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Internal Medicine

AORTIC PULSE WAVE VELOCITY - EVALUATION OF THE AGE-RELATED VALUES IN HEALTHY SUBJECTS USING DOPPLER ECHOCARDIOGRAPHY

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Introduction: Aortic pulse wave velocity (aPWV) is a measure of aortic stiffness, which is an indicator of cardiovascular risk factor and vascular aging. The Doppler echocardiography had been shown to have high correlation with invasive reference method of aPWV based on intraarterial pressure evaluation.

Aim: The aim of the study was to establish reference values of aortic pulse wave velocity, measured by Doppler echocardiography in healthy subjects.

Methods: 121 healthy adults, normotensive, non-smoking, without chronic diseases and not taking medication, were included. All the patients were divided into 5 groups due to age criterion. During the echocardiographic examination with a standard cardiac probe, ten Doppler waveforms were recorded in the distal aortic arch and then in the left external iliac artery. The transit time was calculated as a difference between time delay of the two points of the Doppler recordings relative to ECG signal. aPWV values were calculated according to the formula: PWV = distance/ transit time.

Results: The mean age of the studied group was 42 ± 13 yrs, BMI 24.5 \pm 3.4, SBP 123 \pm 10.39 mm Hg, HR 64 \pm 10 bpm. There was significant positive correlation of aPWV with age and SBP. aPWV did not differ according to sex. Mean aPWV values with 95% confidence interval (95%CI) for each decade of life were as follows: D1-age 21–30, aPWV 4.56 m/s (95%CI 4.41 to 4.72), D2age 31–40, aPWV 4.65m/s (95%CI 4.37 to 4.94), D3-age 41–50, aPWV 5.15 m/s (95%CI 4.88 to 5.43), D4-age 51–60, aPWV 5.96 m/s (95%CI 5.54 to 6.38), D5-age 61–70, aPWV 6.88 m/s (95%CI 6.42 to 7.34).

Conclusion: We report age-related values of aPWV in a healthy population measured by Doppler echocardiography method. This may be helpful in future research exploring the associations between aortic stiffness, cardiac function and cardiovascular prognosis in a large population of patients referred for echocardiography.

THE PREVALENCE OF OTITIS MEDIA WITH EFFUSION IN CHILDREN LESS THAN 2 YEARS OLD AND THE COEXISTING DISEASES

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Introduction: Otitis media with effusion (OME) is a frequent pathology of the childhood and is believed to be the most common cause of conductive hearing loss in children. It is estimated that 90% of children have OME before beginning of school education and the peak of incidence is in children aged between 6 months and 4 years. The characteristic feature of OME is presence of fluid in the middle ear with uninjured eardrum and without symptoms of acute infection.

Aim: The aim of this study was to analyse the prevalence of otitis media with effusion and it's relation to other coexisting diseases.

Methods: Data from the group of 47 children younger than 2 years old, treated in ENT Outpatient Clinic in The University Children's Hospital in Kraków with the primary diagnose of recurrent otitis media with effusion has been analysed in relation to coexisting diseases, in particular the enlargement of tonsils and adenoid, allergies, pulmonological problems, gastro-oesophageal reflux disease (GERD) and immune deficiencies.

Results: Median age was 14 months. Majority of children were boys (3:2). A relation between the prevalence of otitis media with effusion and certain diseases has been confirmed. Almost three quarters of the children had enlargement of tonsils and adenoid (74%) In 59% of the patients allergy has been found, 51% had asthma, 48% eczema, 31% recurrent bronchitis, 61% GERD, 33% laryngomalacia, 36% immunodeficiencies (humoral or cell-mediated), 4% cystic fibrosis, 4% immotile cilia syndrome (ICS).

Conclusion: OME is an insidious disease, developing often without symptoms. It might be caused by dysfunction of Eustachian tube or a complication of acute otitis media. There are many conditions that may increase the risk of OME. As we have found less than half of patients treated for OME didn't have a coexisting disease.

ANALYSIS OF THE FUNCTIONALITY OF DIFFERENT TYPES OF MOISTURE DROPS BOTTLES IN THE EVALUATION OF PATIENTS WITH RHEUMATIC DISEASES

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Introduction: Systemic connective tissue diseases often lead to reduction in the patient's dexterity. In Sjögren syndrome, the secreting function of lacrimal glands is damaged. It's second-ary form may occur with other autoimmune diseases, mainly rheumatoid. Approximately 30% of patients with rheumatoid arthritis also suffer from Sjögren syndrome. Lack of a stable tear film may lead to permanent eye's surface damage. Patient

requires a systematic moisting, but co-existing rheumatic changes can hinder correct application of moisture drops.

Aim: The purpose of this work was to evaluate functionality and self-application comfort of pharmacy-available moisture drops in 6 different types of packaging by patients with different exacerbation of rheumatic changes.

Methods: The study included 24 patients (21 women and 3 men) ophthalmologically-consulted in the rheumological ward. Patients completed the OSDI questionnaire. Schirmer and SICCA tests were performed. Next, patients applied 6 different moisture drops, evaluating them with 5 grade scale: ease of opening the package, comfort and grip's confidence, how easy is to squeeze and instil the drops. The examiner also evaluated the effectiveness of the application

Results: In terms of ease of the package opening, drops number 5 in a large bottle with a vertical pump and side handle have been assased to be the best. Drops No. 6 in a small, traditional bottle were considered to be the most comfortable in grip and the easiest to instil. Drops number 1 in the minims package have been considered the easiest to squeeze

Conclusion: An effective drops application is an important part of treatment which reduces risk of complications and improves the quality of life. Rheumatic changes in the joints and deterioration of the coordination may hinder the proper instil technique. The differences in structure, size and hardness of the bottle vary in patients evaluation. There was no correlation of the advancement of rheumatic changes with the preference of any applicator.

ASPIRIN DESENSITIZATION IN PATIENTS WITH ASPIRIN EXACERBATED RESPIRATORY DISEASE (AERD)

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Introduction: AERD is a chronic medical condition that consists of three clinical features: asthma, sinus disease with recurrent nasal polyps, and sensitivity to aspirin and NSAIDs that inhibit an enzyme called cyclooxygenase-1 (COX-1). Aspirin desensitization (AD) is regarded as an effective and well-tolerated therapy for patients with AERD.

Aim: The aim of our study was to evaluate the influence of AD on asthma control, nasal symptoms, FEV1, total and specific IgE level and blood eosinophil count in AERD patients.

Methods: One-center prospective study involved 37 patients with AERD subjected to 52 weeks of AD with an overall daily aspirin dose of 650 mg. 34 patients received total course of AD. Clinical and biochemical parameters were evaluated during three hospitalizations: at baseline, in 8th or 16th week and in 52nd week of AD. During each hospitalization patients were asked to fill in Asthma Control Test (ACT) questionnaire and Visual Analogue Scale (VAS) for the assessment of nasal symptoms. Statistical analysis was performed using summary statistics and ANOVA post-hoc tests.

Results: The statistically significant improvement was observed in ACT score (p=0,007) and VAS score (p < 0,001) in 52nd week of AD. There was a significant increase in both the absolute count and the percentage of blood eosinophils in 8/16th week (p=0,024 and p = 0,034, respectively) and 52nd week of AD (p = 0,017 and p = 0,014, respectively). There were no significant changes between baseline and following AD FEV1 values. There were also no changes in total or specific IgE level.

Conclusion: Outcomes of our study suggest that AD has a significant positive influence on asthma control and nasal symptoms. AD also leads to the increase in blood eosinophil count. AD did not influence significantly spirometry outcomes and total or specific IgE level.

TALE OF 2 SYNDROMES; ANGELMAN AND PRADER-WILLI'S SYNDROMES; HISTORICAL OVERVIEW, UNDERLYING GENETIC CAUSES & CLINICAL MANIFESTATIONS

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Introduction: Angelman syndrome is a complex genetic disorder that primarily affects the nervous system. Prader-Willi syndrome is a complex genetic condition that affects many parts of the body. Usually, children with Angelman syndrome start walking with a delay and present a specific movement pattern with trembling limb movements, clumsiness and quick jerky puppet like movements.Whilst, Prader Willi syndrome has a number of phenotypic features which include respiratory problems, psychiatric disorders, scoliosis and eating disorders. In babies, reduced fetal mobility, frequently abnormal embryonic position, polyhydrate (excessive amount of amniotic fluid), difficulty in fetus feeding and hypogonadism are mentioned. Seems that both appear multiple anomalies and mental retardation. Despite, some different clinical manifestations, the two syndromes display the same deletion in Chromosome 15, as well. Revealing that particular DNA repeats may be involved with inter - and intra chromosomal misalignment and homologous recombination, leading to the common deletion in both syndromes.

Aim: Our purpose through this systematic meta-analysis is to remind how vital is the role of mitochondrial DNA in many autoimmune diseases and genetic syndromes, giving insight for future research on this unexplored interference as well highlighting new techniques of identification and new therapies related with mitochondrial inheritance. Not all of the DNA resides in nucleus. The mitochondria which is the organelle critical for producing energy for the cell, has its own genome. As you already know, mitochondria are maternally inherited can be used to analyze ancestry from the maternal line.But there's also rare variation in mitochondrial DNA that can lead to disease. Furthermore, genes, which are important for mitochondrial function, re-encoded in the mitochondrial and nuclear genomes while pathogenic mitochondrial variants interfere with energy production in many tissues and cause severe illness. There is a technique called mitochondrial replacement therapy remains in several domains extremely new. The particular therapy includes complete replacement of the cytoplasm of egg/embryo, reducing the transmission of undesired defective mitochondria (mutated mitochondrial DNA: mtDNA) for patients with inherited mitochondrial diseases.

Methods: Charts, figures and tables derived from primary research both on molecular underlying and clinical manifestations. Particularly, show the molecular and clinical similarities and differences of Angelman (AS) and Prader Willi (PWS) Syndromes. We cannot disregard the fact that tables make obvious that the Prader - Willi (PWS) and Angelman (AS) syndromes are clinically distinct developmental and neuro -behavioral disorders, resulting from the loss of imprinted gene expression within chromosome 15q11-q13

Results: OR Diagnostics diagrammes pinpointing international guidelines on diagnosing each syndrome, avoiding the possibility of misdiagnosis. A practical set of molecular genetic testing and reporting guidelines has been developed for these two disorders. In addition, recommendation is given on appropriate reporting policies, including advice on test sensitivity and furthermore the possibility of differential diagnosis is discussed.

Conclusion: Despite the complexity of possible causes, all but the single gene mutation of the Angelman and Prader Willi Syndromes gene can be detected through methylation - sensitive DNA probes, since DNA methylation is process by which the genes for these 2 disorders are imprinted. This unusual property of specific areas of DNA holds promise for future treatment of these and other disorders related to imprinting through reversal of the imprinting process. Phenotype / genotype correlations in both syndromes should be undertaken into careful consideration, identified for each genetic sub-type.

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TOLERABILITY AND EFFICACY OF A FIXED COMBINATION OF CINNARIZINE AND DIMENHYDRINATE VERSUS BETAHISTINE IN THE TREATMENT OF VERTIGO: A META-ANALYSIS

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Introduction: A fixed combination of cinnarizine and dimenhydrinate (Arlevert, [ARL]) is a remarkable bimodal antivertiginous drug; cinnarizine as a calcium channel antagonist and dimenhydrinate as an antihistaminic. It demonstrated high efficacy, compared to placebo in the treatment of vertigo of various origins.

Aim: We aimed at synthesizing evidence from published randomized controlled trials (RCTs) about the tolerability and

efficacy of ARL versus Betahistine in symptomatic treatment of vertigo.

Methods: We searched nine databases for relevant RCTs. Citations were screened for eligibility and data were extracted and analyzed using RevMan. Changes in mean vertigo score (MVS) and mean score of vegetative symptoms (MSVS) were pooled as mean difference (MD). Spontaneous nystagmus and tolerability were pooled as odds ratios (ORs) in a meta-analysis model. Heterogeneity was assessed by Chi-square and I-square tests.

Results: Five low risk of bias RCTs with 292 patients (ARL n = 144, and Betahistine n = 148) were included. ARL was marginally superior to Betahistine in reducing MVS after one week. However, there was no significant difference at the end of follow up (MD = -0.14, 95% CI [-0.29 to -0.001], p = 0.05), MD = -0.08, 95% CI [-0.49 to 0.34], respectively). ARL was superior to Betahistine regarding MSVS after one week and at the end of follow up (MD = -0.34, 95% CI [-0.60 to -0.08]), p = 0.01, MD = -0.30, 95% CI [-0.48 to -0.13], p = 0.0009, respectively). For MSVS, no significant heterogeneity was found (Chi-square p > 0.1 and I₂ = 0%). At the end of follow up, no significant difference was found regarding spontaneous nystagmus or tolerability.

Conclusion: Except for spontaneous nystagmus and patients' tolerability, the ARL achieved significant improvement in MSVS and a slight improvement in MVS. Therefore, larger RCTs are Recommended to guarantee the difference.

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NEW DEFINITION OF KIDNEY ASYMMETRY IN SCREENING FOR RENAL ARTERY STENOSIS

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Introduction: Renal artery stenosis (RAS) is a frequent cause of secondary hypertension. According to the guidelines, discrepancy in size between the kidneys of greater than 15 mm is a clinical indication for the diagnosis of RAS. Doppler ultrasonography is a first choice examination in RAS diagnostics allowing assessment of renal aortic ratio (RAR). RAR above 3.5 is commonly used marker of renal artery stenosis.

Aim: The aim of the study was to verify the arbitrary cut-off value of kidney size difference of 15 mm as clinical indication for the diagnosis of RAS and to find the optimal method of kidney asymmetry assessment.

Methods: The analysis included 1175 of patients who underwent Doppler examination of renal arteries, have measured both kidneys size and RAR. Significant difference in renal dimension was set at more than 15 mm. Significant renal artery stenosis was defined as RAR greater than 3,5. Receiver operating characteristic (ROC) curves were created and analyzed for both absolute and relative differences in kidney size (proportion of kidney size). We calculated area under the curve (AUC), optimal cut-off values and compared the both methods.

Results: 169 patients had significant difference in renal dimension and 61 patients had significant renal artery stenosis. In 44 patients both significant size discrepancy and renal artery stenosis were observed. According to ROC curve analysis the optimal renal asymmetry index was 12 mm, not 15 mm as it is suggested in guidelines. The sensitivity and specificity for this method was 82.0% and 83.3% respectively and AUC 86.3%.

The ROC curve analysis for relative difference of kidney size with cut-off value of 1.1 revealed higher sensitivity 85.2% with specificity 82.0% and better performance with greater AUC 86.9% (p < 0,01) comparing with the absolute difference.

Conclusion: Changing the definition of significant difference of kidney size according to our results may improve the diagnosis of RAS.

MULTIPLE COMORBIDITIES IN COPD -COMPREHENSIVE INTERACTIONS OF CLINICAL VARIABLES

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Introduction: Understanding of multiple comorbidities in COPD and their interactions with clinical variables are important in patient assessment and management planning.

Aim: To study the relationship between echocardiography and pulmonary function test (PFT) parameters and glomerular filtration rate (GFR) in COPD patients with comorbidity.

Methods: 42 COPD patients with comorbidity (arterial hypertension (AH), coronary artery diseases (CAD)) (57.14% males, 42.86% females) on average age 55.0 (50.0; 63.0) underwent clinical examination. Smoking status was 15.16 packs/ years, COPD duration was 6.15 years. Patients are divided into 4 groups depending on airflow limitation severity. According to GOLD criteria (2018) was diagnosed COPD and ESC guidelines (2013) was diagnosed AH and CAD. GFR was assessed (formula CKD-EPI). PFT was studied (Spirograph 'Spirokom'). Transthoracic echocardiography was conducted (Philips HDI – 11).

Results: AH was detected in 50% of COPD patients 1-st gr., in 59.1% - 2-nd gr., in 85.8% - 3-rd gr., in 42.9% - 4-th gr. CAD was registered in 33.3% of COPD patients in 1-st gr., 40.9% - in 2-nd gr., 71.4% - in 3-rd gr., 57.1% - in 4-th gr. In 1-st gr. revealed a positive significant association between PASP and age (R = 0.88). RA ESD correlated with FVC (R = -0.85) and FEV1/FVC (R = 0.89). In 2-nd gr. revealed a significant association between BMI and PASP (R = 0.46) and LV EDD (R = 0.48), between creatinine and age (R = 0.48) and EF (R= -0.55), between LV EDD and urea (R = 0.45), RV EDD (R = 0.78), RA ESD (R = 0.50), LA ESD (R = 0.79). In 3-rd gr. revealed a significant association between BMI and PASP (R = 0.81) and FEV1 (R = -0.94). Among this in 4-th gr. revealed a significant association between GFR and EF (R = 0.82), between FEV1 and creatinine (R = 0.79), LV mass (R = 0.83), LV MI (R = 0.77).

Conclusion: Our data demonstrate comprehensive interactions of clinical variables reflecting the function of the cardiovascular, respiratory and renal systems, aggravating each other's failure.

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THE PROGNOSTIC VALUE OF NEUROPSYCHOLOGICAL PARAMETERS IN PATIENTS WITH HEART FAILURE: AN EXPLORATORY STUDY

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Introduction: Heart Failure (HF) is a complex clinical syndrome with multiple comorbidities. Cognitive impairment, stress, anxiety, depression and lower quality of life are prevalent in HF, but their ability to predict major adverse cardiovascular events (MACE) and quality of life is not known.

Aim: Herein, we explore the value of these parameters in the prediction of MACE in patients with HF with reduced Ejection Fraction (HFrEF), including the Montreal Cognitive Assessment (MoCA) as suggested by the European Society of Cardiology.

Methods: A longitudinal study was conducted using a sample of 65 patients from two hospitals. A battery of tests was performed to assess cognition (MoCA), stress (Perceived Stress Scale-10), anxiety and depression (Hospital Anxiety and Depression Scale) at baseline. MACE were registered using clinical records. Health-related quality of life was estimated using the Kansas City Cardiomyopathy Questionnaire (KCCQ). A descriptive statistical analysis was conducted, as well as multiple linear and Cox regression models to determine the predictive value of neurocognitive parameters and health-related quality of life in MACE.

Results: Both MoCA (hazard ratio (HR) = 0,904; 95% confidence interval (CI) = 0,817–1,001; p = 0,05) and KCCQ (HR = 0,983; 95% CI = 0,970–0,997; p = 0,015) scores were predictors of MACE, but not of overall mortality. Anxiety, depression and stress scores did not predict MACE. However, anxiety ($\beta = -0,326$; p = 0,012) and depression levels ($\beta = -0,309$; p = 0,014) were independent predictors of the KCCQ score.

Conclusion: The MoCA score and health-related quality of life were predictors of MACE-free survival independently of age. Anxiety and depression were good predictors of health-related quality of life, but not of MACE-free survival.

THE ROLE OF PATENT FORAMEN OVALE CLOSURE IN THE SECONDARY PREVENTION OF CRYPTOGENIC STROKE. A META-ANALYSIS REPORT

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¹Faculdade de Medicina, Universidade do Porto, Porto, Portugal; ²Department of Cardiology, Centro Hospitalar São João, Porto, Portugal; ³Department of Neurology, University of Pennsylvania, Philadelphia, USA **Introduction:** Randomized clinical trials have been performed to determine if patent foramen ovale (PFO) closure is superior to medical therapy for secondary prevention of recurrent cryptogenic stroke.

Aim: Our purpose with the current study is evaluate the best management for these patients.

Methods: We performed a search in Medline (PubMed) and in ISI Web of Knowledge databases for all randomized controlled trials that compared PFO closure with medical therapy for preventing recurrent stroke in patients who presented with cryptogenic stroke and who had a documented PFO. The parameters chosen for analysis and meta-analysis were stroke, transient ischemic attack (TIA) and atrial fibrillation (AF).

Results: We included in this study a total of six randomized trials enrolling 3750 patients. Unlike other published meta-analysis on the same topic, in this case only clinical trial data and not follow-up data were used. PFO closure, as compared with medical therapy alone, demonstrated superiority in reducing the rate of recurrent stroke (risk ratio [RR], 0.37; 95% confidence interval [CI], 0.17 to 0.78; P = 0.01). PFO closure did not offer a significant benefit in prevention of TIA (RR, 0.96; 95% CI, 0.64 to 1.44; P = 0.85). Among patients assigned to closure group, an increased risk of AF was seen (RR, 4.64; 95% CI, 2.38 to 9.01; P < 0.01).

Conclusion: In patients with cryptogenic stroke who had a PFO, a protective effect of closure was seen concerning the risk of recurrent stroke, but not regarding the prevention of TIA.

KNOWLEDGE AND ADHERENCE TO WARFARIN'S TREATMENT REGIMEN AMONG PATIENTS IN ALSHAAB AND AHMED GASIM HOSPITALS, SUDAN, 2018

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Introduction: Warfarin is an oral anticoagulant drug that needs continuous clinical and laboratory monitoring due to its narrow therapeutic index and life threatening complications.

Aim: This study aims to assess knowledge and adherence of patients toward their Warfarin treatment regimen and to identify barriers that prevent patients to take their warfarin therapy regularly.

Methods: In this cross-sectional study, a systematic random sample of 307 patients was selected from Alshaab teaching hospital heart section and Ahmed Gasim Hospital. Data were collected by anonymous interview based questionnaires.

Results: Male patients (52.5%) exceeded females (44.8%), the mean age was 48.79. About 57.98% of the studied patients had moderate overall knowledge score, and more than half of them had good adherence levels (62.2%). The study shows that: Forgetting (43.7%) was the main barrier preventing the patients from taking their medication, followed by drug unavailability (36.8%) and high cost (19.5%). There are statistical significant differences between patient's age/education and their level of knowledge (p = 0.008/p = 0.011). The correlations between patients' adherence to Warfarin Oral Anticoagulant and their level of knowledge is statistically insignificant (r = 0.647, p = 0.739).

Conclusion: The majority of the studied patients had moderate overall knowledge score about Warfarin Oral Anticoagulant, and more than half of them had good adherence levels. "Forgetting" was the main barrier preventing the patients from taking their medication.

