. Patient in placebo group will be placed in the same chair and through hidden speaker will be played the same sounds as heard from the device. Two groups we'll be treated on a different days to avoid crosstalk between groups. Patients will be evaluated at baseline, the end of a therapy, 3 and 12 months after treatment using NIH CPSI.

Results: This is double blinded still ongoing study and at this point we can only analyse patients scores prior treatment without knowing which are in active or placebo group. There were 62 enrolled men aged from 28 to 72 years (mean 46,3 SD 11,3) with PSA value of 0,55 (SD 0,35). Total CPSI score ranged from 12 to 38 (mean 22,55 SD 6.04).

Discussion: The use of pelvic floor electromagnetic therapy may be a promising new noninvasive option for chronic pelvic pain syndrome in men.

Acknowledgments: I would like to thank to my mentor prof. Višnja Škerk and all department physicians that helped during this study

MeSH/Keywords: Chronic pelvic pain syndrome, extracorporeal magnetic stimulation

Poster code: B-7-103

POSTER TITLE: INTRINSIC INSULIN RESISTANCE AMONG NONDIABETICS AND OCCURRENCE OF HYPERGLYCEMIA IN CRITICAL ILLNESS

PhD candidate: Edita Lukić, MD, University Hospital Centre Zagreb, Department of Orthopaedic Surgery

Part of the thesis: INTRINSIC INSULIN RESISTANCE AMONG NONDIABETICS AND OCCURRENCE OF HYPERGLYCEMIA IN CRITICAL ILLNESS

Mentor/s: Asst Prof Ivan Gornik, MD, PhD, , University of Zagreb Medical School University Hospital Centre Zagreb, Department of Medicine

Affiliation: Intensive Care Unit, Department of Medicine, University Hospital Centre Zagreb

Introduction: Insulin resistance is characterized by the absence of physiologic response of peripheral tissues to insulin action. It plays a major pathophysiological role in type 2 diabetes and it is tightly associated with major public health problems, including obesity, coronary artery disease and metabolic syndrome. Critical illness or injury can lead to hyperglycemia, insulin resistance and glucose metabolism disorder. Patients without apparent glucose metabolism disorder who had hyperglycemia in critical illness have increased risk for the onset of type 2 diabetes mellitus or impaired glucose metabolism (IFG or IGT).

Materials and methods: This is a prospective study including 99 patients without apparent glucose metabolism disorder admitted to Intensive Care Unit, Department of Medicine, University Hospital Centre Zagreb due to critical illness (acute coronary syndrome, sepsis, pulmonary edema, pneumonia). Patients are divided into hyperglycemia group-HAB (blood glucose level measured during ICU stay >7.7 mmol/L in at least two occasions) and normoglycaemia group-NAB. During their ICU stay following data are collected: age, gender, BMI, WHR, evaluation of physical activity, history of alcoholic and nicotine consumption. Blood tests including: glucose blood level, HbA1c, cholesterol, FFA, RBC, HCT, WBC, platelet count, creatinine, bilirubin are measured. APACHE II and SOFA is calculated.

Follow up of 6-8 weeks is conducted and on the ambulatory appointment insulin resistance is measured by indirect methods (QUICKI, HOMA-IR) and OGTT test is performed. Data will be statistically analyzed.

Results: At the moment we have 48 patients enrolled in our study, 27 patients in HAB group and 21 patients in NAB group. We excluded 26 patients (2 died, 23 rejected follow up, 1 developed IGT). ICU data are gathered for all patients. On ambulatory appointment OGTT test is performed, blood samples are taken and stored according to biochemistry rules. Due to high costs of insulin resistance analysis all blood samples will be analyzed together when collected. We expect to conclude the study in September 2014.

Discussion: Since the study has not been concluded statistical analysis cannot be done. Therefore we cannot discuss so far gathered data. When we conclude the study we expect statistical analysis to show that increased risk for the onset of type 2 diabetes mellitus among patients who had hyperglycemia in critical illness is caused by intrinsically increased insulin resistance.

Acknowledgments:

MeSH/Keywords: : insulin resistance, hyperglycemia, critical illness

Poster code: B-8-15

POSTER TITLE: THE RELATIONSHIP OF PLASMA CONCENTRATIONS OF GLUCAGONE-LIKE PEPTIDE 1 AND FIBROBLAST GROWTH FACTOR-21 WITH GLUCOREGULATION, LIPIDEMIA AND MICROVASCULAR COMPLICATIONS IN DIABETES MELLITUS TYPE 1 INDIVIDUALS

PhD candidate: Karin Zibar

Part of the thesis: abstract of preliminary results

Mentor/s: Prof. dr. sc. Lea Smirčić Duvnjak

Affiliation: Merkur University Hospital, Vuk Vrhovac Clinic for Diabetes, Endocrinology and Metabolic Diseases

Introduction: The roles of glucagon like peptide-1 (GLP-1) and fibroblast growth factor-21 (FGF-21) have become a new scientific interest in the field of pathophysiology of type 1 diabetes mellitus (T1DM), but the results of the published studies were not uniform. The aim of the study was to examine the difference in GLP-1 and in FGF-21 concentrations between T1DM patients and healthy subjects, respectively.

Materials and methods: The cross-sectional study included 30 C-peptide negative T1DM patients, median age 37 years (20-59), the disease duration 22 years (3-45), and 10 healthy controls, median age 30 years (27-47). Fasting and postprandial both total and active GLP-1 and total FGF-21 concentrations were measured by ELISA.

Results: Both fasting the total and the active GLP-1 concentrations were significantly lower in T1DM patients (total median 0.4 pmol/L, 0-6.4, and active median 0.2 pmol/L, 0-1.9) compared with healthy controls (total median 3.23 pmol/L, 0.2-5.5, and active median 0.8 pmol/L, 0.2-3.6),

P=0.008 for total GLP-1, P=0.001 for active GLP-1. After adjustment for confounding factors, binary logistic regression showed that both fasting the total and the active GLP-1 remained significantly independently lower in T1DM patients (total OR 2.43, 95%CI 1.203-4.909 and active OR 8.73, 95%CI 1.472-51.787). The fasting FGF-21 concentration was also significantly lower in T1DM patients (median 28.2 pg/mL, 0-842.4) compared with healthy controls (median 104 pg/mL, 7.7-240.7), P=0.046.

Discussion: Fasting total and active GLP-1 and total FGF-21 concentrations were lower in T1DM patients compared to healthy controls. The results indicated a possible promising therapeutic effect of GLP-1 and FGF-21 analogues in T1DM patients.

Acknowledgments: to laboratory staff

MeSH/Keywords: glucagone-like peptide 1, fibroblast growth factor-21, diabetes mellitus type 1

Poster code: B-9-3

POSTER TITLE: THE CONNECTION BETWEEN HYPOCHLOREMIA AND HYPONATREMIA IN PATIENTS WITH HEART FAILURE

PhD candidate: Bojana Radulović, MD

Part of the thesis: The importance of initial hyponatremia in developing hyponatremia and adverse outcome in patients with acute heart failure

Mentor/s: Vesna Degoricija Professor of Medicine at University of Zagreb School of Medicine and University Hospital Center Sisters of Charity

Affiliation: University Hospital Center Sisters of Charity and University Hospital Center Zagreb

Introduction: Hyponatremia is a significant and independent predictor of outcomes including re-hospitalization and mortality in patients with both acute heart failure and chronic heart failure. Even modest degrees of hyponatremia are associated with a poorer prognosis. Results from some studies of hyponatremia in heart failure suggest the possibility that hyponatremia appears prior to hyponatremia in patients with heart failure.

Materials and methods: The study is designed as a prospective study that will include 276 patients hospitalized through the emergency department for an acute episode of heart failure. Participants will be divided in two groups depending on initial plasma values of chloride (in one group patients with levels of chloride below

97 mmol/L and in the other patients that have higher levels of chloride than 97 mmol/L). The two groups will be compared for development of hyponatremia.

Results: So far we had 15 patients with acute heart failure, two of which had initial hyponatremia. During the hospitalization one of those developed hyponatremia.

Discussion: Our initial results show that a connection between hyponatremia and hyponatremia could be made. Further research is needed.

Acknowledgments:

MeSH/Keywords: Chlorates, hyponatremia, heart failure.

Poster code: B-9-6

POSTER TITLE: CELL-FREE CIRCULATING DNA AS A MARKER IN PATIENTS WITH LYMPHOMA

PhD candidate: Dino Dujmović

Part of the thesis: Cell-free circulating DNA as a marker in patients with lymphoma

Mentor/s: Igor Aurer

Affiliation: Haematology

Introduction: Extracellular circulating DNA can be found in small amounts in the plasma of healthy individuals. Increased levels of cell-free DNA have been reported in a number of clinical conditions such as malignant and autoimmune diseases, myocardial infarction, trauma, and pregnancy-associated complications. Circulating DNA in the blood of patients with cancer is clearly tumor-derived. While it is widely studied in solid tumors, there is much less data on cell-free DNA in hematological malignancies. The aim of this research is to detect the level of circulating cell-free DNA in patients with lymphoma and to evaluate if the cell-free DNA can be used as a marker of disease activity, as a prognostic marker, or as a marker of response to treatment.

Materials and methods: With quantitative real-time PCR we determined the concentration of cfDNA in 129 patients with lymphoma. We correlated our results with other laboratory and clinical parameters as well as OS and PFS

Results: 49(38%) had elevated concentrations of cfDNA. It was higher in patients with advanced stage disease, and also in older patients and

those who had elevated concentrations of LDH and B-2 microglobulin. There was no difference between patients with aggressive or indolent lymphoma. In patients who had concentrations of cfDNA higher than the median value OS and PFS were significantly higher. After treatment all patients had a decrease in cfDNA concentration but it was without clinical significance.

Discussion: In all subgroups elevated concentrations of circulating cell free DNA were found. cfDNA was not shown as an independent marker or as a good prognostic marker in patients with lymphoma. In several subtypes of lymphoma concentration of cfDNA seems to have an influence on event free survival but those results should be tested on a higher number of patients. Until then cfDNA has no role in the prognosis or treatment planning for patients with lymphoma.

Acknowledgments: UHC Zagreb lymphoma team

MeSH/Keywords: cfDNA, Lymphoma,

Poster code: B-9-19

POSTER TITLE: IMPACT OF STRESS HYPERGLYCEMIA ON HOSPITAL OUTCOME OF ACUTE EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

PhD candidate: Marija Zlojtro, MD

Part of the thesis: Stress hyperglycemia is negative prognostic factor for AECOPD

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

Affiliation: General Hospital Zabok

Introduction: Stress hyperglycemia is transient hyperglycaemia during acute illness and was thought to be harmless or even advantageous. However, results of previous studies showed that hyperglycaemia is associated with poor outcomes from pneumonia, myocardial infarction and stroke, but the effect of blood glucose on outcomes from acute exacerbations of chronic obstructive pulmonary disease (AECOPD) has not been established. Current guidelines do not comment on measurement or control of blood glucose in AECOPD. A study was therefore undertaken to determine the relationship between stress hyperglycemia, clinical outcomes and mortality in patients admitted with AECOPD.

Materials and methods: 1-year prospective study with 300 AECOPD non-diabetic patients divided in two groups according to presence of stress hyperglycemia (glucose > 6,9 or 7,8 mmol/L postprandial). After standard corticosteroid therapy each group will be further stratified according to glycemia after 24 hours and before discharge. Beside age, sex, BMI, smoking history, lipid status, CRP, HbA1C, arterial ABS and cardiovascular morbidity, in all groups and subgroups standard variables of lung function, need for mechanical ventilation, sputum culture results, radiological pneumonia finding and outcome will be evaluated.

Results: We descriptively analysed preliminary results for 100 patients. In group I there were

46 subjects (46%) with male dominance (74% vs 26%) and average age of 72,4 years. Most of them were active and former smokers (72%) classified into GOLD C and D group according to the severity of their illness (C 56%, D 21%). Glucose level at admission was 8,9 mmol/L in average, 9,5 mmol/L after 24 hours and 6,3 mmol/L at hospital discharge. In the control group (N 64), no significant differences were found regarding gender, smoking habits and age. Majority of subjects were classified in group GOLD B (N=43, 68%). When comparing results, average CRP values were much higher in test group I (106 mg/L vs 71 mg/L), so was the severity of respiratory insufficiency and need for mechanical ventilation (I-6,II- 0). Subjects in group I had more often verified pneumonia (I- 67%, II - 39%). Average hospital days were 7,6 days for group I vs 6,1 days for group II. Outcome was fatal for 2 patients in group I and none in group II.

Discussion: These preliminary results indicate that stress hyperglycemia in patients with acute COPD exacerbation could be significant negative prognostic outcome factor, which supports original hypothesis.

Acknowledgments: none

MeSH/Keywords: COPD, stress hyperglycemia, exacerbation

Poster code: B-9-38

POSTER TITLE: CAUSES OF DEATH OF 103 PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS – RETROSPECTIVE ANALYSIS OF DEATH CERTIFICATES OF PATIENTS DECEASED FROM 2002 TO 2009 IN CROATIA

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: University Hospital Centre Zagreb and University of Zagreb School of Medicine, Department of Internal Medicine, Division of Clinical Immunology and Rheumatology, Kišpatićeva 12, 10 000 Zagreb

Introduction: Causes of death (COD) of patients with systemic lupus erythematosus (SLE) are commonly classified into the following categories: (1) active disease, (2) acute cardiovascular and cerebrovascular events, (3) infections, (4) malignant tumors and (5) other causes.

Materials and methods: We retrospectively analyzed causes of death of patients deceased from 2002 to 2009 in Croatia, whose death certificates included SLE in the list of diagnoses. Data were extracted from death certificates of identified deceased patients. The frequency of each previously defined COD category was counted.

Results: We identified a total number of 103 deceased patients (85 females and 18 males) with a mean age of 56.5 ± 15.3 (ranging between 7 and 85) years at the time of death. 81/103 patients died in a hospital (17/81 in the intensive care setting), 57/81 in one of the four largest Croatian cities (Zagreb, Split, Rijeka and Osijek). 48/103 patients are included in the large database of SLE patients followed-up by our Division. Infections were identified as the most frequent cause of death (43/103), followed by acute cardiovascular and cerebrovascular events (25/103). A malignant tumor was unexpectedly identified in only one patient (malignant brain tumor), not being the only cause of death of that patient. Active SLE was identified as a cause of death of 14/103 patients. Other causes were identified

in 8/103 patients. Unfortunately, it was not possible to identify causes of death of 24/103 patients because their death certificates were not filled in properly, hence the quality of data was low.

Discussion: Results of this study suggest a high frequency of infections and acute cardio/cerebrovascular events as causes of death of SLE patients. The major limitation of this study is the low quality of data obtained from patients' death certificates. According to results of previous studies, it is reasonable to expect that SLE is not included in the list of diagnoses in death certificates of a large proportion of patients with SLE. Our future research will focus on the analysis of causes of death and SLE characteristics of deceased patients based on data obtained from the large database of SLE patients followed-up by our Division. Combined with data retrieved from death certificates, this will allow us to assess the extent of underreporting of death of SLE patients.

Acknowledgments: I would like to thank my supervisor and all members of the Division for their support.

MeSH/Keywords: systemic lupus erythematosus, cause of death, death certificates

Poster code: B-9-76

POSTER TITLE: EFFECT OF PROLONGED WORKING TIME ON ACTIVATION OF HEMOSTATIC SYSTEM

PhD candidate: Hana Mažibrada

Part of the thesis: Prolonged working time activates hemostatic system resulting with hypercoagulability of the blood

Mentor/s: Petar Gaćina, MD, PhD, assistant professor

Affiliation: KBC Sestre milosrdnice

Introduction: The stress on working place and prolonged working time have affect on hemostatic system what is confirmed by previous studies. A few information is known about the mechanism of activation of the hemostatic system an circadian variation of the coagulation factors and fibrinolysis. This fact is important because the activation of hemostatic system and hypercoagulability of the blood increase risk of morbidity and mortality. The hypothesis of this study is to investigate if the prolonged working time in health workers affects hemostatic system resulting with hypercoagulability of the blood.

Materials and methods: The study group includes thirty physicians age 25-35 who are on education and whose work is occasionally organized as twentyfour hours labour. The control group are physicians matched for ethnicity and age, with same education. Participants excluded from the study are pregnant women, users of hormonal contraception, physicians with positive anamnesis of thromboembolic events, nicotine use, acute infectious disease, BMI <18.5 and >25 kg/m², and those who had last twentyfour hours labor before more than five days. The samples of the vein blood are collected 15 minutes before 24h labor, 12h and 24 hours after the beginning of the 24h labor. We measure the concentrations of fibrinogen, D-dimers, TAT, PAP complexes, factor VIII, activity of vWF, PV, INR, APTV, TV, fibrinolysis and CRP.

Results: The aim of this research is to explore coagulation parameters in study and control group. The specific aims are to measure the concentrations of fibrinogen, D-dimers, TAT, PAP complexes, factor VIII, activity of von Willebrand factor, PV, INR, APTV, TV, fibrinolysis, CRP and also see the dynamic of these measurements. Until this date we measured the concentrations of earlier mentioned factors in ten participants (15% of total participants) and preliminary results showed us shorter time of fibrinolysis in control group which shows that time of the degradation of thrombus is faster in mentioned group.

Discussion: The better knowing of hemostatic system through variations of coagulation parameters and fibrinolysis in circadian rhythm of the health workers occasionally exposed to shift and 24h work would help us to better understand potential danger of prolonged working time on coagulation system. The preliminary results showed us greater effect on duration of fibrinolysis, which results with faster degradation of thrombus in control than study group.

Acknowledgments: I would like to thank my mentor, colleagues and personnel in laboratory in which measurements are done

MeSH/Keywords: prolonged working time, hypercoagulability, fibrinolysis

Poster code: B-9-94

POSTER TITLE: THE CORRELATION BETWEEN SUBCLINICAL HYPOTHYROIDISM AND MORBIDITY AND MORTALITY OF PATIENTS IN END-STAGE RENAL DISEASE

PhD candidate: Nataša Črne Fureš, MD

Part of the thesis: The Correlation between Subclinical Hypothyroidism, Chronic Inflammation and Malnutrition with Morbidity and Mortality of Patients treated with Haemodialysis and Peritoneal Dialysis

Mentor/s: Draško Pavlović, MD, Assistant Professor

Affiliation: Universtiy Hospital Centre

Introduction: Incidence of chronic kidney disease (CKD) rises. Factors like constant inflammation, vascular calcification, malnutrition and many others significantly influence the incidence of cardiovascular complications and mortality of patients treated with hemodialysis. Low triiodothyronine (T3) syndrome is also one of the factors that influence the course of chronic kidney disease. Patients with that syndrome have normal or higher level of thyreotropine-stimulating hormone (TSH) and lower level of T3. In that way the latent hypothyroidism develops, which has a negative effect on the prognosis of CKD.

Materials and methods: The research will be carried out on patients treated with dialysis in three hospitals (about 230 patients) in one year time. Patients that will be acutely ill in the beginning of the research or will have already known thyroid disease, will not be included. In the beginning of the research data concerning gender, age, the main cause of CKD, anamnesis, the duration of dialysis treatment, the sort of dialysis, the presence of AV fistula or central venous dialysis catheter and medical therapy will be collected. In the beginning of the research, 6 months and one year after, and in case of acute illness of a patient, the levels of thyroid hormones and parameters of inflammation and malnutrition will be determined from blood samples.

Results: Blood samples were collected from 18 patients so far. The preliminary results have shown that chronic inflammation is present, according to results of C reactive protein (average mean 8,4 mg/L). Although the average value of body mass index was in the normal range (26 kg/m²), average albumin level was slightly lower (38,5 g/L), which could indicate the presence of chronic malnutrition. Unfortunately, so far the results of thyroid hormones and TSH have not been completed. These results mark only the beginning of my research, and soon there will be more results and more included patients.

Discussion: Most recent research have shown that sudden cardiac death may be influenced by subclinical hyperthyroidism and euthyroid sick syndrome in the short term. Regular assessment of thyroid status may help estimate the cardiac risk of dialysis, but there is a need for further investigation as the prevalence of thyroid disorders and their impact on CV events and mortality in dialysis patients is still largely unknown.

Acknowledgments:

MeSH/Keywords: chronic kidney disease, low triiodothyronine syndrome, inflammation, malnutrition.

Poster code: B-9-120

POSTER TITLE: CLINICAL RISK STRATIFICATION IN CLASSIC HODGKIN LYMPHOMA

PhD candidate: Željko Prka, MD

Part of the thesis: Prognostic significance of Fas, FasL and c-FLIP expression in classic Hodgkin lymphoma

Mentor/s: Professor Vlatko Pejša, MD, PhD, Čedna Tomasović Lončarić, MD, PhD

Affiliation: Clinical hospital Dubrava

Introduction: An accurate assessment of the stage of disease in patients with HL and furthermore their stratification in good or poor prognosis group is critical for the selection of the appropriate therapy. Identifying patients who are at low or high risk for recurrence is most useful in optimizing therapy based on the patient's expected clinical outcome to avoid overtreatment of some and undertreatment of others.

Materials and methods: Ann Arbor staging system was used to assess clinical stage of disease. As for risk stratification, number of poor prognostic parameters and, accordingly, risk group was determined according to appropriate prognostic system. GHSG/EORTC were used for limited stage disease and IPS score for advanced stage. Patients with ≥ 1 parameters in GHSG/EORTC and ≥ 3 in IPS scoring system were placed in poor prognosis group.

Results: So far we evaluated 28 patients with classic Hodgkin lymphoma who were diagnosed in our institution. There were 15 (54%) males. Median age at diagnosis was 39 (range 18-67). Out of 28 evaluated patients nine (32%) of them had limited stage disease (CS I-IIA) at the time of diagnosis and 19 (68%) were in advanced

stage. After risk stratification with aforementioned systems there were seven and eight poor prognosis patients in limited and advanced stage of the disease, respectively.

Discussion: Optimal management of patients with HL requires an accurate diagnosis and careful staging of the disease. Identification of poor prognostic features then allows for risk-adapted therapy to potentially increase the likelihood of cure and minimize toxicity. Our preliminary risk stratification in about half of expected number of patients showed that percentage of patients with limited and advanced disease and their risk stratification profile is in line with literature reports. Due to major technical and staff problems we haven't started with determination of Fas, FasL and c-FLIP expression although all antibodies and other necessary equipment were obtained. We are hoping to show and publish our complete results in next year.

Acknowledgments:

MeSH/Keywords: Hodgkin lymphoma, c-FLIP, Fas, FasL

Poster code: B-9-130

POSTER TITLE: LONG-TERM FOLLOW-UP OF PATIENTS ON SILDENAFIL FROM CROATIAN PULMONARY HYPERTENSION REGISTRY

PhD candidate: Gzim Redžepi, MD

Part of the thesis: Efficacy and Safety of Long-Term Treatment with Sildenafil in Patient with Pulmonary Hypertension

Mentor/s: Professor Miroslav Samaržija, MD, PhD

Affiliation: University of Zagreb School of Medicine, University Hospital Centre-Zagreb, University Hospital for Lung Diseases 'Jordanovac', Zagreb, Croatia

Introduction: Sildenafil is found to improve exercise capacity and haemodynamics in selected patients with pulmonary hypertension. We present data from patients with severe pulmonary hypertension, following their 6 – minute walking distance, right ventricle pressure measured by cardiac ultrasound, Borg dyspnoea score and NYHA class.

Materials and methods: Over 8 – year period we commenced 40 patients on sildenafil 25 – 50 mg tds, NYHA class II-IV, with various etiology of pulmonary hypertension (30 patients with PAH - which included 19 patients with IPAH, 5 with connective tissue disease, 5 with congenital heart disease, 1 with PH associated with anorexigen intake, 8 patients with CTEPH, 1 patient with PH due to COPD and 1 patient with PH due to hematologic malignancy) were followed for mean of 17.3 months (range, 1 to 72 months). Long – term efficacy was assessed by 6 – min walking distance (6MWD), NYHA class, Borg dyspnoea score, and right ventricle pressure measured by cardiac ultrasound. Clinical events were monitored to assess time to disease progression.

Results: Right ventricle pressure was reduced from 94.45 mmHg before treatment to 86.53 mmHg after 12 months of treatment ($p <$

0.05). 6MWD increased from 316 m to 375m after 3 month, then further to 391m at 6 months and further to 414m after 12 months of treatment($p < 0.05$). Seventeen patients (79% of all failures) had failure of treatment after 3 months, additional four after 6 months and two more after 12 months of treatment. Therapy is still ongoing in 38 patients, and in 25 patient is longer than 12 months. In those patients with prolonged benefit, mean duration of treatment is 39.2 months (range 11 to 86 months). In patients with prolonged benefit we noticed improvements in Borg dyspnoea score and NYHA class.

Discussion: Long-term use of sildenafil in patients with severe pulmonary hypertension of various etiologies is associated with a sustained improvement in exercise capacity and right ventricle pressure. Most of the treatment failures were noticed after first three months of treatment.

Acknowledgments:

MeSH/Keywords: pulmonary hypertension, sildenafil, right ventricle pressure

Poster code: B-9-150

POSTER TITLE: BIOLOGICAL, PSYCHOLOGICAL AND SOCIAL FACTORS AS DYSPNEA PREDICTORS AMONG PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASES

PhD candidate: Latinka Basara Toromanović, Professor of Psychology

Part of the thesis: Biological, Psychological And Social Factors As Dyspnea Predictors Among Patients With Chronic Obstructive Pulmonary Diseases

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

Affiliation: University Hospital Centre Zagreb, Department for Respiratory Diseases Jordanovac, Zagreb

Introduction: Dyspnea is a clinical term for shortness of breath, or breathlessness and because of its debilitating characteristics it is the most common complaint among patients with chronic obstructive pulmonary diseases. Although dyspnea is a result of a pathophysiologic process, it is likely to be influenced by factors as psychological state, bodily preoccupation, level of awareness, body weight, state of nutrition, and medications. Biopsychosocial model includes all of these factors into explaining symptoms and disease course.

Materials and methods: In order to gather data for biological variables we used previous medical records, oxygen saturation data (puls oximeter) and lung function tests results. For psychological variables a battery of questionnaires was used: PANAS- Positive and Negative Affective Schedule, ASI – Anxiety Sensitivity Index, Locus of Control Scale, Coping Strategies Questionnaire, Social support scale, COPD Assessment Test, Asthma Control Questionnaire. For assessing social variables we used a demographic questionnaire constructed for the purpose of this study. To assess dyspnea, Borg dyspnea scale was used.

Results: So far data was collected from 14 subjects (from targeted 100 patients with asthma and 100 patients with chronic obstructive pulmonary disease - COPD). Here we bring only descriptive data since no statistically significant differences would be relevant in this early stage of research. Out of 14 subjects, 10 was asthma and 4 COPD patients, 12 female and 2 male, mean age 59.43 years. Majority was married (57.1%), retired (71.4%) with average income. So far, results for anxiety sensitivity in asthma patients suggest higher than average population scores.

Discussion: Because of the very early stage of research and small number of data collected so far, no relevant statistical analysis was done. Majority of subjects are retired, married women with asthma and higher than average population score regarding anxiety sensitivity.

Acknowledgments:

MeSH/Keywords: dyspnea, chronic obstructive pulmonary disease, asthma, biopsychosocial model

Poster code: B-9-152

POSTER TITLE: ROLE OF ARTERIAL STIFFNESS VARIABLES IN ASSESSMENT OF CARDIOVASCULAR RISK IN PATIENTS WITH COPD

PhD candidate: Đivo Ljubičić

Part of the thesis: RELATIONSHIP OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE AND ELEVATED CARDIOVASCULAR RISK

Mentor/s: Professor Neven Tudorić, MD, PhD

Affiliation: Division of pulmonology, Department of internal medicine of Zagreb Medical School, University hospital Dubrava, University of Zagreb

Introduction: Recent studies suggest a possible link between lung and systemic inflammation in chronic obstructive pulmonary disease (COPD) and the progression of atherosclerotic processes, which increases cardiovascular morbidity and mortality. No study has comprehensively investigated the relationship between lung function and arterial stiffness as an independent predictor of increased cardiovascular risk in patients with COPD and healthy smokers, and as a control group of healthy nonsmokers.

Materials and methods: This is a cross-sectional study with a total of 180 subjects, in three groups (COPD, non-COPD-smokers, non-COPD-non-smokers). Beside anthropometric measurements and traditional cardiovascular risk factors assessment, elements of COPD (phenotype of COPD, BODEx index, spirometry, bronchodilation test, and hemoglobin oxygen saturation) were examined with measurement of pulse wave (PWV) velocity and aortic augmentation index (AIx) using TensioMed arteriography. Subjects will be evaluated with SCORE and Framingham 10-year risk for cardiovascular disease.

Results: Preliminary data indicate that there is significant difference in PWV and AIx between COPD group and control groups of healthy smokers and nonsmokers. PWV and AIx are higher in the COPD group and lower in healthy control groups. COPD severity is associated with both

PWV and AIx and that association seems to be independent of traditional cardiovascular risk factors.

Discussion: This study showed that severity of COPD correlates with value of arterial stiffness. This association may be due to the systemic effects of COPD, to environmental factors, or to a shared susceptibility to degradation of elastin. In this cohort, using Arteriograph-measured pulse wave velocity, we were able to replicate the findings reported previously that arterial stiffness is higher in patients with severe COPD than in patients with mild and moderate COPD, and that FEV1 is associated with arterial stiffness. Due to limitation of this cross-sectional study, further longitudinal studies may provide more information about the significance of arterial stiffness as a prognostic tool in assessing the risk of cardiovascular adverse events and overall survival. The results of this study should increase awareness of clinicians about the importance of arterial stiffness measurement in preventing and reducing the increased cardiovascular risk in patients with COPD, which would ultimately lead to a reduction in morbidity and mortality.

Acknowledgments:

MeSH/Keywords: COPD, atherosclerosis, arterial stiffness, cardiovascular risk

Poster code: B-9-168

POSTER TITLE: UNIDIRECTIONAL BARBED SUTURE AS FLEXOR TENDON SUTURE (EX VIVO ANALYSIS)

PhD candidate: Božo Gorjanc,MD

Part of the thesis: Biomechanical characteristics of unidirectional barbed suture as flexor tendon suture (ex vivo analysis on animal model)

Mentor/s: Professor Zdenko Stanec,MD,PhD

Affiliation: Department for Plastic, Reconstructive and Aesthetic Surgery, University Hospital 'Dubrava', Zagreb

Introduction: The treatment of flexor tendon injury in the area of palm and fingers is demanding because of early mobilisation protocol implementation needed to enable tendon gliding, differential gliding, prevent tendon adhesions to soft tissue, and enable better healing. Today suture materials slide in both directions, so we use a number of configurations to make the repair stronger. Suture materials that slide in one direction and resist sliding in other are in clinical use. In theory they show advantages in joining together two ends of tendon (both of them having tendency to diverge).

Materials and methods: Forty-six fresh porcine flexor digitorum profundus tendons will be measured first to unify the tendons and then divided randomly into four groups (with the first group as control group comprised of intact tendon). Tendons will be transected and repaired on following way: four- strand knotless technique with 1 cm purchase, four- strand knotless technique with 2 cm purchase, four strand double Kessler

technique. The cross-sectional area before and after repair, ultimate tensile strength, and the way of repair failure will be recorded

Results: The mean cross sectional area ratio of double Kessler repair was 1.5 - 0.3, whereas knotless repairs was 1.2 - 0.2 ($p=0.0009$). Mean load to failure of modified Kessler group was 41 - 7 N, whereas that of knotless technique with 1 cm and 2 cm purchase was 31 - 5 N ($p=0.32$) and 52 - 6 N ($p=0.03$), respectively.

Discussion: In an ex vivo model of flexor tenorrhaphy, knotless techniques achieved tensile strength comparable to that of four strand double Kessler technique and demonstrated significantly less repair site bunching.

Acknowledgments:

MeSH/Keywords: Flexor tenorrhaphy, core unidirectional suture, barbed suture

Poster code: B-10-23

POSTER TITLE: CHANGES IN THE ELECTRICAL POTENTIAL OF BONE DURING SURGICAL TREATMENT OF FRACTURES.

PhD candidate: Tomislav Žigman, MD.

Part of the thesis: Changes in the Electrical Potential of Bone during Surgical Treatment of Fractures.

Mentor/s: Professor Slavko Davila, MD.

Affiliation: University Hospital Center Zagreb

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. 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. Kirschner wires are connected using clamps to multimeter. Patients are divided into groups depending on the type of fracture (AO classification). Publicly available software 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, 34 patients were fully examined, including the follow-up period of 6 months. Another 30 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 opposed 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 mentor 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: B-10-62

POSTER TITLE: HEAT BUILDUP IN THE BONE DRILLING ZONE: MACHINE VS. HAND GUIDED DRILL

PhD candidate: Tin Ehrenfreund, dr.med.

Part of the thesis: Heat buildup in the bone drilling zone: machine vs. hand guided drill

Mentor/s: Prof.dr.sc. Slavko Davila

Affiliation: KBC Zagreb, Department of Surgery, Kišpatičeva 12, Zagreb

Introduction: The principal operative fracture treatment is open reduction and internal fixation during which the plate is fixed to the bone by screws placed into predrilled holes. The highest increase in temperature occurs around the drill hole. The temperature decreases as the distance from the drill hole increases. One minute of exposure to the temperature of 47°C causes irreversible damage to the bone. Previous research has been based on the linear motion of the drill exclusively. In the clinical environment the direction of the drilling depends on the surgeon so it is not always possible to maintain the direction constantly.

Materials and methods: Hand drilling and machine drilling of fresh cadaver porcine femur according to previously determined protocols.

Results: Hand driven bone drill produces more temperature at the drilling site comparing to machine driven drill.

Discussion: The question of introduction of automatic bone drilling systems into operative fracture treatment still remains open.

Acknowledgments: /

MeSH/Keywords: thermal osteonecrosis, bone drilling

Poster code: B-10-90

POSTER TITLE: ULTRASONOGRAPHY OF EXTRACRANIAL CEREBRAL ARTERIES AND NEUROLOGIC DEFICIENCY DURING CAROTID ENDARTERECTOMY

PhD candidate: Björn Dario Franjić, MD

Part of the thesis: Predictability of neurologic deficiencies during carotid endarterectomy- the role of blood flow through ophthalmic and intracranial arteries.

Mentor/s: Ivo Lovričević, MD, PhD, Professor of Surgery

Affiliation: Department of Surgery, Sestre Milosrdnice University Hospital Center, Zagreb

Introduction: Carotid endarterectomy (CEA) is the most commonly performed procedure within vascular surgery. The aim of this procedure is to reduce the risk of possible future cerebral ischemic events resulting from carotid artery stenosis. One potentially hazardous event that may occur during intraoperative clamping of the internal carotid artery (ICA) is development of cerebral hypoperfusion which leads to neurologic deficiencies. In case of neurologic symptoms, a shunt must be placed in order to restore adequate cerebral blood flow, which usually reverses the neurologic deficiency. So far there has not been established a clear connection between preoperative cerebral blood flow and intraoperative neurologic deficiencies during ICA clamping.

Materials and methods: CEA patients were studied and grouped into two groups: 1) Patients who experienced a neurologic deficiency during ICA clamping (68 patients), and 2) patients without neurologic deficiencies (390 patients). Patients' demographics, clinical stage of disease, type of deficiency and perioperative outcomes were noted. The preoperative ultrasonographic findings of extracranial ICA, vertebral and ophthalmic arteries (OA) and Transcranial Doppler were analyzed. The data were analyzed and compared between the two patient groups.

Results: Neurologic deficiency occurred more frequently in males (70,59% in Group 1 were males vs. 66,41% in Group 2), in older patients (average age 71,91 vs. 69,29 years) and in more

advanced clinical stages of disease (55,71% in Group 1 had symptomatic ICA stenosis vs. 44,58% in Group 2). Left CEA was linked with higher risk of neurologic deficiency (Group 1 58,82% vs. 49,61% in Group 2). Intraoperative ischemic complications occurred more frequently in patients with a neurologic deficiency: TIA in 8,47% vs. 0,52% patients, and stroke in 11,86% vs. none. Inversion of OA blood flow was found more frequently in patients with neurologic deficiencies during ICA clamping: inverted right OA 23,68% vs. 10,92%, and inverted left OA in 18,42% vs. 12,82%. Contralateral ICA was more frequently occluded in patients who experienced neurologic deficiencies (right ICA occlusion: 15,52% vs. 2,80% and left ICA 13,11% vs. 4,33%).

Discussion: Preoperative ultrasonographic study of blood flow through extracranial cerebral arteries, ophthalmic and intracranial arteries may predict the effects of carotid artery clamping and warn about an increased intraoperative risk and more difficult surgery and also contribute to the knowledge of cerebral blood flow.

Acknowledgments:

MeSH/Keywords: Endarterectomy, Carotid Artery. Carotid Artery, Internal. Ophthalmic Artery. Neurologic Manifestations. Ischemic Attack, Transient. Stroke. Ultrasonography, Doppler, Transcranial.

Poster code: B-10-114ž

POSTER TITLE: PROGNOSTIC VALUE OF IMMUNOHISTOCHEMICAL EXPRESSION OF 8-OXO-7,8-DIHYDRO-2'-DEOXYGUANOSINE IN PATIENTS WITH COLORECTAL CARCINOMA

PhD candidate: Petar Matošević, MD

Part of the thesis: Over-expression of 8-oxo-7,8-dihydro-2'-deoxyguanosine in colorectal cancer cells corresponds with higher tumor stage and worse overall survival

Mentor/s: prof. Jasminka Jakić-Razumović, MD, PhD

Affiliation: University Hospital Center Zagreb

Introduction: Oxidative stress impact on carcinogenesis of colorectal cancer is not completely understood. 8-oxo-7,8-dihydro-2'-deoxyguanosine (8-oxodG) is product of 2-deoxyguanosine deoxyribonucleic acid (DNA) oxidation and a potential biomarker for carcinogenesis. We investigated relations of 8-oxodG immunohistochemical expression in colorectal tumor cells to tumor staging and patient survival. We expect to be able to identify high risk patients who would benefit from more radical oncologic treatment in the future.

Materials and methods: Initially, medical records and tumor samples of 146 patients operated because of the colorectal cancer in the 2 years period (years 1999 and 2000) were evaluated. Tumor sample of one patient was not available for immunohistochemical staining, while medical documentation was inadequate in seven patients, leaving 138 patients for the study, 83 (60,1%) male, 55 (39,9%) female. 5-years survival was available for 138 patients, 10-years for 134. Immunohistochemical expression of 8-oxodG compared to over 40 variables per patient was gathered for statistical analysis. Analysis of immunohistochemical 8-oxodG expression with relation to survival and tumor staging were considered most important. Preliminary results are shown.

Results: Preliminary results showed good correlation of survival with clinical tumor staging,

what was expected. Decrease of 8-oxodG detection (percentage of positive cells, immunohistochemical intensity, Allred scoring system) in colorectal tumor cells correlated with better 5 year survival. 10 year survival analysis yield different result, with decrease of only 8-oxodG immunohistochemical intensity in colorectal tumor cells correlated with better survival. Increase in percentage of positive cells for 8-oxodG expression correlated with higher tumor staging.

Discussion: Preliminary results of this research at large met our expectations, although it is hard to draw final conclusions. Research was able to achieve almost all the goals, with results mostly in favor of proposed thesis. Because the results are preliminary, we hope that further statistical analysis of the results will help in achieving satisfactory conclusion.

Acknowledgments: First of all I would like to thank my mentor prof. Jasminka Jakić-Razumović, without her assistance and dedicated involvement in every step throughout the process, this research would have never been accomplished. Also, I thank Ms. Tajana Klepac Pulanić and Ms. Ankica Ajduković who helped me considerably.

MeSH/Keywords: Colorectal Neoplasms, 8-oxo-7,8-dihydro-2'-deoxyguanosine

Poster code: B-10-128

POSTER TITLE: NEUROSURGICAL IMPORTANCE OF SPHENOID ANGLE AND CLIVUS-TENTORIUM ANGLE IN ANATOMICAL VARIATIONS OF SUBTENTORIAL SPACE

PhD candidate: Jakob Nemir, MD

Part of the thesis: Correlation between sphenoid angle (skull base flexion) and clivus-tentorium angle

Mentor/s: Professor Josip Paladino, MD, PhD

Affiliation: Department of neurosurgery, University hospital center Zagreb

Introduction: The anatomical variations of skull base structures have a huge influence in making decisions for the best neurosurgical approach. Due to neuroimaging improvement, especially magnetic resonance (MR) certain structures are more precisely visible. Our hypothesis is that measurement and analysis of topographic anatomical variations in subtentorial space using magnetic resonance (MR) provides the most convenient access to the pathological lesions located in the posterior part of the skull base, brainstem and base of the brain.

Materials and methods: The study includes patients treated in University hospital centre Zagreb in which MR of endocranium and skull base was indicated. Mediosagittal sections taken in different sequences (T1 and T2) in 100 patients were studied. Measurement of sphenoid angle, clivus-tentorium angle, width of prepontine cistern, distance between vermis cerebelli and splenium corporis callosi, upper collicules of lamina tecti and splenium corporis callosi, distance between upper limit of the pons and dorsum sellae, distance between upper part of pons and anterior line of mammilar bodies was noted. Patients with skull base and brain anomalies, previously operated patients, ones with traumatic skull and brain injuries were excluded from study.

Results: Patients' age ranges were from 18 to 87, 44% were male and 56% female. Measures

of certain angles and distances were taken. Measured distances of subtentorial space mentioned above showed variety considering the certain angle. Preliminary results showed differences between age groups, but due to the number of patients there was no statistical significance. Study needs to be finished, so that all results can be statistically relevant.

Discussion: In this study we tried to point out the importance of sphenoid and clivus-tentorium angle for the definite development of infratentorial anatomy which results to anatomical variations. Preoperative planning with high resolution MR is important for choosing the best approach. Knowledge of these angles, distances and various anatomies of skull base and brain base is crucial to avoid neurovascular structure during retraction or manipulation especially during endoscopic and minimal invasive surgical procedures in subtentorial space. We expect the development of new guidelines for best neurosurgical approaches for each individual.

Acknowledgments:

MeSH/Keywords: posterior fossa, sphenoid angle, skull base, tentorium, clivus-tentorium angle, MR

Poster code: B-10-132

POSTER TITLE: THERMAL CHANGES DURING HEALING OF DISTAL RADIUS FRACTURES – PRELIMINARY RESULTS

PhD candidate: Damir Halužan, MD

Part of the thesis: Thermal changes during healing of distal radius fractures

Mentor/s: Prof. Slavko Davila, MD, PhD

Affiliation: Department of Surgery, University Hospital Centre Zagreb

Introduction: Simplified, bone is healing in three basic steps, inflammation phase, repair phase and remodeling phase. Because of the increase in blood flow around the fracture during healing of bones, the temperature of surrounding tissue is increasing which can be then detected by infrared thermography. General aim of this research is to confirm the existence of thermal changes in limb fracture site and in the surrounding area, and to determine the temperature difference between a healthy and a broken arm.

Materials and methods: A prospective study will be conducted. Study will include 50 patients between 50 and 80 years of age with distal radius fracture treated conservatively. Flir ThermaCAM B2 infrared teletermografic camera will be used. Both healthy and broken arm will be recorded on one image in order to compare them. Healthy arm will be a control for the broken arm. During immobilization time temperature of the fingers of both hands will be measured, and after immobilization removal temperature will be measured at both wrists.

Results: So far we have conducted measurements in 25 patients of mean age 67.3 ± 8.0 (range=54-78) with fractures of distal radius in typical place. We performed thermographic recording on the 7th day after fracture, 21st

day after fracture and 6 weeks after fracture. During first recording on the 7th day after fracture the mean temperature of healthy hand was $32.19 \pm 1.68^\circ\text{C}$, and the fractured hand was $33.64 \pm 1.22^\circ\text{C}$. During second recording on the 21st day after fracture the mean temperature of healthy hand was $32.25 \pm 1.36^\circ\text{C}$, and the fractured hand was $33.51 \pm 0.91^\circ\text{C}$. During third recording 6 weeks after fracture the mean temperature of healthy hand was $33.39 \pm 1.41^\circ\text{C}$, and the fractured hand was $34.62 \pm 0.98^\circ\text{C}$. According to our preliminary findings on 25 patients we have found statistically significant temperature changes during different stages of bone healing. We found about 1.3°C temperature difference between fractured and healthy hand.

Discussion: The preliminary results of our study support our hypothesis and show statistically significant temperature changes during fracture healing. Infrared thermography could be used as a good follow up method in traumatology but further investigations are needed on more patients and a longer time period.

Acknowledgments:

MeSH/Keywords: thermal changes, fracture healing, distal radius, infrared thermography

Poster code: B-10-151

POSTER TITLE: OPERATING THEATER STAFF EXPOSURE TO CARBON MONOXIDE DURING PERITONECTOMY PROCEDURE

PhD candidate: Emil Kinda, MD.

Part of the thesis: Levels of carboxihemoglobin and methemoglobin in venous blood of operating staff will be higher during peritonectomy procedure vs. standard colonic resection

Mentor/s: prof. Mate Majerović, MD, PhD. prof. Jadranka Sertić, MD, PhD

Affiliation: University Hospital Center Zagreb

Introduction: The operating room personnel are exposed to inhalation of smoke generated by combustion of tissue when using electrocautery. Following introduction of peritonectomy, in the treatment of malignant neoplasm of the peritoneum, creation of surgical smoke is increased. The surgery consists of removal of macroscopic tumor masses with hyperthermic intraperitoneal chemotherapy. To adequately perform this procedure high power monopolar current is used.

Materials and methods: Research will include measurements of carboxihemoglobin and methemoglobin in venous blood of operating staff on 60 examinees during peritonectomy (3 surgeons at 20 procedures) and 60 examinees during colorectal surgery (3 surgeons at 20 procedures). During every procedure, measurements will be done every 20 minutes in first operating hour and at the end of procedure (time measurement starting with 0, 20, and 40 minutes and at the end). All samples will be collected from heparinised venous blood of examinees.

Results: Preliminary results include measurements of 9 peritonectomy procedures. Increase of carboxihemoglobin and methemoglobin are noticed during peritonectomy procedures, but number of measurements is still not sufficient for statistical data analysis.

Discussion: Preliminary results of this research are as we expected, although it is hard to draw final conclusions because of inadequate number of measurements. Results are preliminary, so we need further measurements to achieve enough data for adequate statistical analysis.

Acknowledgments: I thank mentors prof. Mate Majerović and prof. Jadranka Sertić, without their assistance and dedicated involvement in every step throughout the process, this research would have never been accomplished.

MeSH/Keywords: peritonectomy, electrocautery, carboxyhemoglobin, methemoglobin

Poster code: B-10-154

POSTER TITLE: ANALYSIS OF PAIN INTENSITY AND PAIN DISTRIBUTION PATTERNS IN DIFFERENT TYPES OF CONSERVATIVELY TREATED FRACTURES OF SPINAL THORACOLUMBAR JUNCTION - PRELIMINARY RESULTS

PhD candidate: Tihomir Banić

Part of the thesis: ANALYSIS OF PAIN INTENSITY AND PAIN DISTRIBUTION PATTERNS IN DIFFERENT TYPES OF CONSERVATIVELY TREATED FRACTURES OF SPINAL THORACOLUMBAR JUNCTION

Mentor/s: Gojko Buljat, MD, PhD

Affiliation: Affiliation: Department for spine surgery, University Hospital for Traumatology, Clinical Hospital Center „Sestre milosrdnice“, Zagreb, Croatia

Introduction: The greatest number of vertebral compression fractures affects the last two thoracic and first two lumbar vertebrae. Fractures observed in this study are considered stable, and conservative, non-surgical treatment is indicated. Typically, the immobilization with thoracolumbar orthosis is administered, which reduces further compression of injured vertebra and minimizes micro-movements between fracture fragments, thereby reducing the sensation of pain. However, abovementioned orthosis cannot correct the existing deformity, nor can restore vertebral body height.

Materials and methods: This study includes patients with A1.1, A1.2 and A1.3 type of fracture, according to AO / ASIF-classification. Intensity of pain was assessed by visual analogue scale (VAS), and pattern of pain distribution was determined according to the classification published by the Doo TH, etc. The results were analyzed using chi-square test. Patients' quality of life was assessed using WHOQOL-BREF questionnaire, and analysis of results was carried out by ANOVA.

Results: Different subgroups of fractures (A 1.1., and 1.2. and 1.3.) are linked with different patterns of pain distribution: Subgroup A 1.1. frac-

tures are most often associated with A-type of pain distribution, subgroup A 1.2. with B-type of pain distribution, and subgroup A 1.3. with C-type of pain distribution

Discussion: A1.1. subgroup of spinal fractures represents impaction of vertebral endplate (most often the cranial one), without significant wedging of vertebral body. This causes irritation of synovial nerves, and resulting pain is located in medial line on the level of injury. In A1.2. subgroup of fractures, wedging of vertebral body for more than 5° is present, causing straining of small joints' capsules, paravertebral musculature and dorsal fascia. Medial branches of dorsal rami of lumbar spinal nerves are stimulated, causing paravertebral distribution of pain. In A1.3. subgroup of fractures, collapse of vertebral body can often cause narrowing of intervertebral foramina, with resulting radicular pain distribution.

Acknowledgments:

MeSH/Keywords: Spinal Fractures, Pain Measurement, Quality of Life.

Poster code: B-10-169

POSTER TITLE: IMMUNOGLOBULIN G GLYCOSYLATION IN PATIENTS WITH COLORECTAL CANCER

PhD candidate: Kujtim Thaci mag.pharm.

Part of the thesis: Immunoglobulin G Glycosylation in Patients with Colorectal Cancer

Mentor/s: Gordan Lauc, prof.dr.sc.

Affiliation: Glycobiology laboratory of Genos, Zagreb.

Introduction: Colorectal cancer (CRC) is the third most common malignancy in the world. While TNM and Duke's pathological staging does not fully categorise poor/good prognosis tumours within stage groupings, there have been previous reports that IgG antibodies can act as independent CRC prognostic factors. Aims of this study was to investigate IgG N-glycans as a novel biomarker in survival outcome in CRC.

Materials and methods: This study includes a subset of 1229 with pathologically confirmed colorectal adenocarcinoma and 490 population controls. The IgG was isolated using protein G monolithic plates. Fluorescently labelled N-glycans were separated by hydrophilic interaction chromatography on a Waters Acquity UPLC instrument. Data was analysed using STATA (version 12.0) and R. Initially were examined the association between IgG glycan levels and CRC/all-cause mortality using cox proportional hazards models. Three models were applied: a crude model (Model I), a model where hazard ratios (HR) were adjusted for age at diagnosis, sex and stage of disease (Model II) and a model where HRs were adjusted for age at diagnosis, sex, stage of disease, body mass index (BMI), time from operation to blood collection, type of operation and CRP. $P < 0.002$ was considered statistically significant, after applying the Bonferroni correction for 21 independent tests.

Results: Among the 1229 patients, there were 489 deaths, including 385 from CRC. The IgG

glycan measurement resulted in 23 IgG glycans that were directly measured glycan structures and 54 derived traits that represent common features shared among several measured glycans (sialylation, bisecting GlcNAc, neutral IgG glycans, galactosylation, core fucosylation and bisection GlcNAc). IgG glycans linked to mainly galactosylation were strongly associated with all-cause mortality and CRC mortality. Statistically significant associations were also observed for sialylation, bisecting GlcNAc and core fucosylation.

Discussion: These preliminary results indicated for the first time the significant association between common IgG N-glycans structural features with CRC and all-cause mortality. A number of different studies have made preliminary reports of potentially important glycan biomarkers for cancer and other diseases. Based on these data we conclude that these IgG glycans could be used as a valuable prognostic indicators in survival outcome in CRC.

Acknowledgments: I would like to thank my mentor professor Gordan Lauc for support, guidance and advice through every step of this study.

MeSH/Keywords: Glycans, IgG, Biomarkers, CRC.

Poster code: B-11-81

POSTER TITLE: EFFICACY OF DIFFERENT FOSFOMYCIN DOSAGE REGIMENS IN THE TREATMENT OF URINARY TRACT INFECTIONS CAUSED BY BACTERIAL STRAINS PRODUCING EXTENDED SPECTRUM BETA LACTAMASES

PhD candidate: Luka Bielen, MD, Resident in Internal Medicine

Part of the thesis: Prospective Randomized Controlled Clinical Trial Investigating Efficacy of Different Fosfomycin Dosage Regimens in the Treatment of Urinary Tract Infections Caused by E. Coli and Kl. Pneumoniae Strains Producing Extended Spectrum Beta Lactamases

Mentor/s: Assistant professor Robert Likić, MD, PhD, Specialist in Internal Medicine

Affiliation: University Hospital Center Zagreb, Kispaticeva 12, 10000 Zagreb, Croatia, University of Zagreb School of Medicine

Introduction: Selective pressure of beta lactam antibiotic use resulted in spread of bacteria that produce beta lactamases. The arrival of antibiotics that were resistant to beta lactamases led to the emergence of bacterial strains that produce extended spectrum beta lactamases (ESBL). During the last years there has been a growing interest in investigation of older antibiotics like fosfomycin, especially as it is administered orally in one single dose, which gives it significant potential advantage in comparison to much more expensive carbapenems that are given parenterally. The goal of this doctoral thesis is to investigate in vitro sensitivity of urinary pathogens producing ESBL and to conduct a prospective randomized clinical trial investigating efficacy of different fosfomycin dosage regimens in the treatment of urinary infections (UTI) caused by ESBL bacterial strains.

Materials and methods: Patients with complicated UTI caused by E. coli and Kl. Pneumoniae ESBL producing strains will participate in this clinical investigation. After in vitro testing of susceptibility to fosfomycin, they will be prospectively randomized into two groups. Experimental group will be treated with 3 doses of fosfomycin, while control group will receive single fosfomycin dose. After 8 to 10 days, control urine sample will be taken for bacterial culture. The difference in the proportion of microbiological cure between experimental and control group will be tested by means of Chi squared test.

Results: Preliminary results of this clinical investigation are as follows. Twelve patients fulfilled inclusion and exclusion criteria and were treated with fosfomycin. All of them had one or more complicated factors such as previous antibiotic use, nephrolithiasis, malignancy etc. Seven of them were randomized in experimental, and 5 in control group. Eleven of 12 urinary samples were in vitro susceptible to fosfomycin (one Kl. Pneumoniae sample from control group was resistant). All patients from experimental group and 3 of 5 in control group were successfully cured.

Discussion: According to preliminary results of this clinical investigation and of three previous clinical investigations, fosfomycin is potentially valuable option for the treatment of UTI caused by ESBL producing strains. In patients with comorbidities (so called complicated UTI), it seems that prolonged antibiotic treatment could lead to better clinical outcomes compared to standard single oral dose of fosfomycin. Our preliminary results also point to this conclusion.

Acknowledgments: I thank to my mentor Assistant professor Robert Likić, who helped me with valuable advice in preparing my doctoral thesis.

MeSH/Keywords: fosfomycin, ESBL, urinary tract infections

Poster code: B-13-171

POSTER TITLE: PRO-ANGIOGENIC CYTOKINES AND ITS RECEPTORS IN CORNEAS OF PATIENTS UNDERGOING PENETRATING KERATOPLASTY

PhD candidate: Maja Pauk Gulić, MD

Part of the thesis: The Role of Pro-angiogenic Cytokines and its Receptors in Development of Graft Reaction 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 neovascularization is a major risk factor for graft failure after corneal transplantation and occurs when the balance between angiogenic and antiangiogenic factors is tipped toward angiogenic molecules. Vascular endothelial growth factor (VEGF), one of the most important mediators of angiogenesis, is upregulated during neovascularization. The purpose of the study is to evaluate the quantity of VEGF and its receptors (VEGFR) in the recipient cornea at the time of penetrating keratoplasty (PK) in patients with inflammatory and non-inflammatory corneal diseases.

Materials and methods: The study included 20 eyes (of 20 patients) scheduled for PK. All patients underwent preoperative examination to determine the etiology of corneal disease, and inflammation and vascularisation rate. The quantity of angiogenic growth factors and their receptors: VEGF, sVEGFR1 and sVEGFR3 were analysed using an enzyme-linked immunosorbent assay (ELISA). Postoperatively patients were followed-up for 3 years. The frequency of corneal graft reaction/rejection were recorded, and degree of corneal neovascularisation (NV). Donor corneas obtained from cadaver eyes which were unsuitable for clinical use represented the control group (n=20).

Results: 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. Patients who developed clinical signs of graft reaction during the postoperative follow-up have 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). The statistical method used in data analysis was t-test.

Discussion: Upregulation of VEGF has been associated with neovascularisation in the eye, suggesting that maintaining low levels of VEGF is important for corneal avascularity and intact vision. Our results suggest that graft reaction occur more often in patients with increased levels of VEGF-A in a recipient cornea at the time of PK. 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: Corneal transplantation, corneal neovascularisation, VEGF, soluble VEGF receptor, graft rejection

Poster code: B-14-12

POSTER TITLE: PHYSICIANS' PROFESSIONAL INTERPERSONAL RELATIONSHIPS – THEORY, PRELIMINARY FINDINGS AND FURTHER DIRECTIONS

PhD candidate: Marko Ćurković, MD

Part of the thesis: Development of an instrument for evaluation of physicians' professional interpersonal relationships in hospitals

Mentor/s: Assistant Professor Ana Borovečki, MD, PhD. Milan Milošević, MD, PhD.

Affiliation: University Psychiatric Hospital Vrapče, Zagreb. University of Zagreb School of Medicine, Andrija Štampar School of Public Health

Introduction: From the broad theoretical concept of medical professionalism subcategory of interpersonal relationships can be derived. Alongside the interpersonal relationships involving physicians and their patients, which impersonates the core essence of practical medicine, interpersonal relationships between physician colleagues coexists. There is emerging need for adequate interpersonal relationships among physicians in contemporary medical practice with regard to ever growing complexities of modern medicine and society.

Materials and methods: A survey was conducted using an independently created, web-based questionnaire. There were a total of 120 invited participants, with 80 respondents completing the questionnaire.

Results: When considering frequencies of certain behavioral elements, roughly every sixth physician experienced more than one incident of abuse or belittlement from subordinate or equally ranked colleague during the last year's period, while almost every third physician experienced these incidents from their superior colleague. Every third physician was more than once in verbal conflict, while only two physicians reported being in physical conflict with their colleagues throughout the last year. When concerning respect among colleagues, the most appreciated values were humanity, than knowledge, morality, personality and lastly empathy.

The most desired feeling from their colleagues was respect, while the most undesired one was veneration (even more than competition). Inner hierarchical structure is reflected in finding that almost half of physicians disagreed or neither disagreed nor agreed with the statement that they respect all members of their working team equally, while every third chose those answers when relating to statement about respecting all medical specialties equally. Inconsistencies' regarding self-regulation principle is most obviously reflected in finding that 40% of physicians would almost always or always report their colleague for unprofessional work. Forty percent of physicians agreed with the statement that they receive enough knowledge and skills from their superiors.

Discussion: Although present in everyday's encounters, the concept of medical professionalism is somewhat obsolete and rusty in transitional socio-cultural context. The presented findings, although limited, provide some critical pinpoints regarding future conceptualizations and assessment methods of interpersonal professionalism in practicing physicians.

Acknowledgments:

MeSH/Keywords: medical ethics, medical professionalism, physicians, questionnaire

Poster code: B-15-49

POSTER TITLE: DETECTION OF CAG PATHOGENICITY ISLAND VIRULENCE GENES OF HELICOBACTER PYLORI ISOLATES AFTER FAILED ERADICATION THERAPY

PhD candidate: Dijana Varda Brkić, M.D.

Part of the thesis: Detection of cag pathogenicity island virulence genes and dupA genes of Helicobacter pylori isolates after failed eradication therapy

Mentor/s: Professor Vanda Plečko, M.D., PhD, School of Medicine, University of Zagreb, Zagreb

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

Introduction: Helicobacter pylori is a spiral, microaerophilic, gram-negative bacteria. It plays an important role in the development of chronic gastritis, peptic ulcer, gastric cancer and MALT lymphoma. Several Helicobacter pylori genes, including cagA, are located in the cagPAI (cyto-toxin pathogenicity island) associated with gastro-duodenal diseases and hence the variations in the cagPAI gene structure may be responsible for different clinical outcomes. According to some research, the dupA gene, located in the H. pylori plasticity region, is associated with the development of duodenal ulcers and plays a protective role in the development of atrophy and intestinal metaplasia.

Materials and methods: The research samples used in the study are Helicobacter pylori strains from gastric mucosal biopsy specimens, obtained during routine, clinically indicated gastro-duodenoscopies. The research includes clinical H. pylori strains from patients after multiple failed eradication treatments. conducted research methods shall include: 1. Basic microbiological diagnostics, 2. Molecular microbiological diagnostics - Polymerase Chain Reaction (PCR)

Results: We studied the cag pathogenicity islands of 103 Helicobacter pylori isolates obtained from the patients consisting of 26 men

and 77 women, with a mean age of 55 years (ranging from 28 to 80 years of age). In a total of 103 isolates screened, 16 (15,5%) were found with the cagPAI completely deleted. No isolate was found to carry the complete cagPAI, while 87 (84, 5) carried the cagPAI with partial deletions. The rates of the cagPAI virulence genes in these strains were: 74 (71,8 %) cagA1, 72 (69,9%) cagA2, 6 (5,8%) cagA3, 78 (75,7%) cagE, 74 (71,8%) cagM, 11(10,6%) tnpA, 70 (67,9%) cagT, 65 (63,1%) Apcag, 50 (48,5%) LEC, 8 (7,7%) tnpB

Discussion: The cagPAI genes were most frequent in this study. Further research is necessary to determine the presence of association of this gene with gastric pathology. Variation in the rates of the cagPAI genes in different countries is an indication of its geographical distribution. This study provides important information regarding the prevalence of virulence genes in H. pylori strains in our country.

Acknowledgments: I would like to thank my mentor, professor V. Plečko, M.D., Ph.D., and professor M. Katičić, M.D., Ph.D.

MeSH/Keywords: Helicobacter pylori, genotyping, cag pathogenicity island, dupA gene

Poster code: B-16-41

POSTER TITLE: INVESTIGATION OF NIM GENES AND INDUCIBLE METRONIDAZOLE RESISTANCE IN BACTEROIDES FRAGILIS GROUP ISOLATES

PhD candidate: Aleksandra Presečki Stanko, MD

Part of the thesis: Molecular Analysis of Nim Genes and Inducible Metronidazole Resistance in *Bacteroides fragilis* Group Clinical Isolates

Mentor/s: Associate Professor Vanda Plečko, MD, PhD

Affiliation: University Hospital Centre Zagreb

Introduction: The phenotypic metronidazole resistance in the *Bacteroides fragilis* group could be associated with different resistance mechanisms. A 5-nitroimidazole reductase enzyme encoded by a specific nim gene is the best studied resistance mechanism. Increased lactate dehydrogenase or reduced pyruvate-ferredoxin oxidoreductase activities, as a part of an altered cellular redox system, are some of the other proposed resistance mechanisms. Prolonged exposure of the *Bacteroides fragilis* group strains susceptible to metronidazole to subinhibitory metronidazole concentrations can select for in vitro resistance.

Materials and methods: A collection of *Bacteroides fragilis* group strains recovered from clinical specimens and intestinal microbiota in the two-year period is analysed. The isolate identification is carried out by the api20A kit, bioMérieux and MALDI Biotyper, Bruker Daltonics. The antimicrobial susceptibility testing to metronidazole is performed by the agar dilution method. PCR assay with a specific primer pair is used to detect the nim genes. The selection of metronidazole resistant subpopulations is done by the agar dilution method after passages in subinhibitory and gradually increased concentrations of metronidazole. The resistance stability is tested by the agar dilution method after repeated passages on the medium without metronidazole. In the case of nim-negative metronidazole induced re-

sistance, the lactate dehydrogenase activity will be measured by an enzymatic or qRT-PCR assay.

Results: *Bacteroides fragilis* is the most frequently isolated species. All of the 199 analysed strains are susceptible to metronidazole with minimal inhibitory concentrations (MICs) to metronidazole ≤ 4 mg/L. Molecular investigation of the nim genes reveals that all of the 158 analysed strains are nim-negative. In the subgroup of 52 selected strains, the induced metronidazole resistance is observed in 12 (23%) of them. The resistance is stable with the MICs range to metronidazole from 16 to 128 mg/L.

Discussion: The metronidazole resistance in the *Bacteroides fragilis* group strains is based on the presence of complex mechanisms. A novel nim gene that can not be detected by the current primer pair or other so far unknown mechanisms could be involved in these strains. Detection of nim-negative but metronidazole resistant strains definitely requires further investigation.

Acknowledgments: I would like to thank J. Soki, Institute of Clinical Microbiology, University of Szeged, Hungary for scientific and professional advice

MeSH/Keywords: *Bacteroides fragilis* group, nim gen, metronidazole, resistance

Poster code: B-16-88

POSTER TITLE: SENTINEL LYMPH NODE MAPPING WITH SPECT/CT

PhD candidate: Andrea Mutvar, MD

Part of the thesis: „The value of single photon emission tomography and computed tomography in detection of sentinel lymph node in patients with malignant melanoma and breast cancer“

Mentor/s: Associate Professor Dražen Huić, MD, PhD

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

Introduction: The aim of this study is to investigate whether single photon emission computed tomography with computed tomography (SPECT/CT) is of additional value compared to conventional sentinel node (SN) lymphoscintigraphy in patients who were routinely scheduled for SN mapping.

Materials and methods: 48 consecutive patients with melanoma, head and neck cancer, breast and vulvar cancer scheduled for sentinel node biopsy, underwent conventional lymphoscintigraphy with dynamic and static planar imaging and subsequently SPECT/CT. We used radiopharmaceutical with big particles, Tc99m-albumin colloid (SENTISCINT). Hand-held gamma probe was used for identification of the SLNs. We studied whether SPECT/CT

Results: SPECT-CT detected 122 SNs in 47 patient and conventional lymphoscintigraphy 97 SNs in 45 patients. SPECT-CT found 25 additional radioactive nodes (20,5%) in nineteen patients (39,6 %) of whom 2 patients had non-visualization of SN on planar images (4.16%). SPECT/CT provided additional information that led to an adjustment

of the surgical approach or further patient management in 12 patients (25%). We didn't find SN either on conventional scintigraphy or SPECT-CT in only one patient (2%).

Discussion: SPECT/CT detected additional sentinel nodes and revealed the exact anatomical location of sentinel nodes. SPECT/CT provided relevant additional information in 19 (39,6%) of the 48 patients. Our preliminary results suggest that routine use of SPECT/CT in addition to conventional lymphoscintigraphy may improve sentinel lymph node detection, surgical procedure and patient management.

Acknowledgments: I would like to thank my colleagues from Department of Nuclear Medicine and Department of Surgery who participate in this work

MeSH/Keywords: scintigraphy, sentinel lymph node, single photon emission tomography, computed tomography, SPECT-CT, melanoma, breast cancer

Poster code: B-17-29

POSTER TITLE: URINE IODINE CONCENTRATION IN PREGNANT WOMEN

PhD candidate: Marta Borić, MD

Part of the thesis: An analysis of iodine concentration in urine in pregnant women who are taking iodine supplementation

Mentor/s: Professor Zvonko Kusić, MD, PhD

Affiliation: University Hospital Center

Introduction: People of all ages can be affected by iodine deficiency, but especially, pregnant women and children are at high risk. Because of the changes that occur in maternal thyroid hormone economy during pregnancy and the potential negative effects on neurological development of the offspring that iodine deficiency could cause, an adequate dietary iodine intake throughout the pregnancy period is highly important. Therefore WHO, UNICEF and ICCIDD proposed that the dietary intake of iodine during pregnancy must be 200-300 µg/day to compensate augmented requirements of T4 in pregnant women. Urinary iodine concentration (UIC) median is used as a main indicator of an adequate iodine intake. In countries, such as Croatia, with a longstanding and well-established universal salt iodization program and in which iodine sufficiency has been reached, there is always a fraction of pregnant women that still have an insufficient dietary iodine intake. In the studies performed in such countries there is an accent on how pregnant women should use multivitamin and/or mineral tablets specifically prepared for the needs of pregnancy and containing iodine. Considering all, this study evaluates, on grounds of UIC median and nutrition habits, whether in our country a legitimate need for additional iodine supplementation during pregnancy exists.

Materials and methods: There will be two groups analyzed, each counting 67 pregnant women. Control group will be formed with pregnant women who do not take additional iodine through nutrition additives, and the test group will be formed of pregnant women taking nutrition additives containing iodine. Each examinee will be given an informed consent and a questionnaire that contains general information,

information about thyroid disorders, nutrition additives intake and frequency of certain food containing iodine (range 0-3) intake. Examinees will have to bring next day a sample of the first morning urine in a labeled test tube (5 mL). All pregnant women with any thyroid dysfunction or with any complication during pregnancy will be excluded from the study. The results will be presented tabular and graphically. Descriptive statistic analysis will be applied along with corresponding measures of central tendency for each group and subgroup according to the trimesters. The results will then be compared to "The criteria for evaluation of iodine intake during pregnancy on grounds of urine iodine secretion WHO/UNICEF/ICCIDD 2007". According to obtained results, adequate parametric and nonparametric tests will be used. Predilection of clinical and socio-demographic variables will be analyzed with binary logistic regression. All $p < 0,05$ values will be considered significant.

Results: The study is still in progress, the samples are collecting, but according to the preliminary, though, sparse results, it has been shown that pregnant women taking iodine supplementation in means of multivitamin and/or mineral tablets specifically prepared for the needs of pregnancy and containing iodine have appropriate iodine concentration in urine according to the WHO/UNICEF/ICCIDD recommendation. Also, pregnant women that are not taking those supplements mostly have appropriate iodine concentration, but one part of them has borderline urine iodine concentration according to the same recommendations.

Discussion: Previously described, preliminary results are supporting one of the two hypothesis

and that is that pregnant women who take multivitamin and/or mineral tablets specifically prepared for the needs of pregnancy and containing iodine have sufficient iodine intake according to the WHO/UNICEF/ICCIDD recommendations. The second one is yet to be supported although these early results are showing the tendency of support. Defining, according to the study results, the status of iodine intake in pregnant women we can estimate if there is a need for additional iodine intake during pregnancy in Croatia. With given results, one of the expected scientific

contribution it that to the National program for monitoring of iodine prophylaxis for the purpose of prevention iodine deficiency disorders, which is still of significant meaning for public health.

Acknowledgments: I would like to thank my mentor and all the participants in the study.

MeSH/Keywords: Iodine, pregnancy, WHO criteria

Poster code: B-17-55

POSTER TITLE: PERIPHERAL RETINAL MORPHOLOGIC CHANGES - A NEW PREDICTOR FOR AGE RELATED MACULAR DEGENERATION?

PhD candidate: Tamara Knežević

Part of the thesis: The association of peripheral morphologic retinal changes and genotypic changes in age related macular degeneration

Mentor/s: Associate professor Zoran Vataavuk, MD, PhD

Affiliation: Clinical Hospital Centre Sisters of Mercy, Zagreb, Polyclinic Ghetaldus, Zagreb

Introduction: Age related macular degeneration (AMD) is a multifactorial neurodegenerative disease and the most common cause of legal blindness in developed countries. Over the past decade, risk assesment was based on the clinical examination of macular region which can be easily approached. New studies implicate that the most significant morphologic changes can be found at the peripheral retina and can be a predictor of later clinical development. Likewise, data shows a strong association between genetic polymorphism of complement factor H (CFH) gene and AMD susceptibility. So far there were no clinical studies that sufficiently photodocumented peripheral retina due to lack of wide-angle devices. This study will determine the presence of the association of the peripheral retina and typical genotypic changes in AMD.

Materials and methods: MATERIALS: 150 participants in AMD group and 150 healthy subjects group
METHODS: 1. Slit lamp biomicroscopy and fundus examination with noncontact lens, 2. Optical

coherent tomography of the macular region, 3. Wide-angle fundus camera photodocumentation of the central and peripheral retinal changes, 4. Genotyping of 6ml of the peripheral blood by real-time PCR method.

Results: The preliminary results of morphologic analysis of peripheral retinal changes showed that drusen, reticular pigment changes and paving stone degenerative changes occur more frequently in AMD group than in control group. The genotyping is still underway.

Discussion: If genotyping shows the presence of SNPs for AMD in AMD group, then we expect that the hypothesis will be confirmed.

Acknowledgments:

MeSH/Keywords: Peripheral retinal changes, single nucleotide polymorphism, age-related macular degeneration

Poster code: B-18-31

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: Associate Professor Zoran Vataavuk, 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, glaucoma and diabetic retinopathy. The goal of this study was to correlate morphological and functional outcomes after successful macular hole (MH) surgery using spectral domain OCT and rarebit fovea test.

Materials and methods: Eleven eyes of 11 patients with successfully operated idiopathic full-thickness macular holes were included in this study. Spectral domain optical coherence tomography (Zeiss Cirrus HD OCT) was performed preoperatively and one week, one month and three months after the surgery. Preoperative maximal diameter of the hole and cube volume, as well as postoperative central foveal thickness and cube volume were analysed. Preoperative and postoperative microperimetry (Fovea test, Rarebit perimetry) was also performed.

Results: The median preoperative visual acuity was 0,1 (range 0,05-0,2). The maximal diameter

of macular hole was $371,7 \pm 142,3 \mu$. The mean preoperative microperimetry score was $37,3 \pm 26,4$. Best corrected visual acuity improved to 0,35 at the final follow up visit ($p = 0,01$). There was a statistically significant decrease in central foveal thickness ($F = 6,15$, $p = 0,01$), as well as in cube volume ($F = 6,31$, $p = 0,03$). However, the microperimetry scores did not improve throughout the follow up period, and there was no correlation between microperimetry and visual acuity ($r = 0,14$, $p = 0,69$).

Discussion: In our study no correlation between Rarebit perimetry and visual acuity after successful macular hole surgery was established despite obvious improvement in visual acuity. One possible explanation for this might be that stimulus in Rarebit fovea test is too small for such an extensive neuroretinal damage. In conclusion, Rarebit fovea test is not a reliable indicator of visual function or a good predictor of visual function recovery after macular hole surgery.

Acknowledgments:

MeSH/Keywords: macular hole, microperimetry

Poster code: B-18-37

POSTER TITLE: SYSTEMIC EXPOSURE AND SYSTEMIC ADVERSE REACTIONS (ADRS) TO INTRAVITREAL ADMINISTRATION OF BEVACIZUMAB (IVT-B) IN TREATMENT OF NEOVASCULAR AGE-RELATED MACULAR DEGENERATION (NV-AMD)

PhD candidate: Ivana Mikačić, MD

Part of the thesis: Systemic exposure, systemic adverse reactions and risk minimization measures of bevacizumab applied intravitreally in senile macular degeneration treatment

Mentor/s: Associate Professor Damir Bosnar, MD, PhD, ophthalmologist

Affiliation: University of Osijek School of Medicine, University Hospital „Sveti Duh“

Introduction: NV-AMD is a multifactorial disease of the central retina with vascular endothelial growth factor (VEGF) as the most important individual mediator. Bevacizumab is a monoclonal antibody against VEGF approved for treatment of malignant diseases. Although “off-label”, IVT-B is the most commonly used anti-VEGF treatment of NV-AMD. The most severe ADRs to systemic bevacizumab are cardiovascular (CV) and venous thrombotic events (VTE). Existing data on systemic exposure to IVT-B are sparse. There is no reliable risk estimate of CV/VTE ADRs associated with IVT-B and no recommendations for risk minimization.

Materials and methods: Design: Prospective observational study with pharmacokinetic (PK) evaluation and a systematic review (SR) of published data. Setting: Dpt of Ophthalmology, University Hospital Sveti Duh. Patients: Consecutive pts with NV-AMD and indication for IVT-B once monthly (N=250, PK n=40), who are at a low risk of CV/VTE based on a developed assessment program. Study flow: patients are followed-up over at least 3 treatment cycles. Blood samples for serum bevacizumab and VEGF measurement are taken 1 day before and at days 1 and 8 after each injection. Incidence of CV/VTE is recorded. SR of published data will be performed to yield the best available estimate of CV/VTE risk in unselected patients treated with IVT-B. The observed rates will be assessed vs. this historical reference. Peak and total systemic exposure to bevacizumab will be estimated. Multivariate

methods will be used to evaluate relationships between patient characteristics, systemic exposure to IVT-B and CV/VTE ADRs.

Results: So far, 245 patients have been followed for 3-15 treatment cycles. Preliminary qualitative analysis indicated no targeting ADRs. 20/265 screened patients didn't receive drug due to estimated high CV/VTE risk. Of all monitored laboratory parameters only D-dimer gradually increased with number of cycles administered. To date, 45 serum samples (15 pts x3 cycles) taken in predefined time points are stored according to commercial ELISA set instructions and will be analysed together with all collected samples (around 250).

Discussion: Preliminary data indicate that adequate screening could eliminate systemic ADRs to IVT-B. Certain laboratory parameters could be used to enable safer use of the drug. The present study is to provide the most detailed evaluation of systemic exposure to IVT-B up-to-date and will contribute to optimization of risk-benefit trade-off of its use in NV-AMD.

Acknowledgments: thanks to mentor and Dpt of Ophthalmology

MeSH/Keywords: intravitreal bevacizumab, age related macular degeneration, systemic adverse reactions, anti-VEGF treatment, systemic exposure

Poster code: B-18-47

POSTER TITLE: POSTNATAL WEIGHT GAIN AS PROGNOSTIC FACTOR FOR RETINOPATHY OF PREMATURITY

PhD candidate: Ivana Behin Šarić, MD

Part of the thesis: Postnatal Weight Gain as Prognostic Factor for Retinopathy of Prematurity

Mentor/s: Nenad Vukojević, MD, PhD

Affiliation: University Hospital Centre - Zagreb, General hospital "Dr. T. Bardek" Koprivnica

Introduction: Retinopathy of prematurity (ROP) is a vasoproliferative disease of immature retina whose consequences (low vision and blindness) can be avoided or at least reduced if well designed screening and timely treatment are applied. Guidelines of highly developed countries can not be applied to our population because the prevalence of ROP shows significant geographic variation and depends on the degree of socio-economic development. While the current screening criteria are based mainly on prenatal risk factors (gestational age [GA] and birth weight [BW]), more recent research show that poor postnatal weight gain is a significant predictor of ROP. Our hypothesis is that poor postnatal weight gain is predictive of retinopathy regardless of gestational age and birth weight of preterm infants. If following postnatal weight gain proves predictive, it would be a useful adjunct for ROP screening that identifies high-risk infants early to optimize care.