THE FEATURES OF CENTRAL BLOOD PRESSURE AND ARTERIAL STIFFNESS IN RESISTANT HYPERTENSION PATIENTS IN CROATIA AND INDIA- A COMPARATIVE STUDY

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Introduction: Resistant or refractory hypertension(RH) has been defined as the inability of the body to reduce its blood pressure despite the use of 3 anti-hypertensive drugs of which one is a diuretic. The traditional cuff based methods have been the gold standard for the diagnosis until the non-invasive central blood pressure (CBP) cuff devices have been introduced in the clinical practice lately. CBP and pulse wave velocity (PWV) still remain the surrogate markers of arterial stiffness and predict the early diagnosis of target organ damage in RH patients.

Aim: We investigated the value of CBP and pulse wave velocity (PWV) in group of RH patients non-invasively.

Methods: A bicentered prospective study at Merkur University Hospital, Zagreb, Croatia from 1–31 January 2018 and kasturba Medical college hospital, Mangalore, India in the period 1–31 August 2018 was conducted. Data from 160 patients (80 from each country) with RH (resistance to 3 or more drugs, one is diuretic) without chronic kidney disease, were analysed. The PWV, mean arterial pressure (MAP), pulse pressure (PP), CBP, brachial pressure (BP) were evaluated using the noninvasive Agedio B900 device (Germany). Statistical data was processed in SPSS software, significant differences were considered at p < 0.05.

Results: The mean age was $58,7 \pm 13,5$; 106 (66.3%) were females(F), 64 (33.8%) were males (M). The difference between mean concentration of BP (145,17/21,5; F:144/21 and M:147.2/22.1) and CBP (132,5/92,4; F: 131,33/90,2 and M: 134,9/96,8) was statistically significant for systolic BP (p < 0,01). The mean PWV was found to be higher than reference for all ages in RH 8,9 ± 2m/s. Whereas the MAP and PP was higher than reference (118,3 ± 15 and 48,6 ± 20,4). The difference between sex was statistically significant for PWV (M/F: 8.8/8.9m/s p < 0,01).

Conclusion: PWV and CBP are well documented surrogate markers for arterial stiffness, help in predicting the target organ damage and necessitate the essentiality of chronopreventive therapy.

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PROPORTION OF GAMETOCYTEMIA IN PATIENTS WITH SYMPTOMATIC MALARIA

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¹Kasturba Medical College; ²Department of General Medicine, Kasturba Medical College **Introduction:** Malaria is a life-threatening disease caused by parasites that are transmitted to people through the bite of anopheles mosquitoes. WHO estimates that India accounts for 75% of all malaria cases in South-East Asia and is responsible for an estimated 11.5 million cases and 15400 deaths annually in India. Due to the grave nature of this disease, this study aims at determining the proportion of carriers from amongst the symptomatic patient population in Mangaluru. This would allow us to break the chain in the transmission of malaria and thereby control this dangerous disease.

Aim: To determine gametocyte positivity from amongst the symptomatic patient population in the hospital setup in Mangaluru.

Methods: This is a cross sectional type of study wherein the microscopic parameters of malaria positive gametocyte carriers were analyzed. A simple, descriptive analysis was done to investigate the prevalence of symptomatic gametocyte carriage among the study population.

Results: Malaria was more prevalent amongst men than female. 74.2% of cases were due to Plasmodium vivax, 22.3% of cases were due to Plasmodium falciparum and 3.5% cases were of mixed malaria. 5.9% of cases had scanty parasites. 17.2% of cases had + parasitemia. 23% of cases had ++ parasitemia. 22.7% of cases had +++ parasitemia. 27.7% of cases had ++++ parasitemia. Mixed malaria cases had cumulative of 3.5% cases. 80.5% of cases showed the presence of gametocytes. 97.9% of all cases of Plasmodium vivax showed presence of gametocytes whilst 23.8% of cases of Plasmodium falciparum showed gametocytes.

Conclusion: Patients are thus advised to be on the lookout for the warning signs of malaria and report to a health center as soon as possible. Personal protective measures such as bed nets, full clothing and the use of repellants are to be reinforced. Anti-adult and anti-larval measures must also be put into place for regular usage. Health professionals are advised to modify the treatment regimens by introducing Primaquine from Day 1 to eliminate gametocytes and thus bring down the endemicity of Malaria.

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QUALITY OF LIFE IN PATIENTS WITH NON-ALCOHOLIC STEATOHEPATITIS

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Introduction: Non-alcoholic Steatohepatitis (NASH) is a liver disease that develops in patients who do not abuse alcohol, but it has histological features equivalent to alcoholic hepatitis and is considered to be one of the most serious types of Non-alcoholic fatty liver disease. It is likely to appear asymptomatically, but in some patients there may appear fatigue, exhaustion and dull right-upper-quadrant abdominal discomfort. There is no specific therapy for now.

Aim: The aim of this study was to investigate NASH patient's quality of life through standardized questionnaire, in order to discover potential predictors of quality of life.

Methods: The study included patients older than 18 years, with clinically, laboratorially or phatohistologically confirmed diagnosis of NASH. Their sociodemographic and clinical data were collected through specially constructed questionnaire. The data about quality of life in patients was obtained through two questionnaires: Chronic Liver Disease Questionnaire (CLDQ) and Short-form 36 Questionnaire (SF-36).

Results: The disease differently affected men and women as regards to general symptoms, emotional and social functioning and fatigue. Statistically significant negative correlation was noticed between the body mass index (BMI) and limitation due to physical and general health and also between waist size and abdominal symptoms, fatigue, emotional, physical and social functioning, concern and pain. Albumin levels are in statistically significant correlation with abdominal symptoms, fatigue and emotional functioning. Presence of hypertension had statistically significant influence on limitation due to physical health.

Conclusion: Quality of life in patients with NASH was different in men and women. BMI and waist size have direct negative impact in domains of both questionnaires, and therefore the patient's quality of life. We can conclude that NASH disrupts patient's quality of life, and that further research is necessary as regards to predictors of quality of life and potential therapy for this widespread disease as well.

SEX- RELATED DIFFERENCES IN THE LEFT VENTRICULAR GEOMETRY

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Introduction: It is well recognized that left ventricular (LV) size differs between two genders, even when corrected for body surface area. Numerous processes (ischemia, necrosis, pressure overload, volume overload, aging) and factors (hormones,metabolites) cause cellular and molecular events leading to a change in shape and function of LV. Many studies showed that changes in LV are connected with higher cardiovascular risk.

Aim: The aim of our study is to assess how the same initiators impact on the LV geometry among both: female and male patients with stable coronary artery disease(CAD).

Methods: The analysis was performed retrospectively according to the data collected by the Department of Invasive Cardiology of the Medical University of Bialystok. 1112 patients with stable CAD, admitted for invasive diagnostic or treatment, were included into the study. Analysis comprised medical history, basic laboratory tests and clinical data. Statistical analysis was performed using Kołomogorow-Smirnow, chi-square, odds ratio, Student's t, Mann-Whitney U and ANOVA tests. P value ≤ 0.05 was considered as significant.

Results: In our study women were older and more frequently characterized by chronic renal disease and pressure overload related to LV valvular diseases. Prevalence of hypertension, atrial fibrillation and diabetes mellitus was the same in two groups. Previous myocardial infarction and heart failure were mostly associated with male gender. Female patients less often had normal geometry (16.44% vs. 27.58%; p < 0.0001) and higher rate of concentric hypertrophy (38.63% vs. 17.94%; p < 0.0001). In spite of significantly, more advanced CAD in males we observed no influence of this factor on LV geometry.

Conclusion: Our study shows, that the same factors occur with varying frequency and affect distinctly on the LV geometry among both genders. Therefore, implementation of more personalized prevention based on sex related differences may protect from abnormal LV pattern and through that decrease cardiovascular risk.

THE IMPORTANCE OF MDCT DIAGNOSTICS IN THE DETECTION, MONITORING AND SELECTION OF ACUTE STROKE THERAPY

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Introduction: Stroke indicates a suddenly occurring focal, non-invasive neurological disorder, which is due to vascular damage.

Aim: Follow-up of all patients who came to the Emergency Center for a certain period of time due to the occurrence of some neurological deficit.

Methods: Within a month, we followed 123 patients who were admitted to the emergency diagnostic department with some neurological deficit, and they performed their native CT (computerized tomography) and / or angiographic examination of the endocranium. All examinations were done on the CT 16, GE, Brightspeed, USA. After the initial native CT diagnosis, depending on the finding, the examination was either interrupted, or the contrast medium was administered, and a postcontrast scan or CT angiography was performed.

Results: The largest number of patients with vascular neurological deficits was the life span between 50–59 years, while the smallest number of patients were registered in the group of people under the age of 40 years. Of 94 patients who developed a stroke, 78 (83%) of patients had an ischemic stroke, while 16 (17%) had a haemorrhagic stroke. There is no statistically significant difference in the reporting of ICH and SAH among the poles. The localization of ischemic brain infarction was in the area of vascularization of the frontal cerebral artery (ACA) in 3.2%, the central cerebral arteries in 38.9%, the internal carotid arteries (ICA) in 8.4%, the basilar artery in 13.7% the last cerebral artery in 7.4%, the vertebral artery in 9.5% and in the watershed of supratentoral arterial irrigation zones in 11.7%

Conclusion: A native CT scan is a gold standard for triage of patients with acute stroke. The benefits of CT scanning in assessing patients with acute stroke are convenience, precision, speed and availability of CT devices.

CAUSES OF SECONDARY ERYTHROCYTOSIS AND DIFFERENTIAL DIAGNOSIS TOWARDS TO PRIMARY ERYTHROCYTOSIS

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Introduction: Erythrocytosis presents elevated hemoglobin and hematocrit levels above the range of normal values. Primary

erythrocytosis is characterized by increased erythrocyte production due to disorder at the level of the multipotent stem cell in bone marrow. Diversely, secondary erythrocytosis (SE) is due to bone marrow stimulation by external factor.

Aim: The aim of our study was to determine the common causes of SE as well as parameters which are significant to differentiate SE from primary erythrocytosis (PV).

Methods: This is a retrospective study involving 108 patients (pts) with SE and 111 pts with PV who were diagnosed and treated at the Clinic of Hematology, CCS (december 2005 - november 2018). From the patient record following data were extracted: demographic characteristics, laboratory parameters, comorbidities, spleen size, red cell mass, serum EPO level, and spontaneus growth of BFU-E colony.

Results: The cause of SE in 50 pts (46.3%) was unknown. The most frequent association of SE in patients was with active smoking (24.1%), HOBP (10.2%), Pickwick syndrome (9.3%) and presence of polycistic kidneys (8.3%). SE pts were younger with predominance of male gender with significantly higher serum EPO than in PV pts. PV pts had significantly higher values of BFU-E, and count of leukocytes, platelets, spleen size, level of LDH than SE pts.

Conclusion: Our results showed that the cause of SE in almost 50% of pts is unknown. Red cell mass analysis did not show a differential diagnostic significance. In pts, findings of normal spleen size, normal leukocyte and plate-let count, normal serum LDH, and elevated EPO refer to the diagnosis of secondary erythrocytosis, while the findings of splenomegaly, leukocytosis, thrombocytosis, elevated serum LDH, and decreased EPO favor the diagnosis of poly-cythemia vera.

PREVALENCE OF ANOMALIES OF CORONARY ARTERY ORIGIN IN 11,271 PATIENTS UNDERGOING CORONARY ANGIOGRAPHY – AN 8-YEAR SINGLE-CENTER EXPERIENCE

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Introduction: Anomalies of coronary artery origin are uncommon congenital disorders of the coronary artery anatomy. They are usually accidentally found in coronary angiography (CAG). Their incidence varies between 0.3% and 1,1%. There is no unified classification and nomenclature. Most patients are asymptomatic, or they present nonspecific symptoms (e.g. atypical chest pain).

Aim: To investigate prevalence of anomalies of coronary artery origin in all-comer population of Polish patients undergoing CAG.

Methods: We retrospectively investigated medical records of all patients who underwent CAG at the Jagiellonian University Department of Cardiac and Vascular Diseases from 1 January 2010 to 31 December 2017. Patients with anomalies of coronary artery origin were selected; that is presenting at least one of following features: coronary artery arising outside coronary aortic sinuses, coronary artery arising from the opposite side, absence of left main coronary artery (LMCA), single coronary artery, absence of left anterior descending (LAD) or left circumflex (Cx) artery.

Results: 11,271 patients underwent CAG and 57 (0.506%) of them had 58 anomalies of coronary artery origin. The most prev-

alent anomaly was coronary artery arising from the opposite side (25, 0.222%; 14 Cx from RCA, 2 Cx from right sinus of Valsalva [RSV], 1 LAD from RCA, 3 LMCA from RSV, 2 RCA from left sinus of Valsalva [LSV], 3 RCA from LMCA), followed by coronary artery arising outside of coronary aortic sinuses (15, 0.124%; 14 RCA from the ascending aorta (AoAsc), 1 LMCA from non-coronary sinus (NCS) and LMCA was absent in 14 patients (0.124%). Single coronary artery occurred in 2 patients (0.018%). Left circumflex or left anterior descending artery were absent in 2 patients (0.018%; both absence of Cx). 6 anomalies coexisted with congenital heart disease in 5 patients (8.772%): 2 transposition of great arteries (RCA from LMCA), 2 tetralogy of Fallot (RCA from AoAsc, RCA from LSV, LMCA from NCS) and partial anomalous pulmonary venous connection (RCA from AoAsc).

Conclusion: Anomalies of coronary artery origin occur in 0.5% of all-comer population of Polish patients undergoing CAG. Coronary artery arising from the opposite side was the most common anomaly, followed by absence of LMCA and coronary artery arising outside coronary aortic sinuses. There is little overlap with other congenital heart diseases.

EOSINOPHILS AND INFLAMMATORY RESPONSE IN ASPIRIN EXACERBATED RESPIRATORY DISEASE PATIENTS SUBJECTED TO ASPIRIN DESENSITIZATION

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Introduction: Aspirin Exacerbated Respiratory Disease (AERD) is a chronic medical condition, which includes asthma, chronic rhinosinusitis with nasal polyposis (CRSwNP) and hypersensitivity to aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs). Chronic inflammation is observed in upper and lower airway mucosa. Aspirin Desensitization (AD) is regarded as an effective and well-tolerated therapy for patients with AERD.

Aim: The aim of our study was to investigate the influence of AD on eosinophils count and the expression of several genes in induced sputum (IS) of AERD patients.

Methods: Twenty-four patients were subjected to 52 weeks of AD. At baseline, in 8 or 16th week (short response) and in 52th od AD (long-term response) IS was obtained from all study participants and the following evaluations were conducted: eosinophil count, the expression of LTL4S, EPX, TH2 response cytokines (IL-4,IL-5, IL-13),TNF and protein of eicosanoids pathway – ALOX5. Gene expression was investigated using TaqMan low-density arrays (TLDA).

Results: There were no changes in IS eosinophil count after 52 weeks of AD. The concentration of TNF [p = 0,03] decreased significantly in 8/16th week of AD. We have also observed a decreasing trend in the expression of eosinophil markers (EPX, LTC4S) and TH2 response cytokines (IL4, IL-5, IL-13).

Conclusion: Although AD did not lead to the significant decrease in IS eosinophil count, the IS eosinophil marker (EPX, LTC4S) and TH2 response cytokine (IL-4, IL-5, IL-13) expression tended to decrease in the course of AD. As the mechanisms of AD remain poorly understood, we believe that our study provides some added value to understanding the mechanisms driving its beneficial effects.

LEFT VENTRICULAR PERFORMANCE IN PATIENTS WITH AORTIC STENOSIS AND LOW LEFT VENTRICULAR MASS

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Introduction: Left ventricular hypertrophy (LVH), absent in 10 – 35% of patients with aortic stenosis (AS), is traditionally considered a compensatory mechanism in response to chronic LV pressure overload. However, contrary to this classical paradigm, cardiovascular (CV) outcome appears better, not worse, in AS patients without LVH.

Aim: Our aim was to estimate LV performance in patients with AS and low LV mass (LVM) determined either by traditional mass criteria or in relation to LV afterload.

Methods: We retrospectively analyzed medical records of 123 hospitalized clinically stable subjects with moderate (n = 58) or severe (n = 65) isolated degenerative AS in sinus rhythm with EF>40%, free of relevant non-cardiac coexistent diseases. LVH was identified by means of the recognized cut-off criteria, i.e. LVM > 115 g/m2 in men and LVM>95 g/m2 in women. Inadequately low LVM (i-lowLVM) was defined as the lowest quintile of the ratio of a measured LVM to the LVM predicted from height, gender and LV stroke work by a previously validated formula. Addition, we computed circumferential end-systolic LV wall stress (cESS), an estimate of afterload, and LV fractional shortening at the midwall level (mwFS), considered a better index of LV function than EF in concentric LV geometry.

Results: Clinical characteristics, AS severity and LV diastolic diameter, a raw measure of preload, were similar in patients with (n = 83) and without LVH (n = 40), as well as those with (n = 25) and without i-lowLVM (n = 98). By multiple regression, independently of an inverse association between mwFS and cESS ($\beta = -0.43 \pm 0.08$, p < 0.001), AS patients without LVH had higher mwFS in comparison to subjects with LVH ($\beta = 0.21 \pm 0.08$, p = 0.01). This effect was even more pronounced in patients with i-lowLVM compared to their counterparts with adequate or excessive LVM ($\beta = 0.39 \pm 0.08$, p < 0.001).

Conclusion: Low LVM in AS is associated with enhanced load-independent LV systolic function, especially when LVM is disproportionately low to LV afterload. Thus, enhanced myocardial contractility might offset potential detrimental effects of afterload excess in patients with low LVM, thereby contributing to better CV outcome in AS patients without LVH.

EVALUATION OF INFECTOLOGICAL COMPLICATION OF PATIENTS USING CLEAN INTERMITTENT CATHETERISATION

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Introduction: Clean intermittent catheterization (CIC), where patients are emptying the bladder with single use hydrophilic surface catheters, has been the basis treatment of func-

tional urinary retention for the last decades. Despite long experience with CIC technique there is still no agreement on the use of prophylaxis to prevent lower urinary tract infections.

Aim: The aim of the research is to map the bacteriological burden and hospitalization needs of CIC patients and to evaluate the effectiveness of prophylaxis.

Methods: A two arms study was performed in the CIC patient cohort of the Urological Department of Medical School Pécs with a total number of 28 patients. Antibiotic prophylaxis group was compared with the group without using prophylaxis. Patients in the prophylaxis group received in 6 weekly intervals a 5 days antibiotic therapy with either sulfamethoxazole-trimethoprim or cefuroxime, and diluted povidone iodine solution irrigation on weekly basis. As primary end points asymptomatic and symptomatic bacteriuria and urinary tract infection related hospitalisation were recorded.

Results: Of the 98 positive bacteriological findings, 64 asymptomatic bacteriuria and 34 symptomatic bacteriuria were reported. Both asymptomatic and symptomatic bacteriuria in a one-year interval were lower in the group with prophylaxis (0.347/year vs. 0.656/year and 0.293/year vs. 0.456/year respectively).

Conclusion: Regarding logistic regression analysis, the prophylaxis reduced the likelihood of both asymptomatic and symptomatic bacteriuria. The duration of CIC proved to be a significant protective factor against urinary tract infections, by longer duration lower yearly bacteriuria episodes were observed. The major criticism of our study are the small number of the patients and the non-randomised design. Further prospective, randomised studies are needed the validate our preliminary results.

ASSESSMENT OF HSP70 AND HSP90α EXPRESSION IN NASAL EPITHELIAL CELLS OF PATIENTS WITH CHRONIC RHINOSINUSITIS WITH NASAL POLYPS

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Introduction: Converging lines of evidence indicate that nasal epithelial cells (NECs) are of huge importance for maintenance of homeostasis in upper airways. They act as a barrier and release cytokines such as thymic stromal lymphopoietin (TSLP), IL-25, and IL-33. The epithelium-derived cytokines mentioned above are involved in differentiation of immune cells. Furthermore, it has been reported that NECs undergo epithelial-mesenchymal transition (EMT). EMT occurs when the cells lose their epithelial markers and acquire the mesenchymal ones in response to hypoxia and some pro-inflammatory cytokines. EMT cells gain the ability to migrate to the lamina propria and produce components of the extracellular matrix, contributing to wound healing and fibrosis development. NECs are damaged in chronic sinonasal inflammation called chronic rhinosinusitis, which can be classified into chronic rhinosinusitis with (CRSwNP) and without nasal polyps (CRSsNP). Heat shock proteins (HSPs) are known to promote cell survival under stress conditions. Little is known of their expression in NECs in CRSsNP.

Aim: The purpose of our study was to investigate HSP70 and HSP90 α expression in NECs of patients with CRSsNP.

Methods: Samples of nasal mucosa were collected from 7 patients with CRSsNP and 7 control subjects with deviated nasal septum. They were stained immunohistochemically with antibodies to HSP70 and HSP90 α (Thermo Fischer Scientific, UK) using 3,3'- diaminobenzidine staining for visualization.

Results: HSP70 and HSP90 α expression was found to be weak or absent in some NECs in the control group. In patients with CRSsNP, qualitative evaluation of their expression showed a higher number of both HSP70- and HSP90 α -positive NECs compared with controls. Moreover, the expression of both HSPs was stronger. We believe that HSP70 and HSP90 α overexpression is an adaptation aimed at re-folding of oxidatively modified proteins accumulated due to oxidative stress.

Conclusion: Our findings suggest that CRSsNP is associated with HSP70 and HSP90 α overexpression in NECs.

ARTERIAL STIFFENING AND PRIMARY MYOCARDIAL DYSFUNCTION INDEPENDENTLY CONTRIBUTE TO IMPAIRED LEFT VENTRICULAR MIDWALL PERFORMANCE IN DEGENERATIVE AORTIC STENOSIS WITH CONCOMITANT TYPE 2 DIABETES

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Introduction: Degenerative aortic stenosis (AS), a disease of the elderly, frequently coexists with concomitant diseases, including type 2 diabetes (DM), an adverse cardiovascular (CV) outcome predictor. DM affects LV structure and function via both hemodynamic and metabolic factors.

Aim: To compare clinical and hemodynamic characteristics of patients with AS according to DM status.

Methods: Medical records of patients with moderate or severe AS were retrospectively analyzed. We calculated left ventricular (LV) midwall fractional shortening (mwFS), an index of LV myocardial function, and circumferential end-systolic LV wall stress (cESS) and valvulo-arterial impedance (Zva), estimates of LV afterload. Additionally, systemic arterial compliance (SAC) was derived from stroke volume index and pulse pressure.

Results: Patients with DM (n = 42) and without DM (n = 80) did not differ in age, aortic valve area index, aortic pressure gradients, LV mass, LV diameter and ejection fraction. In comparison to non-diabetic subjects, DM patients had significantly higher body-mass index (p = 0.001), cESS (255 ± 119 vs. 208 ± 86 hPa, p = 0.01) and Zva (5.8 ± 2.2 vs. 5.1 ± 1.8 mmHg per mL/m2, p < 0.04), while SAC (0.5 ± 0.2 vs. 0.6 ± 0.2 mL/m2 per mmHg, p = 0.02) and mwFS (11.7 ± 4.0 vs. 14.1 ± 3.7 %, p = 0.001) were decreased. By multiple regression, higher cESS (p < 0.001) and DM (p = 0.03) were independent predictors of depressed mwFS.

Conclusion: DM can contribute to LV dysfunction by arterial stiffening that increases LV afterload in AS. Additionally, DM appears associated with a load-independent impairment of LV function at the midwall level, corresponding to slightly depressed myocardial contractility.

THE INSULIN PUMP THERAPY IN TYPE 1 DIABETES: THE IMPORTANCE OF GLUCOSE VARIABILITY

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Introduction: Continuous subcutaneous insulin infusion regimen (CSII) has proved the effectiveness over multiple daily insulin injections (MDII). Although HbA1c was brought to an optimal range by CSII, one of the main challenges of this method remains glucose variability.

Aim: The aim of this study was to investigate glucose control and glucose variability in patients switched from MDII to the CSII method.

Methods: We analyzed data from the existent electronic and file database of 65 patients treated at the Clinic for Endocrinology, Diabetes and Metabolic Diseases, the Clinical Center of Serbia. HbA1c levels, frequency of hypoglycemia on a weekly basis and daily glycemic profile - which determined the parameters of glucose variability (mean, standard deviation (SD) - the coefficient of variation (CV) and Mean Amplitude Glucose Excursion (MAGE) were analyzed. All results are expressed as the mean \pm standard error. The significance of the difference of HbA1c, weekly hypoglycemia, mean, SD and CV was tested by Student's t-test for repeated samples. The significance of difference of MAGE was tested in a specific software made for this study. The correlation between variables was tested by Spirman's bivariate correlation test.

Results: HbA1c value was lower after insulin pump therapy than before one (p < 0,01). Glycemic values from daily profiles, mean, SD, CV and MAGE of all glycemic profiles were lower after insulin pump therapy than before it (p < 0,05). The correlation between HbA1c was observed six months after the insulin pump therapy and SD and CV three months after insulin pump regimen (p < 0,01). There was no significant correlation between HbA1c and MAGE values, neither after three, nor after six months of the insulin pump regimen (p > 0,05).

Conclusion: Therapeutic regimen employing CSII regulates the level of HbA1, reduces the values of all glucose variability parameters and reduces frequency of hypoglycemia compared to MDII, thus indirectly improving life quality.

LDL APHERESIS IN TREATMENT OF FAMILIAL HYPERCHOLESTEROLEMIA (FH): EFFECT ON CRP, FIBRINOGEN AND LP(A)

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Introduction: Familial hypercholesterolemia (FH) is an inherited disease characterized by significantly increased levels of low density lipoprotein (LDL) cholesterol (Ch) and premature occurrence and progression of atherosclerosis. In FH patients, when target LDL-Ch level cannot be achieved by maximally tolerated statin dose, the use of LDL apheresis (LA), an extracorporeal method which selectively binds and eliminates LDL-Ch, is indicated.

Aim: The aim of this research is to examine the effects of LA on inflammatory markers (CRP, fibrinogen, Lp(a)), as other important risk factors in the progression of atherosclerosis.

Methods: 10 FH patients (mean age of 47.2 ± 5.3 years) with established cardiovascular disease, treated with LA (DALI method) twice per month, were included in this research. In each

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of them, first 100 DALI treatments (1000 in total) were analyzed. Anthropometric data was measured before every treatment, while biochemical blood analysis of parameters important for this research (total Ch, its subfractions HDL and LDL-Ch, triglycerides, as well as CRP, fibrinogen and Lp(a)) were measured both before and after every LA treatment, along with characteristics of very treatments (treatment duration, volume of blood treated, blood flow speed).

Results: There was a highly statistically significant decrease in total Ch, LDL-Ch, HDL-Ch and triglycerides levels after LA treatment. Also, we found significantly lower levels of all inflammatory markers after LA procedure (percentage of decrease in CRP was 21.4+/-11.0%; in fibrinogen 19.4+/-16.1%; in Lp(a) 32.0+/-50.4%). Strong correlation was found between the fall of CRP and the amount of blood treated, blood flow speed of the treated blood and the duration of the treatment. Fall of Lp(a), expectedly, didn't correlate with treatment characteristics.

Conclusion: Results show that LA is an exceptional method for reduction not only of LDL-Ch, but also of inflammatory markers as important risk factors for the progression of atherosclerosis in patients with FH.

ATG16L1 T300A GENETIC POLYMORPHISM IN HYPERURICEMIA AND GOUT

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Introduction: Autophagy is a sophisticated intracellular recycling system used by cells to degrade cellular material and it is also involved in the modulation of pro-inflammatory cytokine production. The autophagy related 16 like 1 gene (ATG16L1) encodes a protein involved in the formation of the initiation complex of autophagosome formation. A single nucleotide polymorphism in ATG16L1 (T300A) was linked to an excessive production of pro-inflamatory cytokines (IL-1 β), and is a genome widely associated risk variant for Crohn's disease. Autophagy inhibition has also been shown to be a potential mechanism enhancing cytokine production in other autoinflammatory diseases such as gout.

Aim: We investigated a possible association between the AT-G16L1 T300A SNP and the progression to gout in patients with hyperuricemia.

Methods: We performed a case-control study in which we investigated the distribution of ATG16L1 T300A SNP in 147 patients with gout and 127 controls with hyperuricemia. Genotyping of individuals was performed using Taqman SNP genotyping assay. Statistical analysis was performed using Fisher's test and results were considered significant at p-value < 0.05.

Results: Our first findings show a frequency of 0,51 of the variant allele for cases and 0,49 for controls (OR = 1,1; 0,8–1,5 95% CI; p-value = 0.7). The genotype distribution followed similar patterns in cases and controls and our dominant and recessive risk association models showed no significant results.

Conclusion: This is the first study to address the association of this SNP to gout. Our first results did not show a statistically significant difference between the SNP distribution in the two study groups. A limitation of this study could be the small size of the population analysed, nevertheless it has the strength of addressing potential proinflammatory genetic risk variants in a case control

design using hyperuricemic controls, thereby correcting for urate related susceptibility. Further studies in larger cohorts investigating immune related gene variants for gout susceptibility are warranted.

CLINICAL PRESENTATION AND THERAPY OF PRIMARY IMMUNE THROMBOCYTOPENIA RESISTANT TO SPLENECTOMY

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Introduction: A satisfactory therapeutic response is achieved with splenectomy in 60 - 80% patients diagnosed with immune thrombocytopenic purpura (ITP). There is an ongoing consensus on the short - term efficiency of splenectomy, however, its long - term efficiency along with its side effects, clinical presentation and therapy still remains controversial.

Aim: The frequency of resistance and relapse after splenectomy, occurrence of bleeding, infections and thrombolytic events, therapeutic possibilities and medicinal efficiency.

Methods: In a retrospective study, 138 patients that underwent treatment and splenectomy were analysed from 1987 to 2018.

Results: It has been shown that 20.3% of patients were refractory to splenectomy, 11.6% relapsed and 8.7% were primarily resistant. The average post-splenectomy follow-up period was 117 months (range 3–474). The average follow - up period of patients that were resistant to splenectomy was 147 months (range 23–474). The study has found that 67% of cases refractory to splenectomy showed a good therapeutic response, with 48% CR and 18.5% PR. Response usually was achieved using the following therapeutics: romiplostim 100%, eltrombopag 75%, cyclosporine 66.67%, mycophenolate mofetil 50%, danazol 50%, corticosteroids 40.9%. Hemorrhagic syndrome developed in 78.6% patients, while non hemorrhagic complications occurred in 28.6% patients.

Conclusion: Splenectomy remains a very efficient therapeutic modality for the treatment of patients with ITP, with a high percentage of patients resistant to splenectomy achieving remission (67%). Thrombopoietin Receptor Agonists have shown exceptional results so far in the treatment of ITP patients with a refractory form.

PATHOLOGY OF THE PARATHYROID GLAND WITH A SPECIAL REVIEW OF THE PARATHYROID GLANDS THAT HAVE BEEN ACCIDENTALLY REMOVED WITHIN THE THYROID GLAND SURGERY

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Introduction: Clinicopathological correlations of hyperparathyroidism include parathyroid adenoma, hyperplasia and carcinoma. Surgical interventions involving the removal of a part of the tissue or whole thyroid gland can lead to postoperative hypocalcaemia and permanent hypoparathyroidism.

Aim: Analysis of clinical and pathohistological characteristics of pathologically altered and incidentally removed parathyroid glands as part of thyroid gland surgery in the period 2016–2017. **Methods:** Histopathohistological reports from the Center for Endocrine Surgery of the Clinical Center of Serbia and the Pathology Institute of the Medical Faculty in Belgrade were analyzed. This retrospective study included 146 patients with removed parathyroid glands due to hyperparathyroidism and as a part of thyroid hysterectomy in the period from 1.1.2016 to 31.12.2017. An analysis of age, full distribution, mass, diameter, localization, number of removed parathyroid glands, pathological changes of thyroid gland when occasionally removed paratireoid, type of surgery and frequency of removals. Patients were divided into two groups depending on whether the parathyroid glands were removed due to hyperparathyroidism or by accident.

Results: In the group of patients with hyperparathyroidism, 65.91% were women, 34.09% were men. Distribution of the diseases was: adenoma 86.36%, hyperplasia 9.09% and carcinoma in 4.55% of patients. In the second group of 102 patients, 88.24% were women, 11.76% were men, of the average age of 53.04 years. Accidental removal occurred in 71.57% of thyroidectomy and 28.43% of lobectomy. Thyroid gland surgery due to papillary carcinoma is the most common cause of accidental removal of parathyroid glands (39.22%). The parathyroid gland was removed accidentally in 7.4% of all operations of the thyroid gland. One parathyroid gland has been removed in 95.1%, and two glands in 4.9.

Conclusion: Adenoma is the most common pathological change in parathyroid glands. We cannot underestimate the number of accidentally removed parathyroid glands during thyroid gland surgery.

BASELINE INDICATORS OF CORONARY ARTERY DISEASE BURDEN IN PATIENTS WITH NON-ST-SEGMENT ELEVATION ACUTE CORONARY SYNDROME

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Introduction: The non-ST-segment elevation acute coronary syndrome (NSTEACS) is a frequent medical problem in contemporary societies. In patients with hemodinamically significant stenosis in coronary arteries percutaneous coronary intervention is one of the preferred method of treatment. However, due to the diversity of patients with NSTEACS, among this group proper methods of risk and their coronary artery disease (CAD) burden stratification are required.

Aim: We sought to investigate whether baseline characteristics of patients with NSTEACS may predict their CAD burden.

Methods: Baseline clinical, ECG and laboratory data were compared with angiographic findings of 693 consecutive NSTEACS patients. According to the angiography result all patients were assigned to one of the three groups with: significant stenosis of left main and/or three-vessel CAD (LM-3VD, n = 114), single- or two-vessel CAD (1-2VD, n = 335) or without significant CAD (noVD, n = 244).

Results: Baseline characteristics of compared groups were different. By multivariable logistic regression necrotic enzyme negative ACS (odds ratio 5.57, 0.95 confidence intervals 3.74–8.29), female gender (2.23, 1.54–3.24), no previous myocar-

dial infarction (2.06, 1.38–3.08), no diabetes mellitus (1.53, 1.04–2.25), no peripheral arterial disease (1.77, 1.05–2.99) and hematocrit level (0.95 per 1%, 0.91–0.99) independently predicted noVD (2 = 145.8, P < 0.0001) with c-statistics of 0.80. All independent predictors were ranked according to the results of multivariable model and the new score for prediction of noVD was introduced with the area under the ROC curve of 0.77 (CI 0.73–0.80, P < 0.0001) and sensitivity of 70% and specificity of 66% for < 5 points. Also independent predictors of LM-3VD (age, male gender, diabetes mellitus, peripheral arterial disease, necrotic enzyme positive ACS and baseline Killip class 3/4) were determined, however their predictive accuracy was moderate with the area under the ROC curve of 0.69 (CI 0.64–0.75).

Conclusion: In patients with NSTEACS, baseline characteristics are useful in predicting a lack of significant CAD, whereas their correlations with multivessel CAD remain moderate.

HOLTER-ECG BASED APNEA-HYPOPNEA INDEX IN PATIENTS AFTER CRYPTOGENIC STROKE

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Introduction: Obstructive sleep apnea (OSA) is a breathing disorder during sleep regarded as cardiovascular risk factor associated with increased mortality. ECG seems to be potentially the most practical, non-invasive screening tool for sleep disordered breathing (SDB). In patients with Apnea–Hypopnea Index (AHI)>15 risk of SBD is significant. OSA is a modifiable risk factor of acute ischemic stroke (AIS) which is responsible for majority of neurological disabilities in adults.

Aim: The aim of our study was to estimate AHI based on ECG in patients with cryptogenic AIS and in healthy subjects. We wanted to measure if the episode of AIS leads to increased AHI.

Methods: The study group consisted of 92 patients diagnosed with first symptomatic cryptogenic AIS (age: 60 ± 14 ; 51%M) hospitalized in Neurology Department in years 2015–2018. Patients were divided into 2 groups: TACI (anterior ischemia) and non-TACI (posterior ischemia). Each patient had 7-days Holter recording. Control group contained 50 healthy people (age: 55 ± 9 ; 66%M) after Holter ECG monitoring in Cardiology Department. Data was analyzed and automated algorithm was used to estimate patients' AHI. AHI thresholds of <5 and >15 were used to indicate low and high probability of OSA.

Results: AHI was significantly increased in AIS patients in comparison to control group (p = 0,001). AHI in non-TACI patients (14 ± 5,3) was higher than in TACI (10,5 ± 4,8) and control group (8,5 ± 8,4). AHI>15 occurred in 29% AIS patients and in 16% from control group.

Conclusion: Patients after AIS are more likely to have higher AHI and higher probability of OSA. Non-TACI AIS is significantly more predisposing factor of SDB which might be related to localization of respiratory and ANS centers. There is a possibility to use Holter ECG-based AHI in all the patients after cryptogenic AIS as a screening for higher risk of OSA to prevent future cardiovascular complications, but further studies should be performed.

EFFECT OF MINERALOCORTICOID RECEPTOR ANTAGONISTS ON MARKERS OF FIBROSIS IN PATIENTS WITH MYOCARDIAL DYSSYNCHRONY, ON THE BACKGROUND OF CHF OF ISCHEMIC ORIGIN, IN CONJUNCTION WITH DM TYPE 2

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Introduction: Elevated levels of aldosterone contribute to the development of interstitial cardiac fibrosis, consequent upon which the presence of myocardial dyssynchrony (MD) increases, leading to the progression of chronic heart failure (CHF).

Aim: To evaluate the influence of mineralocorticoid receptor antagonists on changes of markers of fibrosis in patients with myocardial dyssynchrony, against the background of CHF of ischemic origin in conjunction with DM type 2.

Methods: 20 patients with CHF of ischemic origin with manifestations of MD were examined. The mean age of patients was (67.45 + 10.32) years. All patients were prescribed mineralocorticoid receptor antagonist - eplerenon at a dose of 50 mg per day. One month after the prescribed therapy, a re-examination was performed. All patients were subjected to a standard 12 leads electrocardiography (ECG), according to the generally accepted method. To detect electrical dyssynchrony, the criteria of a narrow QRS complex <120ms and an extended ORS complex = 120ms were used. Myocardial dyssynchrony was segregated into intraventricular, interventricular, atrial-ventricular (atrioventricular) and combined. The presence of myocardial fibrosis was assessed by the content of galectin (Gal) 3 in the blood serum by an enzyme immunoassay (EIA) and the presence of matrix metalloproteinase (MMP) 1. The interstitial collagen volume fraction (ICVF) was calculated using the J. Shirani method.

Results: There was a decrease in the indices of intraventricular dyssynchrony, and delayed activation of the posterior-lateral wall of the heart: before treatment it was $(355,64 \pm 89,29)$ ms, and after treatment - $(350,5 \pm 123,2)$ ms. (p < 0,05).

After receiving this treatment, a significant reduction in the QRS complex (129.87 ± 48.65) ms. A positive result of treatment was confirmed by a decrease in the activity of markers of fibrosis and in particular, of the volume fraction of interstitial collagen. ICVF before treatment (9,2 ± 3,06) %, and after treatment (7,3 ± 2,4) %. At the same time, the activity of Gal-3 before treatment (7,63 ± 4,77) ng / ml, after treatment (7,61 ± 4,8) ng / ml and MMP-1 before treatment (0,54 ± 1,62) ng / ml and after treatment (0,55 ± 1,63) ng / ml (p < 0,05) did not change.

Conclusion: Inclusion in the complex therapy of the mineralocorticoid receptor antagonist, eplerenon in the dose of 50 mg per day in one month reduces the rates of intraventricular and intraventricular MD, but is accompanied by an increase in atrioventricular MD. It leads to a decrease in the degree of the interstitial collagen volume fraction. To determine the effect on the markers of fibrosis, studies are in place on a larger number of patients and the continuation of supervision over patients for a longer period of time.

LOCATION OF KNOTS AND TYPES OF NOOSES IN CASES OF SUICIDE BY HANGING - ANALYSIS

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Introduction: Suicide by hanging can be performed with different types of materials and knots. Choice of type of noose can be determined by many factors, such as accessibility or cultural influence.

Aim: The objectives of the study were to determine the types of nooses used in suicides by hanging, frequency of different locations of knots and investigate their association with age, gender and place of commiting suicide.

Methods: There were 1373 cases of suicide by hanging in the archives of the Department of Forensic Medicine of Jagiellonian University in Cracow in years 2008–2018. 94,25% of them had documented forensic autopsy and were analyzed in terms of types of used noose and location of a knot.

Results: Most frequently used type of noose was a rope (44,79%). People who used a piece of fabric were younger than the rest (mean age 43,56 vs. 48,06, p-value <0,05) and those who used a rope were older (60,09 vs. 47,77, p-value <0,05). People who committed suicide in hospitals used different types of nooses (a rope was used less frequently, a part of clothing and a belt were more common, p<0,05). The location of a knot on the left side of a neck was present in 299 cases (21,78%), right side of a neck 258 (18,79%), back of a neck 523 (38,09%), front of a neck 23 (1,68%). People who placed a knot at the front of a neck were statistically older (mean age 54.63 vs. 47.73, p-value <0,05).

Conclusion: The most common type of noose in our study was a rope. Easily accessible types of nooses were found very often (cable 12,97%, belt 10,34%). Suicides by hanging that took place in hospitals were performed with different types of nooses. The most common location of a knot is a side of a neck (40,57%; left side 21,78%; right side 18,79%).

ASSESSMENT OF THE ANTERIOR CRUCIATE LIGAMENT LESIONS USING MRI

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Introduction: The anterior cruciate ligament is one of the most commonly injured ligaments in our body. Magnetic resonance imaging is one of the most specific diagnostic methods for early detection of lesions of the anterior cruciate ligament (LCA). Magnetic resonance with its non-active approach, as well as great diagnostic accuracy, found its place in the early diagnosis of knee lesions.

Aim: To prove that magnetic resonance in early lesions detects the presence or absence of LCA lesions with other associated knee lesions.

Methods: The study involved 63 patients grouped in two groups: with LCA treatment and without LCA lesion; lesion LCA served as exclusion criteria. Knee overview was done using a standard protocol using turbo spin echo (TSE), on a 1.5T device: at an axial level in T2w FS, at the sagittal level in T1w, T2w, T2w FS, at the coronal level in T2w FS as well as at a paraxial level parallel to the direction of providing a front cross-link in T2w relaxation time.

Results: Based on statistically studied data, the lesion of the anterior cruciate ligament was not associated with other knee lesions. The most likely reason for this fact is that the injury mechanism is not taken as a criterion factor.

Conclusion: Magnetic resonance imaging is a very effective diagnostic procedure for detecting LCA lesions with a high degree of sensitivity and specificity as well as diagnostic accuracy. Therefore, we consider that the characteristics of magnetic resonance fully justify the role of the gold standard in the diagnosis of LCA lesions.

WELL DEFINED SCAR OR GLOBAL FIBROSIS? NABBING THE CULPRIT OF VENTRICULAR TACHYCARDIA (VT) IN PATIENTS WITH MITRAL VALVE REGURGITATION UNDERGOING STRUCTURAL VT ABLATION

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Introduction: Mitral valve regurgitation (MVR) is associated with burden of ventricular tachycardia (VT) and sudden cardiac death. Recent MRI studies performed in patients with severe MVR associated it with diffuse myocardial fibrosis which may contribute to complex ventricular tachycardia (VT). New data also suggests suppression of VT after MV interventional repair. We aimed to investigate if MVR related VT could be underlying cause of arrhythmia in patients who underwent structural VT ablation in our centre.

Aim: Our goal was to investigate if MVR related complex-VT could be underlying cause of arrhythmia in patients who underwent structural VT ablation.

Methods: We performed retrospective analysis of medical records enrolling 37 consecutive patients referred for structural VT ablation in our centre between 2016 and 2019. We analyzed echocardiographic parameters, follow-up- including implantable cardioverter defibrillator (ICD) memory records and peri-procedural data.