Materials and methods: This is a retrospective study conducted on a population of premature infants (~250) included in the screening program for early detection of ROP in University Hospital Centre – Zagreb from January 2009 to December 2010. Data obtained were gestational age, birth weight, weekly weight measurements and retinal status. Infants will be divided into groups according to their gestational age (≤ 28 weeks, $28^{1/7}$ - $31^{6/7}$ weeks, ≥ 32 weeks), birth weight

(≤ 1000 g, 1001-1499g, ≥ 1500 g) and development of retinopathy according to the Early Treatment of Retinopathy of Prematurity (ETROP) study and compared for postnatal weekly weight gain.

Results: Preliminary results show that poor postnatal weight gain is good predictive factor for ROP development in infants with gestational age ≤ 32 weeks and birth weight < 1499 g but not as reliable in preterm infants of larger GA and BW.

Discussion: Our population, unlike reports from developed countries, shows great variety of both gestational age and birth weight of preterm infants who develop ROP. Postnatal weight gain could be an additional predictive factor in some groups of preterm infants (GA ≤ 32 weeks and BW < 1499 g) but further investigations are needed before we can include postnatal growth in current screening criteria. The close association between poor neonatal weight gain and ROP suggests that optimizing growth may be one way to reduce ROP.

Acknowledgments: I would like to thank my lovely family and my mentors for their understanding and great support

MeSH/Keywords: retinopathy of prematurity, postnatal weight gain

Poster code: B-18-162

POSTER TITLE: PRESBYOPIA TREATMENT BY LENS SURGERY VERSUS LASER IN SITU KERATOMILEUSIS

PhD candidate: Adis Pašalić

Part of the thesis: Ophthalmological clinical prospective study

Mentor/s: prof Iva Dekaris MD PhD

Affiliation: Eye Clinic Svjetlost

Introduction: Presbyopia is the most common refractive disorder of later life, related to decrease of accommodative amplitude. The possibility of „curing“ or reducing the effects of presbyopia is intensively investigated in modern ophthalmology. In the past, the usual remedy was to wear reading glasses or special multifocal lenses (bifocal or progressive) for presbyopia. But in modern times, surgical remedies for presbyopia are also available for qualified candidates. In everyday practice we can see that more and more people want to become independent of glasses. „Monovision“ principle (LASIK) or multifocal IOL are current attempts for presbyopia treatment.

Materials and methods: All patients included in this study are defined age range due to presence of physiological presbyopia and will be aged 40-50 years. Excluding criteria are well defined. Patients younger than 40 and older than 50 will be excluded from the study. Any other ocular pathology that might affect results of surgery as well as effecting presbyopia itself such as glaucoma, cataract, corneal diseases, retina diseases and other systemic disease will be excluding factors for patients election in the study. Patient occupations as professional drivers will also be excluded from the study due to high visual and

professional visual acuity needs, and in other studies reported visual disturbances present primarily in professional drivers patients. Research plan is optimal in length time for reporting visual disturbances and complication rate.

Results: Based on preliminary results all patients aged 40-50 year will have comparable results regarding spectacle independence, visual disturbances and near, intermediate and distance visual acuity. Based on the first results better results are reported for mild to moderate hypermetropic patients in treatment of presbyopia with lens exchange. Moderate myopic patients seem to be more satisfied with LASIK monovision treatment. There is a need for completion of the whole study for more detailed reports and conclusions.

Discussion: Patients aged 40-50 year will have comparable results regarding spectacle independence, visual disturbances and near, intermediate and distance visual acuity in both investigated groups- RLE group and LASIK Monovision group.

Acknowledgments:

MeSH/Keywords: Presbyopia lens LASIK surgery

Poster code: B-18-173

POSTER TITLE: TUMOR CACHEXIA AS A PREDICTOR OF CHEMOTHERAPY TOXICITY AND TIME TO TUMOR PROGRESSION IN METASTATIC LUNG CANCER

PhD candidate: Dražena Srđić, MD

Part of the thesis: Tumor Cachexia in Lung Carcinoma Patients

Mentor/s: Professor Miroslav Samaržija, PhD, MD

Affiliation: University Hospital Center Zagreb, Clinic for Lung Diseases Jordanovac, Department of Thoracic Oncology

Introduction: Cachexia frequently occurs in patients with lung cancer and is associated with reduced physical activity, intolerance to chemotherapy and shorter survival. Until now, in Croatia it is not known what is the prevalence of tumor cachexia in metastatic lung carcinoma. Cachexia has been traditionally understood as a weight loss. Skeletal muscle atrophy is defined as the most important predictor of mortality and functional impairment in cancer cachexia.

Materials and methods: One hundred patients with advanced (IIIB/IV) non-small cell lung carcinoma who were naive to treatment with good performance status ECOG 0-1, were enrolled in this prospective randomized study. Anthropometric, demographic characteristics, laboratory findings and weight loss were assessed and correlated with chemotherapy toxicity and time to tumor progression. CT has proven to be accurate for measuring human body composition. Skeletal muscle cross-sectional area at the third lumbar vertebra was measured by computerized tomography. The directly determined unit was area (cm²) of total skeletal muscle. Chemotherapy toxicity was assessed after cycle 1 of treatment, and time to progression was determined prospectively as the number of days of tumor remission after cycle 1.

Results: A history of weight loss during the 6 mo preceded the referral was common, with an average loss of 6.0 /-8%. Data from the CT image analysis showed sex differences in skeletal mus-

cle area and skeletal muscle index. A very high proportion of men met the criteria for sarcopenia (L3 muscle index <55.4 cm²/m² 54% of men) compared with women (L3 muscle index <38.9 cm²/m² 25% of women). Of these patients with BMI classified as overweight, 55% met the criteria for sarcopenia. Patients with sarcopenia received a higher amount of chemotherapy dose per unit of lean body mass and also presented with a higher prevalence of toxicity (50% vs 20%). Median time to tumor progression was shorter for sarcopenic patients compared to those nonsarcopenic.

Discussion: We observed that skeletal muscle wasting is present in all of the BMI categories. Prevalence of toxicity was significantly higher in sarcopenic compared with nonsarcopenic patients. We showed that the presence of sarcopenia was associated with a significantly shorter time to tumor progression. These preliminary results highlight the potential use of body composition assessment to improve toxicity risk and to individualize drug dosing in a population of patients with advanced lung cancer.

Acknowledgments: To my mentor Professor Miroslav Samaržija

MeSH/Keywords: tumor cachexia, sarcopenia, chemotherapy toxicity, time to tumor progression, lung carcinoma

Poster code: B-19-11

POSTER TITLE: CYTOKERATIN-20 POSITIVE CELLS IN BLOOD OF COLORECTAL CANCER PATIENTS AS A PROGNOSTIC MARKER

PhD candidate: Davor Kust

Part of the thesis: circulating colorectal cancer cells detected by cytokeratin-20 expression analysis as a specific marker

Mentor/s: Ivan Šamija, PhD

Affiliation: University Hospital Center „Sestre milosrdnice“, Zagreb, Croatia, Department of Oncology and Nuclear Medicine

Introduction: Detection of circulating cancer cells by reverse transcription-PCR (RT-PCR) was studied as a prognostic marker in colorectal cancer patients, but so far with conflicting results regarding specificity and prognostic value. In this study, cytokeratin-20 (CK20) will be evaluated as a marker for circulating colorectal cancer cells detection, and also influence of surgical tumor resection on the presence of circulating colorectal cancer cells will be analyzed.

Materials and methods: RNA was isolated from mononuclear cell fraction of blood samples taken from 95 colorectal cancer patients before and after tumor resection and from 23 healthy volunteers and assayed by real-time RT-PCR for CK20 expression.

Results: Patients were followed-up for at least 3 years. Overall survival (OS), disease-free survival (DFS) and progression-free survival (PFS) were calculated, and statistical analysis of collected data is under way.

Discussion: Regarding contrary results of former similar studies, this research will help to evaluate prognostic value of cytokeratin-20 as a marker for circulating cancer cells detection in patients with colorectal cancer. This research could besides scientific also have clinical value, in the sense of introducing new marker which could improve treatment of these patients.

Acknowledgments: I would like to thank my mentor and all employees of Department of Oncology and Nuclear medicine of University Hospital Center “Sisters of charity” on support.

MeSH/Keywords: biological tumor markers, circulating neoplastic cells, colorectal neoplasms, keratin-20, reverse transcriptase polymerase chain reaction

Poster code: B-19-21

POSTER TITLE: EARLY STAGE MELANOMA PROTEOMICS - MISSION (IM) POSSIBLE

PhD candidate: Andro Košec, MD

Part of the thesis: Prognostic significance of tissue proteomic profiling in cutaneous malignant melanoma of the head and neck stage I and II

Mentor/s: Prof. dr. sc. Vladimir Bedeković, Prof. dr. sc. Lovorka Grgurević

Affiliation: Clinical Hospital Center Sestre milosrdnice, Zavod za anatomiju, Centar za translacijska istraživanja Medicinskog fakulteta Sveučilišta u Zagrebu

Introduction: Morphohistopathological parameters are currently the basis for malignant melanoma classification and prognosis. An increasing number of molecular biomarkers offer new potential for refining diagnostic and prognostic disease categories. Early stage disease prognosis is only partially encompassed by morphological and histopathological parameters such as primary tumor localization, patient age and gender, mitotic rate, lesion thickness and ulceration.

Materials and methods: This study is based on tissue proteomic profiling of 40 early stage head and neck malignant melanoma tissue samples and 40 benign pigmented composite skin naevi as a control group for potential identification of biomarkers that will be correlated to known prognostic factors.

Results: The hypothesis that the proteomic profile of cutaneous head and neck melanoma tissue in disease stages I and II correlates with known prognostic factors and disease survival has proven to be quite challenging to pursue. A preliminary study population sample of a 110 patients has been assembled as a retrospective cohort. Follow up information regarding survival and disease specific morbidity and mortality has been assembled. A comprehensive analysis protocol for extracting polypeptides from paraffin-fixed samples has been adapted and tested multiple times, successfully yielding over 900 individual mass-spectrometry recognizable

peptides. The study protocol further plans for a pool of control specimens that will reduce inter-specimen variability of benign pigmented composite skin naevi and the relative difference in individual protein expression levels (fold change values) in melanoma tissue. The pooled protein expression levels will be correlated with well-known prognostic factors. So far, test samples have shown excellent extraction rates for different tissue samples.

Discussion: The principal questions that will be addressed: 1) what is the level of expression of known biomarkers in paraffin-embedded tissue of cutaneous head and neck melanoma in stages I and II, 2) whether paraffin-embedded tissue samples of cutaneous head and neck melanoma expresses new and potentially valuable proteomic biomarkers, 3) does the level of proteomic expression in paraffin-embedded melanoma tissue have a diagnostic or prognostic significance in cutaneous head and neck melanoma stages I and II. All three questions will be answered by using a unique approach to paraffin-fixed protein tissue proteome analysis through an in-house developed protocol.

Acknowledgments: None to be declared.

MeSH/Keywords: proteomics, malignant melanoma, biomarker, prognosis, head and neck

Poster code: B-19-133

POSTER TITLE: MAGNETIC RESONANCE IMAGING FINDINGS OF DISC DEGENERATION IN PATIENTS WITH ADOLESCENT IDIOPATHIC SCOLIOSIS: CORRELATION WITH BACK PAIN

PhD candidate: Matija Žutelija Fattorini, MD

Part of the thesis: Does disc degeneration on magnetic resonance imaging associate with back symptom severity in adolescents with idiopathic scoliosis?

Mentor/s: Associate professor Alenka Gagro, MD, PhD and Associate professor Tomislav Đapić, MD, PhD

Affiliation: University of Zagreb School of Medicine, Children's Hospital Zagreb

Introduction: Scoliosis is the most common deformity of the spine. In most patients with scoliosis, however, the cause is unrecognized. Idiopathic scoliosis is present in 1-3% of adolescents. Back pain (BP) is sometimes the presenting complaint and underlying pathological condition frequently remains unknown. It is reasonable to presume that morphological changes such as disc degeneration (DD) play a role in BP. There are many studies in the literature regarding low back pain in adolescent population confirming aforementioned. The purpose of this study is to determine presence of morphological changes in intervertebral segment at the apex of scoliotic curve, in first place DD, through magnetic resonance imaging. Also we want to investigate the association between DD and back symptom severity among adolescents with idiopathic scoliosis.

Materials and methods: This prospective study will incorporate 120 patients with adolescent idiopathic scoliosis. In the beginning all patient will be examined clinically including gait and posture, detailed neurological examination and Adam's forward bending test using scoliometer. To assess the degree of deformity full length standing posteroanterior and lateral radiographs of the spine will be required. The magnitude of a scoliotic curvature will be determined with the Cobb technique. Then, we will evaluate BP data (visual analog scale), functional limitation (Oswestry Disability Questionnaire and Scoliosis Research Society-22 patient questionnaire) and

thoracic and lumbar magnetic resonance imaging using a 1.5-T scanner. The degree of DD will be graded from T2-weighted images using Pfirrmann classification.

Results: The study is currently in progress (we started data collection in January 2014). Up to now we have completed data for 20 patients and another 40 patients are in process of magnetic resonance imaging (MRI). Preliminary results are showing high prevalence of DD among patients with BP. However, correlation of DD and pain is not statistically significant at this point. We assume that is due to small percentage of fully processed data. It is also important to draw attention that most of processed patients are those with BP.

Discussion: Our preliminary results are showing high prevalence of DD in scoliosis patients. Also we are presuming that those patients with painful scoliosis will have DD on the apex of scoliotic curve. To determinate aforementioned and correlation of DD with back pain we have to complete data collection.

Acknowledgments: I would like to thank my mentors and my colleague Gordana Miličić for their guidance and constant supervision.

MeSH/Keywords: adolescent idiopathic scoliosis, disc degeneration, back pain, magnetic resonance.

Poster code: B-20-102

POSTER TITLE: RELATIONSHIP BETWEEN SPECIFIC AND NONSPECIFIC NASAL HYPERREACTIVITY IN PATIENTS WITH SEASONAL ALLERGIC RHINITIS

PhD candidate: Dejan Tomljenović, MD

Part of the thesis: RELATIONSHIP BETWEEN SPECIFIC AND NONSPECIFIC NASAL HYPERREACTIVITY IN PATIENTS WITH SEASONAL ALLERGIC RHINITIS

Mentor/s: Professor Livije Kalogjera, MD, PhD

Affiliation: University Hospital „Sestre Milosrdnice”

Introduction: Allergic rhinitis is defined as an IgE-mediated inflammation of the nasal mucosa, induced by allergen exposure. Activation of mast cells in the early stage and eosinophils in late stage of allergic reactions, after contact allergen with respiratory mucosa, is the fundamental pathophysiological mechanism which leads to inflammation. Allergic inflammation leads to the characteristic symptoms of allergic rhinitis, such as runny nose (rhinorrhea), postnasal dripping, nasal congestion, nasal itching and sneezing. Nasal symptoms are often combined with ocular symptoms (watery and itchy eyes).

Materials and methods: This study is designed to include 30 patients of both sexes, aged 18 to 65, with monoallergy to grass or ambrosia pollen. An out-of-allergy-season provocation test with allergen, histamine and hypertonic solutions is planned to be administered to the nasal mucosa. Stimulation of two types of nasal mucosa receptors who respond to nonspecific provocation stimulus (H1 and TRPV) is expected. A before and after evaluation of nasal patency, symptom intensity, tryptase concentration, eosinophilic cationic protein and substance P in nasal secretion and tears will be conducted. The markers of inflammation and symptoms in

selected models of nasal provocation will be correlated statistically. The control group encompasses ten patients with symptoms of non-allergic rhinitis, with negative skin prick test and negative specific IgE.

Results: The study is currently in the phase of data analysis, with all of the planned samples collected. Currently, complete laboratory based testing is being conducted for the entire patient group. So far, preliminary results are available for 10 patients, which is insufficient for detailed data analysis. A more comprehensive data review is pending.

Discussion: AIM of the study is to compare the reactivity of inflammatory cells in the early and late phase of allergic reactions, measure non-allergic inflammation intensity and neurokinine release after specific and nonspecific provocation.

Acknowledgments: Prof. Livije Kalogjera, and ENT department University Hospital

MeSH/Keywords: allergy, ambrosia, grass pollen, provocation test, substance P, tryptase, nasal patency.

Poster code: B-21-5

POSTER TITLE: ROLE OF MATRIX METALLOPROTEINASES AND THEIR INHIBITORS IN THE DEVELOPMENT OF CERVICAL METASTASES IN PAPILLARY THYROID CARCINOMA

PhD candidate: Boris Bumber

Part of the thesis: Matrix Metalloproteinases And Their Inhibitors In Papillary Thyroid Carcinoma

Mentor/s: Associate Professor Drago Prgomet, MD, PhD

Affiliation: University Hospital Centre - Zagreb

Introduction: Matrix metalloproteinases (MMPs) thought to play a major role on cell behaviors such as cell proliferation, migration, differentiation, angiogenesis, apoptosis. A number of MMPs have been strongly implicated in multiple stages of cancer progression including the acquisition of invasive and metastatic properties. In particular, MMP-1 (Interstitial Collagenase), MMP-2 (Gelatinase A), and MMP-9 (Gelatinase B) have strongly been implicated in the induction of the local invasiveness, angiogenic switch and metastasis of certain tumors. TIMPs are the major endogenous regulators of MMP activities in the tissue, and four homologous TIMPs (TIMPs-1 to -4) have been identified to date capable of inhibiting the activities of all known matrix metalloproteinases (MMPs) and as such play a key role in maintaining the balance between extracellular matrix (ECM) deposition and degradation in different physiological processes. TIMP-1 and TIMP-2 can inhibit tumor growth, invasion, and metastasis in experimental models which has been associated with their MMP inhibitory activity. TIMP-1 and TIMP-2 have mitogenic activities on a number of cell types, whereas overexpression of these inhibitors reduces tumor cell growth.

Materials and methods: 100 samples of papillary metastatic thyroid cancer (study group) and 50 samples of papillary thyroid carcinoma

without metastases will be analyzed. Resected specimens will be subjected to immunohistochemistry analysis. In the analysis we used semi-quantitative scoring system. Immunoreactivity was assessed by the percentage of positive cells (0-0% 1:1-33% 2:34-66% 3:67-100%) and the intensity of staining (0: no immune reactions, 1: mild immune reaction, 2: moderate immune reaction, 3: strong immune reaction). We scored the tumor and the surrounding tumor tissue.

Results: The rough analysis showed that the study group (100 patients) had an overall score for the MMP 16 (7 for group with metastasis in level VI and 9 for group with metastasis in level II-V of the neck), whereas the control group (50 patients) had an overall score of 5. Unlike matrix metalloproteinase analysis TIMP resulted in a reverse value for a study group 5 and 8 for control group.

Discussion: These preliminary results confirm our hypothesis about the connection between the expression of MMPs and TIMPs and metastatic process, and the connection with the pattern of metastatic process in the neck.

Acknowledgments:

MeSH/Keywords: MMP, TIMP, papillary thyroid cancer, metastasis

Poster code: B-21-73

POSTER TITLE: EXPRESSION OF MATRIX METALLOPROTEINASES (MMP-1, MMP-2 AND MMP-9) AND TISSUE INHIBITORS OF METALLOPROTEINASES (TIMP-1 AND TIMP-2) IN LOCALLY INVASIVE PAPILLARY THYROID CANCERS

PhD candidate: Zgjim Limani MD

Part of the thesis: n/a

Mentor/s: Prof. Dr. Drago Prgomet, Prof. Dr. Damir Babić

Affiliation: Otorhinolaryngology, Pathology

Introduction: Locally invasive thyroid papillary cancer (LI-PTC) is an uncommon disease with significant morbidity and mortality. By definition it is the one that protrudes beyond the thyroid capsule and invades local structures. Over the last years, matrix metalloproteinases (MMPs) have been considered as a target for cancer treatment. They act by invading surrounding stroma. The activity of MMPs is controlled by tissue inhibitors of metalloproteinases (TIMPs). It has been showed that MMP-1, MMP-2, and MMP-9 are most commonly related to malignant tumors and local invasion. Human thyroid carcinoma tissues have been reported to express MMP-1, MMP-2 and MMP-9. The aim of our study is to determine expression levels of MMP-1, MMP-2, MMP-9, and TIMP-1 and TIMP-2 in specimens of invasive and non-invasive papillary thyroid carcinoma (NI-PTC). Our hypothesis is that expression levels of these biomarkers correlate with the development of locally invasive thyroid papillary carcinoma.

Materials and methods: This is a retrospective study of archived tissue specimens of LI-PTC and NI-PTC. We will analyze MMPs and TIMPs Immunohistochemical expression in 50 samples of thyroid tissue diagnosed as LI-PTC and 30 samples of thyroid tissue diagnosed as non-invasive, non-metastatic papillary carcinoma.

Results: Both control and study group were sorted by considering Clinico-Pathologic factors that determine treatment modality. Age group and gender, size of the tumor, lymph node metastasis, multifocality, and localization were used as sorting criteria. Tissue specimens are prepared and in the next step Immunohistochemical analysis will be performed. Based on preliminary tests performed we noted expression levels of MMP-1, MMP-2 and MMP9, but yet it has to be determined if there is a difference in expression levels between study and control group and how it correlates with levels of TIMP-1 and TIMP-2 as well.

Discussion: The availability of a potential marker of prognosis for LI-PTC could have important implications in tailoring therapy, given the morbidity associated with recurrent neck surgeries and external radiation therapy. It could also raise the index of suspicion for occult invasive disease at presentation, indicating the need for wider resection and neck dissection in high-risk patients.

Acknowledgments: n/a

MeSH/Keywords: Matrix metalloproteinases, MMP-1, MM-P-2, MMP-9, TIMP-1, TIMP-2, Papillary Invasive Carcinoma, Thyroid gland.

Poster code: B-21-113

POSTER TITLE: IMMUNOHISTOCHEMICAL EXPRESSION OF PROTEIN NEDD9 IN HEAD AND NECK SQUAMOUS CELL CARCINOMA

PhD candidate: Iva Ledinsky, MD

Part of the thesis: Immunohistochemical Expression of Protein NEDD9 in Head and Neck Squamous Cell Carcinoma

Mentor/s: Professor Božena Šarčević, MD, PhD, Marija Pastorčić Grgić, MD, PhD

Affiliation: University hospital for tumors, University hospital center "Sister of Mercy", Zagreb

Introduction: Head and neck squamous cell carcinoma (HNSCC) is the fifth most common cancer worldwide and the most common cancer of the mucosa of the upper respiratory and digestive system. Although treatment techniques were improved, survival of patients with HNSCC has not been significantly altered in recent decades. New researches are required to discover specific genetic and molecular changes responsible for the onset and development of HNSCC metastatic potential. One of the possible important control points in HNSCC carcinogenesis could be the protein NEDD9. It belongs to a group of CAS proteins, so far the most researched in migration and invasion of cancer. Increased expression of the NEDD9 in breast cancer, melanoma and glioblastoma results in increased metastatic potential and poor patient prognosis.

Materials and methods: In this retrospective study, the immunohistochemical expression of NEDD9 is analyzed in patients with HNSCC who have been treated in our institution in the period from 2000 to 2006. A 140 patients with primary tumors located in the oropharynx, hypopharynx and larynx and who have been followed up for at least 5 years are included in the study. We examine relationship of NEDD9 to the site of the primary process, disease stage, degree of tumor differentiation as well as overall survival. From each paraffin block of primary tumor, three 2-micrometer section were prepared. Two were rou-

tinely stained with HE according to standard histological methods and one was processed with monoclonal antibody for protein NEDD9 (clone number 2G9, AbCam USA) diluted 1:50 in dilution buffer.

Results: So far, we had collected medical data of patients and archived paraffin blocks of primary tumors, then we revised all the biopsy material which was processed by standard histological methods. At this moment, one additional cut from each tumor is being manually immunohistochemically processed with monoclonal antibody for protein NEDD9. Heretofore, 35 processed primary tumors in most cases have shown cytoplasmic positivity. We expect to finish our study until July 2014.

Discussion: This study will contribute to the knowledge on the role of protein NEDD9 in HNSCC carcinogenesis. The prognostic value of protein NEDD9 will be determined on patients five-year survival rate. The study results will clarify the biological behavior of HNSCC and enable more accurate prediction of tumor behavior, and thus more accurate patients treatment planning.

Acknowledgments:

MeSH/Keywords: squamous cell carcinoma of the head and neck, protein NEDD9, CAS proteins, carcinogenesis, survival

Poster code: B-21-163

POSTER TITLE: PRELIMINARY MEASUREMENT OF PLEURAL MESOTHELIOMA USING VIBRATIONAL SPECTROSCOPY

PhD candidate: Fatlinda Sadiku Zehri

Part of the thesis: Comparison of pleural lesions using vibrational spectroscopy

Mentor/s: Prof. Dr. Sven Seiwerth and Doc. Dr. Sc. Ozren Gamulin

Affiliation: University of Zagreb, School of Medicine, Department of Pathology and Department of Physics and Biophysics

Introduction: Vibrational spectroscopy can provide information on biological materials. Any changes leading to disease are due to some biochemical changes in components that it is composed of. The vibrational spectra are sensitive to the structure of these components, so they can change with the diseased state. The aim of this study is to compare the vibrational spectra of normal pleura, pleura with inflammatory changes, with primary neoplastic disease and with metastatic disease. This way we can add vibrational spectroscopy as a possible additional tool in differential diagnosis of pleural lesions.

Materials and methods: We will choose the data for 10 patients who have had a resection of mesothelioma of the pleura, 10 patients with pleuritis, 10 patients with metastatic tumours in pleura and 10 normal pleura. Then, take the paraffin blocks from the archive, from which we will cut and prepare 20 new tissue sections 5 micrometers thick, from each block. New tissue sections will be put on optical grade silicon windows and paraffin will be removed following standard histology protocols. Samples will be placed in vacuum for 10 minutes to extract remaining water. Vibrational spectra of prepared samples will be recorded with PERKIN-Elmer SPECTRUM GX spectrometer. Vibrational spectra of each of tissue type will be recorded for more than 10 spectra for later statistical analysis. Vibrational spectra of each type of lesion will be compared with vibrational spectra of the normal

pleura. Statistical methods which we will use to report the results are multivariate methods PCA, STT and descriptive statistics.

Results: Until now we have recorded infrared spectra of pleural mesothelioma samples. We have to record metastatic tumours in pleura, pleuritis and normal pleura. In first figure we can see original spectra of mesothelioma. In second figure, there are normalized spectra for equal area. Since the infrared spectra of mesothelioma tissue is complex consisting of many spectral bands due to the presence of macro-molecules (lipids, proteins, polysaccharides and nucleic acids), there is absorption in spectral regions: 800 to 1800 and 2800 to 3700.

Discussion: During the recording process of normal pleura, we are faced to a problem. Because of pleural hypocellularity, our samples were very thin and the result was low signal to noise ratio. To increase quality of our spectra, and this is important for further analysis of our measurements, we have to put more than one layer of pleura at optical grade silicon window.

Acknowledgments: I would like to thank Prof. Sven Seiwerth and Doc. Ozren Gamulin for great support, advice and help.

MeSH/Keywords: Pleura, Pleuritis, Mesothelioma, metastatic tumours, vibrational spectroscopy

Poster code: B-23-67

POSTER TITLE: EFFICIENCY OF CARDIOMYOGENESIS IN HUMAN PLURIPOTENT STEM CELLS

PhD candidate: Ana Šepac

Part of the thesis: Cardiomyocytes Differentiated from Human Pluripotent Stem Cells as an Experimental Model for Anesthetic-induced Preconditioning

Mentor/s: Professor Sven Seiwerth, MD PhD and Professor Zeljko J. Bosnjak, PhD

Affiliation: Medical College of Wisconsin, Department of Anesthesiology, and University of Zagreb School of Medicine, Department of Pathology

Introduction: Human cardiomyocytes can be differentiated from various pluripotent stem cells. The aim of this study is to compare in vitro cardiomyogenic properties of human induced pluripotent stem cell (hiPSC) lines, C2a and C6a, and commercially available human embryonic stem cell (hESC) lines, H1 and H9.

Materials and methods: Cardiomyogenesis was induced by treatment with activin-A and BMP4. Genetic labeling of differentiated cardiomyocytes was performed by transducing cells with a lentiviral vector delivering genetic construct that allows expression of reporter enhanced GFP under transcriptional control of cardiac-specific promoter MLC-2v. Immunocytochemistry was performed by labeling cells with primary antibodies against titin, sarcomeric alpha actinin and cardiac troponin T. Differentiation efficiency was determined by counting MLC-2v-positive cardiomyocytes dissociated from beating and non-beating cell clusters. Expression of 18 genes involved in pluripotency and various stages of cardiomyogenesis was determined during differentiation by quantitative PCR.

Results: All tested lines formed spontaneously and rhythmically beating cell clusters following cardiac differentiation, indicating presence of functional cardiomyocytes. H1 line displayed the greatest percentage of cardiomyocytes in beating clusters (86%), while C2a, C6a and H9 cells displayed 65-67% of cardiomyocytes. Im-

munostaining analysis demonstrated existence of a striated pattern of sarcomeric proteins in each line indicating presence of highly organized sarcomeres. In all lines, induction of differentiation diminished levels of pluripotency marker OCT4, which was paralleled by transient expression of mesodermal marker brachiury. Early cardiac differentiation was marked by expression of MESP1, NKX2.5 and ISL1. Markers of terminal differentiation began to rise during the second week of differentiation, including GATA4, MEF2C, TNNT2, TBX20 and MYL7. Expression of various ion channels exhibited steady increase in expression beginning also in the second week, including SCN5A, CACNA1C, KCNH2, KCNJ2 and KCND3. mRNA levels of ISL1, GATA4, TBX20, TNNT2 and MYL7 were greater in hESC lines, while no line-specific differences were noted for other mRNAs.

Discussion: hiPSCs can be differentiated into functional contracting cardiomyocytes, although less efficiently than the hESCs. These results encourage further testing of hiPSC-cardiomyocytes as a patient-specific in vitro disease model.

Acknowledgments: I am grateful to my mentors, Drs. Seiwerth and Bosnjak, lab members and the Graduate School.

MeSH/Keywords: pluripotent stem cells, cardiomyocytes, cell differentiation

Poster code: B-23-110

POSTER TITLE: IMMUNOHISTOCHEMICAL EXPRESSION OF NEDD9 IN PANCREATIC ADENOCARCINOMA

PhD candidate: Petra Radulović

Part of the thesis: Immunohistochemical expression of NEDD9, gamma-catenin and e-cadherin in pancreatic adenocarcinoma

Mentor/s: Professor Božo Krušlin, MD, PhD

Affiliation: Clinical Hospital Centre Sestre milosrdnice

Introduction: Early metastasis is a hallmark of pancreatic ductal adenocarcinoma and is responsible for more than 90% of pancreatic cancer death. Since patient outcome is not reliably predicted using pathological factors (tumor stage, differentiation, resection margin status) alone, markers of tumor behavior are needed. One among candidates is NEDD9 (HEF-1/CAS-L), recently identified as a key protein in tumor cell proliferation and migration. NEDD9 is predominantly cytoplasmic protein that contains many functional modules for protein interaction, leading to its classification as scaffolding protein. It is found to be overexpressed in metastatic melanoma, glioblastoma and metastasizing breast adenocarcinoma.

Materials and methods: Expression of NEDD9 was analyzed in 61 cases of pancreatic adenocarcinoma and 61 samples of normal pancreatic tissue measuring the intensity of immunohistochemical staining as well as the percentage of positive tumor cells in tissue sample and was scored as follows: 1 for weak cytoplasmic staining in less than 25% of tumor cells, 2 for moderate staining in more than 25% of tumor, and 3 for intense cytoplasmic staining in more than 25% of tumor cells. Immunohistochemistry was performed using formalin-fixed, paraffin-embedded tissue sections (thickness 5 μ m). Deparaffinization and immunohistochemical staining were carried out following microwave

streptavidin immunoperoxidase (MSIP) protocol and by use of labeled streptavidin-biotin (LSAB) method on DAKO TechMate™ Horizon automated immunostainer. Monoclonal antibodies against NEDD9 (sab 4200376, dilution 1:200, R Sigma Aldrich, St.Louis, USA) were used.

Results: In pancreatic adenocarcinoma group there was 78.7 % cases with strong expression of NEDD9 and 21.3% of cases with moderate expression while there were no cases with weak expression of NEDD9. Normal pancreatic tissue was strongly positive in 45.9% of cases, while moderate and weak reaction was observed in 31.1% and 23% of cases. Expression of NEDD9 was significantly stronger in pancreatic adenocarcinoma ($p < 0,05$).

Discussion: Our results show that NEDD9 protein is overexpressed in pancreatic adenocarcinoma cells in comparison with normal pancreatic tissue. This study provides evidence of role for NEDD9 in pancreatic cancer progression and invasion and suggests that NEDD9 expression may provide a potential biomarker for tumor aggressiveness.

Acknowledgments:

MeSH/Keywords: pancreatic adenocarcinoma, nedd9, invasiveness

Poster code: B-23-111

POSTER TITLE: SIGNIFICANCE OF MVD (MICRO VESSEL DENSITY) IN DIFFUSE LARGE B CELL LYMPHOMA AND LOW GRADE FOLLICULAR LYMPHOMA

PhD candidate: Labinot Shahini, MD

Part of the thesis: Angiogenesis

Mentor/s: Prof. dr. Gordana Petrusevska, Prof. dr. Slavko Gasparov

Affiliation: Institutes of Pathology, Faculty of Medicine, University of Prishtina and Faculty of Medicine, Cyril

Introduction: The purpose of this study was to evaluate angiogenesis in diffuse large B-cell lymphoma (DLBCL) and low-grade follicular lymphoma (FL). Angiogenesis is essential for the development, growth and progression of solid tumors. It is induced by hypoxia through the mechanism that includes angiogenic transcription factor hypoxia-inducible factor (HIF). Although vascular endothelial growth factor (VEGF) is a well-known proangiogenic factor, its impact on diffuse large B cell lymphoma is still not well understood.

Materials and methods: There have been studied 60 prospective and retrospective cases of DLBCL and FL (30 DLBCL, 30 FL), diagnosed at the Institutes of Pathology, Faculty of Medicine, University of Prishtina, Republic of Kosovo and Faculty of Medicine, Cyril

Results: During our study there have been investigated 30 cases each of DLBCL and FL, analyz-

ing immunohistochemical expression of CD31 in order to determine micro vessel density (MVD). It has been shown that over 60% of cases with DLBCL expressed high MVD, whereas less than 40% of cases with FL expressed high MVD. Furthermore, in cases of DLBCL there have been detected high rates of oxygen and nutrient consumption, as well as small cuffs only two to three cells wide high vascular density.

Discussion: Our data have confirmed the significant association between MVD and high -grade hematological tumors.

Acknowledgments: This study was supported by the Institute of Pathology, Faculty of Medicine, University of Prishtina, Kosovo and Institute of Pathology, Faculty of Medicine, St. Cyril

MeSH/Keywords: DLBCL, follicular lymphoma, hypoxia, angiogenesis, CD31, MVD

Poster code: B-23-158

POSTER TITLE: DETERMINATION OF EARLY ATHEROSCLEROTIC CHANGES IN CHILDREN WHO SUFFER FROM JUVENILE IDIOPATHIC ARTHRITIS

PhD candidate: Iva Rukavina

Part of the thesis: Atherosclerosis in juvenile idiopathic arthritis

Mentor/s: Assistant Professor of Paediatrics, Marija Jelušić Dražić, MD, PhD

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

Introduction: Atherosclerosis commences in childhood but manifests clinically later in life. Besides usual risk factors, nowadays more attention has been given to its inflammatory etiology. Similarity between atherosclerotic process and inflammatory changes in the course of systemic connective tissue disease (included juvenile idiopathic arthritis (JIA)) has been noticed. JIA is arthritis started at child's age, before age of 16. In order to prevent disease progression it is important to look for signs of premature atherosclerosis. Like good and non-invasive methods that can be used in this purpose are measuring of intima media thickness of carotid arteries and determination of parameters of arterial stiffness. Usage of this methods in everyday clinical practice enables identification of signs of premature atherosclerosis, what would be of great benefit for cardiovascular disease prevention.

Materials and methods: The study design is a case – control trial including 60 JIA patients divided into two groups – acute and chronic patients that will be compared to sex matched healthy controls. Intima – media thickness (IMT) of common carotid artery and determination of parameters of arterial stiffness were measured using high – resolution B – mode ultrasound. IMT was evaluated using a high-resolution 10 MHz linear transducer in B mode (Aloka ProSound ALPHA 10) equipped with an E – tracking programme.

Far-wall measurements were obtained. IMT of the far wall was defined as the distance between the leading edge of the lumen-intima interface and the leading edge of the media-adventitia interface. IMT was measured on each side at three sites (1 –2 cm below the carotid bulb) on the longitudinal views. IMT was calculated as the average of measurements from three different sites on each side. Laboratory investigations include total cholesterol, HDL, LDL, triglycerides, lipoprotein (a), C – reactive protein, fibrinogen, factor VIII, aggregation of platelets, MTHFR gene analysis, homocysteine and vitamin D.

Results: Preliminary results show that JIA patients with acute form of the disease have increased IMT compared to chronic patients and control group and this group of patients also have decreased arterial wall elasticity.

Discussion: These very early data from a small number of patients are providing our first insight into the atherosclerotic changes in JIA patients. The results are in line with our expectations. So, it seems that atherosclerosis starts early in the course of JIA.

Acknowledgments:

MeSH/Keywords: Atherosclerosis, juvenile idiopathic arthritis

Poster code: B-24-46

POSTER TITLE: THE CORRELATION OF ANTISTREPTOLYSIN O LEVEL WITH CHILDHOOD ATTENTION DEFICIT, HYPERACTIVITY AND IMPULSIVITY DISORDER

PhD candidate: Tamara Žigman

Part of the thesis: The Correlation of Antistreptolysin O level with Childhood Attention Deficit, Hyperactivity and Impulsivity Disorder

Mentor/s: Prof.dr.sc. Ljerka Cvitanović Šojat

Affiliation: Department of Pediatrics, Clinical Hospital Center

Introduction: In the mid 20th century, rheumatic fever was described as an acute, non-suppurative sequel of acute streptococcal infection. In 10-15% of patients it manifested as Sydenham chorea, sometimes after a very long latency period. In 1998, Swedo et al. described the first 50 patients with PANDAS (Pediatric Autoimmune Neuropsychiatric Disorder associated with streptococcal infections) and set the clinical criteria for the diagnosis of PANDAS. In the year 2006 Pavone et al. pointed to a much wider range of neuropsychiatric disorders that may be associated with acute streptococcal infections, including the symptoms of attention deficit/hyperactivity disorder (ADHD). In May 2012, it was proposed by Swedo herself to change the term PANDAS to PANS/CANS (Pediatric Acute-onset Neuropsychiatric Syndrome/Childhood Acute Neuropsychiatric Symptoms). PANS/CANS includes the simultaneous presence of additional neuropsychiatric disorders, beside obsessive-compulsive activities and tics that were the primary characteristics of PANDAS. ADHD was described for the first time way back in 1902. It is characterized by attention deficit and developmentally inappropriate hyperactivity and impulsivity, and as such may constitute PANS/CANS. Antistreptolysin O (ASO) titer is a landmark of past streptococcal infection.

Materials and methods: The main goal of this study is to determine whether there is association of elevated ASO titer with childhood ADHD.

The study group will consist of 75 children of both sexes, age range 5-15 years, who have symptoms of ADHD. The control group will consist of 150 children without symptoms of ADHD that will be strictly matched with the study group according to age and gender. ADHD will be diagnosed with ADHD-test, standardized test translated to Croatian language. To evaluate the influence of predictor variable (ASO titer) on dependant variables (ADHD quotient, subtest standardized values), the method of multiple linear regression is used.

Results: By now, 37 patients are included (12 in study group and 25 in control group). Higher level of ASO titer can be correlated with higher ADHD quotient, but because of small sample, multivariate analysis has not been done.

Discussion: According to preliminary results, we can conclude that higher level of ASO titer is correlated to higher ADHD quotient, but larger sample is needed to confirm the hypothesis. Environmental factors can influence on the severity of ADHD symptoms including streptococcal infection.

Acknowledgments: I would like to thank to my mentor, professor Ljerka Cvitanović Šojat

MeSH/Keywords: attention deficit, hyperactivity and impulsivity disorder, antistreptolysin O titer, children.

Poster code: B-24-64

POSTER TITLE: SIGNIFICANCE OF PROINFLAMMATORY CYTOKINES, POWER DOPPLER -ULTRASOUND AND NUCLEAR MAGNETIC RESONANCE IN MONITORING DISEASE ACTIVITY AND RESPONSE TO THERAPY IN JUVENILE IDIOPATHIC ARTHRITIS

PhD candidate: Agneza Marija Pasini, MD

Part of the thesis: Laboratory tests and imaging techniques in monitoring disease activity in juvenile idiopathic arthritis

Mentor/s: 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 at least 6 weeks. JIA is one of the most common chronic illnesses in childhood and often persists into adulthood and is an important cause of disability. Chronic synovial inflammation is main pathological process in JIA, and is the result of activation of specific and nonspecific immunity. These processes are mediated by secretion of numerous cytokines. As for adult rheumatoid arthritis, in recent years there has been a growing interest in the use of new imaging techniques, such as magnetic resonance imaging (MRI) and ultrasound (US), in children with JIA. All this radiologic methods have potential application in the evaluation of disease activity, prediction of disease progression and monitoring of response to therapy in JIA.

Materials and methods: The survey will be monocentric, prospective and it will include 30 children with oligo- and polyarticular JIA. In every patient we will determine disease activity based on clinical assessment, laboratory tests and radiological methods. Disease activity will be determined by validated Juvenile Arthritis Disease Activity Score. Laboratory tests include markers of inflammation and levels of cytokines IL-1, TNF- α , IL-6, VEGF, IL-17A i IL-22. Cytokine analysis will be performed in serum samples and

synovial fluid collected from knee joint. Radiologic analysis will include PD-US and MRI of the knee joint. Clinical evaluation of disease activity, the analysis of markers of inflammation in serum, PD-US will be performed before the treatment, 3 and 6 months after treatment. MRI will be done before and after 6 months of treatment.

Results: This is prospective still ongoing study and by now we have enrolled 15 newly diagnosed JIA patients of which 12 females and 3 males of mean age of 8,4 years. All previously mentioned procedures were performed and clinical and radiological data analysis is in progress. Serum and synovial fluid samples taken for cytokine analysis are stored at -80°C until analysis.

Discussion: We will investigate the significance of proinflammatory cytokines in JIA and examine whether their determination improves the algorithm for monitoring of children with JIA in comparison to radiological methods

Acknowledgments: I would like to thank to my mentor and radiologists that helped during this study

MeSH/Keywords: juvenile idiopathic arthritis, proinflammatory cytokines, power Doppler-ultrasound, magnetic resonance imaging

Poster code: B-24-104

POSTER TITLE: CLINICAL AND BIOCHEMICAL CHARACTERISTICS OF ALBANIAN PEDIATRIC CELIAC DISEASE PATIENTS

PhD candidate: Atifete Ramosaj-Morina

Part of the thesis: Clinical, biochemical and immunogenetical characteristics of Albanian pediatric celiac disease patients from Kosovo.

Mentor/s: Assistant Professor Renata Žunec, Professor Mehmedali Azemi

Affiliation: University Clinical Hospital Centre- Zagreb, University Clinical Centre of Kosovo

Introduction: CD is an immune-mediated systemic disorder elicited by gluten and related prolamines in genetically susceptible individuals and characterized by the presence of a variable combination of gluten-dependent clinical manifestations, CD-specific antibodies, HLA-DQ2 or HLA-DQ8 haplotypes, and enteropathy.

Materials and methods: We will analyze all clinical manifestations, biochemical markers including CD-specific serology (tTGA, anti-DGP and EMA), endoscopy with duodenal biopsy and HLA class II polymorphism including presence of DQ2 and -DQ8 heterodimers in a group of at least 60 patients and in a control group consisting of at least 60 age and sex matched healthy Albanian children from Kosovo.

Results: During the year 2013 the incidence of CD was 6.4 per 100,000 children, the study includes 20 out of 27 children diagnosed with CD, from which 66% were females. The median age at diagnosis was 6.2 years (from 1 to 14 years). So far we conducted only clinical and biochemical characteristics. The clinical results are as follows: 13 (65 %) patients had diarrhea, recurrent abdominal pain (70.0%), abdominal distention 80% , weight loss had 85 % of patients, failure to thrive 60%, 70 % had suffered from

malaise, 50% reported nausea / vomiting, short stature (60%) and 80 % of patients were anemic. We classified as "classical" CD 13 patients (65 %) since they had both symptoms, diarrhea and weight loss. All patients tested for tissue transglutaminase and endomysial antibodies were positive, 17 (85%) of them had anti-TG2 antibody levels >10 times ULN (as appropriate for age). Only two patients had positive family (siblings) history with CD. In addition, two patients had type 1 diabetes mellitus, while one had Turner syndrome.

Discussion: The preliminary results of our study support the hypothesis that almost all our CD patients are diagnosed when is manifested in classical form. In meanwhile the atypical and silent forms of celiac disease are very frequent and it is an indication for serological examination in children with unclear clinical picture and genetic predisposition.

Acknowledgments: For supporting me through this endeavor, my sincere thanks and appreciation goes to my Professor Ms. Renata Žunec PhD

MeSH/Keywords: Celiac disease, Kosovo, children, HLA heterodimer, antibodies.

Poster code: B-24-148

POSTER TITLE: ELASTOGRAPHIC VALUES OF BREAST TISSUE IN WOMEN

PhD candidate: Martina Džoić Dominković, MD

Part of the thesis: Characterisation Of Woman Breast Tissue With Elastography And Comparison To Estimated Mammographic Density

Mentor/s: Gordana Ivanac, MD, PhD

Affiliation: 1 - Department for Radiology, General Hospital Orašje 2 - Clinical Institute for Diagnostic and Interventional Radiology, Clinical Hospital Dubrava

Introduction: Elastography is a new quantitative ultrasound technique for measuring tissue stiffness. Breast elasticity can be measured with elastography and it is possible to determine its association with certain parameters, also to determine the difference in elasticity in different breast tissue (fat and glandular). Many physiological changes of breast tissue depend on the age, menstrual cycle and many other parameters.

Materials and methods: We performed a prospective study with 200 women of different age. Women aged > 40 years had mammographic pictures attached with estimated density of breast parenchyma. We performed B-mode ultrasound examination and real-time elastography. Each breast was divided in 4 quadrants and elasticity of glandular and fat tissue in each quadrant was measured. We compared elastographic value with estimated value of mammographic density.

Results: We examined 200 women, 100 of them had mammographic pictures attached, and 100

had only US. We noticed: fat and glandular tissue have different elastographic values, older women have lower elastographic values of breast tissue, women that didn't give birth have higher elastographic values, mammographic and even US estimated density can be correlated with elastographic stiffness.

Discussion: According to our preliminary results, elastographic values of breast tissue can be correlated with density of breast parenchyma which is well known predictor for breast cancer risk. Also we noticed a lot of other correlations (age, parital status, oral contraception) that are not known by now.

Acknowledgments:

MeSH/Keywords: Breast, Elastography, Density of glandular parenchyma, Elasticity of glandular parenchyma, Elasticity of fat tissue

Poster code: B-25-14

POSTER TITLE: ROLE OF DIGITAL TOMOSYNTHESIS IN DIAGNOSIS OF SACROILIITIS

PhD candidate: Luka Novosel

Part of the thesis: Role of digital tomosynthesis in diagnosis of sacroiliitis

Mentor/s: Professor Kristina Potočki, MD, PhD

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

Introduction: Patients satisfy the classification criteria for spondyloarthropathies if they have certain clinical and laboratory findings together with radiological changes on SI joints. Conventional radiography still represents the most available method to depict sacroiliitis, but the complex sinusoidal form of SI joints often makes it difficult to detect pathologic changes in the joints which can therefore sometimes be detected only 5 to 10 years after the condition started. Digital tomosynthesis is a medical imaging technique using a flat panel detector and tube rotation producing a series of slices at different depths. It can provide high resolution images with a considerably lower radiation dose than CT. We would thereby avoid the low sensitivity of conventional radiography due to the complex anatomy and at the same time minimize the radiation dose to the patient that would be delivered by CT.

Materials and methods: The study was conducted on 84 patients who have been referred for radiological analysis because of suspected sacroiliitis. Conventional radiography and digital tomosynthesis were performed in the maximum time period of 2 weeks so that we could avoid significant changes in the radiological manifestation of sacroiliitis. To determine whether digital tomosynthesis is a more exact method for determining structural changes on SI joints two experienced radiologists analyzed, by method of

consensus, the imaging material without any insight into the identity or the clinical and laboratory findings. The changes will be scored by the modified New York criteria. Dosimetry of conventional radiography and digital tomosynthesis was performed according to the anthropometric characteristics of the patients.

Results: Preliminary dosimetric results showed that the radiation dose delivered to the patient during digital tomosynthesis was 3-5 higher than the dose delivered with the use of conventional radiography while the number of discovered structural changes important for the ASAS criteria, such as erosions, sclerosis and ankylosis were significantly higher compared to conventional RTG of SI joints.

Discussion: The results of this study allow insight into the value of digital tomosynthesis as a potential method in the diagnosis of sacroiliitis and set the ground for other studies involving the use of this method in musculoskeletal diseases. The dosimetric analysis of this diagnostic method shows that the delivered radiation dose to the patient is comparable with conventional radiography.

Acknowledgments:

MeSH/Keywords: conventional radiography, digital tomosynthesis, sacroiliitis, dosimetry

Poster code: B-25-124

POSTER TITLE: KIDNEY TRANSPLANTATION OUTCOME FROM EXPANDED CRITERIA DONORS

PhD candidate: Iva Bačak Kocman, MD

Part of the thesis: Short-term And Long-term Outcomes Of Kidney Transplantation From Expanded Criteria Donors

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

Affiliation: University Hospital Centre - Zagreb

Introduction: Kidney transplantation is a method of choice for replacement of renal function while it offers better survival and improve quality of life when compared to dialysis. Kidneys of the expanded criteria donors (ECD) were, until recently, considered unsuitable for transplantation because of the increased incidence of the preservation injury, more frequent acute rejections, delayed graft function and primary afuction. Aim of the present study is to determine characteristics of kidney donors in UHC Zagreb after entering Eurotransplant, with the emphasis on proportion of ECD.

Materials and methods: One-year patient and graft survival of all recipients who received kidney allograft from the deceased donor in UHC Zagreb from 15.8.2007. to 15.08.2011. will be determined, as well as graft function and post-transplant complications. Donors will be compared based on different characteristics which determined them as the ECD (age, comorbidities).

Results: Preliminary results of this study, for the time being are oriented to analysis of kidney donors. In a determined period there is an

increasing number of 388 kidney donors (186 ECD). After joining Eurotransplant, number of ECD in Croatia is increasing. Mean age is increasing in ECD group, in 2007. 60.2 ± 14.2 and in 2011. 62.2 ± 15.1 years, respectively. 122 ECD had arterial hypertension in anamnesis. Leading causes of death in ECD (87%) are vascular incidents (CVI 58%, SAH 41%, ACI 1%). Mean admission ($81.12 \mu\text{mol/l}$ vs $108.82 \mu\text{mol/l}$)and terminal serum creatinine values($95.14 \mu\text{mol/l}$ vs $146.64 \mu\text{mol/l}$) are much higher in the recent years.

Discussion: Results of this investigation will, for the first time, determine the prevalence of ECD in the transplant program in Croatia, as well as outcomes of transplantation from the ECD. Our results may help to improve kidney transplant program in Croatia and could be of the major scientific, practical and social interest.

Acknowledgments:

MeSH/Keywords: Expanded criteria donors, renal transplantation, renal transplant recipient, outcome

Poster code: B-28-101

POSTER TITLE: POLYMORPHISM OF FOLLICULE-STIMULATING HORMONE GENE RECEPTOR IN ALBANIAN MALE POPULATION

PhD candidate: Shkelzen Elezaj M.D. urologist

Part of the thesis: Polymorphism and infertility

Mentor/s: Tamara Nikuševa Martić, Assist Prof. and Feodora Stipoljev, Assist Prof.

Affiliation: Clinic of Urology, General Hospital in Peja, Kosovo

Introduction: Follicle stimulating hormone receptor (FSHR), which mediates the effects of FSH, is essential for normal spermatogenesis and male reproduction. The present PhD investigation is the first screening study for SNP polymorphism at codon 680 in exon 10 of the FSHR and its effect on male infertility in Kosovo Albanian male population.

Materials and methods: So far the study encompassed 82 infertile patients and 24 fertile controls. Genomic DNA was isolated from peripheral blood lymphocytes using the PureLink Genomic DNA mini kit (Invitrogen Life technologies USA) and the polymorphisms at nucleotide position 680 of the FSHR gene were genotyped by TaqMan SNP Genotyping assay (Applied Biosystems, Life technologies, USA) according to manufacturers protocols. The SNP haplotypes for the infertile and control group are compared with the obtained blood hormone levels. Statistical analysis: nonparametric data were expressed as median and range. Mann-Whitney test was used as a test of significance for comparison between two groups. Spearman rank correlation coefficient was done for the relations between variables. Statistical significance was set at < 0.05 .

Results: The results showed that the frequency of FSHR gene variants among fertile men was

41.2% Asn/Asn , 35.2% Asn/Ser, and 23.6 % Ser/Ser, where as among Oligoasthenoteratozoospermija (OAT) men were 34.4% Asn/Asn, 37.5.% Asn/Ser and 28.1.% Ser/Ser and Azoospermic 33.9 % Asn/Asn, 38.0% Asn/Ser and 28.1% Ser/Ser men were respectively with significant differences.

Discussion: Genetic abnormalities of the FSHR would be expected to affect sperm production in males. In the our study, variant screening was carried out among fertile and infertile men (OAT and Azospemic) to determine FSHR variants, Asn680 and Ser680. There was a tendency of Asn/Asn variant of FSHR gene to be higher in fertile men, while Ser/Ser variant to be higher in infertile Azoospermic and OAT men. It is possible that isoforms of the FSHR may have weak and different receptor activities that may result in the physiological conditions such as increased serum FSH concentration or spermatogenic defects.

Acknowledgments: Institute of Molecular Biology Zagreb, Polyclinic Biolab Zafi Klina Kosovo

MeSH/Keywords: Infertility, Polymorphisms, FSHR, FSH, PCR

Poster code: B-28-161

POSTER TITLE: PSYCHOLOGICAL ADJUSTMENT AND SOCIO-CULTURAL ATTITUDES IN ADOLESCENTS WITH ANOREXIA NERVOSA

PhD candidate: Maja Crnković, M.A. Psych

Part of the thesis: Psychological Adjustment And Socio-Cultural Attitudes In Adolescents With Anorexia Nervosa

Mentor/s: Ivan Begovac, MD, Ph.D

Affiliation: Clinical Hospital Centre Sestre milosrdnice, Department of Pediatrics and University Hospital Centre Zagreb, Department of Psychological Medicine

Introduction: Emotional regulation, attachment style, empathy and sociocultural attitudes towards appearance form a key part of conceptual model of anorexia nervosa (AN), but the experimental findings to support this are limited. Anorexia nervosa is an answer of psychological maladjustment to the early adolescent challenges, specifically associated with development of identity, common for females. AN in children and adolescents cannot be considered merely a replication of the same illness in a younger age group. There is evidence to suggest that there are features of the illness unique to Early-Onset AN. The question is: why someone develop AN in early adolescence, and someone in late adolescence? Are there any psychological differences? If so, in which psychological components? Hypothesis: Early onset AN has more severe psychological maladjustment than late onset AN.

Materials and methods: The Questionnaire of General Data, The Questionnaire of sociocultural attitudes towards appearance (SATAQ), Eating Disorders Inventory (EDI-3), Questionnaire Difficulties in Emotional Regulation (DERS), Experiences in Close Relationships-Revised (ECR-R) and Basic Empathy Scale (BES) will be administered to 120 woman adolescents (30 Early Pediatric AN (anorexia nervosa) defined as younger than 15 years old at time of presentation), 30 Later

Pediatric AN (15 years and older at time of presentation), and 60 healthy controls. Statistical comparison of the results and logistic regression will examine whether there are significant differences between groups of subjects relating to the sociocultural attitudes and overall psychological adjustment, with an emphasis on the differences between style attachment, emotional regulation and empathy in early and late adolescent woman with AN, and with consideration of the contribution of specific factors in the prediction of anorexia nervosa.

Results: Currently in the process of collecting data.

Discussion: The data will provide support for conceptualizations of eating disorders that emphasize the role of emotion regulation, attachment and empathy in the prediction of anorexia nervosa.

Acknowledgments: I would like to express my gratitude to all those who gave me the possibility to complete this thesis, especially to my supervisor, PhD Ivan Begovac, MD

MeSH/Keywords: anorexia nervosa, emotional regulation, attachment style, empathy, sociocultural attitudes, adolescence

Poster code: B-29-167

POSTER TITLE: INCIDENCE, ACUTE MANAGEMENT AND LONG-TERM FOLLOW-UP OF PATIENTS WITH VESTIBULAR NEURITIS

PhD candidate: Ivan Adamec

Part of the thesis: ACUTE MANAGEMENT OF PATIENTS WITH VESTIBULAR NEURITIS

Mentor/s: Mario Habek, MD, PhD

Affiliation: UHC Zagreb

Introduction: Aims of this study were: [1] to determine incidence of vestibular neuritis (VN) in Zagreb and Velika Gorica, Croatia, [2] to assess efficacy of intravenous administration of dexamethasone on recovery of clinical symptoms of VN patients treated in the emergency department, and [3] to evaluate clinical, MRI and neurophysiological factors that influence recovery of vestibular nerve function after VN.

Materials and methods: Patients older than 18 years and fulfilling clinical criteria for VN, presenting in the Emergency department of the UHC Zagreb were enrolled. Clinical examination, number of vomiting episodes in the past 24 hours, nausea according to the visual-analogue scale, The European Evaluation of Vertigo scale (EEVS) and need for hospitalization were noted at the time of presentation and 2 hours later. All patients underwent brain MRI during the first 3 months from initial presentation. Patients were randomized into 2 groups: group 1 received intravenous dexamethasone 12 mg and group 2 received placebo. In order to evaluate the recovery of vestibular nerve function after VN, all patients underwent VEMP recordings at 6 days and 1 year after presentation.

Results: The incidence of VN in 2011 was 11.7 per 100000 people, and in 2012 it was 15.5 per 100000 with the peak incidence between the age of 50 and 69. Results of efficacy of dexametha-

sone therapy have shown statistically significant improvement in the EEVS results in group 1 compared with group 2 ($p=0.03$). There was no statistically significant difference between groups regarding other parameters. In the VEMP 12-month follow-up part of the study we included 26 patients (15 with complete clinical recovery and 11 with residual symptoms at month 12). Cerebral white matter changes on brain MRI negatively correlated with clinical recovery ($p=0,001$). Logistic regression analysis showed that positive brain MRI and older age reduced odds for clinical recovery. There was no correlation between clinical recovery and oVEMP asymmetry ratio recovery between groups ($p=0,781$).

Discussion: Based on our study, incidence of VN is higher than previously reported. Intravenous dexamethasone exhibits modest symptomatic relief in patients with VN. Older age and cerebral white matter changes on brain MRI are positive predictors of development of chronic vestibular insufficiency. Finally, this study has identified parameters predicting development of chronic vestibular insufficiency after vestibular neuritis.

Acknowledgments:

MeSH/Keywords: vestibular neuritis, dexamethasone, vestibular evoked myogenic potentials

Poster code: B-30-34

POSTER TITLE: ORTHOSTATIC INTOLERANCE IS FREQUENT IN PATIENTS WITH CLINICALLY ISOLATED SYNDROME

PhD candidate: Iva Milivojević, MD

Part of the thesis: Prevalence of pathological response to orthostatic provocation in patients with clinically isolated syndrome (CIS)

Mentor/s: 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 serum catecholamine levels.

Materials and methods: We included 40 CIS patients, 18 males and 22 females, aged 16 to 53 years. The pain-provoked head up tilt table test (PP-HUTT) was used to provoke an orthostatic reaction. Serum levels of norepinephrine were measured both in supine and standing positions.

Results: Altogether 32 patients (80%) had a pathological response: orthostatic hypotension (OH) (N=13, 32.5%), vasovagal syncope (N=10, 25%) and postural orthostatic tachycardia (POTS) (N=9, 22.5%). There was no significant difference ($p=0.177$) between type of CIS and type of response to orthostatic provocation (OH, POTS or syncope). There was no significant correlation between presence of autonomic dysfunction and presence of lesions in the brain hemi-

spheres ($p=0.403$), brainstem ($p=0.878$), cerebellum ($p=0.346$) or the spinal cord ($p=0.784$). Pathological response to orthostatic provocation correlated with difference in norepinephrine levels (standing – supine) ($p=0.012$), indicating that MS patients with pathological response to orthostatic provocation have higher increase in norepinephrine upon standing. This increase is mainly due to high percentage of patients with postural orthostatic tachycardia who had statistically higher difference in norepinephrine levels (standing – supine) compared to patients with normal response to orthostatic provocation ($p=0.03$).

Discussion: This study has shown that orthostatic intolerance is frequent in the initial phase of MS.

Acknowledgments:

MeSH/Keywords: clinically isolated syndrome, head up tilt table test, autonomic dysfunction

Poster code: B-30-40

POSTER TITLE: IMPACT OF ANTICOAGULANT THERAPY ON THE OUTCOME OF ISCHEMIC STROKE IN PATIENTS WITH ATRIAL FIBRILLATION

PhD candidate: Hrvoje Budinčević

Part of the thesis: IMPACT OF ANTICOAGULANT THERAPY ON THE OUTCOME OF ISCHEMIC STROKE IN PATIENTS WITH ATRIAL FIBRILLATION

Mentor/s: Academician Vida Demarin

Affiliation: Department of Neurology, Sveti Duh University Hospital, Zagreb

Introduction: Oral anticoagulant therapy has the leading role in ischemic stroke prevention in patients with atrial fibrillation, but its impact on clinical outcomes has not been clearly shown. The aim of this Ph.D. thesis was to investigate the impact of oral anticoagulant therapy on stroke outcomes.

Materials and methods: This retrospective study included patients with atrial fibrillation who were hospitalized for ischemic stroke in the period from 1st January 2004 until 31st December 2010 at the University Hospital "Sveti Duh" in Zagreb. Patients were divided into three groups according to the prior antithrombotic therapy usage. The analysis of medical records included: demographic data, stroke risk factors, the stroke severity (assessed according to the National Institute of Health Stroke Scale), and the localization, size and the outcome (modified Rankin scale) of stroke. Data were analyzed using univariate and bivariate statistical analysis.

Results: The study included 821 patients whose mean of age was 77.6 ± 8.2 years. Twenty-one per cent of patients received prior anticoagulant therapy, 30% of patients received prior antiplatelet therapy while 49% of patients were without prior antithrombotic therapy. Patients with prior anticoagulant therapy were the youngest (74.9 ± 7.9 , $p < 0.0001$) among the three groups. These patients had more often previous

ischemic strokes (42.8%, $p < 0.0001$), hyperlipidemia (51.4%, $p = 0.0002$) and chronic myocardial disease (77.5%, $p < 0.0001$). Patients without prior antithrombotic therapy were less often previously diagnosed with atrial fibrillation (59.8%, $p < 0.0001$) and they had the lowest risk for ischemic stroke (CHADS₂ = 2.9 ± 1.2 , $p < 0.0001$). Patients with prior anticoagulant therapy had better clinical outcomes with the lowest disability levels at discharge compared to patients in other two groups, but statistically significant difference was shown only in comparison to patients with prior antiplatelet therapy (mRS 3.8 ± 1.9 vs. 4.4 ± 1.6 , $p < 0.0001$). There were no statistically significant differences between the groups in terms of stroke severity, size and localization of stroke.

Discussion: Our study showed that patients with prior anticoagulant therapy had better clinical outcomes in comparison to patients with prior antiplatelet therapy. Antiplatelet therapy has already a less pronounced role in cardioembolic stroke prevention, and according to the results of our study, its significance can be further questioned.

Acknowledgments: None

MeSH/Keywords: stroke, atrial fibrillation, anticoagulants.

Poster code: B-30-87

POSTER TITLE: LAMOTRIGINE AND RS3812718 POLYMORPHISM – PRELIMINARY RESULTS

PhD candidate: Ivana Marković

Part of the thesis: Influence Of rs3812718 Polymorphism In The SCN1A Gene On Lamotrigine Efficacy In Patients With Partial Epilepsy

Mentor/s: Silvio Bašić, MD, PhD

Affiliation: University hospital Dubrava

Introduction: Despite of good prognosis, one third of epilepsy patients have bad response to antiepileptic drugs which is probably caused by inter-individual genetic variations. Single nucleotide polymorphism rs3812718 was showed to be associated with the drug resistance to the anti-epileptic drugs which act on voltage gated sodium channels.

Materials and methods: The genetic analyse was performed from 28 whole blood specimen obtained from patients after signed informed consent. The analysis was performed using TaqMan® SNP Genotyping Assay™, Applied Biosystems (Foster City, Ca, USA), Assay ID: C_25982233_10. For statistical analysis we have used program SPSS v. 10. Differences between groups have been analysed at the level of statistical significance of 5% ($p < 0.05$).

Results: There is no statistically significant difference between genotype distribution among genders. Patients with AA genotype have higher doses of lamotrigine in therapy than patients

with GG genotype and that despite adequate lamotrigine doses, have higher frequency of epileptic seizures per month than patients with other two genotypes ($p < 0.05$).

Discussion: We have found a positive correlation between AA genotype and resistance to lamotrigine therapy. Our results are concordant with other studies on this polymorphism which found positive correlation between AA and lower efficacy of phenytoin and carbamazepine in therapy. Since there is no published data on lamotrigine efficacy and this polymorphism in the group of patients with partial epilepsy, our results are the first to link rs3812718 polymorphism with possible resistance to the lamotrigine therapy in patients with partial epilepsy.

Acknowledgments:

MeSH/Keywords: epilepsy, lamotrigine, drug resistance

Poster code: B-30-174

1.3.
PUBLIC HEALTH AND HEALTH CARE
– RESEARCH ABSTRACTS

POSTER TITLE: INCIDENCE AND MORTALITY TRENDS OF MELANOMA IN CROATIA

PhD candidate: Jelena Barbarić, MD, MSc

Part of the thesis: Characteristics of incidence and mortality trends of malignant melanoma of the skin in Croatia and South-Eastern European countries

Mentor/s: Ariana Znaor, MD, PhD

Affiliation: Croatian National Institute of Public Health, Rockefellerova 7, 10000 Zagreb, Croatia

Introduction: Compared to other European countries from the GLOBOCAN 2008 database, Croatia had an intermediate melanoma incidence, with the ASR of 8.7/100 000 for men and 7.0/100 000 for women. However, with the ASR of 3.5/100 000 for men and 1.8/100 000 for women, it had the third highest male and fourth highest female mortality rate in Europe. The aim of this study was to analyze melanoma incidence and mortality trends in Croatia 1988-2008, compare them with the trends in other populations, and identify possible changes in the trends.

Materials and methods: Incidence data were obtained from the Croatian National Cancer Registry and the mortality data from the Croatian Bureau of Statistics. United Nations population estimates were used for calculating the age-specific rates. Age-standardized rates were calculated by the direct standardization method, using the world standard population as a reference. To estimate incidence and mortality trends, we performed joinpoint regression analysis.

Results: A significantly increasing incidence trend, with estimated annual percent change (EAPC) of 5.9% for men and 5.6% for women, was

observed over the whole 21-year period and no additional joinpoints were identified. The overall incidence increase between the first and the last five-year period was 149% for men and 130% for women. Significant increase in the mortality trend was observed, with EAPC of 3.0% for men and 2.4% for women. No joinpoints were identified. The overall increase in mortality between the first and the last five-year period was 45% for men and 50% for women.

Discussion: Melanoma rates in Croatia are steadily and markedly rising, with similar trends to those in the countries with lower/intermediate incidence. It is important to further investigate the more specific causes of the increasing trends, as well as to implement effective public policies targeting the melanoma burden.

Acknowledgments: We thank the staff of the Croatian National Cancer Registry for their help with data collection.

MeSH/Keywords: malignant melanoma, time trends, incidence, mortality, cancer registries, Croatia, South-Eastern Europe

Poster code: C-1-59

POSTER TITLE: EXPLORING THE RISK FACTORS FOR THE DEVELOPMENT OF ATOPIC DISEASES FROM MULTIPLE-SOURCE DATA

PhD candidate: Jelena Kovačić

Part of the thesis: Exploring the risk factors for the development of allergic respiratory diseases by Bayesian networks built on multiple-source data

Mentor/s: Veda Marija Varnai, MD, PhD and Anamarija Jazbec, dipl. ing. math., PhD

Affiliation: Institute for Medical Research and Occupational Health, Zagreb

Introduction: The aetiology of atopic diseases has not yet been adequately explained, in part due to high number of interrelated potential risk factors, each exerting low to moderate effect. Using data from multiple observational studies in the same analysis increases power, as is known from meta-analysis. However, only confounders measured across all studies can be accounted for in the standard meta-analysis. Recently, a new method for meta-analysis of partially overlapping data sets in survival analysis models has been proposed. We apply this method, adjusted meta-analysis, in research of risk factors associated with atopic diseases in logistic regression model, and compare it with the standard meta-analysis.

Materials and methods: We compared the methods using simulated data and epidemiological data from four cohorts comprising, in total, 791 subjects aged between 18 and 25. In this preliminary analysis, aimed to test methodology, objective atopy markers (positive skin prick test to at least one standard inhalatory allergen and/or elevated total serum immunoglobulin E level) were selected as an example of outcome variable, while age, sex, smoking status (reported in all four cohorts), urban/rural residence, and family atopy history (reported in two cohorts) were selected as examples of potential confounders. The effects of sex and age on the pres-

ence of atopy markers, adjusted for the smoking status, place of residence and parental atopy, were determined using standard and adjusted meta-analysis of odds ratios.

Results: In 1000 simulations with five fully measured and five partially measured cohorts and mean odds ratio (OR) of 2, mean ORs differed insignificantly between methods (2.03 vs 2.05). However, confidence intervals (CI) of odds ratios in standard meta-analysis were on average 15% wider than in adjusted meta-analysis. Real-life example showed similar ORs and CIs for gender. Males had significantly higher odds for objective atopy markers than females (OR 1.88, CI 1.29-2.84). The OR for age was 1.04 in both analyses, but the CI was 8% wider in standard meta-analysis (0.90-1.20 vs 0.91-1.19).

Discussion: The results indicate that the adjusted meta-analysis can discover associations of lower magnitude in logistic regression than standard meta-analysis models. Further application to larger number of variables and more complex models, such as Gaussian Bayesian networks, is to be investigated.

Acknowledgments:

MeSH/Keywords: atopy, meta-analysis, logistic regression

Poster code: C-1-84

POSTER TITLE: ANTHROPOMETRIC FOOT CHARACTERISTICS IN PRESCHOOL CHILDREN AGED BETWEEN 2 AND 7 YEARS

PhD candidate: Ozren Vrdoljak

Part of the thesis: Anthropometric measurement of growing feet in preschool children

Mentor/s: Associate Professor Mirjana Kujundžić Tiljak, MD, PhD

Affiliation: Children's Hospital Zagreb, Klaićeva 16, 10 000 Zagreb

Introduction: The anatomical specificity of children's feet change during their growth and development, and the foot therefore adapts to its function. When children start walking their feet begin to change shape, and they obtain their final shape when the feet stop growing. The outside shape of the foot is determined by anthropometric measurements: instep length, width, and height, heel width and toe length. Foot length is the basic unit of measurement for monitoring the development and growth of the foot. The existing standards of foot length and shape are not suitable for our population.

Materials and methods: The study will include preschool children between 2 (1.50-2.49) and 7 (6.50-7.49) years of age in Croatia who do not have any congenital or acquired deformities of the foot. The sample will consist of 150 female and 150 male children, totaling to 300 feet in each age group. Some of the data was collected as a part of the project "Anthropometric Measurement of Growing Feet" (code 0072007/2001 of Croatia's Ministry of Science and Technology), a pilot study on a random sample of preschool children between 1.5 and 7.5 years of age. The rest of the data will be a supplement to the sample for each age group. The methodology was developed during the project "Anthropometric Measurement of Growing Feet". The measure-

ment technique will be standardized. Children's feet will be measured without shoes on a specially constructed device using a sliding caliper with a 15 cm range, a tape measure and a pedometer to determine the valgus of the heel.

Results: Previous measurements were performed on a sample of 10 female and 10 male children, totaling to 20 feet in each age group, totaling to 120 feet in 6 age groups of preschool children between the ages of 2 and 7. The Egyptian foot was found in 90% of the children measured, the Greek foot in over 6%, while the least number of children had a square foot.

Discussion: Since the obtained test results were based on a small sample size, we cannot come to a conclusion about the researched growth parameters or about foot development. According to the previous results of this study, it can be concluded that foot development in all age and gender groups demonstrated the expected growth rate, which can be presented by an exponential graph.

Acknowledgments:

MeSH/Keywords: growth and development, anthropometry, reference values

Poster code: C-1-97

POSTER TITLE: POLYMORPHISMS IN CYTOKINE GENES INFLUENCE DEVELOPMENT OF 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, MD, PhD

Affiliation: Institute for Medical Research and Occupational Health, Zagreb, Croatia

Introduction: Cytokine gene polymorphisms TNF α -308G>A and -238G>A, IL1 α -889C>T and IL10 -1082G>A could act as genetic risk factors for the development of atopic respiratory diseases.

Materials and methods: Subjects were 439 students (median age 19 years) from Zagreb University. They filled out the modified ISAAC questionnaire. Skin prick test (SPT) to standard inhalatory allergens and buccal swab collection were performed. Genetic polymorphisms TNF α -308G>A, TNF α -238G>A, IL1 α -889C>T and IL10-1082G>A were genotyped using PCR-based technique. Total IgE was measured using ELISA method, values above 150 kIU/l were considered elevated. Subjects with atopic rhinitis (AR) or atopic asthma (AA) were defined with positive SPT to at least one tested inhalatory allergen and the report of nasal symptoms or asthma symptoms, respectively. Associations of polymorphisms with occurrence of AR and AA, positive SPT, elevated IgE, reported nasal symptoms and asthma symptoms were determined using Pearson's chi-squared test.

Results: There were 77 subjects with atopic respiratory diseases (63 with AR, 3 with AA and 11 with both conditions) while 362 subjects had no atopic respiratory disorder and served

as controls. In the whole sample, there were 92 (21%), 13 (3%), 201 (46%) and 340 (77%) carriers of TNF α -308G>A, TNF α -238G>A, IL1 α -889C>T and IL10-1082G>A polymorphisms, respectively. Higher proportion of carriers of TNF α -238G>A polymorphism was found in subjects with AR and subjects with either AR or AA compared to controls (7.4% in subjects with AR vs. 2.3% in control subjects, $p=0.0331$, and 7.0% in subjects with AR and/or AA vs. 2.4% in control subjects, $p=0.043$). There were no other significant associations between polymorphisms and studied outcomes.

Discussion: Results indicate that TNF α -238G>A polymorphism is a risk factor for occurrence of AR. Further analysis will investigate the influence of genetic polymorphisms TNF α -308G>A, TNF α -238G>A, IL1 α -889C>T and IL10-1082G>A on atopic respiratory diseases while controlling for non-genetic factors of individual susceptibility (age, gender, body mass index), as well as lifestyle and environmental factors (smoking status and area of residency).

Acknowledgments: -

MeSH/Keywords: atopy, rhinitis, asthma, gene polymorphism, cytokine

Poster code: C-1-143

POSTER TITLE: FIRST YEAR NURSING STUDENTS' ATTITUDES TOWARD NURSING AS A PROFESSION

PhD candidate: Snježana Čukljek

Part of the thesis: Correlation of Formal Education and Nursing Students' Attitudes Toward Nursing as a Profession

Mentor/s: Professor Vesna Jureša, MD, PhD

Affiliation: University of Applied Health Studies, Department of Nursing

Introduction: Nurses constitute the largest group of health care professionals, they perform complicated and demanding tasks and even though the roles and responsibilities of nurses have significantly changed over the past twenty years they are still being stereotyped. Nursing is identified as caring for the patient and nurses are associated with the maternal role and feminized stereotypes. Previous studies have shown that the changes in nursing students' attitudes are expected to occur during the course of their study as a result of the educational content. One of the aims of the research was to determine the attitudes of students toward nursing at the University of Applied Health Studies at the beginning of their study program.

Materials and methods: At initial nursing classes, 115 full-time and 151 part-time nursing students anonymously completed Nursing image questionnaire (Toth, 1998). Before the implementation, the questionnaire was translated and cross-culturally adopted. Four factors were derived through factor analysis: nursing roles and responsibilities, professionalism, values, and nursing stereotypes in the society. We compared the main factors' results of the two groups of students, and used the Mann-Whitney U test to compare the differences. A p-value of <0.05 was considered to indicate a statistical significance.

Results: The average age of full-time nursing students (N=115) was 19.6 yrs, with 5% of them

having previous working experience. Mean value for values in nursing was 21.43 (range 13-28) SD 2.67, mean value for nursing stereotypes in the society was 23.04 (range 15-33) SD 2.87, mean value for the nursing roles and responsibilities was 46.33 (range 30-60) SD 5.33, and mean value for the professionalism was 18.53 (range 8-25) SD 2.70. The average age of part-time nursing students (n=151) was 31.7 yrs, with the average work experience of 11.5 yrs. Mean value for values in nursing was 21.30 (range 15-27) SD 2.48, mean value for the nursing stereotypes in the society was 24.24 (range 15-32) SD 3.36, mean value for the nursing roles and responsibilities was 47.63 (range 30-60) SD 5.42, and mean value for the professionalism was 17.21 (range 10-23) SD 2.70.

Discussion: The results show a statistically significant difference in attitudes about nursing roles and responsibilities, professionalism, and nursing stereotypes in the society among full-time and part-time students at the beginning of their study program. There was no statistically significant difference in attitudes about values in nursing.

Acknowledgments:

MeSH/Keywords: nursing, education, attitudes

Poster code: C-2-69

POSTER TITLE: SPORT INJURIES AMONG PROFESSIONAL SOCCER AND HANDBALL PLAYERS AND THEIR MENTAL HEALTH: THE PILOT STUDY

PhD candidate: Tomislav Madžar

Part of the thesis: Psychological predictors of sport injuries among professional soccer and handball players

Mentor/s: Professor Neven Henigsberg, MD, PhD and Milan Milosevic, MD, PhD

Affiliation: MD

Introduction: In order to plan preventive measures to be as accurate as possible it is necessary to know information why an athlete in a particular situation risking injury and how a particular injury occurs. For efficient prevention of sports injuries is necessary to take into account psychological characteristics of athletes.