Results: 11 (29,7%) patients had moderate to severe MVR (group 1), 19 patients(51,4%) mild MVR (group 2). In 7 cases ECHO assessment of MV was not performed.

Peri-procedurally ablation was fully successful in 63,6% (7) of cases in gr.1 and 89,5% (17) in gr.2.

18,2% (2) of cases in group 1 were unsuccessful compared to 5,3%(1) in 2nd group.

Non-clinical VT has been induced in 18,2% (2) cases in gr.1 and 10,5% (2) in group 2.

In the follow-up we collected data of 34 cases, we lost follow-up of 3 patients- 2 in gr.1 and 1 in gr.2.

ICD did not record any sustained VT (sVT) in 54,5% (6) cases from gr.1 and (78,9%) from gr.2.

1 patient from group 1 died shortly after procedure.

2 sVTs were recorded (18,2%) in group 1.

4 ablations from group 2 (21%) had to be redone with good results.

Conclusion: Our results come from a low-volume electrophysiology center, which limits our study by providing us with modest amount of data, impeding reliable statistical analysis. However lower proportion of successful ablations, worse follow-up and higher non-clinical VT induction rate in patients with moderate to severe MVR suggests that performing similar study on significantly bigger population should be considered, especially regarding new research papers proposing mitral valve repair as a suppressor for MVR related VT.

CLINICAL CHARACTERISTICS OF PHEOCHROMOCYTOMA AND PARAGANGLIOMA

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Introduction: Pheochromocytomas and paragangliomas are catecholamine-secreting neuroendocrine tumors originating from chromafin cells. They are mostly benign with a highly variable clinical presentation. As 30–40% of all tumors are hereditary, genetic screening for associated mutations is mandatory. Urinary catecholamine levels, serum levels of the tumor marker chromogranin A (CgA) and pathohistological analysis of tumor tissue are used for diagnostic and prognostic purposes.

Aim: Analyzing the incidence of various clinical characteristics of pheochromocytoms/paragangliomas, the mutual correlations of those characteristics, their reliability and significance in making the diagnosis and evaluating the probability of mortality.

Methods: This retrospective cohort study analyzed the data of 54 pheochromocytoma/paraganglioma patients. We analyzed clinical characteristics, MIBG-scintigraphy sensitivity, measured urinary catecholamine and serum CgA levels, and performed genetic analysis for hereditary forms of the disease. During pathohistological work up proliferative index Ki 67 and PASS score were specifically determined. Finally, we analyzed patients' survival, with potential mortality risk factors. Statistical analysis was performed with SPSS software.

Results: Metastases were present in only 13%, significantly more often in paragangliomas (p = 0.029). Clinical presentation was variable, with some form of hypertension present in 74%. Elevated catecholamines did not significantly correlate with presence of clinical manifestations (p > 0.05). Elevated CgA was verified in 85.4% of patients, with levels significantly correlating with presence of clinical manifestations (p = 0.048) and metastases (p = 0.025). MIBG-scintigraphy was sensitive in 88.9% of cases, and hereditary form of the disease was detected in 26.1% of patients. Median survival time was 271.65 months, and mortality risk significantly depended on presence of metastases (p < 0.001) and CgA level (p = 0.001).

Conclusion: A thorough analysis of variable clinical characteristics of pheochromocytoma/paraganglioma, their cross-comparison, and contextual interpretation represent a very important step in timely diagnosing and treating these tumors.

IMPACT OF MYOCARDIAL INJURY AFTER PERCUTANEOUS TRANSLUMINAL ANGIOPLASTY (PTA) IN PATIENTS WITH CRITICAL LOWER LIMBS ISCHEMIA (CLI) ON MAJOR ADVERSE CARDIOVASCULAR EVENTS

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Introduction: One of common complications after noncardiac surgery is myocardial injury, which is defined as prognostically relevant injury that happens due to ischemia during of up to 30 days after surgery. Endovascular treatment (EVT) in patients with CLI and its impact on myocardial injury related with this procedure has not been well studied yet.

Aim: Our aim was to evaluate myocardial injury after endovascular treatment (MIEVT) and its impact on postoperative major adverse cardiovascular events (MACE).

Methods: In this prospective study we enrolled patients admitted for PTA due to CLI. Blood samples for High Sensitive Serum Troponin (hsTnT) measurement, were collected before procedure, 6–12 hours and 1 day after it. MIEVT criteria have been defined as elevation of hsTnT over 14ng/L after EVT with at least 30% increase from the baseline hsTnT. Patients have been covered with 1-year follow-up observation.

Results: We enrolled 239 patients, 62.1% had preoperative hsTnT above the threshold level of 14ng/L, however it didn't significantly influence MACE (p = 0.89), nor 1-year mortality (p = 0.98). During 1-year observation, cumulative MACE occurred in 48 patients (20.5%) and 34 died (14.2%). Significant dependence of MIEVT (61 patients;25.5%) on death [OR = 2.73(1.3-5.8);p = 0.01] and MACE [OR = 2.94(1.50-5.73);p = 0.003] has been observed.

Conclusion: Troponins, commonly elevated in patients with CLI undergoing PTA, indicate high rate of cardiac diseases. At least one quarter patients undergoing EVT may experience MIEVT. In which at least 25% will die during 1-year indicating on the periprocedural ischemia as a trigger for future outcomes. Significant majority of the patients that experienced MIEVT did not present clinical signs of myocardial ischemia, and may be unnoticed without troponin screening.

COMPARATIVE TREATMENT WITH DYDROGESTERONE AND MICRONIZED PROGESTERONE IN WOMEN WITH RECURRENT MISCARRIAGE

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Introduction: Nowadays there are more and more women with a history of recurrent miscarriage. Various kinds of progesterone are appointed during pregnancy and pre-conception care in such patients.

Aim: To find the most effective progestin with minimal side effects to be used in women with recurrent miscarriage

Methods: A retrospective study initially included 500 singleton pregnant women with recurrent miscarriage in the first half of pregnancy (from 6 weeks 0 days to 22 weeks 0 days). Finally, 93 patients were recruted. All pregnant women were devided in two groups: 49 were treated with dydrogesterone (group1) and other 44 – with micronized progesterone (group 2). All patients were interviewed on the presence of side effects, hospitalizations and their duration.

Results: The main criterion for the therapy effectiveness was prolongation of current pregnancy till 22–27 weeks of gestation.

Treatment with progesterone was effective in 88/93(95%). In group 1 (dydrogesterone) all patients delivered at term, in group 2 (micronized progesterone), the frequency of pregnancy loss was 14% - in 6/44. In patients treated with micronized progesterone 10/44(23%) had nagging pains, 10/44 (23%)-bleeding, 6/44 (14%) - haematoma on ultrasound. While in women received dydrogesterone pain fell out in 3/49(6%), bleeding in 4/49 (8%) and there were no patients with haematoma on ultrasound. 31/44(70%) of interviewed women in group 2 (micronized progesterone) – in 7/44 (16%). The differences among groups were proved statifically, p < 0.05.

Conclusion: The present study suggests that treatment with dydrogesterone demonstrate effectiveness and safety. Dydrogesterone appeared to be optimal for the therapy in women with recurrent miscarriage.

ATOSIBAN VERSUS NIFEDIPINE FOR INHIBITION OF PRETERM LABOR: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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Introduction: Preterm labor (PTL) is associated with high rates of newborns death and serious adverse events. The choice of 1st line therapy lies mainly between two different tocolytic classes, atosiban and nifedipine.

Aim: Our study aimed to compare the clinical efficacy and safety of atosiban versus nifedipine for treatment of PTL.

Methods: PubMed, Scopus, Web of Science, and Cochrane CENTRAL were searched for randomized controlled trials (RCTs) comparing nifedipine with atosiban in women with PTL. Records were screened for eligibility and the authors independently extracted the data which included the following: study design, patients characteristics, risk of bias domains, and study outcomes. We analyzed the data using RevMan 5.2 with a random effect model to pool the safety and efficacy data as relative risk (RR), with their 95% confidence interval (CI).

Results: Seven RCTs with a total of 992 patients were included. There was no significant difference between atosiban and nifedipine regarding efficacy or effectiveness either in pregnancy prolongation \geq 48 hours (RR = 1.06, 95% CI [0.92, 1.22], p = 0.44, RR = 0.93, 95% CI [0.84, 1.03], p = 0.18, respectively), or in pregnancy prolongation \geq seven days (RR = 1.04, 95% CI [0.89, 1.21], p = 0.65, RR = 0.91, 95% CI [0.79, 1.05], p = 0.18, respectively). Atosiban was associated with less adverse events than nifedipine, with statistical significant difference in headache and tachycardia (RR = 0.47, p = 0.05, RR = 0.20, p = 0.02, respectively); while there was no significant difference regarding palpitation, hypotension, vomiting, and nausea (RR = 0.37, RR = 0.30, RR = 1.55, RR = 2.44, respectively). Risk of neonates' adverse events with atosiban was similar to nifedipine.

Conclusion: In PTL women, our findings suggested that atosiban is better than nifedipine regarding maternal adverse

events with no difference in pregnancy prolongation ≥ 48 hours or ≥ 7 days, or in neonates' adverse events. However, further studies with increased sample size are needed.

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MYOCARDIAL BRIDGES OVER THE LEFT ANTERIOR DESCENDING ARTERY IN SYMPTOMATIC PATIENTS UNDERGOING CORONARY ANGIOGRAPHY – INCIDENCE AND CLINICAL CHARACTERIZATION

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Introduction: Myocardial bridge (MB) occurs when coronary artery dips underneath myocardium having an intramural course. In consequence, overlying muscle narrows lumen of the artery during systole. MB may manifest with symptoms of stable coronary artery disease (CAD) or acute coronary syndrome (ACS).

Aim: To investigate prevalence of MB, its coexistence with CAD and its character of symptoms in population of patients undergoing coronary angiography (CAG).

Methods: We reviewed medical records of all patients undergoing CAG at the Jagiellonian University Department of Cardiac and Vascular Diseases from 1 January 2009 to 31 May 2018. Patients who underwent CAG for other reason than suspected stable CAD or ACS were excluded from the study. MB over LAD were recorded and reducing vessel's lumen by \geq 50% were considered significant. Significant CAD was defined by presence of \geq 50% diameter stenosis or coronary stent/CABG.

Results: Of 12,892 patients, 215 (1.67%) were found to have MB over LAD. 196 (35.71% females) patients underwent CAG due to suspected stable CAD or ACS. Median age was 62. 82 (41.84%) MB were significant. In the group with suspected stable CAD, significant MB were more prevalent in men (48.39% vs. 26.42%, p = .009). In females, significant MB were found more often in ACS (41.67% vs 15.22%, p = .031). Fifty patients (25.51%) underwent CAG due to suspected ACS, 27 of them (54%) had no significant CAD. CAD was more prevalent in patients with significant MB (33.63% vs 53.01%, p = .007). In the group of patients without significant CAD, episodes of fainting were more prevalent in patients with significant MB (4.00% vs 18.42%, p = .028).

Conclusion: MB over LAD were found in 1.67% symptomatic patients undergoing CAG. Less than half of them were significant narrowing lumen's diameter at least 50%. CAD was more prevalent in patients with significant MB. Significant MB seem to be associated with fainting.

RHYTHM VERSUS RATE CONTROL FOR ATRIAL FIBRILLATION: A META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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Introduction: Atrial fibrillation (AF) is a common, sustained tachyarrhythmia, associated with an increased risk of mortality and thromboembolic events. The pharmacological management of AF targets either rate control (maintaining the heart rate at normal levels) or rhythm control (restoration of sinus rhythm).

Aim: We performed this systematic review and meta-analysis to compare the clinical efficacy of rate and rhythm control strategies in patients with AF.

Methods: A comprehensive search of PubMed, OVID, Cochrane-CENTRAL, EMBASE, Scopus, and Web of Science was conducted, using relevant keywords. The risk of bias assessment of included trials was performed using the Cochrane risk of bias (ROB) assessment tool. The risk of publication bias was assessed using funnel plot-based methods, whenever 10 or more studies reported on the same outcome.

Dichotomous data on mortality and other clinical events were extracted and pooled as risk ratios (RRs), with their 95% confidence interval (CI), using RevMan software (version 5.3).

Results: Twelve studies (8451 patients) were pooled in the final analysis. The overall effect-estimate did not favor rate or rhythm control strategies in terms of all-cause mortality (RR = 1.13, 95% CI [0.88, 1.45]), stroke (RR = 0.97, 95% CI [0.79, 1.20]), thromboembolism (RR = 1.06, 95% CI [0.64, 1.76]), and major bleeding (RR = 1.10, 95% CI [0.90, 1.35]) rates. These findings were consistent in AF patients with concomitant heart failure (HF). The rate of rehospitalization was significantly higher (RR = 0.72, 95% CI [0.57, 0.92]) in the rhythm control group, compared to the rate control group. In younger patients (<65 years), rhythm control was superior to rate control in terms of lowering the risk of all-cause mortality (p = 0.0003), HF (p = 0.003) and major bleeding (p = 0.02).

Conclusion: In older AF patients and those with concomitant HF, both rate and rhythm control strategies have similar rates of mortality and major clinical outcomes; therefore, choosing an appropriate strategy should consider individual variations, such as patient preferences, comorbidities, and treatment cost. Future trials should compare both strategies in younger patients and those with other comorbidities such as stroke and left ventricular dysfunction.

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THE ERYTHROCYTE CATECHOLAMINE DEPOSITING FUNCTION IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE WITH ACCOMPANYING GASTROESOPHAGEAL REFLUX DISEASE

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Introduction: According to scientific assumption, gastroesophageal reflux in patients with COPD may arise due to background adrenergic imbalance. **Aim:** Studying the intensity of catecholamine (CA) depositing by erythrocytes (Er) in patients with COPD, depending on the concomitant GERD severity.

Methods: The study involved 60 patients, including: 15 patients with COPD (group 1), 15 patients with COPD and endoscopically negative GERD (group 2), 15 patients with COPD and endoscopically positive non-erosive GERD (group 3), 15 patients with COPD and endoscopically positive erosive GERD (group 4).

Results: Patients in group 1 are significantly more likely to have Er, which do not contain granules of CA (category I cells), or contain insignificant number (II category cells) compared with control (1.9 times, p < 0.05). In patients of group 2 the number of cells without CA granules exceeds the control index by 2.5 times (p < 0.05). The percentage of cells containing more than 10 CA granules in this group of patients is reduced by 1.6 times in comparison with the norm (p < 0.05), and the «dark» cells (category VI) are absent. In patients of group 3 present an increase in the percentage of cells category I and II by 4.0 times (p < 0.05), a decrease in the percentage of cells category IV and V by 4.3 times (p < 0.05). Patients in group 4 have the maximum intensity of change: the number of cells without granules of CA exceeds the normative indicators by 3.9 times compared with the control (p< 0.05) and 2.1 times (p < 0.05) compared with a group 1.

Conclusion: Investigation of erythrocyte catecholamine depositing function (ECD) can display the condition of adrenergic receptor apparatus of bronchial smooth muscles. Patients with COPD and GERD revealed a decrease in the ECD, which contributes to the unbalance of sympathoadrenal system and is an adverse prognostic criterion for the development of erosive GERD.

COMPREHENSIVE GERIATRIC ASSESSMENT AS AN IMPORTANT PROCEDURE IN PERSONALIZED CARE PLAN FOR GERIATRIC PATIENT

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Introduction: Comprehensive geriatric assessment (CGA) is a complex diagnostic process, used to collect data on health condition, psychosocial and economic status. Considering the multitude of chronic diseases and big amount of declines in many physiological systems, the traditional procedure - diagnosis and symptomatic therapy are insufficient. Many studies have shown that CGA can improve treatment process and general condition of patients.

Aim: The aim of this study was to evaluate the usefulness and effectiveness of CGA in outpatient clinics.

Methods: A cross-sectional study was conducted among patients aged over 65 in fifteen outpatient clinics in Cracow and outskirts. CGA was performed using following tools: Activities of Daily Living, Mini-Mental State Examination, Geriatrics Depression Scale, Tinetti Test, Mini Nutritional Assessment, Clinical Frailty Scale, Athens Insomnia Scale and EQ-5D-5L.

Results: The study was performed on the group of 438 patients (276 women, 162 men) aged over 65. The main problems in the studied population were: multiple morbidities and the resulting polypharmacy (51% of patients use 6 or more different drugs), depressive disorders (132; 32%), sleep disturbances (182; 42%), risk of fragility syndrome and significantly increased risk

of falls (153; 35%). The most common diseases were: hypertension, sight problems and worsening of hearing. Half of respondents (225; 51%) complained about chronic pain and one third of them (126; 29%) had problems with defecation.

Conclusion: CGA performed in outpatient clinics is a possibility to recognize the previously undiagnosed health problems. This procedure can complement the diagnosis of patients' conditions and their screening. In addition, regularly performed CGA gives the doctor feedback on the effectiveness of treatment and allows its optimization.

Neurosciences

CLINICAL SIGNIFICANCE OF INTRACRANIAL HEMORRHAGE SHAPE IRREGULARITY

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Introduction: Shape and density of intracerebral hemorrhage (ICH) are associated with a higher risk of poor treatment outcome, although mechanisms of such correlation remain unclear.

Aim: The aim of the study was to check whether computationally assessed hemorrhage shape irregularity might indicate presence of other predictors of such outcome.

Methods: We retrospectively analyzed 48 patients with spontaneous ICH. They underwent head CT upon admission, after 24 hours and in case of neurological worsening. Upon admission patients were assessed using Glasgow Coma Scale (GCS) score and had blood test taken. For each slice of CT scan with visible ICH, we extracted its contour and calculated the fractal dimension (FD), compactness (C), and Fourier factor (FF). We also calculated the circle factor (CF), which was defined as the contour perimeter/perimeter of the biggest circle that can be inscribed into the contour

Results: A total of 14 patients (29,17%) had ICH growth. These patients had significantly higher C (0.74 ± 0.23 vs. 0.58 \pm 0.18; p < 0.01), FF (0.96 ± 0.06 vs. 0.84 \pm 0.19; p = 0.03) and CF (0.55 ± 0.27 vs. 0.37 ± 0.18 ; p < 0.01) on primary CT scan. In multivariate logistic regression analysis, after adjustment for all possible confounders C (OR = 2.439; 95% CI: 1.231 – 5.541; p = 0.02) and CF (OR = 1.094; 95% CI: 1.015 – 1.196; p = 0.03) remained independently associated with risk of ICH growth. Also, FD was negatively correlated with GCS score upon admission (R = -0.37; p = 0.01) and positively with blood WBC (R = 0.44; p = 0.02) and INR (R = 0.48; p < 0.01).

Conclusion: ICH shape irregularity can be associated with higher risk of its growth, as well as with worse patient condition upon admission, increased inflammatory response and clotting disorders.

ROLE OF ASTROCYTIC SIGNALING UPON SYNAPTIC PLASTICITY ON AD-LIKE CONDITIONS

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Introduction: Alzheimer's Disease (AD) is a neurodegenerative disease characterized by the loss of cognitive function. Amyloid beta (A β) aggregation contributes to the disease progression, since Ab disrupts long-term potentiation (LTP) [1] – the main physiological mechanism responsible for memory and learning. Astrocytes modulate synaptic transmission and LTP by the Ca²⁺-dependent release of gliotransmitters [2]. A β is able to induce a Ca²⁺-signaling dysregulation in astrocytes [3], which can trigger an abnormal Ca₂-dependent release of gliotransmitters. This atypical release of gliotransmitters can contribute to the increase of neuronal excitability that disrupts synaptic transmission and LTP.

Aim: Thus, the aim of this work was to investigate the role of Ca^{2+} -dependent vesicular gliotransmitter release from astrocytes upon Aβ-mediated deficits in synaptic transmission and plasticity.

Methods: fEPSP were recorded in hippocampal slices from Wildtype (WT) and dn-SNARE mice, in which the SNARE-dependent release of gliotransmitters was selectively impaired in astrocytes. Hippocampal slices were pre-incubated with A β 1-42 oligomers (200 nM) for 3 h. LTP was induced by q-burst stimulation in the CA3-CA1 area. Basal synaptic transmission and presynaptic synaptic function were also evaluated.

Results: In the absence of Ab1-42 oligomers, q-burst stimulation increased LTP magnitude in WT (Dox +) mice, whereas in the presence of A β 1-42 oligomers the same induction paradigm lead to a significant impairment of LTP. However, for dn-SNARE (Dox -) mice, where the SNARE-dependent release of gliotransmitters was compromised, the θ -burst stimulation increased LTP magnitude both in the absence and in the presence of A β 1-42 oligomers. Basal synaptic transmission is compromised in the presence of A β 1-42 oligomers and no differences were found for presynaptic function of all the studied groups.

Conclusion: Considering these results, we hypothesised that astrocytes play a key role in A β -induced deficits in synaptic transmission and LTP, suggesting that the blockade of SNARE-dependent release of gliotransmitters may have a neuroprotective role on AD-like conditions.

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TWO PATTERNS OF ELECTRICAL SYNAPSE DISTRIBUTION IN THE MAMMALIAN RETINA

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¹Institute of Physiology, Medical School, University of Pécs; ²Szentágothai Research Centre, University of Pécs; ³Centre for Neuroscience, University of Pécs; ⁴Institute of Biophysics, Medical School, University of Pécs **Introduction:** Electrical synapses form extended functional syncytia in the retina but little is known about how their organization changes with eccentricity.

Aim: Here, we mapped the expression pattern of connexin-36 (Cx36), the major component of retinal electric synapses across the retinal layers and at a range of eccentricities using fluorescence immunohistochemistry in the cat retina.

Methods: Two morphological measures of electrical coupling, areal density and volume of Cx36 immunoreactive plaques were assessed using Imaris image processing software. Calretinin immunolabelling was used to delineate retinal layers and to highlight certain cell types including AII amacrine cells.

Results: In all retinal regions, Cx36 plaques were found in both synaptic layers and among amacrine cell bodies in the inner nuclear layer (INL). The highest density was found in the ON sublamina of the inner plexiform layer (IPL). Here, plaque density decreased with eccentricity (r = -0.65; p = 0.002) together with the density fall-off of AII amacrine cells. No significant correlation was found in the IPL OFF sublamina, INL or OPL. The mean volume of Cx36 plaques was significantly smaller in the OPL than in other layers. In addition, Cx36 plaque volume decreased with eccentricity (r = -0.70; p = 0.001) in the INL, where an earlier study suggested the existence of gap junctions between All amacrine cell bodies.

Conclusion: In conclusion, we identified two patterns of Cx36 plaque distribution in the cat retina: one that is eccentricity dependent and is linked to AII amacrine cells and another, eccentricity independent pattern. The eccentricity independent pattern suggests that in certain retinal networks, the number of electrical synapses per cell increases in proportion to the increase of dendritic field areas. Electrical coupling in networks involving AII amacrine cells on the other hand appears to decrease towards the retinal periphery.

A LONGITUDINAL STUDY OF COGNITIVE DECLINE IN PARKINSON'S DISEASE: MOTOR AND NON MOTOR PREDICTORS

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Introduction: Cognitive dissorders are one of the most debilitating non-motor syptoms of Parkinson's disease (PD). The rate of cognitive decline varies greatly among individual patients, but the pathophysiological basis of this either relatively stable or more progressive course still remains unclear, as the question whether PD-dementia (PDD) inevitably lies within disease progression or it is a completely separate entity.

Aim: To explore motor and non motor correlates of PD-Mild Cognitive Impairment (PD-MCI) and PDD and their value in predicting conversion from normal cognition to MCI and from MCI to dementia after a four-year follow-up period.

Methods: In this longitudinal study, a comprehensive neuropsychological battery as well as detailed motor and non-motor symptoms measurements were administered to 132 PD patients and 105 healthy matched controls. Patients were classified as having normal cognition (PD-CN), PD-MCI, or PDD. Non-demented patients at baseline were followed during next 4 years. Multinomial logistic regression analysis was used to determine

predicators of PD-MCI and PDD.

Results: At baseline, 61 (46.9%) patient fulfilled criteria for PD-MCI and 23 (17.7%) for PDD. In cognitively impaired patients, PD was characterized by increased motor disability, in addition to more frequent hallucinations and non-motor symptoms. Only axial motor score discriminated between MCI and dementia. PDD patients had more pronounced symptoms of depression and apathy compared to PD-CN. Fifteen (16.66%) patients remained cognitively normal, while 31 (34.44%) developed dementia after four years. Clinical predictors of PDD were: severity of bradykinesia and freezing, stage of the disease, depression and anxiety measures, non-motor symptoms frequency and presence of visual hallucinations.

Conclusion: Our results confirm a complex PD phenotype in cognitively impaired patients with more severe, predominantly axial, motor damage and presence of other non-motor manifestations. Further studies of patient-specific, genetic or environmental factors are nedded to better understand this complexity and improve patient management.

DEVELOPMENT OF A NEURON SPECIFIC NON-VIRAL DELIVERY SYSTEM FOR RHO-KINASE 1 AND 2 SHORT INTERFERING RNA

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Introduction: It has been reported that Rho kinase (ROCK) contributes to nerve regeneration impairment after spinal cord injury, and ROCK expression is higher in the context of neurodegenerative diseases.[1] Current approaches for short-term downregulation through gene therapy include the use of small interfering RNA (siRNA). We have previously reported chitosan nanostructures as promising nucleic acid vectors due to this polymers' biocompatibility and ability to self-assemble into well-defined nanocomplexes that can be functionalized for neuro-targeted therapies.[2]

Aim: We aim to downregulate ROCK expression as an approach to treat neurological conditions in the central nervous system (CNS).[3]

Methods: Nanocomplexes were prepared at different N/P (amine to phosphate) ratios. Briefly, siRNA in 20 mM-HEPES/5%-glucose was added dropwise to thiolated trimethyl chitosan (TMC-SH), and functionalized with PEGylated Hc protein fragment[2].

Cytotoxic profile was obtained by CellTiter-Glo® (Promega), and size was measured by dynamic light scattering (DLS-ZetasizerNano, Malvern) following manufacturer instructions.

Complexes were exposed to HT22 cell line under differentiated conditions for 4 or 24 hours. RNA was extracted by QuickRNA-MicroPrep (ZYMOResearch). cDNA was synthesized using NZY First-Strand Synthesis Kit. ROCK2 gene expression was measured by RT-qPCR.

Results: Diameter of N/P2 to N/P20 of non-functionalized complexes prepared with "siDNA" (siRNA surrogate) ranged from 103 to 160 nm, and all complexes presented a positive zeta potential.

For 24 hours exposure, at siRNA concentration of 100–150 nM, cell viability was reduced to 59%–54% for N/P4 and

87%–79% for N/P8. We report a tendency of increased sensitivity with longer exposure period.

24 hours exposure to nanocomplexes at N/P4 at 100–150 nM siRNA resulted in ROCK2 downregulation of 35%–37%, compared to complexes formed with non-targeted siR-NA. Further experiments at N/P8 and 4 hours of exposure are ongoing.

Conclusion: In conclusion, TMC-SH-PEG-Hc/siRNA nanocomplexes have shown a tendency to downregulate ROCK2 expression, hereby indicating the use of this strategy as a therapeutic approach for CNS pathologies.

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THE ROLE OF GLUTATHIONE TRANSFERASE OMEGA CLASS IN SUSCEPTIBILITY TO PROGRESSIVE MYOCLONIC EPILEPSY

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Introduction: Oxidative stress is considered an important contributing factor in the pathogenesis of progressive myoclonic epilepsy (PME). Glutathione S-transferases (GSTs) are a family of enzymes that play a role in xenobiotic detoxification, but also in antioxidant protection. Polymorphisms in genes encoding antioxidant enzymes lead to complete loss or alteration in enzyme activity, thus affecting antioxidant capacity in certain tissue. The omega class GSTs (GSTO1 and GSTO2) have additional roles and antioxidant mechanisms, while their association with PME has not been examined as yet.

Aim: The aim of this study was to assess the possible association between GSTO1 (rs4925) and GSTO2 (rs156697) polymorphisms and risk of developing PME.

Methods: A hospital-based case control study recruited 26 cases and 333 sex and age-matched controls. The GSTO1 and GSTO2 genotypes were identified by PCR-restriction fragment length polymorphism method (RFLP).

Results: The distribution of individual GSTO1 and GSTO2 genotypes did not differ significantly between PME cases and controls (p > 0.05). In the case of GSTO1 polymorphism, it has been shown that variant A allel could have some effect on reducing the risk of PME (OR = 0.351, 95% CI = 1.70–23.13), but the statistical significance has not been reached. Similarly, the variant G allel in GSTO2 polymorphism contributed to risk reduction in patients with PME (OR = 0.321, 95% CI = 0.041–2.533), however without statistical significance. None of the combined GSTO genotypes showed an impact on the risk of PME, although a discrete reduction in odds ratio was observed. The haplotype analysis confirmed the possible association of variant GSTO1 A allel and variant GSTO2 G allel with decreased risk of PME development.

Conclusion: The presence of variant GSTO1AA and GS-TO2GG genotypes might modulate the risk of developing progressive myoclonic epilepsy.

THE EFFECTS OF KISSPEPTIN-10 NEUROPEPTIDE ADMINISTRATION ON ENERGY BALANCE IN A RODENT ACTIVITY-BASED ANOREXIA MODEL

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Introduction: Kisspeptin (Kp) is a neuropeptide with a critical role in the function of the hypothalamic-pituitary-gonadal axis and energy homeostasis. In neuro-metabolic imbalances e.g. undernutrition status characteristic for anorexia nervosa, alterations of the Kp levels are observed.

Aim: The aim of our study was to evaluate the effects of peripheral kisspeptin-10 administration on weight loss, food intake and extensive physical activity in Activity-Based Anorexia (ABA) model.

Methods: 24 female Wistar rats weighing 170–220 g were included in the experiment. After an initial acclimatization period of 5 days, rats were randomly divided into two equal groups: sham group; ABA with voluntary activity on a reel, restricted feeding schedule and daily s.c. injections of saline solution and experimental group; ABA with voluntary activity on a reel, restricted feeding schedule and daily s.c. injections of Kp-10 (20 nmol/day). Body weight, food intake and physical activity were monitored daily. The experiment was discontinued when the body weight loss exceeded 25%. Plasma FSH and LH levels were assessed by EIA methods, whereas uterus and ovaries were obtained for histological evaluation.

Results: At the beginning of the experiment, the average weight reduction was similar for both groups, on days 3–5 sham group rats showed a significant body weight decrease (day 3: -13% vs.-15%, day 4: -15% vs. -18%, day 5: -18% vs. -21%). Kisspeptin also increased the amount of food consumed but only in the first 3 days of the experiment. There was no effect of Kp-10 on voluntary physical activity in the ABA model. Morphometric analysis of rat uterus and ovaries in sham and study groups has shown a significant difference in a number of ovarian follicles (2 vs. 9, respectively) correlated with the changes in FSH and LH plasma levels.

Conclusion: Kisspeptin alleviated the energy balance in the activity-induced model of anorexia in rats. A positive correlation between hormone plasma levels and histological analysis of uterus and ovaries suggest the possible involvement of the hypothalamic-pituitary-gonadal axis.

INFLAMMASOME ACTIVATION AFTER ACUTE NERVE INJURY

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Introduction: Peripheral and central injuries of the nervous system are often accompanied by inflammatory response, which fundamentally contributes to a "secondary injury", extending neuronal degeneration and inhibiting functional recovery. Emerging evidence highlights the importance of Pattern Recognition Receptors (PRRs), especially NOD-like receptor protein 3 (NLRP3). Activated NLRP3 responds to injury with the formation of inflammasomes and the activation of pro-inflammatory cytokines.

Aim: In this study, we aimed to describe NLRP3 in brain regions that show different susceptibility following peripheral nerve injury. Furthermore, as PRRs might provide a potential therapeutic target for reducing inflammation, we also wanted to determine whether the KATP channel opener diazoxide can reduce the activation of NLRP inflammasome pathway.

Methods: Balb/c mice underwent either surgical axotomy of the hypoglossal nerve or eye enucleation to induce inflammation of the hypoglossal and oculomotor nuclei, respectively. Diazoxide-treated animals recieved treatment for 4 days post-operatively. Brain sections of the two motor nuclei were stained for NLRP3 and evaluated based on the stained profile areas. Astroglia-, microglia-, neuron-, motoneuron- and inflammasome-component-specific antibodies were used to determine cell-type specificity.

Results: NLRP3 expression increased in both the oculomotor and hypoglossal nucleus after nerve injury, however, this elevation was significantly diminished in the oculomotor nucleus. In neurons, NLRP3 translocated from the nucleus (uninjured) to the cytoplasm (injured). Microgliosis and astrogliosis were also observed, but the ratio of NLRP3 positive glial cells did not change. Post-operative diazoxide treatment reduced NLRP3 activation in the hypoglossal nucleus.

Conclusion: Our findings suggest that NLRP3 activation following acute nerve injury is mediated through neurons. This activation was reduced in the oculomotor nucleus, which is considered to be resistant to injury in certain neurodegenerative disorders, suggesting that NLRP3 might contribute to this "resistance". Lastly, NLRP3 activation and microglial reaction could be reduced with post-operative diazoxide treatment, hightlighting the therapeutical importance of PRRs.

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CHARACTERISTICS OF EMOTIONAL ABUSE AND THEIR PSYCHIATRIC AND SOMATIC CORRELATES AMONG CLINICAL GROUP OF ADOLESCENTS

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Introduction: Child maltreatment is a widespread phenomenon that may cause various mental and somatic disorders, with emotional abuse considered as obscure but considerably prevalent and specifically harmful. However, data on the link between the characteristics of emotional abuse and specific clinical correlates of maltreatment characteristics among clinical adolescents is still insufficient.

Aim: The aim of our study was to identify the presence and

the characteristics of emotional abuse in the clinical group of adolescents, as well as to explore associations of these characteristics with psychiatric and somatic features.

Methods: The study sample included 75 older adolescents treated by partial hospitalization, due to the presence of depressive disorder, anxiety disorder, adjustment disorder or mixed disorder of conduct and emotion. The data was collected retrospectively through existing medical records, including general data, data about child maltreatment experiences, diagnosis, psychiatric symptoms, depressive symptom scale scores, and physiological parameters at admission.

Results: In our sample, emotional abuse the most prevalent form of maltreatment (N = 66; 88%),. and within that group, the average maltreatment age of onset was 10.61 ± 3.52 , 42 (63.6 %) adolescents also had other types of maltreatment, and 19 (27.8%) had more than one maltreatment perpetrator. Several multivariate regression models among emotionally abused patients showed that the younger age of maltreatment onset was predictive of social withdrawal (Exp(B) = 0.769, p = 0.02) and higher heart rate at the admission (adjusted R2 = 0.222; beta = -0.521, p = 0.000), while the concomitant presence of other types of maltreatment was predictive of headaches (Exp(B) = 9.396, p = 0.044) and insomnia (Exp(B) = 5.325, p = 0.013). Depression score at discharge was associated with low socio-economic status (beta = 0.332, p = 0.03).

Conclusion: Results indicate high representation of emotional child abuse experience in the group of clinical adolescents, with age of maltreatment onset and the co-occurrence with other maltreatment types as the predictors of several more severe clinical features. These observations may have important preventive implications.

PSYCHOSTIMULANT EFFECTS ON HIPPOCAMPAL NEURONS: FROM MORPHOLOGY TO CYTOSKELETON REMODELLING

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Introduction: The hippocampus is known to contribute to the build-up of addiction. Methamphetamine (Meth) is a powerful psychostimulant abused worldwide. It is known that Meth affects neuronal morphology in the hippocampus, but the mechanisms involved are not clear. The Rho family GTPases are regulators of actin dynamics and among them, cdc42 has been related to changes in dendritic length and stabilization of dendritic spines, being a potential target of Meth.

Aim: To assess the involvement of cdc42 in the alterations induced by Meth in the hippocampus.

Methods: We used primary hippocampal neurons transfected with GFP or a microRNA to knockdown Intersectin1, a specific activator of cdc42, to evaluate the effect of Meth (100 μ M, 24 h). To understand how Meth affected synapses, the colocalization between PSD95 and VGLUT1 (synaptic markers) was assessed. The expression of Itsn1 and downstream effectors of cdc42 was analysed by western blot and immunocytochemistry.

Results: We show that Meth increases dendritic length, ramification and the density of dendritic spines. However, the

head diameter of dendritic spines and the area of PSD95 puncta were reduced. Meth-induced changes in dendritic length and ramifications were not verified when the activation of cdc42 was prevented. However, changes in dendritic spines were only partially prevented. There were no differences in the expression of Itsn1 or downstream proteins by western blot, but the colocalization with PSD95 revealed that these proteins might be altered at dendritic spines. To confirm that, we analysed the signalling pathway in synaptic purified fractions.

Conclusion: Meth increases the maturation of dendritic spines while decreasing its head diameter. Despite this, the number of active synapses was apparently not affected. Itsn1 knockdown prevented the effect of Meth on neuronal network although dendritic spines continued to be partially affected by Meth. This suggests Itsn1-cdc42 pathway is differently disturbed by Meth at distinct cellular compartments.

THE HUMAN VENTRAL AMYGDALOFUGAL PATHWAY: A VIRTUAL GAME OF HIDE AND SEEK

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Introduction: The Amygdala is known to have a role in processes regulated by the limbic system such as emotion, behaviour, and memory. The ventral amygdalofugal pathway is the major efferent fibre bundle that serves as a key output of the amygdala. It divides into five branches terminating at the hypothalamus, dorsomedial nucleus of the thalamus, septal region of the cerebrum, nucleus accumbens and brain stem. The underlying neuronal fibre connectivity has yet to be delineated with standard neuroimaging.

Aim: By using advanced diffusion-weighted magnetic resonance (MR) technologies and virtual reality (VR) we present for the first time a virtual dissection of this tract in-vivo.

Methods: 90 healthy subjects were scanned using High Angular Resolution Diffusion Imaging (HARDI) and high-resolution T1 (1 mm isotropic) MR imaging at Trinity College Dublin (Phillips, Intega 3T). 3D amygdalar and nucleus accumbens volumes were generated by automated cortical segmentation using FreeSurfer 6.0. These digital analogues were used to extract the ventral amygdalofugal pathway and its branches through a neuroanatomically derived boolean logic protocol of the diffusion data. Post-generation tract analogues were converted in 3DS Max and visualised in a Unity3D/Oculus Rift VR environment allowing for intracerebral virtual manipulation and individual isolation of generated elements. Ethics approval was granted by St. James/Tallaght joint REC.

Results: Using our protocol, we were able to delineate the trajectory of the ventral amygdalofugal pathway and it's connections in-vivo. This demonstrates how both neuroimaging and VR techniques can synergise to inform Neuroanatomy. Macroscopic and microscopic data can be calculated from these virtual tracts to provide insight on various neuropsychiatric conditions.

In particular, this tract may show differences in illnesses which involve amygdalar, neuroendocrine and autonomic pathology such as depression, anxiety, PTSD and schizophrenia.

Conclusion: In summary, this is the first time the ventral amygdalofugal pathway and its major branches were virtually dissected and visualised using VR.

TITLE EVALUATION OF REHABILITATION RESULTS ON THE SCALES OF ASHWORTH, BARTHEL AND MACS IN CHILDREN WITH CEREBRAL PALSY: CROSS-SECTIONAL STUDY

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Introduction: Cerebral palsy is accompanied by wide range of problems and symptoms, which makes difficult to assess the patient's condition and to set the goals of rehabilitation. Program of rehabilitation of children with CP should be appropriate (the age and functional status). The concept of CP rehabilitation changed in recent years and focuses on patient participation in daily activities. We evaluated the results of inpatients with CP rehabilitation at the rehabilitation department in Aktobe.

Aim: The aim of the study is to evaluate the results of inpatients with CP rehabilitation at the rehabilitation department in Aktobe.

Methods: The cross-sectional study was conducted in 52 patients with CP who are on rehabilitation department with the use of physiotherapy, therapeutic gymnastics, massage. The effectiveness evaluation was carried out on scales of Ashworth, Bartel, MACS before and after rehabilitation. We used descriptive statistics.

Results: Spastic type was the most common and accounted for 73% of all cases. Assessment of daily life on Barthel scale showed children with dyskinetic form after rehabilitation increase from 85 (95% CI 66–103) to 89 points (95% CI 80–107), in children with spastic form from 105 (95% CI 87 - 122) before rehabilitation to 112 points (95% CI 93–129) after rehabilitation. 7 children (50%) with dyskinetic paralysis and 31 children (82%) with spastic paralysis had increase of 5 or more points on] Barthel scale (p < 0.02). There was a spasticity reduction according to Ashworth scale of 1 (p < 0,00) in 4 of the 14 children with dyskinetic form and in 36 children with spastic form of 38.

According to the MACS, level of the scale decreased slightly in both groups of children with dyskinetic form and with spastic form of CP, by 21% and 13%, respectively (p < 0.4).

Conclusion: The most effective rehabilitation was in children with spastic paralysis than children with dyskinetic form. The results of rehabilitation on the scales were not significant than expected, which requires an interdisciplinary approach that takes into account the needs of patients more than the disease.

COPING WITH JUVENILE LUPUS - DEALING WITH EMOTIONS MAY PREVENT DEPRESSIVE SYMPTOMS

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¹Faculty of Medicine, University of Porto, Department of Clinical Neurosciences and Mental Health; ²Pediatric and Young Adult Rheumatology Unit, Centro Hospitalar e Universitário São João, Faculty of Medicine, University of Porto **Introduction:** Juvenile Systemic lupus erythematosus (JSLE) is a multiorgan autoimmune disease with onset age below 18 years old. Patients cope with physical and neuropsychiatric symptoms such as depression, anxiety and fatigue. The disorder may interfere with academic, social or professional activities and entail mild cognitive impairment.

Aim: The present study examines the sociodemographic and psychological characterization of a group of young adults with JSLE.

Methods: Twenty-seven patients followed in Centro Hospitalar São João were evaluated between October 2018 and May 2019. Sociodemographic, clinical and psychological data was collected through the Portuguese versions of validated questionnaires and clinical records. Statistical analyses were performed with SPSS software, version 25.

Results: The mean age was 23 years (SD 5.5) with 89% females. Cognitive assessment showed a mean Mini Mental State Examination score of 27.7 (SD 1.9). The mean fatigue score in the Fatigue Severity Scale was 4.2 (SD 1.3), which shows high severe fatigue. The screening for anxiety and depressive symptoms using the Hospital Anxiety and Depression Scale revealed a mean anxiety score of 8.9 (SD 4.5) and a mean depression score of 3.8 (SD 3.4). Brief Cope assessment identified coping mechanisms used by patients, with a score of 0.69 (SD 0.23) in problem-focused, 0.55 (SD 0.19) in emotion-focused, 0.45 (SD 0.25) in social-supported and 0.26 (SD 0.12) in avoidant coping. A statistically significant negative correlation was found between the risk of depression and emotion-focused coping (r = -0.541, p = 0.006).

Conclusion: Our population, although presenting high levels of fatigue and anxiety appear to cope efficiently with a disabling disease. Most patients reported adaptive coping skills, enabling them to better deal with physical and psychological suffering imposed by Lupus. However, there was still a significant population using less adaptive mechanisms, showing a need to psychologically assess JSLE patients and assist them in dealing with their disease.

ELUCIDATING THE AFFERENTS OF THE DORSAL HIPPOCAMPAL COMMISSURE AND CHANGES IN MAJOR DEPRESSIVE DISORDER

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Introduction: The human dorsal hippocampal commissure (DHC) is a major neglected fibre bundle within the limbic system, with potential roles in memory, mood regulation and emotional processing. Though considered a nexus between the bilateral hippocampal subfields in humans, animal tracer studies suggest that this bundle is composed primarily of extrahippocampal fibres. This has yet to be thoroughly investigated in humans.

Aim: This study aimed to develop a method of establishing the loci of origin of the DHC. Given the limbic locus of this tract, potential implications in Major Depressive Disorder (MDD) were also investigated.