Materials and methods: This pilot study is a part of prospective cohort study that is conducted during a 2013/2014 sports season and includes all professional players with the first team contract in the Croatian football and handball league. Athletes who are acutely injured and who are not able to actively participate in the competitions are not included in the study. A stratified sample of 63 male athletes (32 football players and 31 handball players) has been selected for assessment. They were surveyed during preparation period before the beginning of the season and are still under monitoring during season for occurrence of newly developed sports injuries. Seriousness of the injury was assessed depending on the length of non-participation in sports activities which was obtained from the history of attending a sporting event through the course of the study. Psychological characteristics were assessed with General Anxiety Disorder Scale (GAD-7), Self-report Depression Scale for Research in the General Population (CES-D Scale) and questions about impulsive behaviour.

Results: 45 (71,4%) of athletes experienced sports injuries and 29 (46,0%) some acute or chronic disease in previous 12 months. Athletes who had acute/chronic disease in previous 12 months had significantly higher CES-D score ($15,03 \pm 9,53$ vs. $10,13 \pm 5,27$ $P=0,014$) although this difference was not significant between those players who suffered only injuries ($P=0,728$). Differences in GAD-7 scores and impulsive behaviour were not significant. Significant negative correlation was between CES-D score and duration of professional sport engagement ($r=-0,270$ $P=0,039$) indicating that those players who have been in professional sport longer have lower depression level

Discussion: Findings from this pilot study suggests that mental health of professional players differs regarding perception of their injury or acute/chronic disease. Athletes take diseases more seriously compared to injuries which have higher impact on their depression levels.

Acknowledgments:

MeSH/Keywords: professional athletes, soccer, handball, psychological characteristics, sports injuries

Poster code: C-3-149

2. RESEARCH PROPOSALS

2.1. BASIC MEDICAL SCIENCES – RESEARCH PROPOSALS

POSTER TITLE: SEXUAL DIMORPHISM IN EXTRAORBITAL LACRIMAL GLANDS IN SF-1 KNOCKOUT MICE

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. SD of mice extraorbital lacrimal gland is well documented. Also, a major testosterone effect on the formation of male and female GL is proven. It remains unclear whether SD is solely determined by hormonal factors. Steroid factor-1 (SF-1) is nuclear receptor essential for steroid organs embryonic survival. Knockout Sf-1 gene (Sf-1 KO) mice are born without gonads and adrenal glands and therefore are not exposed to sex hormones. In this study we will use GL of Sf-1 KO male and female mice.

Hypothesis: In Sf-1 KO mice, stereological measurements and comparison of male and female extraorbital lacrimal gland will demonstrate the existence of sexual dimorphism. Higher androgen receptor expression is expected in mice that received testosterone substitution therapy.

Aims: The aim of this study is to investigate whether SD in mouse GL is present if hormonal effects are excluded.

Materials and methods: This study will include 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 (0.1 mg TP sc) 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 in corn oil (400µg/ml

hydrocortisone, 40ng/ml dexamethasone and 25 ng/ml of fludrocortisone acetate). 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 to the subaxillary region of Sf-1 KO pups with transdermal puncture. The animals were sacrificed after 6 months, GL removed and placed in Bouin's fixative. The tissue will be subjected to standard histological procedure. Paraffin sections will be dyed with H-E, modified method by Masson and PAS method. Stereological and immunohistochemical analysis will be done.

Expected scientific contribution: The model of Sf-1 KO mice is unique because these animals are not exposed to sex hormones. The results of this study would provide new insights on the impact of sex chromosomes on development of SD. In the light of present knowledge that SD is more pronounced in men than previously thought, this study could contribute to understanding the causes of SD and perhaps turning to "sex related medicine" in future.

Acknowledgments: I would like to thank to my mentors and to all employees of 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: A-3-100

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: Associate 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.

Hypothesis: GABA neurotransmitter is involved in regulation of the cervical mucus secretion.

Aims: The aim of this research is to explain a part of the mechanism of cervical mucus secretion according to the proposed model of the participation of GABA in the regulation of mucus secretion.

Materials and methods: We will analyze histological structure and secretory activity of the

endocervical glands and perform immunohistochemical detection and localization of the molecules involved in the GABA pathway of mucus secretion regulation (GABAAR, GAD, VGAT, ER α , etc.). 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 will be performed on the samples of the healthy human uterine cervix obtained after therapeutic operative procedures (usually hysterectomy).

Expected scientific contribution: The expected scientific contribution of this research is to prove the role of GABA in the regulation of the cervical mucus secretion as a scientific novelty. This could give new insights into the mechanisms of the regulation of intracellular signal transduction and deepen our understanding of the role of the cervical mucus in women fertility. This will provide a new potential to develop diagnostic, therapeutic and prevention strategies that will help in the struggle against the infertility, one of the major health and social problem nowadays.

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

MeSH/Keywords:

Poster code: A-3-136

POSTER TITLE: THE EFFECT OF BPC 157 ON FRACTURE HEALING, ECTOPICAL BONE AND HETEROTOPIC OSSIFICATION IN THE RAT

PhD candidate: Neven Starčević, MD

Part of the thesis: The Effect Of BPC 157 On Heterotopic Ossification And Fracture Healing In The Rat

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

Affiliation: Zagreb School Of Medicine, University Hospital

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. Given the known beneficial effects of BPC 157 on ligament, tendon and muscle healing and it's known anti-inflammatory effects, coupled with the fact that there is no medicamentous therapy for developed HO it would be useful to investigate the effect of BPC 157 on HO in rats.

Hypothesis: The application of BPC 157 will prevent the development of heterotopic ossification, enable the resorption of developed heterotopic ossification, enable the resorption of ectopic bone, and simultaneously improve fracture healing.

Aims: Prevent the development of heterotopic ossification, improve fracture healing, improve the motor function of the leg.

Materials and methods: In this study we will investigate the effects of pentadecapeptide BPC 157 on heterotopic ossification in rats using two models. The first one consists of bone marrow aspiration from the iliac crest and injection into the quadriceps muscle. The second one involves

removing a corticospongious cylinder from the iliac crest, and implantation into the quadriceps muscle of the hind leg. Pentadecapeptide BPC 157 dissolved in saline solution will be applied in doses of 10 µg/kg i 10 ng/kg PO according to the experimental group. Throughout whole duration of experiment we will conduct functional measurements (SFI—sciatic functional index, MFI- modified motor function index, shortening of the leg). After euthanasia, X rays will be performed on the donor site and the locus of the induced HO, afterwards the samples will be processed for histology, and the mass of soleus muscle will be taken as a measure of the leg function.

Expected scientific contribution: according to the duration the animals will be divided into 4 series (from 1 to 4 weeks). In the post-treatment arm of the experiment animals will be allocated according to the dose in one of two groups: BPC157 µg, and drinking water

Acknowledgments:

MeSH/Keywords: pentadecapeptide BPC 157, heterotopic ossification, rat

Poster code: A-4-16

POSTER TITLE: HEPATOPROTECTIVE EFFECT OF BPC 157 ON MODEL OF BILIARY CIRRHOSIS IN RATS

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: Long-term biliary obstruction causes liver damage resulting in liver cirrhosis and liver failure. Despite numerous previous studies the problem of biliary cirrhosis therapy isn't yet resolved. Pentadecapeptide BPC 157 has already proved hepatoprotective effect in liver damage caused by alcohol, insulin and non-steroidal inflammatory drugs.

Hypothesis: Pentadecapeptide BPC 157 is hepatoprotective agent and reduces the development of liver fibrosis on model of surgically induced biliary cirrhosis in rats.

Aims: Preservation of liver parenchyma, biochemical and functional liver recovery, reduced collagen production in pentadecapeptide BPC 157 treated animals.

Materials and methods: In our experiment we'll use male Wistar rats weight 180-200 g. Animals will be randomized in pentadecapeptide BPC 157 and control group. After the operation, the animals will receive pentadecapeptide 157 daily, dissolved in saline at a dose of 10µg/kg and 10ng/kg intraperitoneally or orally. The control group will receive the equivalent volume of 0.9% NaCl. After a time interval of 2, 4, 6 and 8 weeks the animals will be sacrificed. Blood samples will be taken for measurement liver enzymes (AST,

ALT, GGT, ALP), bilirubin, PT and albumin serum levels as indicators of liver function. We'll measure the body weight, spleen mass, liver mass with and without expanded main bile duct and liver volume. Liver tissue samples will be taken, fixed and embedded in paraffin blocks. Further histopathological analysis will be performed on hematoxylin-eosin, Gomori's, Mallory stain and immunohistochemical analysis α SMA. The fibrosis degree (0-6) and liver necroinflammatory activity (0-18) will be determined by Ishak classification. Liver fibrosis extent will be assessed morphometrically as collagen area percentage within microscopic field. Hepatocyte proliferative ability will be determined according to the average number of double nuclei in five HPF within the sample.

Expected scientific contribution: The contribution of our research is to define pharmacological effect of pentadecapeptide BPC 157 on liver fibrosis

Acknowledgments: Professor Predrag Sikirić, Assistant Professor Marijana Ćorić

MeSH/Keywords: Common bile duct ligation, biliary cirrhosis, pentadecapeptide BPC 157

Poster code: A-4-28

POSTER TITLE: EFFECTS OF PENTADECAPEPTIDE BPC 157 IN AMINOGLYCOSIDE NEPHROTOXICITY IN THE RATS

PhD candidate: Ivan Vukoja

Part of the thesis: Pentadecapeptide BPC 157 has Nephroprotective Effect in Aminoglycoside Nephrotoxicity in the Rats

Mentor/s: Professor Predrag Sikirić, MD, PhD

Affiliation: University of Zagreb – School of Medicine, County Hospital Požega

Introduction: In this research we will investigate the effect of pentadecapeptide BPC 157 on aminoglycoside nephrotoxicity in the rats after application of high dose of gentamicin 100mg/kg body weight. We assume that BPC 157 is causing nephroprotective effect by modulating overstimulative activity of iNOS in aminoglycoside nephrotoxicity. Therefore we will also apply various combinations of L-NAME and L-arginin with BPC 157 and gentamicin.

Hypothesis: Pentadecapeptide BPC 157 has a nephroprotective effect in aminoglycoside nephrotoxicity in the rats.

Aims: General aim is to prevent or mitigate aminoglycoside nephrotoxicity by application of pentadecapeptide BPC 157 in aminoglycoside nephrotoxicity in the rats. Specific aims are to prevent or reduce acute tubular necrosis, to maintain glomerular filtration and kidney function by application of pentadecapeptide BPC 157, and to demonstrate that the effect of pentadecapeptide BPC 157 is mediate by NO-system.

Materials and methods: Animals: We will use male Wistar albino rats, body weight 150-200 grams. Rats will be randomized in groups, 10 rats per group, with totally 17 groups. Every rat will be situated in metabolic cage with free access to water and food. Drugs: Gentamicin (gentamicin Belupo) in dose 100 mg / kg of body weight will be administered to rats in all groups. Pentadeca-

peptide BPC 157 in attributable groups will be administered intraperitoneally (10 µg/kg and 10 ng/kg) and per orally (0,16 µg/ml and 0,16 ng/ml at 12 ml water ad libitum per day) in attributable groups. L-NAME (5 mg/kg intraperitoneally), L-arginin (200 mg/kg intraperitoneally) and adequate combination will be administered in attributable group. Experimental protocol: During the research clinical appearance will be measured and scored (1-3) by two independent persons. Daily diuresis will be measured in metabolic cage. For biochemical analysis rats will be narcotized by ketamine (100 mg/kg) and after laparotomy blood will be sampled by venepunction from vena cava. Serume levels of creatinine, urea, potassium, sodium, calcium and magnesium will be analyzed. After that rats will be sacrificed with double dose of ketamine and kidneys without perirenal tissue will be taken. Relative mass of kidney will be measured and macroscopic appearance will be photodocumented. Finally, kidney samples will be patohystologically analyzed.

Expected scientific contribution: Prove nephroprotective effect of pentadecapeptide BPC 157 in aminoglycoside nephrotoxicity in the rats.

Acknowledgments:

MeSH/Keywords: pentadecapeptide BPC 157, aminoglycoside nephrotoxicity, rat

Poster code: A-4-105

POSTER TITLE: EFFECT OF RETROBULBAR APPLICATION PENTADECAPEPTID BPC ON EFFECT OF RETROBULBAR APPLICATION L-NAME

PhD candidate: Mirna Zlatar, MD

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

Mentor/s: Professor Predrag Sikirić, MD, PhD

Affiliation: University of Zagreb School of Medicine, 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.

Hypothesis: Retrobulbar application of BPC 157 prevents / removes vasoconstrictor activity retrobulbar application of L-NAME.

Aims: To investigate the effect of retrobulbar application of human gastric pentadecapeptide BPC 157 on vasoconstrictive effect of L-NAME on retinal arteries in rat.

Materials and methods: 54 Wistar rats, 3 groups. After retrobulbar application of L-NAME (2mg/kg), we monitored the effects of retrobulbar application of BPC 157 (2µg/kg, 2 ng/kg) on retinal arteries. Fundus of the eye was re-

corded with the USB microscope camera before retrobulbar application of L-NAME and BPC, 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 stained.

Expected scientific contribution: Retrobulbar application of BPC 157 prevents / removes the effect of vasoconstriction caused by retrobulbar application of L-NAME, and thus prevents loss of vision.

Acknowledgments:

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

Poster code: A-4-115

POSTER TITLE: CHANGES IN GENE STRUCTURE AND PROTEIN EXPRESSION OF DVL1, DVL2, DVL3 AND TRANSCRIPTION FACTORS TCF1 AND LEF1 IN ASTROCYTIC BRAIN TUMORS

PhD candidate: Anja Kafka, BS, MS

Part of the thesis: Changes in Gene Structure and Protein Expression of DVL1, DVL2, 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, University of Zagreb School of Medicine

Introduction: Astrocytomas are the most common and deadliest form of primary brain tumors. Despite recent advances in diagnosis and therapies the prognosis and survival times remains poor. WHO classified astrocytomas into four clinical grades on the basis of their histology and prognosis. Wnt signaling pathway is one of the basic mechanisms of cell signaling as evidenced by its participation in a numerous processes in the cell. New insights showed that molecular key components of the wnt signaling pathway play crucial roles in the process of tumorigenesis of the central nervous system.

Hypothesis: DVL1, DVL2, DVL3, TCF1 and LEF1 are involved in the formation and malignant progression of astrocytic brain tumors and changes in the genes, and increased expression of the protein indicate a higher degree of malignancy.

Aims: We aim to investigate the incompletely understood role of Dishevelled (DVL) gene family, which is considered to be the central hub of wnt signaling. We also want to clarify the role that transcription factors TCF1 and LEF1, the central mediators of transcription of wnt signaling pathway, have in the development and progression of astrocytic brain tumors.

Materials and methods: Scientific research will be conducted on tumor tissue, blood and paraffin sections of 80 patients with astrocytic brain tumors (15 pilocytic astrocytoma, 15 diffuse astrocytoma, 15 anaplastic astrocytoma, 35 glioblastoma). Genetic changes will be analysed by PCR/loss of heterozygosity (LOH)/microsatellite instability (MSI) methods using Spreadex electrophoresis. Protein expressions and localizations will be analyzed by immunohistochemistry.

Expected scientific contribution: Since the genetic profile of astrocytic brain tumors is still unclear the results of the proposed research could contribute to the elucidation of the mechanisms of initiation and progression of these tumors. More precise, the results could contribute to a discovery and better understanding of the role of DVL gene family and transcription factors TCF1 and LEF1 which could be responsible for the onset and progression of astrocytic brain tumors.

Acknowledgments:

MeSH/Keywords: wnt signaling pathway, astrocytic brain tumors, Dishevelled (DVL), TCF1, LEF1

Poster code: A-6-85

POSTER TITLE: THE ANALYSIS OF SERUM ANTIBODIES FOLLOWING AN ADMINISTRATION OF RECOMBINANT HUMAN BMP6 (OSTEOGROW) IN RATS AND PATIENTS WITH A BONE FRACTURE

PhD candidate: Mehmed Jamakosmanović, MD

Part of the thesis: Immunogenicity of BMP6 administration in animals and humans

Mentor/s: Professor Slobodan Vukičević, MD PhD

Affiliation: Laboratory for Mineralized Tissue and Centre for Proteomics, School of Medicine, University of Zagreb, Croatia, Department of Orthopaedic Surgery University Clinical Centre Sarajevo

Introduction: Approximately 6 million fractures are sustained in EU each year with up to 11 % resulting in delayed or impaired healing. A significant need for development of a novel osteogenic device that will improve fracture healing, with no inflammatory response and low dosage and cost, as OSTEOGROW BMP6 osteogenic device offers. Immunogenicity of BMP6 administration to animals and humans has not been thoroughly investigated and will be assessed in this research, as part of OSTEOGROW project.

Hypothesis: A single local administration of rh-BMP6 at the fracture site in patients and rats will induce an immunogenic response. Additionally, the neutralizing or non-neutralizing antibodies will be transient and will not significantly affect any of the pleiotropic BMP6 functions.

Aims: To characterize immunogenic response to rhBMP6 therapy in OSTEOGROW clinical trial Phase I in patients with distal radius fracture and in rats with induced femur fracture.

Materials and methods: I Pre-clinical Study will be conducted on Sprague Dawley laboratory rats, by testing appearance of BMP antibody in circulation after a single subcutaneous administration of BMP6, using indirect ELISA and C2C12 Luciferase assay. II Pre-clinical Study will be conducted on 2 groups of laboratory rats, with induced femoral fracture. The rats will be randomly assigned into groups: A) control (n=8)

and B) group receiving osteogenic device at fracture site (BMP6 carrier) (n=8). The effects on fracture healing will be monitored by μ CT after four weeks. III Clinical Study will include 12-15 subjects undergoing distal radius fracture surgical procedure. A single dose of 500 μ g BMP6 in WBCD will be administered intraoperatively to the fracture site. Potential development of antibodies toward rhBMP6 will be assessed before and after operation, using Western blot analysis and C2C12 cell assays.

Expected scientific contribution: First study to extensively characterize potential immunotoxic effects of newly induced antibodies following application of rhBMP6. It will describe new in vitro assays and in vivo models for testing short and long term toxic effects of preclinical and clinical use of rhBMP6.

Acknowledgments: I would like to acknowledge my mentor professor Slobodan Vukičević for his support in preparation of this thesis, as well as all the staff of the Laboratory for Mineralized Tissue and Centre for Proteomics.

MeSH/Keywords: OSTEOGROW, bone morphogenetic protein 6 (BMP6), whole blood-derived coagulum device (WBCD), BMP6 induced neutralizing antibodies, human radius fracture, rat femur fracture.

Poster code: A-6-95

POSTER TITLE: ASSOCIATION OF DNA SINGLE NUCLEOTIDE POLYMORPHISMS WITH DEVELOPMENTAL DYSPLASIA OF THE HIP

PhD candidate: Tomislav Čengić

Part of the thesis: Association of DNA single nucleotide polymorphisms with developmental dysplasia of the hip

Mentor/s: Vladimir Trkulja, Robert Kolundzic, Sandra Kraljevic Pavelic

Affiliation: University of Zagreb, School of Medicine, University Hospital Centre Sestre Milosrdnice, University of Rijeka, Department of Biotechnology

Introduction: Developmental dysplasia of the hip (DDH) is a congenital malformation that increases the risk of severe adult hip osteoarthritis (OA). Just like OA, DDH has a strong genetic component. So far, association studies have identified several DDH-susceptibility genes within transforming growth factor β (TGF- β) superfamily. Vitamin D-binding protein gene VDBP polymorphisms as well as vitamin D receptor (VDR) gene polymorphisms have already been associated with growth complications and bone and joint disease.

Hypothesis: Our hypothesis is that propensity to DDH is in great way associated with molecular pathway determined by genome.

Aims: Study aim is to test potential associations between TGF- β 1 signal sequence, IL-6 promoter region and VDBP and VDR genes SNPs, with DDH.

Materials and methods: To test the hypothesis that the polymorphisms are associated specifically with DDH, in the current case-control study 150 consecutive adult patients with severe hip OA secondary to DDH (“cases”) and 100 consecutive adults with severe hip OA not related to DDH (“controls”) are genotyped at these loci.

Expected scientific contribution: To indicate a possibility of TGF- β 1, IL-6, VDR and VDBP interaction in DDH pathogenesis.

Acknowledgments:

MeSH/Keywords: Developmental dysplasia of the hip, Single nucleotide polymorphisms, TGF- β 1, IL-6, VDBP, VDR.

Poster code: A-6-99

POSTER TITLE: THE ROLE OF DIHYDROPYRIMIDINE-DEHYDROGENASE AND UDP-GLUCURONYL TRANSFERASE POLYMORPHISMS IN FLUOROPYRIMIDINE AND IRINOTECAN TOXICITY

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: Associate Professor Nada Božina, MD, PhD

Affiliation: University Hospital Centre Zagreb, Department of Laboratory Diagnostics, Department of Oncology

Introduction: Toxic cytostatic treatment including fluoropyrimidines (5-fluorouracil, capecitabine) and irinotecan is foundation of therapy in oncology. Dihydropyrimidine-dehydrogenase (DPD) is the rate-limiting enzyme of the fluoropyrimidine metabolism, responsible for bulk degradation of injected drug (up to 80%). Irinotecan is to similar extent inactivated by glucuronidation through UDP-glucuronyl transferase (UGT1A1). Deficiency of aforementioned enzymes elevates drug level, and increases risk for toxicity. DPD-gene (DPYD) and UGT-gene contain polymorphisms with potentially lethal functional consequences, but risk-level varies considerably. Fluoropyrimidine and irinotecan-treated patients will be sampled, and DPYD and UGT polymorphisms will be analyzed.

Hypothesis: Dihydropyrimidine-dehydrogenase polymorphisms DPYD*2A (IVS 14 1 G>A) and M166V (496 A>G) are more frequent among patients with fluoropyrimidine toxicity than in fluoropyrimidine-tolerant patients. UDP-glucuronyl transferase polymorphism UGT1A1*28 is more frequent among patients with irinotecan toxicity.

Aims: We will test influence of the aforementioned polymorphisms on development of chemotherapy toxicity. Frequency of the polymorphisms among patients with fluoropyrimidine and irinotecan toxicity will be determined and

compared with patients treated with same drugs without toxic complications.

Materials and methods: Test-group will contain patients experiencing high grade toxicity of fluoropyrimidine and/or irinotecan (grade III and IV according to CTCAE v4.0 - Common terminology criteria for adverse events v 4.0). Patients receiving same drugs, without or with minimal toxic consequences (grade I and II), will be recruited as control-group. Patients will be treated with cytostatic therapy in Department of Oncology, University Hospital Centre Zagreb. Genotyping of aforementioned polymorphisms of DNA isolated from patient whole blood samples (3ml) will be performed in Department of Laboratory Diagnostics, Unit for pharmacogenomics, University Hospital Centre Zagreb, by means of real-time PCR methods.

Expected scientific contribution: Data on polymorphisms of DPYD and UGT1A1 and their relation to chemotherapy toxicity in Croatian cancer-patients are not available. Study may provide clinically significant insight in pharmacogenomic characteristics relevant for individualization of cancer-therapy.

Acknowledgments:

MeSH/Keywords: DPYD, UGT1A1, 5-FU, irinotecan, chemotherapy, toxicity, pharmacogenomics

Poster code: A-6-131

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, BSc

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, PhD

Affiliation: University Hospital

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.

Hypothesis: Examining the micronucleus frequency among young couples who had one or more pregnancies and/or children with Down syndrome, the susceptibility to chromosome malsegregation during the mitotic division of peripheral blood lymphocytes will be determined. Assuming that the same susceptibility to chromosome malsegregation exists in gametes, micronucleus frequency could be proposed as a biomarker for risk assessment of numerical chromosomal aberrations in subsequent pregnancies.

Aims: The aim of this study is to evaluate the application of micronucleus assay and fluorescence in situ hybridization in estimation of chro-

mosome instability and occurrence of regular form of Down syndrome within young couples. According to the results, significance of micronucleus assay as a prognostic biomarker for assessment of risk of aneuploidies in subsequent pregnancies would be determined.

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 in 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.

Expected scientific contribution: Considering the fact that it is still not known the cause of appearance of such a large number of trisomy 21 pregnancies among young mothers, 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: A-6-139

POSTER TITLE: THE RISK OF BORRELIA BURGdorFERI INFECTION FOLLOWING TICK BITE IN PRISTINA REGION, KOSOVO

PhD candidate: Albina Ponosheci-Biçaku MD, PhD candidate

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

Mentor/s: 1.Assoc.Professor Goran Tešović, MD, PhD, 2.Professor Salih Ahmeti, MD, PhD

Affiliation: 1.University Hospital for Infectious Diseases, Zagreb University of Zagreb, School of Medicine 2.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 manifestations can vary from subclinical – asymptomatic through mildly symptomatic to severe forms with significant organ damage resulting in death in severe Lyme carditis cases. Lyme borreliosis 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.

Hypothesis: 1. Lyme borreliosis is endemic infection in Prishtina region. 2. The seroprevalence of Lyme borreliosis in Prishtina region is low. 3. Occupational and recreational activities have influence on incidence of Lyme borreliosis after a tick bite.

Aims: The main objective is to define the risk of developing Lyme borreliosis after a tick bite in Kosovo.

Materials and methods: The study will be conducted during a one-year-period (January-December 2015) and will include all seronegative subject older than 18 years of age recently bitten by Ixodes ticks in the region of Prishtina, Kosovo. The risk of acquiring Lyme borreliosis after a tick bite will be assessed through serologic testing using ELISA. All subjects included in study will be followed up for the next six months.

Expected scientific contribution: The assessment of the risk of acquisition Lyme borreliosis after a tick bite in Prishtina region, Kosovo will be done according to the results of present study. The results of our research will complete the knowledge on the epidemiology of Lyme disease in southeastern Europe.

Acknowledgments: Clinic of Infectious Diseases at University Clinical Center of Kosovo, National Institute of Public Health of Kosovo

MeSH/Keywords: tick bite, Lyme borreliosis, Kosovo

Poster code: A-8-18

2.2.
CLINICAL MEDICAL SCIENCES
– RESEARCH PROPOSALS

POSTER TITLE: SYNERGISTIC EFFECT OF LOCAL ANESTHETICS ON HEMODYNAMIC CHANGES DURING PARAVERTEBRAL BLOCK

PhD candidate: Miroslav Župčić, MD

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: Regional anesthesia is a technique when the injection of local anesthetic near a nerve or spinal cord inhibits pain, sensation and motor stimuli. 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.

Hypothesis: The application of one local anesthetic solution compared to the solution with two local anesthetics in the paravertebral block causes smaller hemodynamic changes.

Aims: Overall objective: To determine which of the two solutions of local anesthetics in paravertebral block has the most favorable effect regarding hemodynamic and analgesic activity. Specific objectives: To monitor Stroke Volume Variation (SVV) within and between groups of patients, monitor changes in SVV depending on the time of injection of local anesthetic within the same group, to determine the existence of differences in reimbursement volume crystalloid between groups, establish the need for the application of vasoactive drugs and achieve satisfactory postoperative analgesia.

Materials and methods: The study has been planned as a prospective, randomized double-

blind study. 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 by measuring by the visual analgesic scale (by Rawal) every 3 hours with the application of appropriate analgesic measures.

Expected scientific contribution: Determine the optimal solution of one or two local anesthetics regarding hemodynamic and analgesic stability, which would allow wider use of regional anesthesia.

Acknowledgments:

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

Poster code: B-1-2

POSTER TITLE: INTRAPERITONEAL INSUFFLATION OF LEVOBUPIVACAINE FOR POSTOPERATIVE ANALGESIA IN LAPAROSCOPIC CHOLECYSTECTOMY - DETERMINING THE EFFECTIVE DOSE OF LEVOUPIVACAINE FOR YOUNG ADULT POPULATION AND ELDERLY POPULATION

PhD candidate: Vanja Crnica, MD

Part of the thesis: Intraperitoneal insufflation of levobupivacaine for postoperative analgesia in laparoscopic cholecystectomy - determining the effective dose of levobupivacaine for young adult population and elderly population.

Mentor/s: Professor Mladen Perić, MD PhD

Affiliation: Mentor: University Hospital Centre Zagreb, Department of Anesthesiology and ICU. Candidate: University Hospital Merkur, department of Anesthesiology and ICU

Introduction: Pain following laparoscopic cholecystectomy is multifactorial, but the dominant source is the peritoneum. Intraperitoneal application of local anesthetics is an efficient analgesic modality, with best results achieved when local anesthetics are nebulized prior to insufflation. The exact effective dose, ED₉₅ required to achieve adequate analgesia is unknown. Pharmacokinetics and pharmacodynamics of local anesthetics change with age.

Hypothesis: The ED₉₅ of intraperitoneally insufflated local anesthetics for postoperative analgesia following laparoscopic cholecystectomy will be significantly lower for the elderly patients.

Aims: A) Determine ED₉₅ of levobupivacaine effective for postoperative analgesia after laparoscopic cholecystectomy for two groups of subjects – younger adults (18 – 45 yr) and the elderly (> 65yr). B) Check for a difference between ED₉₅ for the two groups by calculating the potency ratio.

Materials and methods: “Bias coin design” study. Subjects: Sequentially allocated patients undergoing elective laparoscopic cholecystectomy. Two groups of patients: A) 50 younger adults aged 18 – 45. B) 50 elderly patients aged >65. Research plan: The same basic anesthetic and surgical technique will be applied for all patients. All patients will be insufflated with a designated quantity of nebulized 0,5% levobupi-

vacaine towards the end of surgery. The initial dose applied to the first patient in each of the two groups of patients will be 50 mg of levobupivacaine, with subsequent increments of 5 mg, depending on the outcome of the previous patient. If the outcome is negative, the following patient will receive a larger dose. If the outcome is positive, the following patient will receive a smaller dose with probability of 5%, or the same amount will be insufflated with probability of 95%. Variables: 1.) Primary outcome: Abdominal pain at rest 4h postoperatively, measured using the visual-analogue scale: a. Positive outcome – no pain to mild pain = VAS value 0-3. b. Negative outcome – moderate pain to unbearable pain = VAS value 4-10. 2.) Secondary outcomes: a. Abdominal pain while straining. b. Shoulder pain. c. Postoperative nausea and vomiting (PONV).

Expected scientific contribution: The planned study will demonstrate the influence of age on the dose of local anesthetics insufflated during laparoscopic cholecystectomy required for effective postoperative analgesia.

Acknowledgments: I would like to thank all of the colleagues from my department, especially Jadranka Pavičić Šarić, MD, PhD.

MeSH/Keywords: local anesthetics, intraperitoneal nebulization, laparoscopic cholecystectomy, postoperative analgesia, elderly patients

Poster code: B-1-68

POSTER TITLE: EXPRESSION OF THE PLACENTAL VEGF AND EARLY NEUROLOGICAL OUTCOME OF INFANTS FROM PREGNANCIES COMPLICATED WITH INTRAUTERINE GROWTH RESTRICTION

PhD candidate: Maja Predojević

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

Mentor/s: Prof. Aida Salihagić Kadić, MD, PhD

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

Introduction: Intrauterine growth restriction (IUGR), most frequently caused by placental insufficiency, is a risk factor for early and late brain disturbances. Because of inadequate supply of the fetus with oxygen the redistribution of blood flow to the vital organs develops, especially towards the fetal brain. Although this phenomenon can be detected using the Doppler, neurological damage cannot be predicted with certainty. The brain disturbances can occur even without Doppler signs of hypoxia. Furthermore, caused by impaired placental development, hypoxia takes place in placental tissue too and increased placental expression of vascular endothelial growth factor (VEGF) has been proven. However, there is no data whether the expression of placental VEGF correlates with neurological disturbances in IUGR.

Hypothesis: Increased expression of placental VEGF could be associated with early morphological and/or functional brain disturbances in neonates with IUGR.

Aims: To assess differences in placental VEGF expression in relation to the early neurological outcome of neonates with IUGR.

Materials and methods: The study will include 50 pregnant women hospitalized due to IUGR

caused by placental insufficiency. Umbilical artery resistance index, middle cerebral artery resistance index, and cerebro-umbilical ratio will be followed during the pregnancy. Neurological outcome of neonate will be evaluated during the first week of life according to brain ultrasound findings and Amiel-Tison neurological assessment at term. Immunofluorescence staining will be used to quantify the VEGF expression in the placentas. Expression of VEGF in the placentas from pregnancies with IUGR will be also compared with VEGF expression in the placentas from normal pregnancies.

Expected scientific contribution: For the first time a correlation of the placental VEGF expression and early neurological disturbances in neonates with IUGR will be established. The results will provide a better understanding of the pathophysiology of placental insufficiency and its impact on the brain development.

Acknowledgments: This work was supported by a grant from the University of Zagreb and Ministry of Science, Education and Sport of the Republic of the Croatia.

MeSH/Keywords: IUGR, hypoxia, VEGF, neurodevelopment

Poster code: B-5-91

POSTER TITLE: HIGH-RISK HPV INFECTION IN KOSOVAR FEMALE POPULATION

PhD candidate: Pranvera Zejnullahu-Raci

Part of the thesis: High-risk HPV infection in Kosovar female population

Mentor/s: Prof.dr. Adriana Vince MD, PhD

Affiliation: University Clinical Center of Kosova, and Department of Cell Immunology and Molecular Diagnostics at University Hospital for Infectious Diseases "Dr. Fran Mihaljevic" Zagreb.

Introduction: Statistical analyses released from the World Health Organization (WHO) suggest that cervical cancer is the second most common cancer in women worldwide. The most important risk factor for the development of cervical cancer is the presence of human papillomavirus, HPV type, and persistence of HPV infection. Recently, it has been demonstrated that over 99% of cervical cancers have detectable HPV infection. In Kosovo, till now, there are no data about the prevalence of HPV infection, neither which high-risk HPV types are related with cervical cancer.

Hypothesis: To prove that HPV 16 and 18 are more prevalent high-risk HPV subtypes in Kosovar female population.

Aims: AIMS: to study the prevalence of HPV infection and the prevalence and distribution of HPV high-risk subtypes among Kosovar female population. To find the correlation between the HPV genotypes and cytological findings. To find out if the prevalence and specific genotypes are related to certain sociodemographic characteristics, ethnical background, sexual behaviours.

Materials and methods: Our study is designed as observational cross-sectional study. The study will include in total 360 women from 5 regions

of Kosovo to represent the real distribution and prevalence of HPV infection. Prior to enrolment in the study, all participants will fill out a questionnaire. The women included in our study the conventional PAP test smear will be performed, and analysis of PAP smear will be done in the Laboratory of Cytology, Clinic of Obstetrics and Gynecology in the University Clinical Center of Kosova. The samples collected for HPV detection and Genotyping will be collected, preserved and then will be transported in the Department of Cell Immunology and Molecular Diagnostics at University Hospital for Infectious Diseases "Dr. Fran Mihaljevic" in Zagreb for further processing. HPV detection will be performed by Hybrid Capture 2 HPV test (Qiagen, USA, FDA approved).

Expected scientific contribution: It is the first time that in Kosovo will be studied the prevalence of HPV and these study will help to reveal the real situation with HPV infection among female population. The study of high-risk HPV subtypes in Kosovar women will give an idea, if already existing vaccines will cover the women in risk for cervical cancer.

Acknowledgments:

MeSH/Keywords: High risk HPV, cervical cancer

Poster code: B-5-160

POSTER TITLE: PROGNOSTIC IMPACT OF INCREASED PRESEPSIN CONCENTRATIONS ON SEPSIS OUTCOME

PhD candidate: Ajete Aliu-Bejta

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

Mentor/s: prof.dr.Bruno Baršić, prof.dr.Shemsedin Dreshaj

Affiliation: Clinic of Infectious Diseases-Prishtina and Clinic of Infectious Diseases-Zagreb

Introduction: sCD14-ST (Presepsin) is a glycoprotein on the surface membranes of monocytes/macrophages that plays a role of a specific receptor for lipopolysaccharide. CD14-LPS-LBP complex is released into circulation, creating a new form, known as soluble CD14. sCD14 under the action of plasma protease is transformed into sCD14-ST (presepsin).

Hypothesis: 1.Levels of presepsin in septic patients correlate with patients outcome 2.The concentration of presepsin in plasma in patients with sepsis is a good indicator of the adequacy of appropriate antibiotic therapy

Aims: to assess the impact of presepsin concentration on patients outcome and to evaluate presepsin concentration as a prognostic marker of antibiotic response

Materials and methods: A prospective observational study will be conducted in the Clinic of Infectious Diseases, in Prishtina, and the Clinic of Infectious Diseases in Zagreb. 100 patients will be included in the research, children and adults of both sexes that satisfy criteria for sepsis. The impact on the sepsis outcome will be evaluated with comparison of presepsin concentration in patients with defined favorable and unfavorable outcome. It will also be assessed the impact of appropriate antibiotic treatment in presepsin

concentrations. Presepsin concentration will be measured at admission (T0), after 24 hours (T1), after 72 hours (T2) and day 7 (T3). Blood samples will be taken from cubital vein after initial skin disinfection with 70% alcohol. Plasma will be collected using tubes with ethylenediaminetetraacetic acid/heparin (EDTA/heparin), or citrate as an anticoagulant. Blood will be centrifuged within 30 minutes of collection than samples will be stored at -20°C. Presepsin levels will be measured with a quantitative enzyme linked immunosorbent assay (ELISA).

Expected scientific contribution: Sepsis is a state that complicates severe infections and a leading cause of death in critically ill patients. Early diagnosis is crucial for a favorable outcome. Our research will show the importance of presepsin for identifying high-risk patients with unfavorable outcome of disease and/or poor therapeutic response. Our attempt is also to show the possibility of antibiotic guidance based on presepsin levels, which is crucial for patients with severe sepsis.

Acknowledgments: Clinic of Infectious Diseases, Prishtina

MeSH/Keywords: presepsin, sepsis, antibiotic therapy

Poster code: B-7-42

POSTER TITLE: SPECKLE TRACKING ECHOCARDIOGRAPHY IN TRANSPLANTED HEARTS

PhD candidate: Željko Baričević, MD

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: Allograft 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.

Hypothesis: Deformation indices are reduced immediately after HTx when compared with normal subjects, despite preserved systolic function and the absence of rejection and vasculopathy.

Aims: The goals of the study are to determine the value and dynamics of global and regional LV myocardial deformation markers in “healthy” subjects within 1 year of HTx, to assess the contribution of individual components of myocardial deformation (longitudinal, radial and circumferential) and to test the feasibility and limitations of ST echocardiography in patients with transplanted hearts.

Materials and methods: ~20 adult Htx patients with 1-year follow-up period will be enrolled. Ten standard check-up visits will include clinical examination, 12-lead ECG, laboratory tests, endomyocardial biopsy and echocardiography. Coronary angiography will be made at the end of the follow-up year. The study will include “healthy” HTx patients only, which implies normal LV ejection fraction (Simpson 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 valvular disease, major cardiovascular events or poor quality echocardiographic records will be excluded. Echocardiographic images will be obtained with acquisition of parasternal and apical views using the highest possible frame rates (50-90 frames/s) for adequate speckle tracking. Global and segmental strain values will be determined and compared to normal subjects’ reference values.

Expected scientific contribution: Baseline deformation values obtained in “healthy” HTx patients might be used as a reference for early non-invasive detection of myocardial abnormalities.

Acknowledgments:

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

Poster code: B-9-8

POSTER TITLE: MYOCARDIAL DEFORMATION ABNORMALITIES IN HYPERTENSIVE PATIENTS WITH BASAL SEPTAL HYPERTROPHY

PhD candidate: Vlatka Rešković Lukšić, MD

Part of the thesis: Myocardial Deformation Abnormalities in Hypertensive Patients with Basal Septal Hypertrophy

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

Affiliation: University Hospital Centre - Zagreb

Introduction: Hypertension is one of the leading problems in everyday clinical practice. As a result of chronic pressure overload, structural concentric remodeling occurs. Hypertrophy pattern is determined by fibre orientation, interaction with local wall stress and is the most prominent in the region of basal interventricular septum. In many previous researches of myocardial deformation, complex changes in shape and dimensions of myocardium and whole ventricle were found. Every single segment deformats during systole in three dimensions- longitudinal, radial and circumferential, depending on fibres orientation. By analyzing standard echocardiographic parameters, no reduction in global ventricular function is to be found in this early phase of geometric changes, but longitudinal fibres are affected and longitudinal function is already reduced.

Hypothesis: We hypotese that patients with basal septal hypertrophy already have more significant deformation abnormalities and that this changes in hypertensive patients occure in exact moment when longitudinal function deteriorates with compensatory increased myocardial deformation in all other directions.

Aims: We would like to investigate wether if there is a difference in shape, magnitude, localization and time when myocardial deformation

abnormalities occure in hypertensive patients depending on presence of the basal septal hypertrophy.

Materials and methods: To analyse myocardial deformation, new echocardiographic metod by “speckle tracking” is going to be used on 140 hypertensive patients. They are going to be divided into two groups, depending on presence of basal septal hypertrophy. Differences between left ventricular segments in their longitudinal, radial and circumferential deformation are going to be analysed.

Expected scientific contribution: These results could lead to better understanding of pathophysiology of myocardial structural remodeling in hypertensive patients and its influence on deformation changes. Importance of basal septal hypertrophy in those patients and the exact moment in which longitudinal function deteriorates could be defined. All of this could help us recognize patients at high risk of progression to heart failure.

Acknowledgments: I would like to thank my mentor and my family for all the support

MeSH/Keywords: Hypertension, Myocardial deformation imaging, Echocardiography, Hypertensive cardiomyopathy.

Poster code: B-9-32

POSTER TITLE: EXPRESSION OF WNT 4 IN TRANSPLANT KIDNEYS

PhD candidate: Ines Mesar

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

Mentor/s: Prof.dr.sc.Nikolina Bašić Jukić

Affiliation: Nephrology

Introduction: Transplantation is the method of choice for patients with end stage renal diseases. 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 repair 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.

Hypothesis: Expression of WNT 4 is increased in transplanted organs in comparison with healthy kidneys, and the expression varies in relation to the cause of graftectomy.

Aims: This research would determine the expression of WNT 4 in the surgically removed transplanted kidneys. Followed to the extent of the pathological changes in transplanted kidneys and compared with normal kidney tissue. Aim is to contribute to the clarification of the process of fibrosis as a major causal factor of function of transplanted kidneys.

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. For all the patients basic anamnestic data will be collected. All the tissue samples are in the archive of Department of pathology UHC Zagreb. In all the samples expression of the WNT4 will be done by immunohistochemical method. Expression will be quantified by the percent of positive tubul cell from O-III.

Expected scientific contribution: This research would determine the localization patterns in humans of WNT 4 expression in healthy kidney tissue as well as expression of WNT 4 in kidney tissue after surgical removal of the transplanted organ. Based on this, we would get an insight into the changes in expression of WNT 4 during different pathological changes that were the reason for surgical removal of the transplanted kidney. We hope that the results will contribute to knowledge about the etiology of renal fibrosis, which is an important factor in the loss of graft function.

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

MeSH/Keywords: WNT4, kidney, transplantation, tubulointerstitial fibrosis

Poster code: B-9-39

POSTER TITLE: PLASMINOGEN ACTIVATOR INHIBITOR 1 IN ACUTE MYOCARDIAL INFARCTON

PhD candidate: Marin Pavlov, MD

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: Professor Vesna Degoricija, MD, PhD

Affiliation: Sestre milosrdnice University Hospital Centre, Zagreb

Introduction: Cardiovascular diseases are the main cause of death in Croatia. In 2012, coronary artery disease was the most common cause of death. 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.

Hypothesis: 1. In acute ST elevation myocardial infarction (STEMI) patients, PAI-1 correlates with infarction size measured by peak creatine phosphokinase (CPK) level. 2. PAI-1 is elevated in acute STEMI patients treated with primary PCI in whom "slow-flow" phenomenon is observed after successful recanalisation of coronary artery with culprit lesion. 3. In acute STEMI patients, PAI-1 measured in acute phase predicts long-term (6 months and 4 years) outcomes (death, acute coronary syndrome and stroke).

Aims: 1. To determine correlation between peak CPK as a surrogate marker of infarction size and PAI-1 dynamics in acute STEMI patients treated with primary PCI. 2. To determine correlation between PAI-1 dynamics and presence of "slow-flow" phenomenon in acute STEMI patients with successfully recanalised coronary artery with

culprit lesion. 3. To determine predictive value of PAI-1 measured in acute phase of STEMI on long term outcome.

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.

Expected scientific contribution: This study will help elucidate the potential pathophysiologic role of PAI-1 in slow-flow phenomenon. If proven to correlate with incidence of slow-flow, it could serve as potential treatment target in future. Predictive value of PAI-1 in acute STEMI patients treated with primary PCI is not established. With this study, more clear insight on significance of measuring PAI-1 in acute STEMI patients and its role in predicting long term outcome will be determined.

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: B-9-43

POSTER TITLE: ARTERIAL STIFFNESS AS A MARKER OF VASCULAR AGING IN IBD PATIENTS

PhD candidate: Radovan Prijčić, MD

Part of the thesis: Arterial stiffness as a marker of vascular aging in IBD patients

Mentor/s: Assistant Professor Silvija Čuković Čavka, MD, PhD

Affiliation: University Hospital Center Zagreb, Department of Internal Medicine, Division of Gastroenterology and Hepatology

Introduction: It has been reported that diseases characterized with chronic inflammation are associated with increased risk of cardiovascular events (myocardial infarction, stroke). Recent researches have demonstrated higher risk of developing atherosclerosis-associated diseases in inflammatory bowel disease (IBD). Chronic systemic inflammation can be a contributor to development of vascular changes, arterial stiffness increase and accelerated vascular aging. Role of arterial stiffness in cardiovascular diseases' development is well established. Noninvasive measurement of aortic pulse wave velocity (PWV) and augmentation index (Aix) has predictive value for future fatal cardiovascular events and total cardiovascular mortality in general population.

Hypothesis: IBD patients have increased arterial stiffness (measured by PWV and Aix) and accelerated vascular aging compared to healthy controls.

Aims: The aim of our study is to assess the level of arterial stiffness by measuring aortic pulse wave velocity in IBD patients compared to healthy controls. In addition, to determine differences within IBD patient groups, according to disease phenotype, disease length and treatment regimens.

Materials and methods: Our study will comprise adult IBD patients and healthy sex- and age-matched controls. All participants will un-

dergo complete physical examination. In addition, detailed medical history will be obtained. Laboratory tests from peripheral blood will be performed (complete blood count, electrolytes, urea, creatinine, cholesterol, liver function tests, CRP, erythrocyte sedimentation, fibrinogen, uric acid). In order to measure PWV and Aix, validated and non-invasive medical device TensioMed Arteriograph will be used. Creatinine clearance and microalbuminuria will be determined from 24 hour urine sample. To assess target organ damage 24 hour continuous arterial blood pressure monitoring, echocardiogram (to measure left ventricular hypertrophy) and carotid artery ultrasound (to measure carotid intima-media thickness) will be utilized.

Expected scientific contribution: We expect our research to provide insight into vascular aging of IBD patients in everyday clinical practice. Furthermore, to contribute to clarification of pathogenesis of IBD by finding relationship between the level of vascular aging and specific IBD phenotypes. Finally, to establish better monitoring and prevention of cardiovascular events in these patients.

Acknowledgments:

MeSH/Keywords: inflammatory bowel disease (IBD), atherosclerosis, pulse wave analysis, vascular stiffness

Poster code: B-9-44

POSTER TITLE: ASSESSMENT OF EARLY SIGNS OF MACROVASCULAR COMPLICATIONS IN CROHN'S DISEASE BY MEASURING ENDOTHELIAL FUNCTION WITH FLOW MEDIATED VASODILATATION AND THE NUMBER OF CIRCULATING ENDOTHELIAL PROGENITOR CELLS

PhD candidate: Nikola Perković, MD

Part of the thesis: Assessment of early signs of macrovascular complications in Crohn's disease by measuring endothelial function with flow mediated vasodilatation and the number of circulating endothelial progenitor cells

Mentor/s: Miroslav Šimunić, MD PhD, Ante Obad MD PhD

Affiliation: University hospital Split, Department of Medicine

Introduction: Crohn's disease is an inflammatory bowel disease of unknown etiology and can be present in any part of the gastrointestinal tract with inflammation affecting all layers of the intestinal wall with frequent local complications. Several reports stated that endothelial dysfunction might be involved in the pathogenesis of this disease. Given that endothelial dysfunction is directly involved in the pathogenesis of atherosclerosis and more specific coronary artery disease it can be assumed that Crohn's disease patients have an increased cardiovascular risk.

Hypothesis: 1.) Crohn's disease patients have an endothelial dysfunction that can be measured with flow mediated dilatation. 2.) Crohn's disease patients have an increased cardiovascular risk due to reduction of the endothelial progenitor cell number.

Aims: The aim of this study is to quantify the level of flow mediated dilatation and circulating endothelial progenitor cells in Crohn's disease compared to healthy controls.

Materials and methods: The total number of 30 patients and 30 healthy controls will be included in this study. Crohn's disease activity will be assessed by CDAI (Crohn disease activity index) and patients with the score 150 or higher will be included (moderate and severe disease). Endothelial function will be assessed by ultra-

sound measurement at the brachial artery level after reactive hyperemia had been caused by cuff insufflation. Flow mediated dilatation will be determined as the relative increase in brachial artery diameter compared to basal levels. A venous blood sample will be taken and 1 mL of whole blood will be incubated with CD 34, CD 45 and KDR as markers of endothelial progenitor cells. Afterwards we shall use the sequential strategy according to the modified ISHAGE protocol to determine the level of circulating endothelial progenitor cells. The adequate statistical analysis will be used according to data distribution.

Expected scientific contribution: Revealing the level of endothelial dysfunction in Crohn's disease by measuring flow mediated dilatation and by quantifying the level of circulating endothelial progenitor cells will increase our knowledge of cardiovascular risk in this patient group. As well, this is the first study to use modified ISHAGE protocol for quantifying endothelial progenitor cells in the context of flow mediated dilatation measurement in Crohn's disease patients.

Acknowledgments:

MeSH/Keywords: endothelial dysfunction, endothelial progenitor cells, flow-mediated dilatation

Poster code: B-9-45

POSTER TITLE: TRANSRECTAL ELASTOGRAPHY IN INFLAMMATORY BOWEL DISEASES

PhD candidate: Matea Majerović, MD

Part of the thesis: The Role of Transrectal Elastography in Differentiation between Crohn's Disease and Ulcerative Colitis

Mentor/s: Professor Nadan Rustemović, MD, PhD

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

Introduction: Inflammatory bowel diseases include two major disorders: ulcerative colitis and Crohn's disease. Each possesses distinct macroscopic and microscopic features with transmural bowel inflammation being the hallmark of Crohn's disease, as opposed to mucosal inflammation in ulcerative colitis. However, there are many similarities making the diagnostic procedure challenging. The diagnosis is based on a combination of endoscopic, histological, radiological, and biochemical investigations as a single gold standard is missing. Despite this complex approach, in up to 10% of cases we are unable to make definitive diagnosis. Therefore, new diagnostic methods that could help us differentiate the two disorders are needed, with real-time elastography being one of the promising.

Hypothesis: Transrectal real-time elastography is a diagnostic procedure that can help us differentiate Crohn's disease and ulcerative colitis.

Aims: The aim of this study is to analyse tissue stiffness of rectal wall and perirectal tissue in active phase of Crohn's disease and ulcerative colitis, as well as in control group, by using transrec-

tal real-time elastography and measuring strain ratio and hue histogram ratio.

Materials and methods: Our study will include approximately 100 patients divided into three groups: Crohn's disease and ulcerative colitis patients with active disease assessed endoscopically, and control group, patients with no clinical or endoscopic signs of inflammatory bowel disease. All patients will undergo transrectal real-time elastography with strain ratio and hue histogram ratio measurements. Cut-off value for every method, that differentiates the two disorders, will be determined.

Expected scientific contribution: Results obtained in this study would enable the use of transrectal real-time elastography as a diagnostic procedure in inflammatory bowel diseases, thus contributing to the overall process of making the definitive diagnosis.

Acknowledgments:

MeSH/Keywords: Inflammatory bowel diseases, Elasticity imaging techniques

Poster code: B-9-51

POSTER TITLE: SERUM LEVEL OF ENDOTHELIAL LIPASE, LIPID PROFILE AND INFLAMMATORY MARKERS IN ACUTE HEART FAILURE PATIENTS WITH OVERLAPPING 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. Since MS is present in many patients with acute HF (AHF), this overlapping is important for further investigation.

Hypothesis: Elevated serum level of endothelial lipase, inflammatory markers and lipid profile in AHF patients with overlapping MS produce worse outcome.

Aims: 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: The study will be observational, prospective and performed on AHF patients recruited from the Sisters of Charity University Hospital Center, Zagreb, Croatia, in a roughly estimated period of 12 months. Patients will be divided in two groups depending on the presence of MS. The groups will be compared by analysing lipid profile and inflammatory biomarkers considering the following parameters: total lipids, cholesterol, HDL, LDL, triglycerides, VLDL, endothelial lipase (EL), lipoprotein A, hs-CRP, TNF α , IL6, IL8, paraoxonase activity in HDL, and its total anti-inflammatory activity. Patients will be treated according to standard treatment protocol. The study will be performed according to Good Clinical Practice and Helsinki Declaration's principles, and approved by the local Eth-

ics Committee. Input parameters will include the patients' data: medical history, current clinical status, laboratory and diagnostic procedures. Additionally, 3x6mL of full blood samples will be collected, two at admission, and one on the third day of hospitalisation, immediately centrifuged, with serum divided into plastic tubes, and frozen at -30°C. Once sample collection is completed, serum biochemical analysis will be performed at Institute of Molecular Biology and Biochemistry, Center of Molecular Medicine, Medical University Graz, Austria. Output parameters will include outcome measures: treatment duration, performed procedures, mortality and NYHA classification.

Expected scientific contribution: The results should determine that investigated increased laboratory markers can be predictors of morbidity and mortality of AHF patients with overlapping MS.

Acknowledgments: I would like to thank all team members and principal investigators for collaboration on this project: Vesna Degoricija^{1,2}, and Saša Frank³. ¹Sisters of Charity University Hospital Center, Zagreb, Croatia, ²University of Zagreb, School of Medicine, Zagreb, Croatia, ³Institute of Molecular Biology and Biochemistry, Center of Molecular Medicine, Medical University Graz, Austria. A special appreciation for informatics support goes to Dubravko Rotalj. 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: B-9-53

POSTER TITLE: ACOUSTIC FEATURES OF VOICE ANALYSIS FOR ASSESSMENT OF FATIGUE IN PATIENTS WITH MYELOFIBROSIS

PhD candidate: Dubravka Čaržavec, MD, prim.

Part of the thesis: Voice Analysis for Assessment of Fatigue in Patients with Myelofibrosis

Mentor/s: Professor Rajko Kušec, MD, PhD, Professor Krešimir Čosić, B.Sc.E.E., PhD

Affiliation: Clinical Hospital Center Sestre Milosrdnice, Dubrava University Hospital, University Hospital Merkur, Faculty of Electrical Engineering and Computing

Introduction: Myelofibrosis (MF) is a myeloproliferative neoplasm (MPN) associated with dysregulated JAK/STAT signaling. Typical manifestations of MF are splenomegaly, anaemia and debilitating symptoms, which commonly include fatigue. JAK inhibitors are effective in diminishing the constitutional symptoms and fatigue. Quality of life assessments are included in clinical studies of patients with MF. Myeloproliferative Neoplasm Symptom Assessment Form-Total Symptom Score (MPN-SAF TSS) consists of 10 questions that are answered in scale of 0-10, depending on the symptom severity. Answers of patients are susceptible to subjective feeling and cannot completely objectively reflect their condition. Fatigue related physiological changes indirectly influence acoustic voice features. Voice analysis with standard acoustic feature computation procedures can objectively and in real time assess intensity of physiological disorders.

Hypothesis: Acoustic features of voice analysis is efficacy and sensitive method for evaluation and stratification of patients with MF.

Aims: Computing analysis of voice is complementary to MPN-SAF TSS and both methods could be used together in clinical drug research and clinical practice.

Materials and methods: 25 patients with MF will take part in a study voluntarily. The control group consists of 25 healthy and rested subjects

consistent with the age and sex. After inclusion in the study the risk group of patients with MF by IPSS will be determined. All participants will fill out a MPN-SAF TSS questionnaire. Based on the results TSS and MPN-SAF TSS quartile will be calculated. The voice recording takes place in a quiet room using high-quality microphone and personal computer. It will be recorded A. basic data - reading always the same fragment from "The little prince" B. vocalization data - pronouncing of vowel "a" with intensity of 40-60 dB lasting five seconds. From recorded material relevant acoustic features of voice will be extracted and build statistical models of the fatigue ratings based on the acoustic features. The results obtained for each participant will be correlated with its calculated TSS and with associated risk group by IPSS.

Expected scientific contribution: Computer voice analysis so far has not been used for the assessment of fatigue in patients with myelofibrosis. Implementation of computer analysis of voice as a non-aggressive, objective and sensitive method for the assessment of fatigue in patients with myelofibrosis and their response to treatment with JAK2 inhibitors.

Acknowledgments:

MeSH/Keywords: myelofibrosis, fatigue, voice analysis

Poster code: B-9-57

POSTER TITLE: THE ROLE OF ADIPOCYTOKINES 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, MMedBiochem, PhD

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

Introduction: The development of New-Onset Diabetes After Transplantation (NODAT) has the highest negative impact on long-term survival of liver transplant patients. It is associated with increased infection, chronic kidney disease and cardiovascular risk. NODAT pathogenesis is most likely similar to that of diabetes mellitus type 2. 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.

Hypothesis: The decreased concentration of serum adiponectin and an increased concentration of serum leptin prior to transplantation increases risk of NODAT after liver transplantation. Serum concentrations of adipocytokines correlate with insulin resistance, beta-cell function and biochemical and clinical indicators of increased cardiovascular risk after transplantation.

Aims: This study will determine the incidence of NODAT in the first posttransplant year, as well as risk factors associated with NODAT after liver transplantation. Relationship between NODAT and episodes of acute graft rejection, infectious complications and cardiovascular events will also be assessed, as well as the role of immunosuppressive protocols on the concentrations of serum adipocytokines. The predictive value of adiponectin and leptin as independent risk fac-

tors for the development of NODAT will be assessed. The final aim is to assess the relationship between serum concentrations of leptin and adiponectin with markers of insulin resistance and beta-cell function.

Materials and methods: The prospective study will follow the metabolic status and development of NODAT in 150 patients undergoing liver transplantation at University hospital 'Merkur' 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 (including serum leptin and adiponectin concentrations). At 3, 6 and 12 months postoperatively metabolic reevaluation will be conducted, with the diagnosis of NODAT being made in concordance with WHO/ADA criteria.

Expected scientific contribution: Apart from determining the incidence of NODAT and its influence on the development of unwanted events in the first posttransplant year, this study will help elucidate the role of adiponectin and leptin in the development of NODAT.

Acknowledgments:

MeSH/Keywords: liver transplantation, new-onset diabetes after transplantation, adipocytokines, adiponectin, leptin

Poster code: B-9-65

POSTER TITLE: COMPERATIVE STUDY OF CHARACTERISTICS AND OUTCOMES BETWEEN PATIENTS WITH STEMI IN TWO DIFFERENT COUNTRIES (KOSOVO AND CROATIA)

PhD candidate: Rreze Koshi Cardiolog

Part of the thesis: Comparative study of characteristics and outcomes between patients with STEMI in two different countries (Kosovo and Croatia)

Mentor/s: Prof Dr sci Maja Strozzi

Affiliation: KBC REBRO University of Zagreb.MF

Introduction: STEMI is among most comon risks of mortality in patients with coronary disease. That is also known that female gender is conected with more complications and higher mortality comparing to male patients. There are some differences in risk factors, clinical characteristics and time of presentation in female gender in comparison to men. The differences in the clinical characteristics, risk factors, treatment modalities and prognosis of STEMI in different countries, health systems and cultural and educational societies are nearly investigated.

Hypothesis: Patient from two different countries, will have different risk factors, presentation characteristics and presentation times in STEMI, and outcomes according to differences in economic situation, health system and cultural background.

Aims: The aim of this study would be to compare two different groups of female and male

patients with STEMI one from Croatia and other from Kosova. To compare STEMI causes, presentation, treatment and outcome differences in two different countries.

Materials and methods: In a prospective manner we will analyse the 160 patients presenting with STEMI in Clinical Hospital Center Zagreb Croatia (80) and Regioanl Hospital Isa Grezda Gjakova -Kosova (80).

Expected scientific contribution: Our assumption is that these two groups will significantly differ. These results will help us to improve acute coronary treatment in female patients and male patients, and maybe enlighten some specific characteristics and risks in some subgroups.

Acknowledgments: Thank you very much.

MeSH/Keywords: ST elevation acute myocardial infraction, (STEMI), female and male patients.

Poster code: B-9-89

POSTER TITLE: QUALITY OF LIFE AFTER LIVER TRANSPLANTATION

PhD candidate: Nino Kunac, M.D. ¹

Part of the thesis: Part of a 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.¹, Full professor Vesna Medved, M.D., Ph.D.²

Affiliation: University hospital Merkur¹, University hospital center Zagreb²

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.

Hypothesis: Better clinical parameters in patients with liver cirrhosis before and after liver transplantation are associated with better quality of life after liver transplantation. Less comorbidities, liver cirrhosis etiology other than chronic hepatitis C, lower Child Turcotte Pugh (CTP) and Model for end stage liver disease (MELD) score, lower Donor risk index (DRI) and less post-transplantation complications, are considered as better clinical parameters.

Aims: General aim: to evaluate the impact of pre- and posttransplantation clinical condition of patients and liver graft quality on quality of life after liver transplantation. Specific aim: to evaluate the dynamics of quality of life change after liver transplantation, and to verify parameters associated with positive and negative quality of life dynamics.

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 posttransplantation quality of life.

Expected scientific contribution: 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 postransplantation patient care.

Acknowledgments:

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

Poster code: B-9-106

POSTER TITLE: THERMOGRAPHY IN ULCERATIVE COLITIS

PhD candidate: Tonći Božin, MD

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, clinical (endoscopy), imaging (CT, MR) or laboratory (C-reactive protein, calprotectin) give an insight into disease activity, but are possibly associated with significant discomfort for the patient and/or increased risk of irradiation and potential allergic reactions on contrast agents. For that reason there is a need for a noninvasive, biologically inert method for evaluation of disease activity in IBD. Thermography possesses most of these characteristics. The aim of this study is to find potential link between pathological thermographic signs and endoscopic findings, serum CRP and calprotectin in the stool of patients with active and extensive ulcerative colitis.

Hypothesis: Documenting pathological thermographic signs in patients with extensive ulcerative colitis we will demonstrate pathological thermography criteria that correlate with standard inflammatory markers such as Mayo ESS, CRP and calprotectin in patients with ulcerative colitis.

Aims: The aim of this study is to record abdominal thermographic images of patients with active ulcerative colitis (UC), to create interpreta-

tional thermographic criteria for these images and to compare them to abdominal IR images of healthy volunteers. Furthermore we intend to correlate these criteria with standard markers of inflammation such as CRP and calprotectin in patients with UC at the beginning of treatment and at the end.

Materials and methods: For the purpose of this work, 30 patients with extensive UC and 30 healthy individuals will be put through thermographic imaging, have their stool tested for calprotectin and their blood for CRP. In addition, patients with UC will receive colonoscopy evaluations.

Expected scientific contribution: The results of this paper would give additional contribution to existing tools for pursuing ulcerative colitis activity thus demonstrating the potential of thermography as a complementary method to standard methods in assessing disease activity. Establishing diagnostic criteria for this method would be a good addition to present clinical practice.

Acknowledgments: I would like to thank Professor Banić and Doctor Svetlana Antonini for providing material and moral support.

MeSH/Keywords: Ulcerative colitis, thermography, colonoscopy, calprotectin

Poster code: B-9-119

POSTER TITLE: CORRELATION OF GHRELIN AND GHRELIN RECEPTOR WITH THE GRADE OF DYSPLASIA IN COLONIC ADENOMAS

PhD candidate: Sanja Stojšavljević, 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. Consumption 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 concentrations 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 concentrations will be determined with RIA 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 colonic 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: B-9-121

POSTER TITLE: ENDOTHELIAL LIPASE PLASMA LEVELS AND FUNCTIONAL PROPERTIES OF HIGH DENSITY LIPOPROTEIN IN PATIENTS WITH VARIOUS DEGREES OF CORONARY ARTERY DISEASE

PhD candidate: Tomislava Bodrožić Džakić

Part of the thesis: Endothelial lipase plasma levels and functional properties of high density lipoprotein in patients with various degrees of coronary artery disease

Mentor/s: Professor Vesna Degoricija, MD, PhD

Affiliation: University of Zagreb School of Medicine, Zagreb, Croatia Department of Medicine, Sisters of Charity University Hospital Center, Vinogradska 29, 10 000 Zagreb, Croatia Department of Medicine, Universit

Introduction: Atherosclerotic coronary artery disease is one of the leading causes of morbidity and mortality worldwide. High levels of low-density lipoprotein density (LDL) and low levels of high-density lipoprotein (HDL) contribute to initiation and progression of atherosclerosis. Endothelial lipase (EL) is a recently discovered triglyceride lipase which affects the HDL and changes its activity and plasma level.

Hypothesis: Concentration and / or activity of endothelial lipase correlate with different clinical presentations of coronary artery disease. Certain isoforms of EL affect the properties of HDL and patients with various degrees of coronary heart disease have different characteristics of HDL.

Aims: To determine the concentration and enzyme activity of EL and structural and functional characteristics of HDL in patients with acute coronary syndrome (ACS) and in patients with a symptoms and signs of stable angina pectoris (AP) and compare them. To explore if the concentration and / or activity of EL can be used as a biomarker and / or predictor of progression of coronary heart disease. To determine the structural and functional characteristics of HDL in patients with ACS and stable coronary artery disease and compare them, to determine if lev-

els of EL correlate with structure and function of HDL.

Materials and methods: The study includes patients with acute coronary syndrome and patients who have clinical presentation of stable angina pectoris (two groups of patients). We gather data on patients medical history, physical characteristics, routine laboratory tests, data on electrocardiography, echocardiography and coronary angiography (Gensini score). Specific laboratory tests include measuring of levels of EL and the isolation of HDL. Isolated HDL will be used for testing of the structural and functional characteristics. Structural properties of HDL will be tested by mass spectrometry, while the functional characteristics will be tested in vitro in cell culture (human aortic endothelial cells).

Expected scientific contribution: To determine if there is any difference in the concentration of endothelial lipase in patients with ACS and stable angina pectoris, and thus determine whether the level of EL could be used as a biomarker of different stages of coronary heart disease.

Acknowledgments:

MeSH/Keywords: endothelial lipase, HDL, coronary heart disease

Poster code: B-9-129

POSTER TITLE: QUALITY OF LIFE AND PSYCHOLOGICAL STATUS OF PATIENTS WITH IMPLANTIBLE CARDIOVERTER DEFIBRILLATORS

PhD candidate: Ivan Bitunjac, MD

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

Mentor/s: Professor Martina Lovrić Benčić, MD, 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.

Hypothesis: 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.

Aims: 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.

Materials and methods: Three self-administered questionnaires will be used. Quality of life will be evaluated using SF-36. The 20-item CES-D Scale will be used for severity measuring of depressive symptoms. GAD-7 test will be used for severity measuring of generalized anxiety disorder. 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, and deterioration in quality of life will be measured regarding delivered therapy, indications for implantation, age and gender of patients.

Expected scientific contribution: 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 my mentor for advices and support during this investigation.

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

Poster code: B-9-134

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.

Hypothesis: Exposition to cardiotoxic treatment in childhood cause aortic elasticity changes which can be evaluated using echocardiography methods.

Aims: The purpose of this study is to determine the impact of cardiotoxic therapy on aortic elasticity.

Materials and methods: Fifty adult childhood cancer survivors will be matched healthy volunteers. Aortic elasticity will be examined by using echocardiography device. Systemic arterial blood pressure will be measured by manual sphygmomanometer in supine position, simul-

taneously with the echocardiographic examination of the ascending aorta. The indexes of aortic stiffness and distensibility will be calculated and statistically analyzed.

Expected scientific contribution: 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. 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: B-9-137

POSTER TITLE: EFFECT OF IMMUNOSUPRESIVE 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. The success of transplantation depends largely on immunosuppressive therapy. Different combination regimens with immunosuppressive agents like corticosteroids, azathioprine, mycophenolate mofetil (MMF), cyclosporine, tacrolimus, everolimus, and sirolimus are used. Immunosuppressive therapy is associated with an increase risk of thromboembolic complications and morbidity and mortality from cardiovascular disease.

Hypothesis: Platelet aggregation in renal transplant patients varies depending on the type of immunosuppressive agent used in the prevention of acute rejection.

Aims: Main goal of the study is to investigate the effect of different immunosuppressive agents on platelet aggregation in renal transplant patients with stable graft function. We will also analyse potential risk factors (age, sex, comorbidities, etc.) on platelet aggregation. Finally, we will compare platelet aggregation in renal transplant patients with the control group (with normal renal function).

Materials and methods: The study will include renal transplant patients which are controlled in

the Department of Nephrology, Hypertension, Dialysis and Renal Transplantation in Clinical Hospital Center Zagreb, during 3 months period, after providing the informed consent. Ethical approval was obtained from Ethics Board of Clinical Hospital Center Zagreb. During regular visit, together with blood sampling for standard laboratory parameters, platelet aggregation test would be done. Platelet function testing will be conducted on platelet function analyzer (PFA-200) that „in vitro“ simulates the process of aggregation and platelet activation. Data for analyses for renal transplant patients will be taken from the medical records. Control group will include healthy individuals.

Expected scientific contribution: We would investigate the effect of everolimus on platelet aggregation in renal transplant patients, and the impact of different immunosuppressive agents on platelet aggregation in renal transplant patients, in terms of increased risk of cardiovascular disease with the long term immunosuppression therapy.

Acknowledgments:

MeSH/Keywords: platelet aggregation, immunosuppression, everolimus

Poster code: B-9-138

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) developed classification criteria for SLE in 1982. After their revision in 1997 they have not changed and have been used for standardization of patients for clinical researches. The patient will be diagnosed with SLE if a minimum of 4 criteria of 11 is fulfilled. Not all of the criteria have the same weight and not every manifestation of SLE is included in the classification. In 2012 a new set of criteria has been derived and validated, with the same specificity, but greater sensitivity in comparison with the ACR criteria. On our group of patients, the sensitivity and specificity of the new classification criteria will be tested and compared with ACR classification criteria. We presume to have a better defined patient group at the end of our research.

Hypothesis: Application of the SLICC criteria will, with high specificity and sensitivity, recognize patients with SLE, especially in the early stages of the disease. Our research will efficiently validate the current ACR criteria for SLE and help in clarifying some ambiguous cases.

Aims: The aim of our research is to validate SLICC criteria on our group of patients and to determine if they are a better diagnostic tool for SLE. Sensitivity and specificity of the SLICC criteria will be compared with the ACR criteria and we presume that the SLICC criteria will better identify patients in the early stages of the dis-

ease. The specific aim of the dissertation is forming a well defined group of patients which will be useful in further clinical research.

Materials and methods: During the past few years, in our Division medical records of patients diagnosed with SLE or SLE associated disease have been sorted out (1918 patients). There are 968 patients diagnosed with SLE or incomplete SLE (< 4 ACR criteria). Two patient groups will be formed: patients who fulfill 4 or more of 11 ACR criteria and patients who are diagnosed with SLE, but fulfill less than 4 ACR criteria, each group will consist of 150 patients minimally. A team of rheumatologists will revise patient charts and see if they agree with the diagnosis. On every patient the new criteria will be applied.

Expected scientific contribution: Current classification of SLE patients has not shown enough sensitivity, especially in the early stages of the disease. With our research, we expect to contribute in better defining the group of SLE patients. This will be of great importance for further investigations of the disease.

Acknowledgments:

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

Poster code: B-9-141

POSTER TITLE: SERUM PHOSPHORUS

PhD candidate: Dajana Katičić, dr. med.

Part of the thesis: Serum phosphorus as a risk factor for cardiovascular morbidity in patients with diabetes mellitus type 2

Mentor/s: Doc. dr. sc. Draško Pavlović, Prof. dr. sc. Lea Smirčić-Duvnjak

Affiliation: University hospital Center Sisters of mercy, Department of nephrology and dialysis

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.

Hypothesis: Serum phosphorus is an independent risk factor for cardiovascular morbidity in patients with type 2 diabetes.

Aims: To determine the association between serum phosphorus and the risk of cardiovascular complications in patients with type 2 diabetes and chronic kidney disease stage <3B.

Materials and methods: It is a cross-sectional study on a sample of 280 patients at University Hospital Center "Sisters of Mercy". 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 groups 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 groups 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.

Expected scientific contribution: This would stimulate new research to justify therapeutic approaches that would reduce the risk of adverse clinical consequence. Certain contribution would be a justification for routine serum phosphorus determination in patients with type 2 diabetes, not only those in advanced stage of chronic kidney disease.

Acknowledgments: No acknowledgments

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

Poster code: B-9-159

POSTER TITLE: UROMODULIN IN PREHYPERTENSION

PhD candidate: Josipa Josipović, MD

Part of the thesis: Uromodulin in 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. GWAS Study of blood pressure extremes identified variants near UMOD gene associated with hypertension. The UMOD gene encodes the Tamm Horsfall protein (THP)/uromodulin which is expressed primarily in the thick ascending limb of the loop of Henle. Clinical functions studies have shown that the minor allele of rs13333226 is associated with a lower risk of hypertension and lower urinary uromodulin excretion. The plan of this study is to analyze potential value of uromodulin as a new biological marker in prehypertension.

Hypothesis: Uromodulin urinary excretion is independent risk factor for the development of prehypertension.

Aims: To determine urinary uromodulin levels in prehypertensives compared with subjects with hypertension stage 1. The specific aim is to analyse the associations of uromodulin with circadian BP characteristics, renal function, salt load and other CVR factors with uromodulin levels and BP, uromodulin excretion and overall CVR, and to determine value of uromodulin as a new biomarker.

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. Participants excluded from the study are those with BP beyond the set limits, diabetes, heart failure, atrial fibrillation, pregnancy, chronic kidney disease (GFR <60 ml/min), acute infectious disease, NSAR abuse, oral contraceptives, amputation of one limb. Anamnesis and physical examination will be done, and structured questionnaire will be filled out. Blood pressure with electronic device and ABPM will be measured. The samples of the vein blood will be collected for measurements CBC, glucose, creatinine, uric acid, sodium, potassium, CRP, lipids profile. 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.

Expected scientific contribution: To determine uromodulin as potential novel biomarker in better categorization of prehypertensives in regards to cardiovascular risk and pharmacotherapeutic options.

Acknowledgments:

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

Poster code: B-9-172

POSTER TITLE: CARDIAC ALLOGRAFT VASCULOPATHY AFTER HEART TRANSPLANTATION

PhD candidate: Jana Ljubas Maček, MD

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: Heart transplantation (HTx) is the most effective treatment for patients with terminal heart failure. Except graft rejection, cardiac allograft vasculopathy (CAV) considerably contributes to higher mortality.

Hypothesis: Early troponin T correlates with longer ischemic time, which further predisposes to higher rate of myocyte as well as vascular injury, so longer ischemic time could be the trigger for early and/or progressive CAV. The more immunogenic graft generates stronger immunological response which could be manifested with more frequent episodes of cellular, humoral or mixed graft rejection. Higher heart rates after HTx could also reflect stronger tendency to graft rejection, because they are indirectly correlated with late graft reinnervation, possibly related to CAV and rejection predisposition. Platelets could also be one of the cofactors involved in the development of CAV, especially if platelet hyperreactivity is found in HTx patients.

Aims: The aim of the study is early recognition of risk factors important for CAV development and stratification of patients with higher risk for CAV, as well as to examine the influence of graft damage and platelet function on CAV. Further, the aim is to investigate whether patients with late or absent graft reinnervation have a higher rejection tendency, worse CAV or development of graft dysfunction.

Materials and methods: 120 HTx patients included in retrospective study, from the begin-

ning of 2001 to October 2013. The prospective study will include patients transplanted in period from October 2013 to the end of 2014. 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).

Expected scientific contribution: To identify potential biomarkers pointing out to the risk of development of CAV in HTx patients, to explore the consequences of graft ischemic injury and lack of reinnervation on CAV development. Also to prove that platelet hyperreactivity could favor CAV development and to investigate the potential advantages in CAV prevention by use of antiplatelet drugs in patients with higher risk of CAV.

Acknowledgments:

MeSH/Keywords: heart transplantation, cardiac allograft vasculopathy, graft reinnervation, ischemic time.

Poster code: B-9-175

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 osteosynthetic 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.

Hypothesis: Our 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.

Aims: General aim: Prove that the drill with open type internal cooling made out of medical steel lowers the temperature at the site of drilling of the bone below the critical temperature of 47 °C
Specific aims: 1) Strength comparison between drill with and without open type internal cooling, 2) Determination of the interconnectedness of the coolant flow and the degree of reduced temperature, 3) Comparing the impact of internal cooling on the drilling temperature at various stages of drill wear, 4) Prove that the flow in the cooling system does not cause a pressure increase in medullar canal above the critical pressure of 50 mmHg, 5) Prove that the drill with

open type internal cooling is possible to sterilize and resterilize.

Materials and methods: Research will be carried out on pig cadaveric femur. The temperature on drilling site will be measured with thermocouples which will be located at distance of 5 mm from the drilling site. Pressure sensor will be placed in the medullar canal. Drilling will be 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 will be 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 and intramedullar pressure will be recorded and analyzed. Before first use and after completion of each series of measurements all drill will be cleaned and sterilized which will be followed by control of sterility in the microbiology lab.

Expected scientific contribution: Newly designed drill should significantly reduce temperature at the drilling site of the bone compared to standard drills that are used in bone and joint surgery.

Acknowledgments:

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

Poster code: B-10-30

POSTER TITLE: IMPORTANCE OF CIRCUMCISION IN PREVENTION OF INFLAMMATORY AND INFECTIOUS DISEASES IN POPULATION OF THE REPUBLIC OF KOSOVO

PhD candidate: Hysni Jashari MD, Pediatric Surgeon

Part of the thesis: Thesis proposal

Mentor/s: Prof.Božidar Župančić MD, PhD

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

Introduction: About a third of the world's male population aged 15 and older are circumcised, according to the World Health Organisation. Except for medical reasons, in many countries circumcision is performed for religious and cultural reasons. Lichen sclerosus atrophicus (LSA) is a chronic skin condition of unknown cause that most often affects the glans and prepuce but sometimes extends into the urethra. LSA can lead to phimosis and urethral stenosis, affecting both urinary and sexual function.