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Methods: 54 healthy control and 38 subjects with MDD were scanned using high-resolution T1, T2 MR imaging (1 mm isotropic) and High Angular Resolution Diffusion Imaging (HARDI) at Trinity College Institute of Neuroscience. Digital analogues (masks) of the hippocampus, parahippocampal gyrus (PG), amygdala and temporal pole (TP) were generated using Freesurfer 6.0. Following manual isolation of the DHC using boolean logic regions of interest (ROIs) around neuroanatomical landmarks in Explore DTI, Freesurfer-generated masks were employed as ROIs in an anatomically derived sequence to determine and capture fibres terminating at specific subregions. Ethics approval for this work was granted by St James'/Tallaght joint REC.

Results: Macroscopic and microscopic values for all tracts were statistically examined. The majority of DHC fibres stem from TP, a significant portion from PG and a minutia from the hippocampus and amygdala. No differences were observed in MDD patients.

Conclusion: This study is the first to investigate the connections of the DHC in-vivo and to explore alterations in this tract in MDD. Our work is the first to show that the DHC connects to the amygdala and to show the stability of this tract in MDD. This opens avenues for further understanding this enigmatic commissure and hints at the elusive function underlying it.

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VERTEBRAL ARTERY HYPOPLASIA AND ITS ASSOCIATION WITH HIGHER INCIDENCE OF BASILAR ARTERY ANEURYSMS

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Introduction: Hypoplasia of the vertebral artery is associated with higher prevalence of ischaemic stroke, vertebral artery dissection and vertebral artery aneurysms. This vascular disorder affects 2–26% of population.

Aim: The aim of this study is to evaluate the association of vertebral artery hypoplasia with higher incidence of basilar artery aneurysms.

Methods: The group of 25 patients treated for basilar artery aneurysms in University Hospital in Cracow from 2015 to 2018 was collected. The inclusion criterion for this retrospective study was undergone Computed Tomography Angiography examination. Average age in this group was $59,2 \pm 10,6$ years old. Women constituted 64% (n = 16). Control group was matched for age and sex. Following parameters were assessed: incidence of BA aneurysms, vertebral artery hypoplasia, aplasia and diameter and posterior cerebral artery hypoplasia, aplasia and diameter. Statistica software was used for statistical analysis.

Results: Hypoplasia of at least one vertebral artery occured in 60% of patients with basilar artery aneurysm and in 20% of patients without aneurysm (p < 0,05). Diameter of vertebral artery in patients with basilar artery aneurysms was 2,4 ± 0,8 mm on the left side and 1,9 ± 0,8 mm on the right side, whereas in patients without basilar artery aneurysm 2,2 ± 0,5 mm on the left side and 1,9 ± 0,6 mm on the right side (p > 0,05). At least one hypoplastic posterior cerebral artery occured in 24% of patients with basilar artery aneurysm and in 8% of patients without aneurysm (p > 0,05).

Conclusion: Vertebral artery hypoplasia is associated with higher prevalence of basilar artery aneurysms. Hemodynamic changes caused by vertebral artery hypoplasia may contribute to basilar artery aneurysm development.

EFFECTS ON BEHAVIOUR AND NEUROGENESIS OF PRETERM BIRTH IN RATS

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Introduction: Encephalopathy of prematurity is the result of disorganized reparative phenomena in the developing brain that occur in response to the global neurological lesion caused by preterm birth. Consequently, many premature infants suffer from major or minor neurodevelopment disorders. Preterm birth accounts for one-tenth of all births worldwide, amounting to 15 million premature birth annually, making it a major health problem.

Aim: Characterize hypoxia-ischemia and mifepristone non-inflammatory models of preterm birth by assessing the neurologic outcome in the neonatal period and anxiety, cognition in adulthood, and neurogenesis.

Methods: Pregnant Wistar rats were submitted to laparotomy on embryonic day (ED) 18 for occlusion of uterine arteries during 60 min (TSHI). In another group of Wistar rats, preterm parturition (ED21) was induced by RU486 administration on the previous day (ED20). Sham rats were also laparotomized but received no treatment. Rat pups were then tested through neonatal developmental milestones. After weaning, they were submitted to the following tests: Morris water maze, elevated plus-maze and open-field tests. Two months after weaning, rats were deeply anesthetized, perfused and processed for immunohistochemistry for doublecortin (DCX). The areal densities of DCX-immunoreactive neurons was estimated by counting the number of cells within a given area of the hippocampus.

Results: Rat pups from TSHI group showed several significant changes in neonatal developmental milestones, as well as in anxiety, fear and cognition. TSHI animals also had an increased density of DCX neurons in the subgranular layer, and showed aberrant cell location. Dendritic arborizations were also altered in the TSHI. Rats from ED21 group showed no differences on the analyzed parameters.

Conclusion: Hypoxia-ischemia induced changes in anxiety, fear and cognition. These behavioural changes were associated with an increased neurogenesis, that was in part aberrant, and alterations in the pattern of dendritic arborization. Rats of ED21 group showed no changes in behaviour and had unaltered neurogenesis.

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EMBOLIC AND HEMODYNAMIC TYPE OF STROKE IN PATIENTS WITH CAROTID ARTERY STENOSIS

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Introduction: Stroke is an acute neurological deficit lasting more than 24 hours and caused by cerebrovascular aetiology. It is further subdivided into ischemic and hemorrhagic stroke. Increasing age, hypertension, diabetes mellitus, smoking, and cardiovascular diseases are risk factors for stroke. Approximately 20% of all strokes are caused by atherosclerosis of blood vessels, mostly by atherosclerotic stenosis of internal carotid artery and medial cerebral artery.

Aim: To determine gender and age of patients with embolic and hemodynamic stroke. To investigate if there are significant differences in average values of blood pressure, NIHSS score, mRS and differences between frequency of the most common risk factors in these two groups.

Methods: Retrospective study. Research considered 61 patients divided in two groups, both sexes, with stroke and carotid artery stenosis - with embolic (42), and hemodynamic (19) type of stroke. Average values of blood pressure, NIHSS, mRS and frequency of the most common risk factors for stroke were considered.

Results: In both groups there were more men. There were no statistically significant differences in average values of blood pressure, initial NIHSS, and NIHSS score after treatment between these two groups (p > 0.05), and there were statistically significant differences in values of mRS after treatment (p < 0.05). Chi-square test did not show statistically significant differences between frequency of the most common risk factors in these groups (p > 0.05).

Conclusion: Acute ischemic stroke is more often in men. There are no significant differences in average values of blood pressure and NIHSS score between patients with embolic, and those with hemodynamic stroke. Differences in frequency of the most common risk factors between these two groups are not significant. There are significant differences in mRS between these two groups.

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SIDE EFFECTS OF BOTULINUM TOXIN INJECTIONS IN PATIENTS WITH HEMIFACIAL SPASM

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Introduction: Hemifacial spasm (HFS) is a rare neurological movement disorder characterized by involuntary contractions of muscles on one side of the face innervated by the facial nerve. Although the disorder does not have life-threatening consequences, it strongly decreases the quality of patients' life. The main ways of treatment are medication, botulinum toxin A injections (BTI) and microvascular decompression of the facial nerve. In the majority of cases BTI is the treatment of first choice. There are three commercially available forms of botulinum toxin: onabotulinumtoxinA, abobotulinumtoxinA and incobotulinumtoxinA. Considering long-term therapy, knowledge about side effects (SE) of BTI is crucial for successful treatment.

Aim: To estimate the frequency of SE in treatment with BTI and its dependency on patients' sex, age, duration of treatment, number of injections and type of toxin.

Methods: The observational retrospective study was performed on medical records of 261 patients with HFS treated with BTI at the outpatient clinic of the University Hospital in Cracow. Collected data was analyzed using U Mann-Whitney test and chi-squared test as appropriate.

Results: SE occurred in 10,73% patients (28 of 261). The most common SE were ptosis presented by 14 patients (5,36%) and temporary facial palsy presented by 11 patients (4,2%). 19 patients had SE after onabotulinumtoxinA and 9 patients after abobotulinumtoxinA (67,86% and 32,14% respectively). There was correlation between the frequency of SE and the total number of injections (p < 0,01) and duration of treatment (p < 0,01). We did not find statistically significant correlation between SE and sex (p = 0,16) and age of patients (p = 0,14).

Conclusion: Outcomes of our study suggest that major factors affecting incidence of SE of BTI are total number of botulinum toxin A injections and duration of the therapy. This study provides only preliminary data which need to be confirmed by prospective studies on this topic.

METHAMPHETAMINE AND NEUROINFLAMMATION: UNVEILING THE CROSSTALK BETWEEN GLIAL CELLS AND NEURONS

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¹I3S - Instituto de Investigação e Inovação em Saúde, Universidade do Porto, Portugal; ²IBMC - Instituto de Biologia Celular e Molecular, Portugal; ³ICBAS - Instituto de Ciências Biomédicas Abel Salazar; ⁴FMUP - Faculdade de Medicina da Universidade do Porto; ⁵INEB - Instituto de Engenharia Biomédica, Portugal; ⁶Discovery Centre for Regenerative and Precision Medicine, Porto Campus, Portugal **Introduction:** It is now accepted that addiction results also from the interaction between neuronal and glial cells, that under exposure to psychoactive drugs may lead to inflammation. As the crosstalk between neurons and microglia depends both on soluble and contact dependent factors, we used different experimental paradigms to unveil how methamphetamine (Meth) affects it.

Aim: In previous studies we have seen that Meth activates microglia cells through a crosstalk with astrocytes which relies on the release of TNF and glutamate. Here, we aim at characterizing the role of the crosstalk neurons-microglia.

Methods: Primary hippocampal neurons and microglial cells were seeded in a microfluidic chamber in opposite sides. The following parameters were used to evaluate the effects of Meth (100 μ M): 1) immunohistochemistry for iNOS, arginase1 and iba1; 2) mRNA expression levels (qRT-PCR) for the cytokines IL-1beta, IL-6, and IL-10, and the factors TNF and TGF; 3) mRNA expression levels for the ligands CD200, CD22, CX3CL1 and its myeloid receptors CD200r, CD45, CX3CR1 and CD95; 4) phagocytic efficiency.

Results: In our co-cultures of neurons-microglia exposed to Meth, neurons seem to shift microglia to a more anti-inflammatory profile, as evidenced by the decrease of pro-inflammatory markers (iNOS, IL-1 β) and the increase of the anti-inflammatory arginase1. We found also that the CD95 receptor (also known as Fas, apo-1 or TNF receptor superfamily member 6) was increased, matching our in vivo results. This receptor is involved in intrinsic and extrinsic apoptotic mechanisms and may be a good target for genetical manipulation under Meth.

Conclusion: The present results indicate that neurons may play an important role in shifting microglia to a less inflammatory profile under Meth exposure, which may be an important neuroprotective pathway. Further studies are ongoing to better understand the mechanisms that underlie this crosstalk.

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GUILTY OR INNOCENT? THE EFFECTS OF FOCAL LESIONS OF THE PREFRONTAL CORTEX UPON HUMAN BEHAVIOR: A META-ANALYSIS

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Introduction: The prefrontal cortex (PFC) represents a cortical region considered in the past functionally insignificant, known nowadays that by its extensive connections, it is placed in a particular position to orchestrate a wide range of cognitive and affective neural functions.

Aim: The purpose of our study is to emphasize the importance of consequences following PFC damage, thus addressing an important question: do these patients intend to or perform harmful actions because of a failure to process harmful outcomes? **Methods:** We performed a meta-analysis based on 11 studies selected from PubMed database, consisting of 236 subjects with focal PFC lesions (114 = stroke, 90 = tumors, 32 = TBI) and 287 healthy subjects. In order to evaluate the behavioral effects of the lesions, fMRI, Voxel-based Lesion Symptom Mapping and neuropsychological tests were performed.

Results: 33,4% presented decreased ERP amplitudes following dorsolateral-PFC damage and difficulty performing Wisconsin Card Sorting Task, demonstrating increased distractibility. 5.9% with ventrolateral-PFC damage were significantly slower when performing the Stop Signal Reaction Time Task. 5% with orbitofrontal lesions made riskier decisions when performing Iowa Gambling Test, even when outcome probabilities were made explicit. 12,7% with rostral-PFC damage failed the Faux Pas Test, presented impairments in creativity measured by Torrance Test of Creative Thinking and performed poorly on tasks that investigated multitasking ability. 27,1% with ventromedial-PFC lesions had pronounced cortisol levels after Trier Social Stress Test and presented impairment in moral judgment after specific presented scenarios. 12,2% with both dorsolateral-PFC and ventromedial-PFC damage had significant levels of aggression following Voodoo Doll Task and Taylor Aggression Paradigm. 3,3% with dorsomedial-PFC damage presented abulia.

Conclusion: Based on the analyzed data, it seems that PFC lesions present a crucial role in altering the behavior, supporting the claim that these patients may not be guilty for their actions after all.

THE HUMAN STRIA TERMINALIS: A NOVEL APPROACH TO DISSECTION IN THE VIRTUAL REALM

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Introduction: The stria terminalis is the primary output tract from the amygdala to the hypothalamus. In humans, the stria terminalis follows a course similar to and tightly aligned with the fornix. This close anatomical arrangement has posed difficulty in tractographically separating these tracts in the past.

Aim: To radiologically separate the stria terminalis from the fornix using a novel neuroanatomically driven protocol, to a greater degree of precision than the protocols implemented previously.

Methods: 90 subjects underwent DW-MRI using high angular resolution diffusion imaging (HARDI) and high-resolution T1 (1 mm isotropic) MR imaging at Trinity College Dublin (Phillips Intega 3T). A combination tract involving the Fornix and the Stria Terminalis was isolated using a previously demonstrated technique. Amygdalar volumes were generated using the automated segmentation module of FreeSurfer 6.0. These digital amygdalar analogues were then employed in a Boolean logic driven protocol to virtually extract the stria terminalis from the fornix-stria combination. Ethics approval was granted by St James/Tallaght joint REC. Post-generation tract analogues were converted in 3DS Max and visualised in a Unity3D/Oculus Rift VR environment allowing for intracerebral virtual manipulation and individual isolation of generated elements. Ethics approval was granted by St. James/Tallaght joint REC.

Results: Using this technique we were able to reliably visualize and quantify the stria terminalis. This is the most precise virtual dissection of the Stria Terminalis to date and demonstrates how both new neuroimaging and VR techniques can synergise to inform neuroanatomy.

Conclusion: As this white matter tract provides the majority of the amygdalar drive to the hypothalamus, this protocol could be used to study neuropsychiatric diseases. In particular, this will permit interrogation of illnesses that involve amygdalar, neuroendocrine and autonomic pathology. The salience of this study can be marked by the potential of opening therapeutic avenues for depression, anxiety, post-traumatic stress disorder and schizophrenia.

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WHY DOES PRESENTATION WITH SEIZURES PROGNOSTICATE WELL IN LOW-GRADE GLIOMA?

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Introduction: Glioma is the most common primary intra-axial brain tumour, conferring a grim prognosis. So far, molecular profile of glioma-associated epilepsy (GAE) remains poorly understood, despite being observed in over 80% of patients and half of those patients remaining pharmacoresistant[1]. Although impairing life quality in glioma patients, seizures prognosticate well[2]. Therefore, molecular characterization of GAE could yield new glioma prognostic markers.

Aim: This study undertakes systems biology approach to the puzzle of positive prognostic value of seizures in glioma.

Methods: Whole-genome expression profiles of samples from 475 primary grade II and III gliomas were downloaded from The Cancer Genome Atlas and analysed in R[3]. The differentially expressed genes (DEGs) in samples with seizure history were identified[4], characterized using gene set enrichment approach[5] and their prognostic value was compared with established biomarkers in Cox model. Additionally, multifaceted approach to identifying associated epigenetic features was undertaken[5–8] and verified with ENCODE database experiments[9,10].

Results: Among the upregulated genes, the majority prognosticated positively and some, like SEZ6, SLC6A11 and CRH, have established roles in epileptogenesis[11]. Signature derived from DEGs was superior in predicting survival to that based on established prognostic factors. GAE samples were enriched in expression of neurotransmitter and neuropeptide signalling genes whereas those without seizure history displayed traits of higher aggressiveness and invasiveness. This was attributed to increased activity of the Neuron-Restrictive Silencer Factor (REST) in those samples. REST is a negative

prognostic feature in glioma[12] and its inactivity in GAE may explain better prognosis in this setting. Moreover, molecular signatures of antiepileptic pharmaceuticals were analysed, supporting use of those with calcium channel modulating properties in GAE.

Conclusion: REST is a master regulator of glioma biology with profound impact on seizures. The genes associated with epileptogenesis are valuable prognostic features. Overall, systems biology approach has yielded insight into GAE symptomatic and causative treatment.

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DISSECTING THE MOLECULAR CAUSES OF NDE1-ASSOCIATED MICROCEPHALY

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Aim: We hypothesize that, in addition to Dynein-1, NDE1 might also regulate Dynein-2 and therefore ciliogenesis and/or cilium-dependent signaling. We aim to dissect the contribution of NDE1 for Dynein-1 and Dynein-2 functions during neocortical development.

Methods: To address this, we use in utero electroporation of rat embryos to deplete NDE1 in neural progenitors and to express NDE1 point mutants incapable of binding specific Dynein subunits or other regulators. In parallel, we use C. elegans as a complementary model, where cilia are dispensable for survival but are essential for key sensory functions in neurons. Using knockout of the NDE1 ortholog nud-2, we perform live fluorescence microscopy to study the contribution of NUD-2 for cilia formation, Dynein-2-mediated transport, and sensory cilia functions.

Results: So far, our results suggest that the Dynein-1 regulator LIS1 is required for all NDE1 functions in the RGPs cell cycle, especially in the cilium-dependent G1-to-S transition. We also found that loss of the NDE1 ortholog in the C. elegans, nud-2, results in altered distribution of cargoes along cilia and reduces the velocity of Dynein-2-mediated transport without significantly perturbing cilia length.

Conclusion: Our data in neural progenitors provides new insights into how NDE1 contributes to the functions of cytoplasmic Dyneins during brain development. Furthermore, our data in C. elegans reveals a role for NUD-2 in regulating Dynein-2-mediated transport in cilia. We speculate that this function influences cilia-mediated signaling and C. elegans behavior.

RESULTS OF THROMBOLYTIC THERAPY (TLT) IN PATIENTS WITH ISCHEMIC STROKE IN DISTINCT CEREBROVASCULAR VESSELS

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Introduction: In recent years the effectiveness of TLT in the period up to 4.5 hours was efficiently proved. Circulatory features have a greater influence on the dynamics of neurological symptoms regression in ischemic strokes in the brainstem, which is explained by the lower sensitivity of cells to ischemia and more pronounced intracerebral collateral blood flow.

Aim: To study the dynamics of neurological symptoms recovery in patients with ischemic stroke (hemispheric and the brain stem) receiving TLT.

Methods: The course of ischemic stroke was analyzed in 36 patients (hemispheric) and 12 (brainstem) using rtPA TLT from 3 to 4.5 hours using the standard procedure. A neurological examination and CT scan of the brain was conducted. The results were evaluated by the regression of neurological symptomatology on the 2nd and 10th day of the disease.

Results: On admission in patients with vertebro-basilar stroke, bulbar syndrome was noted in 7 patients and regressed a day after TLT by 37%. After 10 days, in 6 patients the regression was about 57%. Vestibulo-atactic syndrome was seen on admission in 5 patients, regressing after 2 days in 2, and by 10th day was noted only slightly expressed in 1 patient. Hemiparesis (2.6 points) on admission was seen in all patients; a day later in 3 patients full recovery was noted; in 4 severity decreased by 2 points, in 3 patients - by 1 point. In 2 patients there were no manifestations of motor deficit; in 4, regressed by 2 points, in 2 by 1 point.

Conclusion: In the late lines of TLT, there is a more pronounced regress of neurological symptoms in the group of patients with vertebrobasilar stroke, which allows the use of TLT in the later periods and in the presence of severe stem disorders.

THE INFLUENCE OF ZALEPLON ON BEHAVIOUR OF RATS IN THE ACTIVE AVOIDANCE TEST

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Introduction: Zaleplon, the "Z" drug, is a pyrazolopyrimidine hypnotic which is structurally distinctive from benzodiazepines and other hypnotics. It bounds selectively to benzodiazepine site on GABA-A receptor which contains $\alpha 1$ subunit, resulting in specific effects with ultra-short elimination half-life. Having specific pharmacological effects like shortening of sleep latency, recruitment of sleep continuity and increase in slowwave phase duration, it is commonly used in pharmacotherapy of sleep disorders.

Aim: To evaluate the influence of increasing doses of zaleplon on cognition and learning processes in active avoidance test in rats, as well as evaluation of inter-trial crossings representing locomotor activity.

Methods: Wistar albino rats were used (n = 30), weighing 200–240 g, which were divided into 5 groups (n = 6). Increasing doses of zaleplon (0.625, 1.25, 2.5 and 5 mg/kg) were applied i.p. 30 minutes before the test of active avoidance, while the control group received saline solution. During the experiment, number of successful active avoidance responses were counted as well as number of inter-trial crossings.

Results: There was a statistically significant number of successful responses in active avoidance in comparison to the control group. Dose of 0.625 mg/kg was found to facilitate learning process in rats. There were not noticed any significant differences of applied doses in active avoidance in other groups when compared to the control. Furthermore, analysis of inter-trial crossings did not show significant differences between groups.

Conclusion: We have shown that zaleplon influences process of active avoidance in such a way that in low doses it facilitates learning, while in high doses it does not have any prominent memory effect neither does have prominent influence on locomotor activity. Facilitating effects of zaleplon are probably mediated by other mechanisms/receptors taking into the consideration results of so far conducted researches implying selective and specific properties of zaleplon which other "Z" drugs do not have nor do classic benzodiazepines.

THE ASSOCIATION OF BRAIN ISCHAEMIC CHANGES WITH CALCIFIED ATHEROSCLEROTIC PLAQUES AND ABNORMAL GEOMETRY OF ARTERIES SUPPLYING THE BRAIN

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Introduction: Coronary Artery Calcium Score is a wellknown predictor of cardiovascular risk, but existence of analogous risk factors of brain ischaemic disease are still a matter of debate.

Aim: The objective of the study was to evaluate the correlation between brain ischaemic changes and the presence of calcified carotid atherosclerotic plaques as well as abnormal geometry of arteries supplying the brain.