Hypothesis: Circumcision is a justified surgical procedure in children with recurrent urinary infections, disuric complaints, phimosis and changes in prepuce that could resemble LSA.

Aims: To establish whether circumcision is a curative surgical procedure in recurrent urinary infections, determine frequency of Lichen Sclerosus Atrophicus as a cause of phimosis, determine the prevalence of penile carcinoma in population of Kosovo and to conclude the percentage of these patients circumcised before the disease occurred.

Materials and methods: Patients included in the study are children with recurrent urinary infections (UTI), disuric complaints, phimosis and children with changes in the prepuce and glans penis that could match the Lichen Sclerosus Atrophicus. The sample size is 100 patients. Patients are divided into age groups of 0-5, 5-10 and 10-15 years of age. Before circumcision, a urine sediment and urine culture are taken, a

swab of the inner leaf of the prepuce for microbiological analysis. Control swab after circumcision will be taken 4 weeks after surgery. At intervals of 3, 6 and 12 months after circumcision, urine sediment and urine culture will be taken for analysis. Preliminary results of more than a quarter of samples examined so far show almost no recurrence of urinary infections after circumcision, while the incidence of LSA is low, proving the hypothesis of impact of surgery on UTI and aims of the study. Data analysis will be performed with statistical SPSS software package as appropriate given the size, distribution and type of data collected from our samples.

Expected scientific contribution: The doctoral dissertation would be a significant scientific contribution to the medicine of Kosovo because to date, there are no professional-scientific papers on the field, it would enable us to come to the recommendation when and by whom should children be operated on. The results of this doctoral dissertation would prove the importance of circumcision not only as a medical indication, but as a religious and cultural as well.

Acknowledgments: I would like to thank University of Zagreb, School of Medicine and University Clinical Centre of Kosova, Pediatric Surgery Clinic for their support.

MeSH/Keywords: Circumcision, lichen sclerosus atrophicus, cancer of penis, urinary tract infections, sexually transmitted diseases.

Poster code: B-10-61

POSTER TITLE: THE INFLUENCE OF DECONTAMINATION PROTOCOLS ON STRUCTURAL CHARACTERISTICS OF HEART VALVE ALLOGRAFTS

PhD candidate: Ivica Šafradin, MD

Part of the thesis: The influence of decontamination protocols on structural characteristics of heart valve allografts

Mentor/s: Bojan Biočina, MD, PhD

Affiliation: Department of cardiac surgery, University Hospital Centre Zagreb

Introduction: Heart valve allografts are well established substitutes used for heart valve replacement. Microbiological decontamination is a standard procedure in heart valve allografts preparation. Although an increase in temperature of microbiological decontamination could increase its efficacy, there is no published data about its influence on structural characteristics of heart valve allografts. Functional durability of heart valve allografts depends on remodeling capacity of extracellular matrix. Remodeling capacity of extracellular matrix depends on the balance between biosynthetic and proteolytic activity. The aim of proposed study is to analyze influence of different protocols of microbiological decontamination on remodeling capacity of extracellular matrix of heart valve allografts.

Hypothesis: Increase in temperature of microbiological decontamination does not influence structural characteristics of heart valve allografts

Aims: The aim of proposed study is to analyze influence of different protocols of microbiological decontamination on remodeling capacity of extracellular matrix of heart valve allografts.

Materials and methods: Heart valve allografts used in this study do not meet functional and morphological criteria for the storage in Cardiovascular tissue bank at UHC Zagreb. Heart valve allografts will be incubated in antibiotic solution at 4°C and 37°C. Tissue samples will be taken at beginning of decontamination and after 6 and 24 hours. Tissue samples will be routinely processed in pathohistological laboratory. Immunohistochemical analysis of expression of matrix metalloproteinase 2 and procollagen type I will be performed and tissue samples for fibroblast culture will be taken.

Expected scientific contribution: Results of this research will help in understanding how to maintain original characteristics of heart valve allografts during processing which could be crucial for their performance after implantation.

Acknowledgments:

MeSH/Keywords: Heart valve, allograft, decontamination, extracellular matrix

Poster code: B-10-108

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, MD

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

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

Affiliation: Affiliation(s): University Hospital Merkur, Zagreb

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.

Hypothesis: Morphological features and characteristics of atherosclerotic unstable plaques analysed by MRI and immunohistochemical staining of MMP-9 and COX-2 protein would be highly expressed in symptomatic patients with indication for carotid endarterectomy. Atherosclerotic plaque features analysed by MRI would be able to distinguish patients with unstable atherosclerotic carotid plaque.

Aims: The aim of the research is to analyse the characteristics of atherosclerotic plaque by magnetic resonance imaging, morphological features of plaque and expression of MMP-9 and COX-2 proteins, to determine their correlation and identification of unstable atherosclerotic plaques in patients with an indication for carotid endarterectomy.

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 morphologically using H&E and special histochemical trichrome staining. Semi quantitative analysis of collagen fibres will be performed. Immunohistochemical staining of MMP-9 or 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.

Expected scientific contribution: Research results may indicate a better definition of patients with an indication for carotid endarterectomy as well as a possibility to predict the outcome of surgery.

Acknowledgments: 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: B-10-127

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POSTER TITLE: FREQUENCY OF AGT, ADRB1, UMOD, AGTR1, ACE AND ADIPOQ GENETIC POLYMORPHISM IN PREHYPERTENSION

PhD candidate: Livija Šimičević, MMedBiochem

Part of the thesis: Frequency of AGT, ADRB1, UMOD, AGTR1, ACE 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: Arterial hypertension (AH) is a major independent risk factor for mortality and burden of cardiovascular, cerebrovascular and renal diseases. AH prevalence in Croatia is near 40% of the adult population and over 1/3 has high normal blood pressure (BP) or prehypertension. Clinical studies suggest that early treatment of prehypertension might have a positive influence on AH progression making it important to detect persons in the early stage of the cardio-renal continuum. Various environmental and endogenous factors influence development of AH and determine the clinical course. The role of individual genes and their interactions with external factors is not yet elucidated.

Hypothesis: ACE, AGTR1, AGT, ADRB1, UMOD and ADIPOQ genes polymorphisms associated with hypertension and metabolic syndrome are more frequent in patients with high normal BP than in those with normal BP.

Aims: The aim of this study is to assess the frequency of ACE, AGTR1, AGT, 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: This study will include 300 prehypertensive patients (130-139 / 85-89 mmHg), 20-45 years old, and 300 normotensive

subjects as a control group. All subjects will fulfill a questionnaire detailing family history, drug therapy, smoking, alcohol, diet type, physical activity and socio-economical status. BMI, systolic and diastolic BP will be measured and the following blood tests will be performed alongside genotyping: glucose, creatinine, lipid status, adiponectin, leptin, and aldosterone. Urine samples will be tested on albumin, alpha-1-microglobulin and creatinine.

Expected scientific contribution: Study results will determine the clinical and epidemiological characteristics of prehypertensives, correlating their present cardiovascular and renal risk factors to the gene polymorphisms involved in the cardio-renal continuum. Likewise, the results should 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 hypertension.

Acknowledgments:

MeSH/Keywords: prehypertension, arterial hypertension, genetic polymorphism, metabolic syndrome

Poster code: B-11-25

POSTER TITLE: CHARACTERISTICS OF PATIENTS WITH RHEUMATOID ARTHRITIS IN KOSOVO

PhD candidate: Blerta Rexhepi

Part of the thesis: Thesis proposal

Mentor/s: Prof.dr.sc. Nada Čikes, dr.med/ Prof.asoc. Vjollca Sahatçiu-Meka Physiatrist-rheumatologist

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

Introduction: RA is a chronic inflammatory rheumatic disease with prevalence 0.5 to 1% of adults in the developed world.

Hypothesis: There is no data about RA in Kosovo population. In the group of 100 patients with RA we expect to define specific pattern of clinical and laboratory data in patients with RA and comorbidity in well defined Albanian ethnic group from Kosovo.

Aims: The aim of this study is to define the characteristics of the populations of RA patients in Kosovo.

Materials and methods: Data from the University Clinical Center of Kosovo, Rheumatology Clinic will be used to define characteristics of patients with RA from Albanian ethnic group from Kosovo, based on questionnaire, analysis of sociodemographic data, disease characteristics, laboratory and radiological findings. The prevalence of criteria for the RA in Kosovo population of RA

patients and comorbidity of RA patients will also be evaluated. The cytokines pattern IL-6, IL-17 and TNF alpha in RA patients in Kosovo will be defined.

Expected scientific contribution: Kosovo is a development country. Because of low income, there is not enough research projects in the field of medicine and data from clinical research are missing. With this study we expect to define specific clinical and laboratory data as well as comorbidity in patients with RA in well defined Albanian ethnic group from Kosovo.

Acknowledgments: Prof.dr.sc. Nada Cikes- Principal Mentor and Prof.dr.Sylejman Rexhepi, Head of Rheumatology Clinic in University Clinical Center of Kosova for help and support

MeSH/Keywords: Rheumatoid arthritis, characteristics, epidemiology

Poster code: B-14-78

POSTER TITLE: PREVALENCE OF METABOLIC SYNDROME IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

PhD candidate: Goran Šukara, MD

Part of the thesis: Prevalence of Metabolic Syndrome in Patients with Systemic Lupus Erythematosus

Mentor/s: Professor Branimir Anić, MD, PhD

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

Introduction: Cardiovascular incidents are an important cause of mortality in patients with systemic lupus erythematosus (SLE). This phenomenon is explained by the accelerated atherosclerosis, which is the consequence of chronic inflammatory disease. Metabolic syndrome is the strongest predictor of cardiovascular morbidity and mortality in patients with SLE. Prevalence of metabolic syndrome was significantly different in SLE populations studied so far. Primary goal of this research is to analyse the prevalence of metabolic syndrome in the defined group of patients with SLE listed in the Division of Clinical Immunology and Rheumatology, University Hospital Centre Zagreb register.

Hypothesis: Higher prevalence of metabolic syndrome in patients with systemic lupus erythematosus is associated with specific clinical, laboratory, pharmacological and demographic parameters.

Aims: To define prevalence of metabolic syndrome in the population of patient with systemic lupus erythematosus registered in the database of Department of Clinical Immunology and Rheumatology, University Hospital Center - Zagreb. To connect the occurrence of metabolic syndrome in patients with systemic lupus erythematosus with specific clinical, laboratory, pharmacological and demographic parameters.

Materials and methods: Study will be conducted as part of the project: Epidemiological characteristics of systemic lupus erythematosus in Croatia. It will be conducted as a combination of cross-sectional and retrospective study. Patients with systemic lupus erythematosus included in the database of Department of Clinical Immunology and Rheumatology will be included in the study. Required data (clinical, laboratory, pharmacological and demographic parameters) will be collected from patient during their regular controls in the Department. Metabolic syndrome will be defined according to International Diabetes Federation criteria. Statistical analysis will be performed to determine the association of metabolic syndrome with specific clinical, laboratory, pharmacological and demographic parameters.

Expected scientific contribution: Results of the study will help in better understanding of the pathogenesis of metabolic syndrome in patient with systemic lupus erythematosus. Gathered data and the results will improve the standard of care and therapy of patients with systemic lupus erythematosus.

Acknowledgments:

MeSH/Keywords: Lupus Erythematosus, Systemic, Metabolic syndrome

Poster code: B-14-156

POSTER TITLE: INCREASED IN VITRO EFFICACY OF COMBINATION OF SELECTED ORAL ANTIBIOTICS AND FOSFOMYCIN AGAINST CLINICAL ISOLATES OF METHICILLIN – RESISTANT STAPHYLOCOCCUS AUREUS

PhD candidate: Nataša Firis, MD

Part of the thesis: Increased In -Vitro Efficacy of Combination of Selected Oral Antibiotics and Fosfomycin against Clinical Isolates of Methicillin – Resistant Staphylococcus Aureus

Mentor/s: Associate Professor Vanda Plečko, MD, PhD, Assistant Professor Robert Likić, MD, PhD

Affiliation: University Hospital Centre Zagreb

Introduction: Methicillin - resistant Staphylococcus aureus (MRSA) is one of the most important causes of nosocomial infections and a significant factor in development of life threatening clinical conditions in patients such as pneumonia, sepsis, infective endocarditis, bone and joint infections, infections of prosthetic devices with biofilm, as well as skin and soft tissues infections. Vancomycin is the standard of therapy for severe MRSA infections. However, other treatment options ought to be examined, especially for patients who can not tolerate or are allergic to vancomycin or when MRSA strains show heteroresistance or reduced sensitivity to this drug. In the past few years some new antibiotics became available including linezolid, daptomycin, tigecycline, a new lipoglycopeptides telavancin, oritavancin and dalbavancin. MRSA is typically resistant to all beta-lactams antibiotics and other groups of antibiotics including macrolides, lincosamides, quinolones, cotrimoxazole, rifampicin and fusidic acid. However, we can try treating MRSA with antibiotics which were for various reasons therapeutically neglected in the past such as fosfomycin or fusidic acid in monotherapy or try and explore their possible synergistic effects with other oral or parenteral antibiotics, particularly for cases of severe MRSA infections.

Hypothesis: There is a detectable, positive in vitro synergistic effect between fosfomycin and antibiotics that act on the inhibition of protein

synthesis, as well as the group of antibiotics that act on nucleic acid synthesis.

Aims: The aim of this study is to evaluate in vitro effects of a combination of erythromycin, clindamycin, cotrimoxazole, ciprofloxacin and linezolid with fosfomycin.

Materials and methods: A total of 200 MRSA clinical isolates will be identified by MALDI BIOTYPER, BRUKER Daltonics. Sensitivity will be done by standard antimicrobial tests according to CLSI and EUCAST (disc diffusion and MIC). Synergism testing will be done by Broth Microdilution Checkerboard Methods. The interpretation is given in the calculation of a synergistic effect $F_{ICI} < 0.5$, antagonism $F_{ICI} > 4$ or indifference with values $0.5 < F_{ICI} < 4$.

Expected scientific contribution: MRSA is a global health problem. Synergistic effect of two antibiotics can improve the effectiveness of treatment, reduce the appearance of resistance, have fewer side effects and decrease the costs of health care.

Acknowledgments:

MeSH/Keywords: Methicillin - resistant Staphylococcus aureus (MRSA), drug synergism, fractional inhibitory concentration index, fosfomycin, erythromycin, clindamycin, cotrimoxazole, ciprofloxacin, linezolid

Poster code: B-16-145

POSTER TITLE: HISTOPATHOLOGY OF INVOLUTIONAL LOWER EYELID ENTROPION

PhD candidate: Daliborka Miletić, MD

Part of the thesis: 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 is 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 includes 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: B-18-93

POSTER TITLE: MONOVISION VRS MULTIFOCAL – CAN OPTICAL AIDS TRULY BE AVOIDED?

PhD candidate: Lidija Andrijašević, MD

Part of the thesis: Part of a Thesis: Can The Available Refractive Surgery Methods Achieve Satisfying Visual Acuity At Near And Distance At The Same Time?

Mentor/s: Professor Vladimir Trkulja, MD, PhD and Professor Mladen Bušić, MD, PhD

Affiliation: University Eye Clinic, University Hospital „Sv. Duh“, Zagreb

Introduction: Weakening of accommodation and consequently reduced visual acuity at near occurs after the age of forty. In patients with pre-existing refractive error, after the onset of presbyopia, correction of visual acuity at near and distance is necessary. This 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 at the same time - multifocal approach and monovision. Both approaches include several methods: procedures on the cornea (laser) and lens implantation (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.

Hypothesis: Refractive surgical methods used to induce monovision or multifocal vision are successful in achieving satisfying visual acuity at near and distance and provide independence of optical aids. The two main method groups differ in postoperative visual acuity and complications.

Aims: To evaluate and compare the benefit-risk ratio for each of the methods used to achieve monovision or multifocal vision. Both objective (visual acuity at near and distance) and subjective (patients using/not using optical aids

Materials and methods: Patients' satisfaction outcomes will be evaluated. Satisfying visual postoperative acuity is defined as 1.0 without correction or with ± 0.50 Spherical equivalent (objectively) or if patients declare not to be using optical aids (subjectively). Postoperative complications will be evaluated for each method (type and intensity).

Expected scientific contribution: Systematic literature review with qualitative and quantitative data synthesis. Randomized controlled trials, non-randomized case-control and observational studies will be included.

Acknowledgments:

MeSH/Keywords: -

Poster code: B-18-122

POSTER TITLE: SLEEP QUALITY AND CATARACT SURGERY

PhD candidate: Ivan Škegro, MD

Part of the thesis: Correlation Between Cataract Surgery And Type Of Implanted Intraocular Lens With Sleep Quality

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

Affiliation: Department of Ophthalmology of University Hospital Centre Zagreb and University of Zagreb School of Medicine

Introduction: Sleep pattern is regulated via the retinohypothalamic tract by stimulation of retinal ganglion cells, primarily with short wavelength light (blue light). With aging, the natural human lens opacifies and prevents passage of light to retina, and that may influence on entrainment of circadian rhythms. Intraocular lenses with blue light filter were developed in order to prevent adverse effects of blue light to retina.

Hypothesis: Although every removal of cataract improves the quality of sleep, implantation of blue-light-filtering lens improves the quality of sleep less than implantation of intraocular lens with UV filter only.

Aims: To confirm that cataract surgery improves the quality of sleep. To determine the difference in improving of sleep quality between patients with implantation of blue-light-filtering lens and ones with implantation of conventional intraocular lens (UV filter only).

Materials and methods: In this randomized control trial we will administer the Pittsburgh Sleep Quality Index questionnaire. It is a self rated questionnaire which assesses sleep quality and disturbances over one month time interval. Eighteen individual items generate seven component scores. The study will include patients older than 60 years who already have an appointment for cataract surgery at the Department of Ophthalmology of University Hospital

Center Zagreb. We will not include patients who have had previous eye surgeries, those with diseases and disorders of the retina, those who have only one eye, patients with terminal stages of glaucoma and those who have some other reason that prevents the passage of light to the retina (eyelid ptosis, pterygium, opaque cornea). Also the patients with verified sleep disorders and those who are taking psychiatric drugs won't be included due to altered sleep architecture. Subjects in whom there is a change in the type or dose of taking medicines and those who had complication during surgery will be excluded from the research. The research plan is to allocate 90 patients to group which would receive conventional IOL and 90 patients to group with blue-light-filtering lens. The results will be statistically processed with appropriate parametric or non-parametric alternative tests for pairs of samples. They will be interpreted in at least a 5% significance level.

Expected scientific contribution: Determining the difference in changing the quality of sleep after cataract surgery due to the type of implanted intraocular lens.

Acknowledgments:

MeSH/Keywords: cataract, blue-light-filtering intraocular lens, quality of sleep

Poster code: B-18-123

POSTER TITLE: ROLE OF THE MTOR INHIBITOR METFORMIN IN TREATMENT OF PATIENTS WITH METASTATIC COLORECTAL CARCINOMA

PhD candidate: Domina Kekez, m.d.

Part of the thesis:

Mentor/s: Stjepko Pleština, MD, PhD

Affiliation: Klinički bolnički centar Zagreb

Introduction: Colorectal cancer is one of the most common and lethal cancers in the world. mTOR signaling pathway is included in pathogenesis of colorectal cancer. It is serin/treonin kinase involved in cellular growth and proliferation. As mTOR integrates inner- and extracellular signaling pathways, logical attempt is to try blocking it. Numerous studies showed that patients who were taking metformin had lower incidence of colorectal adenomas and carcinomas. In vitro and in vivo studies proved effectiveness of mTOR inhibition, so metformin is logic choice in trying to prevent malignant proliferation.

Hypothesis: Metformin is effective in treatment of metastatic colorectal cancer. We presume that combination of metformin and chemo-immunotherapy will be more effective than chemo-immunotherapy alone.

Aims: The main aim is to test the effectiveness (improvement of response rate) of metformin in combination with chemo-immunotherapy in standard protocols for treatment of metastatic colorectal carcinoma. Secondary aims are to test progression free survival, toxicity of combine therapy, and effect of metformin on the activity of mTOR signaling pathway.

Materials and methods: All new diagnosed patients with metastatic colorectal cancer will be included in the study. Patients will be randomized into two groups, one group will receive standard first line chemo-immunotherapy, and other

group will receive metformin plus chemo-immunotherapy. Data collected prior to inclusion are: age, sex, histological type and tumor grade, TNM classification, type of surgical procedure, tumor markers and activity of phosphorilated mTOR. Patients will be evaluated on a monthly basis (clinical examination, standard laboratory tests) and every three months MSCT of thorax, abdomen and pelvis with tumor markers and activity of phosphorilated mTOR will be performed. Extent of the disease will be classified by TNM classification after classical patohistological analysis. Response to treatment will be evaluated by RECIS criteria every three months. Study is designed as prospective intervention randomized study which will test efficacy of metformin in combination with chemo-immunotherapy in treatment of patients with metastatic colorectal carcinoma.

Expected scientific contribution: Considering that randomized interventional prospective study of metformin in combination with first line chemo-immunotherapy for disseminated colorectal carcinoma has not been conducted yet, contribution of this study might be a proof of eventual effectiveness of the treatment protocol.

Acknowledgments:

MeSH/Keywords: Colorectal carcinoma, mTOR, metformin

Poster code: B-19-27

POSTER TITLE: BONE MORPHOGENETIC PROTEIN 6 (BMP 6) EXPRESSION IN SQUAMOUS CELL CARCINOMA OF ORAL CAVITY

PhD candidate: Petar Suton, MD

Part of the thesis: Prognostic significance of bone morphogenetic protein 6 (BMP 6) expression in squamous cell carcinoma of the oral cavity on the development of local recurrence, regional metastases, distant metastases and survival

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 BMP6 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 BMP6 expression in squamous cell carcinoma of the oral cavity remains unknown.

Hypothesis: Increased expression of BMP6 molecule in squamous cell carcinoma of the oral cavity is a negative prognostic factor associated with the development of local recurrence, regional and distant metastasis and patient's survival.

Aims: GENERAL AIM: to determine BMP6 expression in squamous cell carcinoma of the oral cavity. SPECIFIC AIMS: 1) to associate BMP6 expression with the disease recurrence and survival of patients, 2) to compare the level of BMP6 expression with parameters that have prognostic value (tumor size, depth of invasion, tumor grade, perineural/perivascular invasion, periosteal involvement and bone invasion, number and the lowest region of affected lymph nodes, extracapsular spread).

Materials and methods: The study included 120 patients with T1-T3N0 squamous cell carcinoma of the oral cavity who were primary surgically treated at the Department of Maxillofacial Surgery of the University Hospital Dubrava, from January 1, 2003 to December 31, 2008. The immunohistochemistry and semiquantitative analysis will be used to determine the expression of BMP6 in tissues of these patients. These values will be correlated with clinical and pathohistological prognostic factors, disease recurrence and survival, by use of univariate and multivariate statistical methods, in order to identify statistically significant and independent factors for survival.

Expected scientific contribution: Due to the lack of data and papers which analyze BMP6 expression in squamous cell carcinoma of the oral cavity as well as unknown prognostic significance of this protein in head and neck tumors, the study will make an important scientific contribution to a better understanding of predictors factors for recurrence and patient's survival.

Acknowledgments:

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

Poster code: B-19-33

POSTER TITLE: IMPAIRMENT OF COGNITIVE FUNCTIONS ASSOCIATED WITH ADJUVANT CHEMOTHERAPY OF BREAST CANCER

PhD candidate: Ivana Kukec, MD

Part of the thesis: Impairment Of Cognitive Functions Associated With Adjuvant Chemotherapy Of Breast Cancer

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: Extension of overall survival for cancer patients has brought to phenomenon in oncology that, besides the struggle with cancer, the patients are more occupied with unwanted effects of treatment. Impairment of cognitive functions associated with chemotherapy is still not well recognized.

Hypothesis: Adjuvant chemotherapy of breast cancer patients is connected with impairment of cognitive functions.

Aims: Analysis of connection of adjuvant chemotherapy for breast cancer patients with cognitive function disorder considering the influence of anxiety and depression. Specific aims: following up the incidence, beginning,dynamics and reversibility of impairment of cognitive functions among breast cancer patients during and after adjuvant chemotherapy.

Materials and methods: Prospective research on impairment of cognitive functions will be done within 120 breast cancer patients (after signing Informed Consent) who will be treated with adjuvant chemotherapy considering the influence of anxiety and depression. By testing of cognitive functions and by testing of general intellectual status before the start of specific oncological treatment, impairment of cognitive functions will be associated with adjuvant che-

motherapy. Further testing of cognitive functions will be done after 2, 4 and 6 cycle of chemotherapy and during the period of 6 months after the end of adjuvant chemotherapy, if the impairment of cognitive functions will be still present then further testing of cognitive functions will be done during 12 months period after the end of adjuvant chemotherapy. Tests which will be used are: Standard Progressive Matrices, Beck Anxiety Inventor, Beck Depression Inventor Hopkins Verbal Learning Test-Revised (HVLTR), Trail Making Test (TMT),Controlled Oral Word Association Test (COWAT).

Expected scientific contribution: Impairment of cognitive functions associated with chemotherapy is still not well researched. These prospective longitudinal study will be done with more breast cancer patients, then previous studies. Influence of initial cognitive function and influence of anxiety and depression will be considered. Tests of cognitive functions are selected by international guidelines for homogenization of future studies of cognitive impairment associated with adjuvant chemotherapy of breast cancer patients.

Acknowledgments:

MeSH/Keywords: cognitive functions, adjuvant chemotherapy, chemobrain

Poster code: B-19-56

POSTER TITLE: LACUNARITY AND TUMOR BUDDING IN COLORECTAL CARCINOMA

PhD candidate: Martina Šarec, MD

Part of the thesis: Part of a Thesis: The comparison of lacunarity and tumor budding in colorectal carcinoma

Mentor/s: Mentor 1: Assistant professor Gorana Aralica, MD, PhD Mentor 2: Paško Konjevoda, MD, PhD

Affiliation: School of Medicine University of Zagreb and Clinical Hospital Dubrava Zagreb

Introduction: Colorectal cancer is a major health issue, with a pathohistological assesment of preoperative colonoscopic biopsy specimens is the "golden standard" for diagnosis of this type of cancer. Beside the standard prognostic parameters, the invasive front of colorectal carcinoma should be described and peritumoral budding could be recognised. Tumor budding is considered a parameter of tumor progression and is an indicator of tumor aggressiveness. Biopsy sample taken during the colonoscopy is the basic material for the preoperative diagnosis of colorectal cancer. Therefore, an additional histological parameter is used - intratumoral budding. The semiquantitative methods for budding assessment are difficult to reproduce and this is a limiting factor in routine pathology practice. In this study, we will analyze lacunarity using computer based image analysis, as a more objective method.

Hypothesis: Lacunarity of epithelial elements of colorectal carcinoma in different parts of tumor correlates with intratumoral and peritumoral budding and so reflects biological behavior of the tumor.

Aims: 1.To determine the extent of epithelial elements lacunarity in preoperative biopsy specimens that may predict the stage of colorectal carcinoma. 2.To determine the relationship between epithelial elements lacunarity and tumoral budding assessed by Nakamura method. 3.To determine the relationship between the lacu-

narity in preoperative biopsy specimen and the invasive front lacunarity of the colorectal cancer. 4.To determine if the lacunarity, as objective quantitative method, is more valid then tumor budding which is a semiquantitative method, in assessment of disease spread.

Materials and methods: -110 pathohistological specimens of surgical resection specimens and corresponding preoperative colonoscopic biopsies -Tumor budding - assesed by 2 pathologists on HE stained specimens using Nakamura method -Lacunarity – computer based image analysis using imunohistochemical slides (cytokeratin AE1/AE3) Data analysis according to AJCC criterias using multivariate tests and algorithms rpart and party.

Expected scientific contribution: The lacunarity of epithelial elements of colorectal carcinoma as a predictor of biological tumor behavior has not been determined by now. This study would contribute to better understandig of: 1.The relationship between lacunarity and biological behavior of colorectal carcinoma, 2.The relationship between lacunarity and tumor budding, 3.Similarities and differences in conclusions using classification algorithms rpart and party.

Acknowledgments:

MeSH/Keywords: carcinoma, biopsy, morphometry, lacunarity, tumor budding

Poster code: B-19-60

POSTER TITLE: PROFILE OF LONG-TERM SURVIVING PATIENTS WITH METASTATIC BREAST CANCER

PhD candidate: Martina Bašić Koretić

Part of the thesis: Long-term Surviving Patients with Metastatic Breast Cancer : Profile of Patients and Tumour Characteristics.

Mentor/s: Professor Fedor Šantek, MD PhD

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

Introduction: Metastatic breast cancer (mBC) is heterogenous disease with various and unpredictable duration. However, there is now a wide range of therapeutic approaches in current clinical use, in scale from very radical multimodal therapies to paliative care only. And new therapies are emerging. Although metastatic breast cancer is considered to be incurable disease, a certain subset of patients achieves long-term survival.

Hypothesis: patient characteristics and tumour characteristics, both primary and secondary, have an influence on survival of patients with metastatic breast cancer

Aims: identifying variables of long-term metastatic breast cancer survivors that may be associated with favorable long-term outcomes and which could have an impact on therapeutic approach.

Materials and methods: covering retrospective data from those patients with metastatic breast cancer which have survived more than 24 months. Analysis of therapeutic approach, containing several lines of systemic (both che-

motherapy and hormonal therapy)and local therapies , site and number of metastases will be done. Tumor parameters and such as hormonal and HER-2 status, initial morphological tumour characteristics, proliferation index, inflammatory response of of tumour surroundings. Although there are no definitive results, there are data that suggest that patients with hormone positive hormonal tumour status, bones as only metastatic site, oligometastatic disease, good general condition and more active multimodal therapy applied, are in connection with prolonged survival of these patients.

Expected scientific contribution: identifying characteristics of metastatic breast cancer patients and influence of various therapies on long-term surviving, identifying factors that will help clarify clinical course and improve treatment outcome

Acknowledgments:

MeSH/Keywords: long-term surviving, metastatic breast cancer.

Poster code: B-19-116

POSTER TITLE: BIOMECHANICAL ANALYSIS OF NOVEL STABILIZATION SYSTEM FOR THORACO-LUMBAR SPINE FRACTURES TREATMENT

PhD candidate: Krešimir Saša Đurić

Part of the thesis: Biomechanics of the spine

Mentor/s: Prof. M. Stančić, MD, PhD and Prof. J. Sorić, PhD

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

Introduction: Posterior stabilization and the reconstruction of the anterior column, according to most authors is the method of choice in the treatment of thoracolumbar spine fractures AO A3, B2, B3 and C. This approach is invasive it is often unfeasible in polytrauma patients.

Hypothesis: By combining two posterior stabilization systems (transpedicular screws and sublaminar hooks and rods), stabilization that allows a range of motions approximately equal to the undamaged spine can be achieved while using a single surgical approach.

Aims: GENERAL AIM: To compare biomechanical properties of three stabilization systems: the system of transpedicular screws, combined anterior and posterior stabilization and combined posterior stabilization system on the LI corporectomy and spondilectomy vertebrae model. To compare them with each other and with the spine model. SPECIFIC AIMS: To separately analyze and compare with one another: 1. Stress forces in transpedicular screws, hooks and rods of each individual system separately in both models, 2. The deformation of bones at juncture of bones and hooks, 3. Based on the obtained values of stress forces, to analyze whether obtained values are within permissible limits for screws, hooks and bones, 4. Analyze the range of mo-

tion of the original model of the spine, and the corporectomy and spondilectomy model stabilized with three systems.

Materials and methods: To verify our hypothesis, we will conduct the biomechanical analysis using the engineering numerical finite element analysis on the corporectomy and spondilectomy LI vertebrae model. Corporectomy LI model imitates the biomechanical characteristics of AO A3 fractures and AO B2, B3 and C spondilectomy.

Expected scientific contribution: Based on the results of our study, a new stabilization system that would be much more efficient than those applied nowadays will be proposed. The proposed system should greatly improve the treatment of the patients with thoracolumbar fractures AO type A3, B2, B3 and C. The study is a contribution to the efficiency assessment of the posterior surgical approach in the treatment of thoracolumbar spine fractures.

Acknowledgments:

MeSH/Keywords: biomechanical analysis, human spine, finite element analysis, thoracolumbar fractures, posterior surgical approach

Poster code: B-20-7

POSTER TITLE: TREATMENT OF ARTICULAR CARTILAGE DEFECTS WITH BIOREACTOR ENGINEERED AUTOLOGOUS OSTEOCHONDRAL GRAFT

PhD candidate: Tadija Petrović, MD

Part of the thesis: Evaluation of intraarticular inflammatory markers following cartilage reconstruction with autologous osteochondral graft engineered in a perfusion bioreactor

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, Cro

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.

Hypothesis: 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.

Aims: To analyze the changes that occur in subchondral bone and surrounding synovium during the healing process, integration and remodeling of osteochondral graft grown in the bioreactor.

Materials and methods: 24 sheep will be divided into four groups of six sheep. Osteochondral defects will be 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 will be sacrificed after 6 weeks, next 2 after 3 months and the rest after 12 months postoperatively. Collected samples of subchondral bone and synovium will be analyzed histologically and immunohistochemically for the presence of inflammatory markers IL-1, TNF and MMP-13.

Expected scientific contribution: This research will help to evaluate the possibility that autologous osteochondral grafts cultured in a bioreactor become the first choice in the treatment of focal osteochondral defects in joints.

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: B-20-112

POSTER TITLE: DETERMINING THE MAXIMAL AMOUNT OF SAFE COTYLOPLASTY FOR TOTAL HIP ARTHROPLASTY IN DYSPLASTIC HIPS

PhD candidate: Katarina Barbarić, MD

Part of the thesis: Cotyloplasty in dysplastic hip arthroplasty

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

Affiliation: University of Zagreb School of Medicine, University Hospital Centre Zagreb, Department of orthopedic surgery

Introduction: Total hip arthroplasty (THA) in patients with dysplastic acetabulum represents a significant challenge for orthopedic surgeons. Because they are mainly younger people, with increased functional requirements, it is necessary to achieve the ideal biomechanical conditions by placing the acetabulum in the ideal center of rotation with maximum medialization, what sometimes require even controlled iatrogenic fracture of the medial wall of the acetabulum (cotyloplasty).

Hypothesis: Total hip arthroplasty (THA) in patients with dysplastic acetabulum represents a significant challenge for orthopedic surgeons. Because they are mainly younger people, with increased functional requirements, it is necessary to achieve the ideal biomechanical conditions by placing the acetabulum in the ideal center of rotation with maximum medialization, what sometimes require even controlled iatrogenic fracture of the medial wall of the acetabulum (cotyloplasty).

Aims: On animal model (pig or sheep pelvis, not alive) we will measure acetabular component stability depending on the diameter of cotyloplasty following with monitoring of clinical and radiological parameters in patients who underwent cotyloplasty

Materials and methods: On the animal model of the pelvis cotyloplasty in different diameters (0.5, 1, 1.5, 2 cm) will be done followed with acetabular components placement (sizes 44 and 46). Acetabulum will be loaded with 70 kg for determining to which diameter of cotyloplasty acetabular component of the THA remains stable, or at which point the remaining medial wall of the acetabulum can't withstand the load and endoprosthesis breaks through the pelvis. Additionally, we will prospectively analyze patients with osteoarthritis as a result of developmental dysplasia of the hip in which we planning to do THA. Before the surgery, and 6 months after, clinical analysis of functional status and filling the questionnaires will be done. Also, radiographic examination and analysis of the acetabular component stability will be performed.

Expected scientific contribution: Defining maximal amount of safe cotyloplasty which leads to significantly better biomechanical conditions for achieving longer survival of THA, without reducing the acetabular component stability. We expect significantly better long-term results with this treatment method.

Acknowledgments:

MeSH/Keywords: cotyloplasty, hip dysplasia, arthroplasty

Poster code: B-20-126

POSTER TITLE: ARE THERE BENEFITS OF TOURNIQUET USE IN ANTERIOR ANKLE ARTHROSCOPY?

PhD candidate: Damjan Dimnjaković

Part of the thesis: Use of the tourniquet in all arthroscopic surgeries is taken for granted worldwide.

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

Affiliation: Department of Orthopaedic surgery of the University hospital center Zagreb and 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 made which did not confirm the advantages of tourniquet use in knee arthroscopy.

Hypothesis: Postoperative bleeding will not be greater without the use of the tourniquet in anterior ankle arthroscopy, compared to anterior ankle arthroscopy with use of the tourniquet.

Aims: The goal of this research is to clarify if there are differences in course and outcome re-

lated to tourniquet use in anterior ankle arthroscopy.

Materials and methods: The patients will be randomized into two groups, consisting of 25 patients in each. AOFAS, FADI and Tegner score will be used preoperatively and 3 and 6 months postoperatively to determine the function of the operated ankle. Surgery log will be filled out by the surgeon. Postoperative pain diary will be filled by patients. Any complications will be noted.

Expected scientific contribution: To determine if anterior ankle arthroscopy is possible without the use of the tourniquet.

Acknowledgments:

MeSH/Keywords: arthroscopy, ankle, tourniquet

Poster code: B-20-164

POSTER TITLE: THYROTROPIN RECEPTOR MRNA AS A NOVEL MARKER FOR THYROID CANCER

PhD candidate: Tomislav Novosel, MD

Part of the thesis: Molecular Marker for Thyroid Cancer

Mentor/s: Professor Vladimir Bedeković, MD, PhD

Affiliation: The Cleveland Clinic, Cleveland, Oh, USA, Universiti Hospital Center

Introduction: Early thyroid malignancy and early recurrence detection improves patients survival rate. New thyroid cancer tumor marker for thyroid cancer or thyroid cancer recurrence identification would improve patient care and outcome. Existing thyroid tumor marker, thyroglobulin, is overall good marker for recurrence detection but it has limitations.

Hypothesis: Thyrotropin receptor mRNA (TSHR mRNA) detection in peripheral circulation is correlated with differentiated thyroid cancer diagnosis.

Aims: The aim of this study is to investigate TSHR mRNA presence in patients with differentiated thyroid cancer, measure TSHR mRNA in peripheral circulation and correlate TSHR mRNA concentration with thyroid cancer presence.

Materials and methods: In this study thyrotropin receptor messenger RNA (TSHR mRNA) concentration will be analyzed in patients with differentiated thyroid cancer. Blood samples from all patients with fine needle aspiration biopsy proven thyroid cancer, follicular neoplasm and

benign goiter referred to surgery will be collected and TSHR mRNA concentration will be measured using quantitative real-time transcriptase polymerase chain reaction. This method extracts total RNA from the cellular fraction of a peripheral blood sample, and then amplifies mRNA specific for the TSHR using specifically designed primers. TSHR mRNA concentration will be correlated with thyroid cancer presence. The data will be analyzed using JMP 7.0 (SAS Institute Inc.) software.

Expected scientific contribution: TSHR mRNA has potential to become relevant tumor marker for thyroid cancer identification as well as thyroid cancer recurrence. With this study we will try to validate TSHR mRNA as useful tumor marker improving thyroid cancer patient care, increase survival rate with early diagnosis and identify thyroid cancer recurrence.

Acknowledgments:

MeSH/Keywords: Thyroid cancer, follicular neoplasm, TSHR mRNA, tumor marker

Poster code: B-21-82

POSTER TITLE: CHARACTERISTICS OF GLOMERULAR BASEMENT MEMBRANE IN ALPORT'S SYNDROME AND THIN BASEMENT MEMBRANE NEPHROPATHY

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: Associate Professor Danica Galešić Ljubanović, MD, PhD

Affiliation: Dubrava University Hospital Zagreb

Introduction: Alport's syndrome (AS) and thin basement membrane nephropathy (TBMN) are structural disorders of glomerular basement membrane (GBM) with its genetic bases lying on mutations of collagen IV isoforms.