Methods: The study group consisted of 201 patients, who underwent unenhanced computed tomography (CT) of head with subsequent CT angiography (CTA) of head and neck. 57.2% of patients were female. Mean age was 52.6 ± 19.6 years. Firstly, the presence of calcified carotid atherosclerotic plaques, complete carotid occlusion, carotid artery kinking and vertebral artery hypoplasia were assessed in CTA. Then head CT scans were screened for ischaemic stroke, minor ischaemic changes, leukoaraiosis and global cortical atrophy.

Results: The incidence of calcified atherosclerotic plaques in carotid arteries was 50.2%. Patients with calcified plaques were more likely to have ischaemic stroke (p = 0.003, OR = 4.356), minor ischemic changes (p < 0.001, OR = 5.041), leukoaraiosis (p < 0.001, OR = 16.970) and global cortical atrophy (p < 0.001, OR = 9.129). Unilateral complete carotid occlusion was associated only with higher ischaemic stroke incidence (p < 0.001, OR = 58.667). Stroke significantly more often was located ipsilateral to carotid occlusion (right side: p < 0.001, OR = 40.500; left side: p < 0.001, OR = 31.000). Carotid artery kinking correlated with increased prevalence of leukoaraiosis (p = 0.030, OR = 2.236) and cortical atrophy (p = 0.028, OR = 2.894). Hypoplasia of vertebral artery predisposed to posterior circulation infarction (p < 0.001, OR = 18.400).

Conclusion: There is a strong correlation between the presence of calcified carotid atherosclerotic plaques and the occurrence of ischemic changes in the brain. Abnormal geometry of brain vascular supply (carotid kinking, vertebral artery hypoplasia) are also associated with increased incidence of particular brain ischaemic changes.

IN VIVO CHEMOBRAIN STUDY: THE EFFECTS OF DOXORUBICIN AND MITOXANTRONE IN THE BRAIN OF DIFFERENTLY AGED MICE

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Introduction: Hemobrain is the designation given to the long-term cognitive dysfunction caused by systemic chemotherapy. Doxorubicin (DOX) and mitoxantrone (MTX) are topoisomerase II inhibitors extensively used to treat a wide range of tumours. Despite their effectiveness in cancer treatment, their long-term toxicity has been established in several organs, but its brain toxicity is still poorly understood.

Aim: Our work aimed to evaluate the brain's redox and energetic status of male CD-1 mice at three different ages [juvenile (4 weeks), adult (3 months) and old (18–20 months)], after exposure to clinically relevant doses of DOX and MTX.

Methods: The mice received biweekly intraperitoneal administrations of each drug, for 3 weeks. Mice received a total cumulative dose of 6 mg/kg MTX or a total cumulative dose of 18 mg/kg DOX, except the oldest group that received a total cumulative dose of 9 mg/kg DOX. Throughout the experiment, animal's well-being, as well as body weight and food and water consumption were evaluated. Mice were euthanized one week (adults and old animals) or seventeen days (juvenile) after the last injection. To assess the brain's oxidative stress, total glutathione (GSHt), reduced glutathione (GSH) and oxidized glutathione (GSSG) levels were determined, as well as the GSH/GSSG ratio. To evaluate the brain's energetic status, ATP was measured.

Results: In adult and juvenile mice, DOX (18 mg/kg) caused weight decrease after the last injection. Brain levels of GSHt, GSH and GSH/GSSG ratio were decreased in DOX adults, but DOX infant brains had no changes in spite of equal cumulative dose. Nevertheless, DOX (18 mg/kg) increased brain ATP levels in juvenile mice.

Conclusion: MTX did not cause significant changes neither in glutathione nor ATP brain levels in any of the groups tested. This data suggest that DOX has a great potential to damage the brain, and DOX neurotoxicity requires further research.

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THE HUMAN PARALAMINAR NUCLEUS AND THE HPA AXIS: SALIENCE IN MAJOR DEPRESSIVE DISORDER

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Introduction: Embedded beneath the lateral, basal and cortico-amygdaloid regions of the amygdala is the paralaminar nucleus (PL), a poorly understood structure that has evolved to be relatively larger in humans and non-human primates. Studies show that it has dense mood regulatory serotonergic connections and indicate it to be a site for amygdalar neuroplasticity. Until recently, neuroimaging was unable to visualise this enigmatic nucleus in vivo.

Aim: The purpose of this study was to investigate the involvement of the PL in Major Depressive Disorder (MDD) and evaluate whether the cortisol awakening response (CAR), a measure of HPA axis function, was related to its volumetrics.

Methods: 20 healthy and 15 depressed subjects were scanned using high-resolution T1 magnetic resonance imaging at Trinity College Institute of Neuroscience. Paralaminar volumes were generated using state-of-the-art automated amygdalar segmentation in FreeSurfer-6.0. Participants also provided three-morning salivary cortisol samples (0, 30, 60 mins after waking). The CAR was calculated using two well-defined calculations; area under the curve with respect to ground and increase (AUCg and AUCi respectively). Ethics for this study was granted under the Tallaght hospital REC.

Results: Results showed a smaller left PL in MDD and that which inversely correlated with AUGi. This indicates a smaller left PL may impact the normal cortisol response to waking, a known neuroendocrine disturbance in the disorder. The relationship between the AUCg and the right PL in MDD also showed that total cortisol output may be associated in right PL volumes in MDD. These results were consistent with the hypothesis of cortisol oversecretion in MDD and previous findings of larger right amygdalae in MDD and right-sided amygdalar affective dominance for negative emotions.

Conclusion: In summary, this study suggests a role for this nucleus as a potential nexus in the regulation of stress in MDD. **Acknowledgements:**

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MICRO AND MACROSCOPIC ANALYSIS OF THE GENICULATE GANGLION OF THE FACIAL NERVE

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Introduction: The geniculate ganglion (ganglion geniculi) is a triangle-shaped collection of fibers and sensor neurons located at the first knee of facial nerve level, in petrosal part of temporal bone. By analysing its morpho-functional characteristics we strive to ensure saver microsurgery preocedures in this field.

Aim: Potential clinical ambitions that are essentially based on the results of this paper, by determining the periganglionic and intraganglionic vascular network and the clinical significance of vascularisation of geniculate ganglion in terms of possible performing more secure microsurgical procedures is the goal of this study.

Methods: Blood vessels of fourteen temporal bones were studied by stereo microscopy after injecting with a mixture of India ink and gelatine in the arterial system. In addition, the histological preparations of the geniculate ganglion were painted trichromatically by Masson for the analysis of the intraganglionic vascular network. **Results:** The geniculate ganglion was irrigated by a petrosal artery, singular in all the specimens, except in one, where there were two of them. The mentioned originated from the middle meningeal artery (a. meningea media). A.petrosa averaged 17.1 mm in lenght. From this artery branched out approximately 1.6 branches intended for periganglionic arterial network, whose average diameter was 0.029 mm. Microscopic section fields of the ganglion slides contained in average 99.8 microvessels.

Conclusion: The observed characteristics of the geniculate ganglion vasculature, could be the useful base for decompressive neurovascular surgery and provides the basis for further examination of the geniculate ganglion from both the scientific and clinical aspect.

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SLEEP QUALITY AND DEPRESSIVE SYMPTOMATOLOGY IN PATIENTS WITH MULTIPLE SCLEROSIS

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Introduction: Changes in sleep quality and depression are common in patients with multiple sclerosis (MS). The quality of sleep can be related to many affective and physical symptoms that occur within this disease. Affective symptoms, socio-demographic and clinical features are some of the potential factors that have been evaluated in previous researches.

Aim: To determine the frequency of changes in sleep quality, depression, anxiety, and stress in MS patients using screening tests: PSQI test Pittsburhg Sleep Quality Index and DASS test (Depression, Anxiety and Stress Scale) taking into account socio-demographic characteristics, duration of disease and EDSS score (Extended Disability Status Scale). To determine the relationship between the global PSQI score and gender, age, marital status, EDSS score, and duration of illness in the examined group. To examine the relationship between the global PSQI score and DASS subscores of depression, anxiety and stress.

Methods: 53 patients (32 women, 21 men) were studied, aged 19 to 56, with relapsing-remitting form of MS, treated with Interferon β . The testing was conducted using: PSQI index that evaluates sleep quality, DASS scale for assessing depression, anxiety, and stress and EDSS score that evaluates the severity of the disease.

Results: A sleep quality disorder exists in 44.4% of the examined sample. Depression (p = 0.001), anxiety (p < 0.001) and stress (p < 0.001) were shown as predictors of poorer sleep quality. A statistically significant correlation between the years of the subjects and sleep quality was determined (p = 0.047).

Conclusion: In multiple sclerosis patients, with relapsingremitting form under immunomodulatory therapy, a correlation between sleep quality and depression, anxiety and stress was detected. As far as the socio-demographic characteristics are concerned, the only established association was the relation between the age structure and the quality of the sleep measured by PSQI index.

THE SIGNIFICANCE OF FDG/PET IN DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS OF DEMENTIA

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Introduction: Dementias are neurodegenerative diseases whose diagnosis is based on clinical examination, neurological, cognitive and psychological tests, as well as morphological imaging. Recently, the positron emission tomography with fluoro-deoxiglucose (FDG PET), method which evaluates the intensity of brain metabolism, plays an important role in the diagnostics of these diseases.

Aim: The aim of this study will be to evaluate the role of FDG PET in dementia diagnostics, as well as to analyse the significance of this method in determining the differential diagnosis.

Methods: In this study, a total of 60 patients were included in whom FDG PET tests was made from July 2017 to December 2018. Patients were neurologically examined and MRI scanned, before they were required to be FDG PET scanned.

Results: In 57.1% of the cases the referral diagnosis matched with PET diagnosis, while in the remaining 42.9% PET changed the referral diagnosis in to another type of dementia.

Conclusion: FDG PET has proven to be a very useful method in evaluation of the patients with cognitive disorders. In addition to high sensitivity in the detection of hypometabolism in the brain, FDG PET has shown a particular importance in the ascertaining the correct diagnosis of dementia.

CAFETERIA-DIET EFFECTS ON COGNITION, ANXIETY, NEUROGENESIS AND ON THE GABAERGIC AND CHOLINERGIC SYSTEMS IN THE HIPPOCAMPUS OF JUVENILE RAT

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Introduction: Obesity prevalence has increased in the past few decades. Diet has been the main factor in this increase. The consequences of high fat and/or high sugar consumption go beyond obesity and have impact also in the brain and even on cognitive performance. Adolescence is the period in which the brain goes through great development, and so is more susceptible to impairments. It is also a period in which individuals start gaining independence on their choices and are prone to succumb to bad eating behaviors.

Aim: As animal submitted to caloric diets show impaired spatial memory and increased anxiety, we aimed to find neurochemical changes causing these effects. Since hippocampus is a mediator of learning and memory, we focused our attention on this structure.

Methods: Male wistar rats, 4 weeks old were randomly allocated to control (C), high-sugar diet (HS) or cafeteria diet (CAF) groups and fed accordingly for 8 weeks. After treatment, behavioural tests were performed to analyse anxiety and cognition. Animals were sacrificed and the brains collected for immunohistochemical studies targeting parvalbumin, calretinin, calbindin, neuropeptide Y, somatostatin, and vesicular acetyl-choline transporter.

Results: We have found that CAF diet is associated with impaired spatial learning and memory, and increased anxiety levels. Moreover, we have found that CAF diet induces alterations in neurogenesis. Relative to GABAergic circuit, CAF diet induced alterations in the expression of the calcium-binding proteins, namely a reduction in the expression of parvalbumin and an increase in the expression of calbindin in the dentate hilus, that was accompanied by an increase the density of cholinergic varicosities.

Conclusion: These results suggest that cafeteria diets, rich in saturated fats and sugar, are more detrimental for juvenile rats than diets with high-sugar content alone. These findings

may help explain the cognitive disturbances observed in obese human adolescents, who consume high-caloric diets.

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VASCULAR LESIONS IN DEMENTIA

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Introduction: Background: Dementia is a term for an umbrella of progressive diseases usually present in the elderly at an early prodromal stage and include, most prominently, Alzheimer's disease (AD) and dementia with Lewy bodies (DLB). Both diseases are associated with protein accumulation and cerebrovascular lesions have been identified as a key feature of end-stage AD. However there is limited research into the vascular aspect in the prodromal stage of these diseases.

Aim: To improve the knowledge surrounding white matter hypersensitivities (WMH), a major vascular lesion, in brains of patients as a potential marker in differentiating between DLB and AD. For this, WMHs were assessed in the brains of DLB and AD patients at prodromal and established stage.

Methods: 211 patients including 66 prodromal (pro)-DLB, 42 DLB, 28 pro-AD, 45 AD and 30 controls underwent a detailed clinical and neuropsychological examination along with a T2 weighted FLAIR MRI scan which was repeated after a year. Analysis was undertaken using the Itksnap software for volumetry and the Fazekas grading scale.

Results: Fazekas grade results show that both AD and DLB patients have a significantly greater grade of WMHs lesions than controls and pro-DLB (p < 0.005). No difference is observed between pro-AD and pro-DLB. In addition, the difference between pro-DLB and established DLB is more marked in comparison to that of pro AD and AD

Conclusion: This suggests that the progression from pro-DLB to established DLB is more vascular loaded than the evolution from pro-AD to AD. However more research is needed to to confirm whether WMH can differentiate between both diseases.

EFFECT OF ORALLY ADMINISTERED SOMATOSTATIN 4 RECEPTOR AGONISTS IN NEUROPATHIC PAIN, ANXIETY AND DEPRESSION-LIKE BEHAVIOUR IN MOUSE MODELS

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¹Department of Pharmacology and Pharmacotherapy, University of Pécs Medical School, Pécs, Hungary; ²Szentágothai Research Centre, Centre for Neuroscience, University of Pécs Medical School, Pécs, Hungary **Introduction:** Neuropathic pain is a chronic pain syndrome caused by different etiological factors. This disease is usually associated with anxiety and depression. The medication currently in use is not specific, furthermore long term use has several side-effects. Development of new analgesic drugs with novel mechanism of action would be important. Somatostatin besides the well-known general hormonal influence, is also known to mediate analgesic, anti-inflammatory and antidepressant effects, which are transmitted by the somatostatin 4 receptor (sstr4) without accompanying endocrine effects.

Aim: In our study our aim was to examine orally active, small-molecular sstr4 agonists (Vichem Ltd.) in mice models of neuropathic pain, anxiety and depression-like behaviour.

Methods: In male NMRI mice the mechanonociceptive threshold of the hind paw was measured by dynamic plantar esthesiometry (DPA), followed by a Seltzer-operation (traumatic sensory mononeuropathy caused by partial ligation of sciatic nerve). On the 7th postoperative day, when neuropathic pain fully developed, we performed post operative control measurements. Then the mice received orally active agonists or vehicle, and 60 minutes thereafter we repeated the DPA measurements. Depression-like behaviour was examined by tail suspension (TST) test. We examined anxiety behaviour with elevated plusmaze test (EPM) furthermore spontaneous locomotor activity by open field test (OFT).

Results: All our examined agonists significantly and dose-dependently decreased the operation-induced mechanical hyperalgesia. The most effective substrates were investigated further. These agonists significantly decreased the depression-like behavior in TST. In higher doses one agonist also showed a significant anxiolytic effect in the EPM.

Conclusion: Orally acting sst4 agonists effectively reduced neuropathic mechanical hyperalgesia and depression-like behavior.

These new, small molecule sst4 agonists can provide novel perspectives for the development of new combined analgesic and antidepressant agents.

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CHEMOGENETIC MODULATION OF SEIZURE ACTIVITY IN FREELY BEHAVING MICE

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Introduction: Background Epilepsy is often characterised by a disruption to the normal balance between excitation and inhibition of the neuronal networks in the brain. Parvalbumin-expressing (PV), somatostatin-expressing (SST) and vasoactive intestinal peptide-expressing (VIP) interneurons are thought to differentially regulate network activity by targeting distinct sub-cellular post-synaptic domains, such as the cell body or distal dendrites of excitatory neurons, or even other inhibitory interneurons.

Aim: Our objective was to establish a reliable murinein in vivo seizure model, and to use excitatory DREADDs (designer receptors exclusively activated by designer drugs) to explore the capacity of PV, SST and VIP interneurons to modulate epileptic behaviour.

Methods: We used three strains of mice expressing Cre recombinase in either of the PV, SST or VIP interneuron populations. Adeno-associated virus (AAV) delivering the double-floxed DREADD construct was used to transduce hippocampi bilaterally. The seizure model consisted of gradual intra-hippocampal infusions of 4-aminopyridine (4-AP) in tethered mice, while DREADDs were activated byintraperitoneal injections of clozapine-N-oxide (CNO). EEG activity was recorded and the animals' behaviour was scored using the Racine scale.

Results: The probability of reaching a generalised seizure decreased by 45% when PV interneurons were recruited, whereas no significant probability change was recorded when SST or VIP interneurons were stimulated. Epileptic behaviour was confirmed to be associated with seizure-specific EEG alterations.

Conclusion: Our study stands as a proof of concept, indicating that specifically stimulating distinct interneuron populations of the hippocampus via excitatory DREADDs has the potential to significantly alleviate epileptic behaviour in freely behaving mice, depending on which interneuron subtype is recruited.

ALTERATION IN MOTOR NEURONAL CALCIUM LEVEL INDUCED BY ACUTE SERUM INOCULATION OF AMYOTROPHIC LATERAL SCLEROSIS PATIENTS WITH GENETIC MUTATIONS

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Introduction: Amyotrophic lateral sclerosis (ALS) is a progressive and fatal neurodegenerative disorder, which is characterized by the loss of motor neurons. There has been a number of mutations implicated in the pathomechanism of ALS. The genetic screening of a subpopulation of Hungarian ALS patients revealed mutations on the superoxide dismutase 1 (SOD1) and chromosome 9 open reading frame 72 (C9ORF72) genes [1]. Our previous results demonstrate that ALS serum can transfer motor neuron disease to mice [2,3].

Aim: Our aim was to determine the importance of different neuropathological hallmarks in each observed mutation, such as intracellular calcium increase, mitochondrial ultrastructural alterations and survival of motor neurons.

Methods: Balb/c mice were treated intraperitoneally (1 ml/ day) for 2 days with blood serum of ALS patients with identified mutation or sporadic ALS patients without mutation (n = 3-6/group). Non-treated and healthy serum treated groups served as controls. Electron microscopic detection of intracellular calcium level and ultrastructural changes of motor neurons were examined in the lumbar enlargement of the spinal cord and in the axon terminals of musculus interosseus samples. Number of motor neurons in the spinal cord was measured with the disector method.

Results: Acute passive transfer with blood serum of ALS patients induced elevation of intracellular calcium level and increase of lipofuscin vesicle volume. Significant decrease could be documented in the number of motor neurons in the spinal cord. Changes in calcium homeostasis and motor neuronal loss were most prominent in C9ORF72 mutation. Furthermore, partial mitochondrial volume decreased in SOD1 point mutations.

Conclusion: Our previous experiments demonstrated the central role of intracellular calcium level elevation in ALS. Our current findings proved that different mutations induced similar morphological alterations, but to different extent. The extensive loss of motoneurons and changes in intracellular calcium level suggest that C9ORF72 mutation might present a more progressive phenotype.

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HEART RATE VARIABILITY CORRELATES OF EXPRESSIVE WRITING

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Introduction: Numerous studies have used the expressive writing task (writing about a personally upsetting experience) and have shown benefits on physical and mental health in various pathologies. These pathologies include eating disorders, depression, anxiety, and cancer.

Aim: Despite the awareness of these positive health outcomes, the underlying relationship between expressive writing and health is yet to be understood. By understanding this

relationship, we can develop expressive writing as a complementary treatment method in disease.

Methods: Participants were first-year university students at the University of Porto (n = 57). Each participant was randomly assigned to one of two groups. They either described their daily routine (control group) or a traumatic experience (expressive writing group) for 15 minutes. During the writing task electrocardiogram (ECG) data was recorded. The recorded ECG was divided into five, 5-minute parts (1' baseline; 3' writing; 1' post-writing). Data analysis was conducted by calculating three heart rate variability measures (HRV): SDNN, RMSSD, and LF/HF ratio, representing respectively, overall HRV, parasympathetically mediated HRV and sympathovagal balance. Writing measures were calculated using HandSpy 2.3, to assess for writing processes correlates of expressive writing.

Results: Results showed that HRV seems to increase from the beginning to the end of the task, regardless of the assigned group, with the expressive group showing significantly higher sympathetically mediated HRV.

Conclusion: These findings suggest that expressive writing has a physical effect on the body through cardiovascular changes, with HRV patterns differing significantly between groups. This could indicate that emotional regulation and coping mechanisms are active while writing about a personally upsetting experience, but not during a neutral writing task.

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Oncology & Molecular Biology

DETERMINATION OF ANDROGEN RECEPTOR METHYLATION PATTERN IN THREE PROSTATE CANCER CELL LINES THROUGH BISULFITE SEQUENCING

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Introduction: When diagnosed, most of prostate cancer (PCa) patients display androgen-dependent tumors, but an important proportion of those tumors progress to a castration-resistant state after androgen-deprivation therapy (ADT). This progression is due to androgen receptor (AR) signaling pathway deregulation by several genetic mechanisms, regardless of androgen circulating levels. From these, 20–30% of androgen-independent cancers that display AR loss of expression do not harbor AR genetic alterations. DNA promoter methylation

have been also suggested to associate with AR loss, but consistent data is still lacking.

Aim: Characterize the methylation status of CpG dinucleotides in AR regulating sites in three different PCa cell lines.

Methods: AR gene was divided into three different regions, each one with a specific pair of primers. DNA from three wild-type prostate cancer cell lines (RWPE: non-malignant, DU145 and PC-3: androgen-independent responsive and unresponsive to epidrugs, respectively) was extracted according to the standard phenol-chloroform protocol and modified with sodium bisulfite to discriminate between methylated and unmethylated cytosines. After amplification of the three AR regions, the PCR product was subcloned into TOPO TA vector and transformed in competent E. coli bacteria. Afterwards, bacteria were plated and incubated overnight and colonies were collected to perform colony PCR. Subsequently, the samples were purified and sequenced by Sanger sequencing.