Hypothesis: Immunofluorescent/immunohistochemical (IF/IHC) analysis of $\alpha 3$, $\alpha 4$ and $\alpha 5$ chain of collagen IV significantly improves diagnostic differentiation between AS and TBMN and subtyping of AS in native and transplant kidney biopsy specimens analysis.

Aims: Aim of our research is to elucidate concept of "thin GBM" and evaluate IF/IHC analysis for COL4A3, COL4A5 and COL4A4 in differentiation TBMN from AS and subclassification of AS.

Materials and methods: Our retrospective research will have two parts. In first part (research on native kidney biopsy samples) we will define referential span of normal GBM thickness for our laboratory. On biopsy samples of AS and TBMN patients, we will determine accurate GBM thickness. Kidney samples will be analyzed by IF/IHC for $\alpha 3$, $\alpha 4$ and $\alpha 5$ chains of collagen IV. By patterns in IF/IHC analysis patients will be categorized as: TBMN, heterozygous carriers of X-linked AS, X-linked male AS, autosomal recessive AS, and patients with disturbed patterns of COL4A4 staining. For these groups, data about histological appearance, GBM ultrastructure and GBM thickness will be compared. In second part

(research on transplanted kidney biopsy samples) we will on "zero" renal biopsy specimens determine accurate GBM thickness and number of TBMN patients. Renal samples from those patients will be analyzed and categorized with IF/IHC as previously described. Data about renal function parameters and Banff scores will be collected and compared between categorized patients and other transplanted patients. We will also test if there is any difference in GBM thickness among transplanted patients at the point of "zero" kidney biopsy and the same transplanted patients who have EM analysis after more than six months after kidney transplantation and if there is difference in GBM thickness between transplanted patients and control group of patients.

Expected scientific contribution: This research will elucidate complex disorders TBMN and AS in histopathologic, ultrastructural and clinical sense. Accurate diagnosis and categorization of patients will enable correct approach regarding treatment and monitoring of patients. This methodology will also be applicable in transplanted patients.

Acknowledgments:

MeSH/Keywords: Alport Syndrome, Thin Basement Membrane Nephropathy

Poster code: B-23-142

POSTER TITLE: MOLECULAR PROFILING OF TUBULOCYSTIC RENAL CELL CARCINOMA

PhD candidate: Faruk Skenderi

Part of the thesis: Molecular Profiling of Tubulocystic Renal Cell Carcinoma

Mentor/s: Ondrej Hes, MD, PhD - Semir Vranić, MD, PhD - Božo Krušlin, MD, PhD

Affiliation: Department of pathology, Clinical Center of the University of Sarajevo, Sarajevo, Bosnia and Herzegovina. Department of Pathology, Charles University in Prague, Faculty of Medicine in Plzeň, Czech Rep

Introduction: Renal tumors are diverse group of neoplasms in regards to their morphology, genetic features, biological behavior, prognosis and potentially therapy. Besides the surgery, there is no specific targeted therapy for existing particular subtypes of RCC. Vasculature plays a key role for the growth and further spreading of these tumors. Angiogenic inducers and other markers play a critical role in tumor progression and metastasing and could be potentially influenced by RCC subtype specific therapy. There are insufficient data dealing with biological behavior, molecular genetic features and potential targets for biological treatment of rare renal tumors. Tubulocystic Renal Cell Carcinoma (TCRCC) is a recently recognized distinctive subtype of renal cell carcinoma.

Hypothesis: Molecular profile of TCRCC includes distinct chromosomal and gene abnormalities of which some could be targeted with novel therapeutic agents.

Aims: Our aim is to explore the molecular genetic characteristics of the TCRCC by detecting of the common mutations and chromosomal abnormalities which could be potential candidates for available targeted therapeutic agents or provide a rationale for development of new therapeutics.

Materials and methods: TCRCCs will be selected from 17,000 cases of renal carcinomas that

are registered in the Tumor Registry in Plzen, Czech Republic. Cases from the Department of Pathology, University of Sarajevo Clinical Center, Bosnia and Herzegovina and Ljudevit Jurak Department of Pathology, University of Zagreb, Croatia, will also be included. The selected cases will undergo a comprehensive molecular genetic analysis. Fluorescent in-situ hybridisation (FISH), Comparative Genomic Hybridization (array CGH) will be used as screening method for major chromosomal numerical alterations. Polymerase chain reaction (PCR) and DNA sequencing will be used for detection of families of vascular-endothelium-specific growth factors and their transmembrane receptors and VEGF responsive genes. Tumor oncogenes and tumor-suppressor genes will be analyzed.

Expected scientific contribution: Molecular genetic profiling of the TCRCC will give the results which could potentially have impact on the treatment of patients with TCRCC with available targeted therapy agents, or provide a rationale for novel therapeutic agents.

Acknowledgments: Professor Zoran Gatalica, MD, DSc, Caris Life Sciences, Phoenix, Arizona, United States of America

MeSH/Keywords: kidney, carcinoma, Tubulocystic renal cell carcinoma, biomarkers, mutation, genetic profiling

Poster code: B-23-153

POSTER TITLE: MUTUAL CONTRIBUTION OF NOVEL BIOMARKERS AND ADVANCED HEMODYNAMIC MONITORING IN UNDERSTANDING ACUTE KIDNEY INJURY PATHOGENESIS AFTER PEDIATRIC CARDIOPULMONARY SURGERY

PhD candidate: Slobodan Galić, MD, M.S.

Part of the thesis: Mutual Contribution of Novel Biomarkers and Advanced Hemodynamic Monitoring in Understanding Acute Kidney Injury Pathogenesis after Pediatric Cardiopulmonary Surgery

Mentor/s: Professor Danko Milošević, MD, PhD

Affiliation: University Hospital Centre Zagreb

Introduction: Acute kidney injury (AKI) is known and common complication after pediatric cardiopulmonary bypass (CPB) surgery, the diagnosis of which depends on serum creatinine (Scr). Unfortunately, Scr is a delayed and unreliable indicator of AKI during the early postoperative period. Recent research led to the discovery of numerous molecules which are released in blood and urine during early kidney injury (AKI biomarkers). It is believed that biomarkers could guide to the earliest possible and reliable warning of AKI. Some of the most important biomarkers are neutrophil gelatinase-associated lipocalin (NGAL), kidney injury molecule 1 (KIM-1), and cystatin C. It is believed that AKI ensues as a result of hemodynamic matching disturbances during and after CPB, resulting in kidney ischemia. However, previous investigations are still inconclusive to the fundamental question: are those biomarkers predictive factors for AKI at all, and if yes, which of them are the most reliable? Their relationship with cardiocirculatory disturbances which lead to AKI are still debated.

Hypothesis: AKI in children after CPB surgery ensues due to kidney ischemia in early perioperative period. We believe that the degree of kidney ischemia and related dynamics of AKI biomarkers appearance in plasma and urine, beside duration and quality of CPB, depends also patient's cardiocirculatory condition in early postoperative period.

Aims: The aim of the study is to investigate if measured values of biomarkers have predictive values for AKI in children who underwent CPB surgery, does multiple biomarkers determination have an advantage against a single one and can the comparisons of dynamics of AKI biomarkers appearance in plasma and hemodynamic parameters explain the true nature of AKI.

Materials and methods: The study is clinical and prospective and includes children who underwent CPB surgery. The study has Central Ethic Committee approval of Medical Faculty, University of Zagreb. Signed parental consent will be obtained before investigation. Blood and urine samples will be obtained immediately before and after CPB surgery, thereafter at every 6 hour interval during the next 24 hours. All patients will be monitored with application of advanced hemodynamic monitoring based on transpulmonary thermodilution technology (Pulsion, Germany).

Expected scientific contribution: Expected scientific contribution is better understanding of AKI pathogenesis in children after CPB surgery.

Acknowledgments:

MeSH/Keywords: Acute Kidney Injury, Biological Markers, Cardiopulmonary Bypass, Hemodynamics and Children

Poster code: B-24-20

POSTER TITLE: CHILDREN BORN FROM ASSISTED REPRODUCTIVE TECHNIQUES

PhD candidate: Sonja Anić Jurica, MD

Part of the thesis: Outcome differences between children conceived spontaneously and from assisted reproductive techniques

Mentor/s: Professor Miro Kasum, MD, PhD

Affiliation: Division of Neonatology, Division of Human Reproduction, University Hospital for Obstetrics and Gynecology, University Hospital Center Zagreb, School of Medicine, University of Zagreb

Introduction: It is a widespread opinion that children born from assisted reproductive technique (ART) have worse outcome than those spontaneously conceived. ART proved to be followed by perinatal complications such as premature birth and small birth weight for gestational age (SGA). Majority of complications stem from prematurity due to prevalence of multiple pregnancies following ART. Higher incidence of SGA in multiple pregnancies results from placental, umbilical cord and uterus factors as well as genetic potential divergency and growth discordancy between children. In single pregnancies premature birth and SGA are also recorded and considered to be a result of hypofertility basis of the couple, maternal age and oftenly a single pregnancy resulting from multiple after vanishing twin. Both prematurity and SGA have impact on neurological outcome. Progress of ART procedures, decreased number of multiple pregnancies, shortened hypofertility duration, upgrading of perinatal and neonatal care have critical roles in outcome of the ART children.

Hypothesis: Adverse outcome of children conceived by ART in general can be annuled when parental factors and characteristic as well as ges-

tational age and multiplicity are encountered.

Aims: To compare outcome of ART children and spontaneously conceived children.

Materials and methods: In our Center 200 children are born after ART conception per year. Outcome of ART children will be analyzed and compared to those spontaneously conceived. Incidence of prematurity, small birth weight for gestational age and concomitant complications with an accent on brain lesions and neurological outcome will be compared. Indications for ART, parental age, course of pregnancy, duration of pregnancy and termination method will be included in the analysis with individual adjustment in comparison to spontaneous pregnancy.

Expected scientific contribution: To define procedures and treatments of perinatal and neonatal care that can be improved to ameliorate outcome of children born after ART.

Acknowledgments:

MeSH/Keywords: neonatal outcome, assisted reproduction techniques, perinatal complication

Poster code: B-24-75

POSTER TITLE: ROLE OF INNATE IMMUNE SYSTEM IN PATHOPHYSIOLOGY OF JUVENILE IDIOPATHIC ARTHRITIS IN MULTIPLEX JIA FAMILIES

PhD candidate: Marija Perica, MD

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 with still undefined role of innate and adaptive immune system in the disease development. Multiplex families represent rare entity, defined by two or more members diagnosed with JIA, in contrast with simplex families, with only one member diagnosed with JIA. Pathophysiology underlying disease development in multiple members of the same family has not been clarified.

Hypothesis: Single nucleotide polymorphisms (SNP) and altered gene expression of the innate immune system components IL1 β , IL18, NOD2/CARD15, CARD 8, NLRP3, TLR 2,TLR 4 i ATG16L1 contribute to the development and clinical characteristics of juvenile idiopathic arthritis (JIA) in multiplex families

Aims: 1. To compare the prevalence of gene expression alterations and SNP's of innate immune system components in multiplex and simplex JIA families and among healthy and JIA affected members of the same multiplex family. 2. To determine correlation of gene expression alterations and SNP's with disease activity and clinical phenotype

Materials and methods: Using PCR-based methods, 39 JIA patients from multiplex families, 40 JIA patients from simplex families (control

group) and 40 healthy members of multiplex families will be genotyped for NLRP3 (Q705K), CARD8 (C10X), NOD2/CARD15 (SNP 8, SNP 12, SNP 13), caspase 1(8404 A/G), TLR4 (Asp299G-ly, Thr399Ile), TLR2 (R753Q i R677W), IL1 β (-511, 3954), IL18 (-607,-137) and ATG16L1 SNP's. Standardized assays will be used for gene expression determination. Levels of proinflammatory cytokines and alarmines (TNF- α , IL-1, IL-6, IL-18, caspase 1,S100A8/A9 and hs CRP) will be determined at the time of inclusion in the study and six months later. Medical records of all patients will be used to compare clinical phenotypes of the disease. PRINTO criteria will be used for disease activity assessment.

Expected scientific contribution: By comparing polymorphisms of innate immune system's key components and gene expression in multiplex and simplex families, we will note the differences in signal pathways and discover new, easily measured biomarkers useful for early diagnosis, better disease activity assessment and potential therapeutic targets.

Acknowledgments:

MeSH/Keywords: juvenile idiopathic arthritis, multiplex families, innate immune system, polymorphisms, gene expression

Poster code: B-24-140

POSTER TITLE: VALIDATION OF COLOR DOPPLER USAGE IN DIAGNOSING ACUTE SACROILIITIS IN PATIENTS WITH ENTHESITIS-RELATED ARTRITIS

PhD candidate: Dubravko Bajramović, MD

Part of the thesis: 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: Imaging methods have an important role in diagnostics, classification and treatment efficiency monitoring in patients with juvenile idiopathic arthritis. 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.

Hypothesis: Color Doppler is a valid diagnostic method in detection of sacroiliitis in patients with enthesitis-related arthritis (ERA).

Aims: General aim is to determine validity of Color Doppler in detection and follow-up of sacroiliitis in patients with ERA in comparison with MRI. Specific aims include determination of prevalence of sacroiliitis in patients that fulfil the ILAR criteria for ERA, analysis of radiological correlation with clinical and laboratory findings, determination of value of Color Doppler in appraising the response to applied therapy and analysis of MRI techniques for detection of acute sacroiliitis.

Materials and methods: 62 patients that fulfil the ILAR criteria for ERA will be enrolled in this study. During initial visit ultrasound imaging and MRI of sacroiliac (SI) joints will be performed for each patient. Ultrasound examination will be performed on a high-quality device with high-frequency linear array using B-mode and Color Doppler imaging in order to determine degree of synovial vascularity. Results will be recorded using two semi quantitative methods. Values

of vascular resistance index (RI) which may be used as a quantitative measure for acute synovitis will be recorded. MRI of SI joints will be performed on 1.5T machine in standard series of sequences. Presence of synovitis, joint effusion, subchondral bone marrow oedema, erosions and marginal appositions will be analysed. Inflammatory changes will be quantified using SPARCC (Spondyloarthritis Research Consortium of Canada) method. Clinical appraisal of disease activity will be conducted using JADAS-10 composite score and JAMAR questionnaire. Therapeutic effect will be determined based on ACR criteria. Results of standard laboratory findings will be also collected. All imaging and clinical workup will be repeated after 6 months in order to determine the effects of applied therapy.

Expected scientific contribution: Confirming validity of Color Doppler use in diagnostics of acute sacroiliitis in patients with ERA would lead to improvement of diagnostic procedure in regard of simplicity, price, time needed to perform an examination and possible risks for patients.

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: B-25-9

POSTER TITLE: CORRELATION OF MORPHOLOGICAL AND KINETIC MR FEATURES WITH PROGNOSTIC AND PREDICTIVE FACTORS IN BREAST CANCER

PhD candidate: Ana Marija Alduk, MD

Part of the thesis: Correlation Of Morphological And Kinetic Mr Features With Prognostic And Predictive Factors In Breast Cancer

Mentor/s: Maja Prutki, MD, PhD

Affiliation: University Hospital Centre Zagreb, Clinical Department for Diagnostic and Interventional Radiology

Introduction: Breast magnetic resonance imaging (MRI) is a highly sensitive modality for imaging of breast cancer. MRI provides important information not only on the morphology of lesions but also on the functional aspects reflected by the temporal and spatial uptake of contrast medium. Integration of both morphological and kinetic features is important for accurate diagnosis. Göttingen score is a multifactorial evaluation protocol that enables integration of these MRI features. The correlation between MRI features with prognostic and predictive factors in breast cancer has been studied. However, these studies showed variable results.

Hypothesis: Due to difference in histology and biological characteristics, breast carcinomas show different morphological and kinetic MRI features. These MRI features may be used for the assessment of prognostic and predictive factors of breast carcinoma. Breast cancers with unfavorable prognostic and predictive factors will show higher Göttingen score.

Aims: To analyse the correlation of morphological and kinetic MRI features with prognostic and predictive factors in breast cancer.

Materials and methods: 112 women with invasive ductal carcinoma of no special type (NST) who underwent preoperative breast MRI will be included in this retrospective study. MRI findings will be interpreted with a multifactorial classification system according to Göttingen. The difference in morphological and kinetic MRI features of NST breast carcinoma depending on prognostic factors will be analysed (including tumor size, lymph node status, nuclear and histological grade, lymphatic and vascular invasion, estrogen and progesterone receptors, oncogene HER2 expression, and proliferation marker Ki-67).

Expected scientific contribution: Considering variable results published so far, this study could contribute to understanding of the relationship of MRI features and prognostic factors of breast carcinoma. Establishing association between MRI features and prognostic factors would be valuable in the development of clinically useful MRI-based predictive models that could be used in the preoperative assessment of breast cancer.

Acknowledgments:

MeSH/Keywords: breast neoplasm, magnetic resonance imaging, prognostic factors, kinetic characteristics

Poster code: B-25-52

POSTER TITLE: THE ROLE OF THORACIC MAGNETIC RESONANCE IMAGING IN LYMPHOMA PATIENTS

PhD candidate: Nikola Ivan Leder

Part of the thesis: The Role of Magnetic Resonance Imaging of the Thorax in Treatment Response Evaluation of Hodgkin and Non-Hodgkin Lymphoma Patients

Mentor/s: Asst. Prof. Vinko Vidjak, MD PhD

Affiliation: Clinical Department of Diagnostic and Interventional Radiology, University Hospital Merkur

Introduction: This study is aimed to prove that modern magnetic resonance imaging (MRI) techniques including electrocardiogram (ECG) gating can provide images of thorax and mediastinum of adequate diagnostic quality to replace the need for computerized tomography (CT) imaging with its inherent radiation dose. Secondary, the diffusion weighted (DWI) and dynamic contrast enhanced (DCE) imaging will be evaluated to determine the predictive ability of MRI for treatment response.

Hypothesis: MR imaging can replace the CT imaging in detection and staging of lymphoma. Information gained through added DWI and DCE imaging will enable earlier prediction of response to treatment.

Aims: 1. To assess the feasibility of MR imaging in comparison with CT imaging in lymphoma patients. 2. Comparison of changes in contrast uptake dynamics and DWI properties in MR imaging of lymph nodes and correlation with the clinical findings of lymphoma activity. 3. Radiation protection by introducing MR imaging in regular practice in lymphoma patients.

Materials and methods: Inclusion criteria includes: - lymphoma patients with mediastinal involvement of the disease, - preserved renal function (for contrast medium application), - no ferromagnetic metal implants, metal foreign bodies or electrostimulators in the body, - no allergies to contrast media. All imaging will be

performed on a 1.5 Tesla MR scanner (Excelart Vantage Atlas-Z, Toshiba Corporation, Tokyo, Japan). MR imaging technique will include: - Ultra fast spin echo localizer, - Axial and coronal T2 weighted FSE sequence with ECG gating during breath hold, - Axial T1 weighted in and opposing phase GRE with ECG gating during breath hold, - Axial DWI with b value of 0, 400 and 800, - Axial T1 weighted spoiled GRE DCE series. All MR imaging will be performed 1-3 weeks after CT imaging. This interval should provide sufficient time to preserve renal function while still being short enough that no significant changes due to treatment are expected. Statistical analysis will be performed with appropriate tests for parametric and nonparametric variables.

Expected scientific contribution: Analysis of the changes in MR properties of lymphomatous masses during treatment and possibility of introducing MR imaging in staging of lymphoma with thoracic involvement. Results of the study will also include the most adequate MR imaging protocol.

Acknowledgments: I would like to thank Asst. Prof. Jelena Popić Ramač, MD PhD and radiographers Demir Puljizović, Mladen Radošević and Kristijan Ristović.

MeSH/Keywords: Magnetic Resonance Imaging, Diffusion Magnetic Resonance Imaging, Thorax, Mediastinum, Lymphoma

Poster code: B-25-86

POSTER TITLE: OSTEOMETRIC SEX DETERMINATION FROM THE AURICULAR AND RETROAURICULAR SURFACE AND ACETABULUM OF PELVIC BONE

PhD candidate: Pero Bubalo MD

Part of the thesis: A new discriminant function of pelvic bone in sex determination

Mentor/s: Assistant Professor Davor Mayer MD PhD

Affiliation: Department of Forensic Medicine University of Zagreb School of Medicine

Introduction: Pelvis is the most sexually dimorphic area of the adult human skeleton. Therefore, sexing a pelvis is one of the fundamental bases of forensic identification. It has long been customary among anatomist, anthropologist, and forensic medicine experts to determine the sex on the skeletal material by non-metric morphological observations. Over time, confirming sexual divergence by osteometric analysis of the bones became increasingly recognized. For that purpose, creating the discriminant function formulas from osteometric data are the most common methods. It is widely argued in the literature that these formulas are population specific. Some recent works pointed to acetabulum features as being useful in determining the sex while at the same time using the auricular and retroauricular surface for the same purpose is completely uncovered topic in the literature.

Hypothesis: Osteometric parameters obtained by measuring the auricular and retroauricular surface and acetabulum of pelvis will differ significantly between males and females.

Aims: This study aims to assess the validity of the osteometric analysis of auricular and retroauricular surface and acetabulum in distinguishing male from female pelvis and to develop new standards for sex determination of human adult skeletal material based on these specific areas of pelvis.

Materials and methods: The material for this study will be recruited from skeletal remains of the victims of Croatian Homeland War. This skeletal remains have already undergone the identification process at the Institute of Forensic Medicine and Criminalistics in Zagreb so their sex is already known. One hundred female and one hundred male individuals will be included in the study. Using a flexible meter and sliding caliper, we will measure seven parameters on the auricular and retroauricular surface and two parameters on the acetabulum. The measurement will be taken from both sides of the pelvis. Data will be subjected to statistical analysis using the SPSS program.

Expected scientific contribution: We expect that the results of the work will yield a new method for sex diagnosis using pelvic indicators of sex that we propose could be added to the standard set of osteological measurements and will have practical application in forensic medicine and forensic anthropology. Those new indicators could be particularly useful in cases where the skeleton is badly fragmented, which prevents routine measurements to be taken.

Acknowledgments:

MeSH/Keywords: pelvic bones, acetabulum, sex determination, analysis

Poster code: B-27-26

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.

Hypothesis: Peritoneal dialysis before transplantation with early removal of peritoneal catheter after transplantation will result with the same outcome and lower overall treatment cost when compared to haemodialysis.

Aims: Outcome of renal transplantation with respect to pretransplant dialysis modality. Specific aims: 1. Patient and graft survival, 2. Incidence of urinary tract, wound, intraabdominal infections and sepsis in first three months after transplantation, 3. Estimate of kidney function 6 and 12 months after transplantation, 4. The cost of transplantation and duration of first hospitalization.

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.

Expected scientific contribution: Results of this study will show the relationship of dialysis modality before transplantation with the outcome and cost of transplantation, which could contribute to the choice of the dialysis modality in patients who are candidates for renal transplantation.

Acknowledgments:

MeSH/Keywords: peritoneal dialysis, haemodialysis, kidney transplantation, infection, surgical wound infection

Poster code: B-28-17

POSTER TITLE: CLINICAL CHARACTERISTICS OF HGPIIN AND THEIR CORRELATION WITH PROSTATE CANCER

PhD candidate: Igor Grubišić, m.d.

Part of the thesis: Localisation of PIN in prostate biopsy

Mentor/s: assistant professor, Borislav Spajić, MD, PhD

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

Introduction: Prostate cancer is the most common cancer in elderly males in Europe. The need for a prostate biopsy should be determined on the basis of the PSA level and a suspicious DRE. According to European association of Urology indications for repeat biopsy are rising or persistently elevated PSA, suspicious DRE, atypical small acinar proliferation (ASAP) and extensive (multiple biopsy sites) prostatic intra-epithelial neoplasia (PIN). High grade prostatic intraepithelial neoplasia (HGPIIN) is a cytoarchitectural modification of the prostatic tissue, with pre-existing acini and ducts lined by cytologically atypical cells. It has long been considered the pre-neoplastic lesion of prostate cancer but in 2010. it is no longer indication for repeat biopsy. In EAU guidelines 2014 high-grade PIN as an isolated finding is no longer considered an indication for repeat biopsy. A repeat biopsy should therefore be prompted by other clinical features, such as the DRE findings and the PSA level. Extensive PIN (i.e. in multiple biopsy sites) could be a reason for an early repeat biopsy because the risk of subsequent prostate cancer is slightly increased. The prognostic value of HGPIIN, clinical markers (age, digital rectal examination, PSA, etc) and widespread HGPIIN in men after multiple diagnoses of isolated HGPIIN remains controversial.

Hypothesis: Patients with HGPIIN in prostate apex have increased risk for prostate cancer in repeat biopsy.

Aims: To determine is localization of HGPIIN in prostate apex associated with higher risk of prostate cancer in repeat biopsy. 1. Define the number of patient with HGPIIN in first biopsy and prostate cancer in second biopsy, 2. Compare clinical characteristics (PSA, DRE, Volume, Age) in biopsies with and without cancer, 3. Compare the localisation and number of HGPIIN in first biopsy in patients with prostate cancer in second biopsy.

Materials and methods: Find all patients with HGPIIN in first prostate biopsy done from 2003. till 2013. in our clinic. Compare the results with repeat biopsy and clinical findings and determine connection of localization of HGPIIN and prostate cancer in repeat biopsy.

Expected scientific contribution: HGPIIN (PIN) is still controversial in scientific literature, ten years ago it was considered as precancerous pathological finding. The attitude of scientific community is that HGPIIN is no longer precancerous pathological finding, with some exceptions. We want to prove that HGPIIN is still precancerous finding if it is connected with localization (apex of prostate) and some other clinical characteristics.

Acknowledgments:

MeSH/Keywords: HGPIIN, prostate biopsy, repeat prostate biopsy, prostate cancer, prostate apex

Poster code: B-28-96

POSTER TITLE: ATTACHMENT STYLE AND EMOTIONAL REGULATION IN PATIENTS WITH BULIMIA NERVOSA

PhD candidate: Trpimir Jakovina, psychologist

Part of the thesis: Attachment style and emotional regulation in patients with bulimia nervosa

Mentor/s: Ivan Begovac, MD, PhD

Affiliation: University Hospital Centre Zagreb

Introduction: Theoretical models of eating disorders associate bulimia nervosa (BN) with insecure attachment style, as well as with dysfunctional emotional regulation. Studies on BN are rare, with limited scientific evidence to support such a perspective.

Hypothesis: Insecure attachment style and dysfunctional emotional regulation are positively associated with the presence of symptoms of bulimia nervosa

Aims: The aim of the study is to examine the relationship between attachment styles and emotional regulation with symptoms of bulimia nervosa.

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 years of age. Clinical group will include 50 participants with BN, and control group will include 50 healthy matched participants. Statistical comparison of the results and logistic regression will determine whether there

are differences in factors of attachment styles and emotional regulation between group of female subjects suffering from BN and control group, as well as determine whether insecure attachment style and dysfunctional emotional regulation are positively associated with the presence of BN symptoms.

Expected scientific contribution: This study will contribute to a better understanding of the specific psychological concepts (attachment styles and emotional regulation) in explaining the eating disorder BN. If the hypothesis of the research will be confirmed, the existing theoretical models will be supported, and the findings will contribute to the therapeutic approaches to the treatment of BN, which to a greater extent should focus on attachment style and emotional regulation in treating patients with BN.

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: B-29-13

POSTER TITLE: PERSONALITY, COGNITIVE BIASES AND POSTTRAUMATIC STRESS DISORDER (PTSD)

PhD candidate: Nenad Jakšić, MA

Part of the thesis: Complex Relationship among Personality Traits, Cognitive-affective Biases and Posttraumatic Stress Disorder (PTSD)

Mentor/s: Professor Miro Jakovljević, MD, PhD

Affiliation: Department of Psychiatry, University Hospital Center Zagreb, Zagreb, Croatia

Introduction: The idea of trauma experience as the only etiological factor in the development of PTSD has been rejected by empirical data. There are numerous pre- and post-traumatic factors responsible for the variations in the development, symptomatic expression and clinical outcome of PTSD. Personality dimensions (e.g., novelty seeking) and cognitive-affective biases (e.g., intolerance of uncertainty) are such entities of research and clinical relevance with regard to posttraumatic reactions. This research field can be further improved by integrating these two fundamental perspectives, such that cognitive affective biases might be elaborated as more proximal and situation-related mediators in the relationship between distal personality dimensions and the development and expression of PTSD.

Hypothesis: 1. There is a statistically significant prospective association between personality dimensions and PTSD symptoms. 2. There is a statistically significant prospective association between cognitive-affective biases and PTSD symptoms. 3. Cognitive-affective biases are statistically significant mediators of the perspective association between personality dimensions and PTSP symptoms.

Aims: To examine the complex associations between personality dimensions, cognitive-affective

biases and PTSD among psychiatric patients who experienced interpersonal trauma.

Materials and methods: The study will be conducted with psychiatric outpatients who have experienced interpersonal trauma within the last month. They will be approached during their first psychiatric consultation, after which they will be assessed with the structured clinical interview and several self-report measures of personality dimensions, cognitive-affective biases, PTSD symptoms, depressive symptoms, perceived social support. Finally, patients are going to be contacted after 3 months and they will be invited to a follow-up session.

Expected scientific contribution: Prospective investigation of personality dimensions and cognitive-affective biases can help better understand the etiopathological development and symptomatic expression of PTSD, as well as enhance the implementation of more efficient treatment methods.

Acknowledgments:

MeSH/Keywords: PTSD, interpersonal trauma, personality, temperament, character, cognitive bias, mediation

Poster code: B-29-155

2.3.
PUBLIC HEALTH AND HEALTH CARE
– RESEARCH PROPOSALS

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: Metabolic syndrome is a cluster of interrelated risk factors for development of cardiovascular disease and diabetes mellitus type II. Prevalence of the metabolic syndrome in children and adolescents ranges from 3-11%, depending on the applied criteria. The prevalence is higher among population of overweight and obese children, in boys and in aged group of adolescents compared to younger children. In the literature there is no data on the prevalence of the metabolic syndrome in children and youth in Croatia. Development and presence of metabolic syndrome are still discussed topics with an opened question whether there is a tracking phenomenon. Opened questions also include clustering risk factors of the metabolic syndrome and whether the interaction between BMI and other risk factors contribute to the development of metabolic syndrome more than the individual effect of one single factor.

Hypothesis: Overweight in early school age is a predictor of metabolic syndrome development in adolescence.

Aims: The aim of this thesis is to determine ability to identify risks at an early school age for

development of metabolic syndrome in adolescence and suggest protocol for early diagnosis of metabolic syndrome in schoolchildren and youth.

Materials and methods: Longitudinal study includes 500 students (aged 18) which is 50% proportional sample of the initial cohort from a representative sample of first-grade students of elementary school year 2003/2004. Respondents will complete questionnaire, and anthropometric measurements and laboratory analysis of blood will be carried out. Data will be processed by appropriate statistical and analytical procedures.

Expected scientific contribution: Results will contribute to recognition and understanding of retention of risk factors for metabolic syndrome from early school age to adolescence, in order to facilitate development of early detection and prevention programs.

Acknowledgments:

MeSH/Keywords: children, adolescent, metabolic syndrome x, early diagnosis, prevention

Poster code: C-2-54

POSTER TITLE: OUTPATIENT UTILIZATION OF CARDIOVASCULAR DRUGS

PhD candidate: Maja Marić Bajš, 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: Institute of Public Health „Dr. Andrija Štampar“

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.

Hypothesis: The quality and rational prescribing cardiovascular drugs in outpatient health care in the City of Zagreb during the 2001-2012 periods increased.

Aims: The aim of this study is to determine trend of outpatient utilization of cardiovascular drugs as the largest generator in the total utilization of drugs. Specific goal is to evaluate the quality and rational prescribing of cardiovascular drugs using the “Drug utilization 90%” (DU90%) method and the method of adherence to relevant professional guidelines.

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.

Expected scientific contribution: The establishment of scientifically evaluated methodology and implementation of methods for evaluating the quality and rational prescribing of cardiovascular drugs on the population level.

Acknowledgments:

MeSH/Keywords: outpatient, utilization, cardiovascular drugs, ATC/DDD methodology, Zagreb

Poster code: C-2-107

POSTER TITLE: DETERMINANTS OF MAMMOGRAPHY SCREENING RESPONSE-WOMAN 50-69 YEARS OF AGE FROM TYPICAL URBAN AND RURAL AREA

PhD candidate: Jasmina Kovačević, MD, MPH

Part of the thesis: Utilization and Determinants of Response Rate to Free Breast Examination as Part of a National Screening Program for Early Detection of Breast Cancer “MAMMA”- Woman 50-69 Years of Age Living in a Typical Rural and Typical Urban Environment

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

Affiliation: Public Health Institute of Pozega-Slavonia County

Introduction: In the Republic of Croatia there are three systematic National screening programs for early detection of breast, colon and cervical cancer followed by public health campaign about the importance of early cancer detection. The main outcome measure of the screening program is coverage rate. Neither program has met its objectives with regard to expected coverage rate, observed at the national level. The long-term goal of National screening programs is early cancer detection and mortality reduction from breast, colon and cervical cancer that can not be achieved without achieving an adequate response rate. The focus of our research is the National screening program for early detection of breast cancer “MAMMA”.

Hypothesis: We start from the hypothesis that poorly informed women have lower response rate to mammography screening for breast cancer, and that there are differences in the reasons for response and non-response with respect to the life in a typical urban and typical rural environment.

Aims: In the Republic of Croatia the reasons why woman respond or not respond to mammography screening as part of the National screening program for early detection of breast cancer are not sufficiently explored and examined. Our goal is to explore the reasons of response and non-response in typical urban and rural areas. We will consider the social and economic context,

the impact of insufficient information on the response and the involvement of elected doctors and nurses in the program.

Materials and methods: The subjects are women 50-69 years of age included in the National screening program for early detection of breast cancer living in predefined areas. We plan to use a multidimensional questionnaire. Research will be carried out in Pozega-Slavonia County, in two typical urban and two rural areas. Interview will be conducted by final year students studding at University of Zagreb School of Medicine over the course “Community Health” under the expert guidance and supervision of PhD candidate. Returned questionnaires will be verified and entered into the database and analyzed using statistical software. The most important data will be presented by descriptive statistics.

Expected scientific contribution: Better understanding of the reasons for response and non-response to preventive mammography screening in order to improve the implementation of the National screening program for early detection of breast cancer.

Acknowledgments:

MeSH/Keywords: National cancer screening programs, breast cancer, response/non-response reasons, urban/rural area

Poster code: C-2-118

POSTER TITLE: RELATIONSHIP BETWEEN ANTHROPOMETRIC CHARACTERISTICS, MOTOR ABILITIES, HEALTHY HABITS AND SELF-ESTEEM AMONG MEDICAL STUDENTS

PhD candidate: Tonći Mašina, prof. kinesiology

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 Štampar 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.

Hypothesis: Better anthropometric characteristic and motor abilities, healthy lifestyle (regular physical activity, eating habits, health care, interpersonal relationships, self-actualization, and adequate coping with stress) conditional on greater self-esteem in medical students

Aims: General aim is to examine anthropometric characteristics and body composition, motor abilities, healthy habits and self-esteem among first two years medical students. Specific aims are to: assess differences in healthy habits, level of physical activity and self-esteem regarding to gender and year of study, get information about anthropometric characteristics and body composition, determine level of some motor abilities, calculate metric characteristics of HPLP II questionnaire to the population of students in Croatia, get information about physical activity, eating habits, concern about their own health, self-actualization, interpersonal relationships and stress management, determine the level

and type of engagement in physical activity, design a proposal for the physical education program

Materials and methods: Studied population is 1200 students first two years of the Medical Faculty, University of Zagreb. Subjects will fill in a questionnaire about healthy lifestyle (HPLP II), international physical activity questionnaire (IPAQ) and Rosenberg self-esteem scale. Furthermore, they will be tested in some anthropometric characteristics and motor abilities.

Expected scientific contribution: The scientific contribution of this research is evident in the results of the analysis of the obtained data on anthropometric characteristics, motor skills, healthy habits, self-esteem and their interrelations. Thanks to the data collected on the population of students of the Medical Faculty, University of Zagreb, the same can be compared with the population of students and medical students all over the world. Knowing the state of objects and relations of this research will enable appropriate intervention within the curriculum in PE classes.

Acknowledgments:

MeSH/Keywords: healthy habits, physical activity, psycho-social well-being

Poster code: C-3-66

POSTER TITLE: PSYCHOSOCIAL DETERMINANTS OF SATISFACTION WITH HOSPITAL CARE IN ADULT PATIENTS WITH ADVANCED CANCER

PhD candidate: Maja Boban

Part of the thesis: The aim of the research is to determine the moderator and mediation effect mechanisms of coping styles on the relationship of symptoms of depression, anxiety, hopelessness and pain with satisfaction with hospital care in patients with advanced cancer.

Mentor/s: doc. dr. sc. Marijana Braš

Affiliation: research place: Clinical Hospital Center Zagreb, Oncology department. Job post: Agency for quality and accreditation in health and social welfare

Introduction: According to Engel's biopsychosocial model, human beings and their diseases are complex system, caused by interplay of many factors. Direct observation of the outcome of the disease through one or more of the factors is insufficient, that it is necessary to understand and indirect (moderator and mediator) effects in order to obtain a complete picture of the needs of patients. Because of the long duration of treatment and invasive treatment satisfaction medical care is particularly important in the field of oncology, and can be thought of as the success or failure of oncology. Research on possible intervening factors correlation of symptoms of depression, anxiety, hopelessness and pain with pleasure medical care in patients with advanced cancer, almost nonexistent.

Hypothesis: There is a significant moderator and mediation effects of coping with the stress on the relationship between symptoms of depression, anxiety, hopelessness and pain with satisfaction with hospital care in patients with advanced cancer.

Aims: To determine is there moderator and mediation effects of stress coping styles on the connection between symptoms of depression, anxiety, hopelessness and pain with satisfaction with hospital care in patients with advanced cancer.

Materials and methods: The study will engage adult patients of both sexes suffering from advanced cancer (N = 250-300) who are being treated at the Clinical hospital center Zagreb, Department of Oncology. Inclusion Criteria: TNM classification of advanced malignancies,

inability second curative approach. The criteria for non-inclusion: proven metastatic disease of the central nervous system and/or a primary malignancies of the central nervous system, presence of acute psychosis, delirium, dementia and psychoorganic syndrome. Exclusion criteria: inadequately completed questionnaires. Instruments: general questionnaire, Beck's depression scale, Beck anxiety scale, Beck hopelessness scale, EORTC cancer in-patient satisfaction with care measure, Inventory Coping with stressful situations.

Expected scientific contribution: With the obtained data we will be able to more clearly define the needs of patients with advanced cancer, to clarify the relationship between the mechanisms of coping with stress, symptoms of psychological distress and satisfaction with hospital care that will, hopefully, contribute to the improvement of care for this very vulnerable group of patients.

Acknowledgments: The survey is conducted as part of Palliative Medicine in Croatia needs and attitudes of patients with advanced malignant disease and their physicians conducted by the Center for Palliative Medicine, Medical Ethics and Communication Skills School of Medicine, University of Zagreb (CEPAMET) and funded by the Adris Foundation.

MeSH/Keywords: patients with advanced cancer, depression, anxiety, hopelessness, pain, satisfaction with hospital care, coping with stress

Poster code: C-5-117

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