Results: The majority of cytosines were unmethylated in all studied CpG dinucleotides of the three regions for both RWPE and PC3 cell lines. Contrarily, DU145 displayed a high number of methylation sites in two specific regions.

Conclusion: RWPE and PC-3 have few methylated dinucleotides in AR regulating sites whereas DU145 depicted multiple methylated CpGs in two regions, which might inhibit AR expression. If proven, AR methylation in specific CpG sites may lead to AR downregulation in a subset of PCa lesions and consequently associate with ADT resistance.

TAZ AS A POTENTIAL PLAYER IN DEVELOPMENTAL LUNG METABOLIC REWIRING

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Introduction: Hippo signaling is a highly conserved kinase cascade that it is known to be involved in organ size control and has recently emerged as a key player in lung branching. However, the correlation between Hippo and metabolism in early lung development has not been explored so far.

Aim: The aim of this work is to unravel the influence of TAZ in the metabolic signature of the developing lung.

Methods: Embryonic chicken lungs were used to perform in vitro lung explant culture supplemented with a specific TAZ-enhancer or DMSO (control), for 48 hours. Cultured lung tissue was morphometrically analyzed, and the expression levels of metabolic-related genes assessed by qRT-PCR. Culture medium was collected and 1H-NMR spectroscopy was performed for a metabolomic analysis. To confirm TAZ translocation into the nucleus, in situ hybridization for runx2 was performed.

Results: Lung explants treated with TAZ-enhancer showed an increase of around 12% in branching, in a dose-dependent manner when compared to controls. The increase in branching was accompanied by a mild increase in runx2 expression. qRT-PCR analysis revealed an increase of glut8, mct8, pdh and ldh expression levels when compared to controls. 1H-NMR spectroscopy revealed an increase in the levels of succinate and acetate after treatment.

Conclusion: TAZ manipulation, validated by runx2 increase, had a mild impact in lung branching nonetheless it induced alterations in the expression levels of different enzymes/ transporters of glucose catabolism. Furthermore, alterations in the amount of certain key metabolites was also noticed. Taken together, these results point to a potential role of TAZ in the regulation of the metabolic profile of the embryonic lung.

This is the first study that demonstrates the contribution of Hippo signaling to metabolic reprograming of early lung development through the modulation of gene expression. These findings may contribute to uncover new therapeutic targets to treat lung developmental disorders.

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MODELLING OF RADIATON-INDUCED HEART DISEASE (RIHD) ON CARDIOMYOCYTE-BASED CELL CULTURE

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Introduction: Nowadays the increasing incidence of cancer is a major problem worldwide. One of the therapeutic approaches is radiotherapy, using ionizing radiation in order to kill the malignant tumor cells. However as the survival rates are increasing, we have to cope with more and more chronic complications associated with radiotherapy. In the case of thoracic tumors, the radiation has long-term cardiovascular consequences, such as fibrosis or cardiomyopathy, called radiation induced heart disease (RIHD).

Aim: The aim of the study is to create an in vitro cardiomyocyte-based cell culture model in which this phenomenon and its cellular mechanisms can be examined.

Methods: We isolated hearts from neonatal Wistar rats in order to make a primer cardiomyocyte culture. On the following day cells were exposed to once 10, 15 and 20 Gray ionizing radiation. To establish the viability rates after the irradiation, we performed Calcein viability assay with a microplate reader. To confirm one possible cellular mechanism we measured the oxidative stress by performing DHE (dihydroetidium) assay.

Results: We could establish that all of the applied doses were able to significantly reduce viability compared to the control group (10 Gray: 66.39 ± 1.61%; 15 Gray: 62.19 ± 1.75%; 20 Gray 61.61 ± 1.97% vs. control group, p < 0.05, One-way ANOVA). For futher analysis we used the most optimal dose, which was 10 Gray. The oxidative stress significantly increased in the treated (10 Gray) group compared to the untreated group (control: 0.28 ± 0.02; 10 Gray: 0.43 ± 0.08, p < 0.05; Two-sample T-test).

Conclusion: Based on our data, the modell of a radiation-induced heart disease on an in vitro cardiomyocyte-based cell culture was successfully performed. In addition we also detected the presence of oxidative stress in the radiation exposed group. The results are promising, but further studies are needed in order to find out more about the exact mechanisms undergoing in the cells.

CANCER CACHEXIA PREVENTION: THE USAGE OF DIMETHYLAMINOPARTHENOLIDE AS A NF-KB INHIBITOR

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Introduction: It is of current knowledge, that changes in the nuclear factor kappa light chain enhancer of activated B cells (NF-kB) expression are connected with progression of certain cancers. This protein complex is essential in regulating the innate immune response, namely, against pathogens as viruses and bacteria. The human papilloma virus (HPV) has the ability to regulate the KF-kB pathway in order to promote malignant progression. Furthermore, this opportunistic regulation of the KF-kB pathway can lead to a state chronic inflammation followed by cachexia.

Aim: It was our aim to evaluate if the dimethylaminoparthenolide (DMAPT) was able to inhibit the progression of HPV-induced lesions and cachexia since this compound is a NF-kB inhibitor.

Methods: For 6 weeks, HPV-transgenic mice received, once a day, an oral DMAPT dose (100 mg/kg/day). The food and water intake, as well as the body weight were registered every week. At the end of the 6 weeks, the animals were humanly sacrificed, and gastrocnemius samples were harvested, their mass was registered, and they were analyzed for the expression of NF-kB subunits p50, p52, p65 and Rel-B.

Results: Overall, the treated mice bodyweight and strength was partially preserved. These findings were independent of the expression levels of the NF-kB subunits analyzed in the muscle.

Conclusion: To conclude, the usage of DMAPT as a NF- κ B inhibitor can be a potential strategy to prevent cancer cachexia. Its effects may be amplified by the use of combined therapies.

ELECTRON MICROSCOPIC ANALYSIS OF AUTOPHAGIC VESICLES IN LYMPHOCYTES OF TYPE 2 DIABETES MELLITUS PATIENTS WITH HYPERLIPIDEMIA

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Introduction: Autophagy is the process responsible for the degradation of cell components. Type 2 Diabetes Mellitus (T2DM), a global illness, linked to obesity and hyperglycemia, develops as a result of tissue resistance to insulin. One of the

many disturbances that accompany T2DM are elevated levels of lipids in blood (hyperlipidemia). Studies have shown that there is a correlation between autophagy and T2DM. Some of the studies indicate that there is an increase, while others show decrease of the autophagy induction in T2DM patient's cells.

Aim: The aim of our study was to determine if the autophagic structures are more frequently present in lymphocytes of T2DM patients with hyperlipidemia compared to healthy individuals.

Methods: Peripheral blood was obtained from the T2DM patients with hyperlipidemia and from the healthy individuals. Mononuclear cells, isolated from the peripheral blood, were fixed in glutaraldehyde and rinsed in 0.1 M cacodylate buffer. The cell precipitate was additionally fixed in osmium tetroxide and contrasted with uranyl acetate. The samples were then dehydrated in alcohol and embedded in Epoxy resins. The embedded samples were cut on ultramicrotome, contrasted with lead citrate and uranyl acetate and analyzed using the transmission electron microscope. The autophagy analysis was based on manual counting of the autophagic vesicles in lymphocytes of the T2DM patients with hyperlipidemia and in lymphocytes of the healthy individuals.

Results: There were more autophagic vesicles in lymphocytes of the T2DM patients with hyperlipidemia than in lymphocytes of healthy individuals (p < 0.05).

Conclusion: The higher number of autophagic vesicles detected in lymphocytes of the T2DM patients with hyperlipidemia indicates that autophagy may be induced in lymphocytes of T2DM patients compared to lymphocytes of healthy individuals.

EPITRANSCRIPTOMIC DEREGULATION IN BLADDER CANCER: IMPLICATIONS FOR TUMOR AGGRESSIVENESS

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Introduction: Bladder cancer (BlCa) is the tenth most incident cancer worldwide and the thirteenth leading cause of death from cancer. Currently, BlCa patients' management is a major health concern, due to the frequent recurrences and progression to muscle invasive disease. Thus, there is a need for the understanding of the molecular pathways underlying the pathology to improve patients' clinical outcome.

Recently, a new layer of gene expression regulation at the RNA level named "epitranscriptomics" has been identified. Specifically, it refers to the study of reversible chemical modifications of messenger RNAs (mRNAs). N6-methyladenosine (m6A), that is written by METTL3, is the most abundant mR-NAs chemical modification in eukaryotes, and has been associated to tumorigenesis. Indeed, METTL3 and m6A deregulation have been implicated in several cancer hallmarks (proliferation, invasion, migration, among others). However, limited data is available regarding BlCa.

Aim: Assess the expression levels of METTL3 in a set of BlCa samples and evaluate the potential impact in patients' prognosis.

Methods: METTL3 protein expression was evaluated by immunohistochemistry in 190 samples of primary bladder cancer patients. Moreover, METTL3 protein expression was characterized by western blot and cellular location was evaluated by immunofluorescence in seven BlCa cell lines and one normal bladder cell line.

Results: No significant differences were found between muscle invasive and non-muscle invasive bladder cancer. The expression levels and cellular distribution was rather heterogeneous among the studied cell lines.

Conclusion: Although it was not observed statistical differences, complementary studies are been performed to further elucidate METTL3 and m6A role in BlCa's progression.

K14-HPV16 TRANSGENIC MICE: A MOUSE MODEL FOR CANCER-ASSOCIATED CACHEXIA

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Introduction: Most advanced cancer patients suffer from cachexia, a syndrome characterized by involuntary weight loss, muscle wasting and systemic inflammation, affecting the tolerance and response to cancer treatments, quality of life and survival. Current therapeutic options for cancer cachexia are extremely limited and animal models are essential for developing effective treatments.

High-risk human papillomavirus (HPV), such as HPV16, are among the best-established etiological agents of cancer.

Aim: This study aims to assess the presence of cancer cachexia in K14-HPV16 transgenic mice with or without exposure to the tobacco-related carcinogen 7,12-dimethylbenz(a) anthrancene (DMBA).

Methods: A total of 39 male, 9–11 weeks-old mice were randomly divided into four experimental groups: wild-type without (wt) and with DMBA (wtDMBA); K14-HPV16 without (khpv) and with DMBA (khpvDMBA). Topical DMBA application occurred weekly during 17 weeks. Food intake and body weight of the animals were assessed weekly. The animals were sacrificed at 31–33 weeks-old. Body and gastrocnemius weights were measured at the sacrifice.

Results: Our results show that although transgenic mice seem to have a higher food intake, they presented lower body weights during the experiment when compared to wild-type animals (wt VS khpv: p = 0.025; wtDMBA VS khpvDMBA: p = 0.003). Additionally, body weight was lower in transgenic mice with DMBA application when compared to transgenic without DMBA (p = 0.003).

At the time of the sacrifice, transgenic mice continued to present a lower body weight compared with wild-type animals (wt VS khpv: p = 0.041; wtDMBA VS khpvDMBA: p = 0.002). Among K14-HPV16 mice, DMBA exposure was associated with significantly reduced bodyweight at sacrifice (p = 0.005). The same pattern was observed concerning the gastrocnemius weights (wt VS khpv: p = 0.025; wtDMBA VS khpvDMBA: p < 0.001; khpv VS khpvDMBA: p = 0.001).

Conclusion: Thus, K14-HPV16 mice may be a potential model to study cancer cachexia and we hypothesize that DMBA could have an enhancer effect on the wasting syndrome of these mice.

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THE ROLE OF APOPTOSIS IN MECHANISM OF ACTION OF THE CARDIOCYTOPROTECTIVE KYNURENIC ACID

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Introduction: Endogen tryptophan metabolite kynurenic acid (KYNA) is a widely investigated neuroprotective and immunosuppressive agent that reduces excitotoxicity, inflammation and oxidative stress. These effects are studied in several experimental setups, however, the potential roles of KYNA in the cardiovascular system are poorly understood.

Aim: In this study, we aimed to reveal the effects of KYNA against simulated ischemia/reperfusion-induced cardiac cell injury and determine the altered cellular pathways focusing on the involvement of apoptotic processes.

Methods: We employed the model of simulated ischemia/ reperfusion (SI/R) injury in ventricular heart muscle cells,
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isolated from neonatal Wistar rats. Our protocol included 4 hours of simulated ischemia and 2 hours of reperfusion. Based on our previous experiments, the most effective KYNA concentration (128 μ M) was used to uncover the role of apoptosis and the well-known reperfusion injury salvage kinase (RISK) pathway in the cardiocytoprotective effect of KYNA. The cell cultures were treated with KYNA or its vehicle during the 6 hours of SI/R which were followed by viability measurement. For the estimation of the apoptotic processes, we measured caspase-3 activity by immunostaining and determined the protein levels of pro- and cleaved caspase-7, B-cell lymphoma protein 2 (Bcl-2), phosphorylated and total forms of protein kinase B (Akt) and extracellular signal related kinase 1/2 (ERK1/2) via Western blot.

Results: Our results demonstrated that KYNA has a dose-dependent cardiocytoprotective effect against SI/R-in-duced cell death. Attenuation of apoptotic processes may have an important role in this as KYNA administration significantly reduced the SI/R-induced increase in caspase-3 and caspase-7 and increased the level of antiapoptotic Bcl-2. Our treatment had no effect on Akt or ERK1/2.

Conclusion: We conclude that KYNA protects cardiomyocytes from SI/R via antiapoptotic mechanisms. The RISK pathway is not involved in KYNA-induced cytoprotection.

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GENOMIC CHARACTERIZATION OF THE PROSTAGLANDIN E2 (PGE2) PATHWAY IN GASTRIC CANCER DEVELOPMENT - THE ASPIRIN AS AN OPPORTUNITY FOR PREVENTION?

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Introduction: Gastric cancer (GC) is the fifth most common cancer worldwide and the third leading cause of cancer-related deaths. Prostaglandin E2 (PGE2) has a key role in virtually all hallmarks of cancer and its levels are mainly regulated by COX-2 and MRP4, responsible for PGE2 synthesis and transport to the extracellular milieu, respectively, and 15-PGDH and PGT, responsible for its inactivation. Even though there are distinct genetic and molecular signatures across ethnic populations, most published studies are focused on Asian populations.

Aim: Thus, our main objective was to characterize the genomic profile of the four genes, that encode the proteins mentioned above (PTGS2, ABCC4, HPGD, and SLCO2A1), associated with gastric cancer risk. Additionally, we decided to explore the genetic expression of those genes in FFPE slides (normal and tumorous mucosa) from a subset of 250 Caucasian patients with histological confirmation of intestinal-type GC, consecutively selected after reviewing the histopathological database from the Pathology department at IPO-Porto.

Methods: The nucleic acids were extracted, after macrodissection, quantified and their quality assessed using a spectrophotometric approach. Approximately 55 tagSNPs were retrieved

from the Genome Variation Server and successfully converted to the Sequenom Platform. SNP genotyping will be performed using the MassARRAY iPLEX Gold Technology.

Results: Focusing on gene expression, the most suitable reference gene has already been selected from a panel of six genes previously reported (B2M, HPRT1, GUSB, IPO8, RPL29, PPIA) using Normfinder and GeNorm softwares and will be used to normalize the target gene expression.

Conclusion: We expect to have characterized the role of COX-2-derived PGE2 pathway in gastric cancer by the beginning of the conference and to suggest a targeted chemopreventive approach using aspirin, a COX-2 inhibitor shown to have beneficial effects on gastric cancer prevention.

ELECTRONIC CIGARETTE AEROSOL: IMPACT ON EMBRYONIC LUNG MORPHOLOGY

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Introduction: Smoking is a major public health problem responsible for 700000 deaths/year in Europe. Conventional cigarettes (c-cig) exacerbates several health issues, such as chronic obstructive pulmonary disease, fibrosis and cancer. Tobacco use during pregnancy has serious consequences to infants, since they become more susceptible to develop congenital disorders, lung diseases and sudden death. Electronic cigarettes (e-cig) have emerged as an alternative to c-cig. Previous studies revealed that c-cig exposure impairs lung development, aggravates wheezing and triggers inflammation. However, nothing is known about the impact of e-cig aerosol during pulmonary development.

Aim: Our aim was to evaluate the effect of e-cig aerosol and c-cig smoke in the early chick embryonic lung.

Methods: Ex vivo lung explants were cultured in smoke/ aerosol medium or unexposed medium (control) for 48 hours. Explants were assessed morphometrically. Additionally, TNF- α levels were evaluated by ELISA.

Results: When compared to controls, c-cig treated explants revealed a significant decrease, in all morphometric parameters, between 15 to 30%, while e-cig treated explants displayed a significant reduction only in lung total area and mesenchymal perimeter (roughly 10%). Lastly, c-cig explants presented a decrease in all morphometric parameters, between 11 to 26%, when compared to e-cig treated explants. Additionally, e-cig and c-cig treatment induced similar TNF- α release, that was nearly 7 times higher than control.

Conclusion: This study describes, for the first time, the impact of e-cigs on early lung development. The results revealed that e-cig aerosol impairs lung growth and promotes lung inflammation. However, its impact on early lung growth seems to be less detrimental than conventional cigarette smoke. Nevertheless, more

studies are required to fully understand the effect of the aerosol in embryo development. The validation of these effects will eventually lead to the development of new tobacco control recommendations to pregnant women in order to protect the fetus and child's health.

T CELL POLARIZATION INFLUENCES THE DEVELOPMENT OF IBD-ASSOCIATED NEOPLASIA

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Introduction: Inflammatory bowel disease (IBD) is a chronic relapsing inflammatory disorder of the gastrointestinal tract, being an example of the widespread concept that chronic inflammation is a cancer risk factor. Classically, this association has been explained by the establishment of an inflammatory environment that favours cell proliferation, angiogenesis and, ultimately, neoplastic risk.

Aim: The objective of this work is to demonstrate that, besides inflammation itself, the polarization of T helper (Th) cells towards branches that are pro- or anti-tumourigenic is an important cancer risk factor in chronic inflammation, namely IBD, and that Th1 cells are anti- while Th17 cells are pro-tumourigenic in this setting.

Methods: To recapitulate tumour development in the context of chronic colitis we used the azoxymethane and dextran sulphate sodium (AOM+DSS) chemical carcinogenesis mouse model. Cytokines produced by each of the cell subsets - IFN- γ for Th1 cells or IL-17F for Th17 cells - were administered to AOM+DSS treated C57BL/6 mice to polarize inflammation differentially. Tumour number and area were quantified macroscopically and tissue was collected for histological and immunohistochemistry analysis.

Results: The cytokine treatment influenced neoplasia development. Macroscopically, IL-17F treated mice had more lesions than IFN- γ treated mice (m = 12.9 lesions vs. m = 5.4 lesions, P = 0.004), with a stronger impact in females. Histologically, only 28% of IFN- γ treated mice had neoplastic lesions. That number was higher in both the control (66%) and the IL-17F group (62%), although not significantly. No major differences were observed in the tumour CD4+, CD8+ and Ror γ t+ cell densities between the groups.

Conclusion: We confirmed that polarizing the Th cell immune response influences tumour development. Polarization towards a Th1 phenotype decreased tumour number, whereas polarization towards a Th17 response increased that number.

DIMETHYLAMINO-PARTHENOLIDE AS CACHEXIA REDUCTANT IN MICE GENETICALLY MODIFIED FOR HPV16

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Introduction: The nuclear factor kappa light chain enhancer of activated B cells (NF- κ B) has been implicated in the progression of cancers induced by high-risk human papillomaviruses (HPV). It is known that in patients with NK- κ B cancer leads to a chronic systemic inflammatory state which leads to cachexia.

Aim: This work aimed to study the ability of DMAPT, a water-soluble NF- κ B inhibitor, as a blocker for the development of lesions and cachexia in mice genetically modified for HPV16.

Methods: Over 6 consecutive weeks, the animals received DMAPT once daily (100 mg / kg / day). Body weight was recorded weekly. After 6 weeks the animals were submitted to a grip strength test and sacrificed for specimen collection. Skin samples were histologically and histologically analyzed for expression of NF- κ B-regulated genes Bcl2 and Bcl2l1.

Results: The results were very interesting DMAPT reduced the incidence of epidermal dysplasia (18.2% versus 33.3% in HPV16+/- untreated mice). This was associated with reduced expression of Bcl2 and Bcl2l1 (p = 0.0003 and p = 0.0014 respectively) and reduced neutrophilic infiltration (p = 0.0339).

Conclusion: With these results we can suggest that the inhibition of NF- κ B appears as a strategy against in vivo HPV-induced lesions and which justifies the additional preclinical tests, essentially in the set of combined therapies. Thus, the data obtained allow us to conclude that inhibition of NF- κ B can prevent cancer cachexia.

ANXA1 AS A PREDICTIVE BIOMARKER OF TRASTUZUMAB RESISTANCE IN BREAST CANCER

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Introduction: Breast cancer (BrC) is the most commonly diagnosed cancer and the leading cause of cancer-related death among women, being responsible for high morbidity and mortality rates, and so, constitutes a major health issue and economic burden worldwide.

There are different molecular subtypes of BrC which, in clinical practice, can be identified by a panel of biomarkers including estrogen (ER) and progesterone receptors (PR) and the human epidermal growth factor receptor-2 (HER-2). HER-2+ (non-luminal) and a subset of Luminal B overexpress HER-2 and/or have amplification of the HER-2 gene. Despite having different molecular features and prognosis, all HER-2 positive patients, either true HER2+ and Luminal B (HER2+) are treated with Trastuzumab. Indeed, Trastuzumab revolutionized precision medicine and became a standard of care in the HER-2+

disease. Nevertheless, a substantial part of the patients develop resistance to the therapy (~20%). Our current inability to effectively stratify patients for Trastuzumab therapy highlights the need to find new predictive biomarkers that can tackle this issue.

Annexin A1 (ANXA 1) has already been identified as a possible biomarker of Trastuzumab resistance. Nonetheless, the studies were performed through an in sillico approach and not in patients' samples.

Aim: Assess the value of ANXA1 expression as predictive marker for Trastuzumab resistance in HER-2+ BrC patients.

Methods: Immunohistochemistry for ANXA1 was performed for 218 HER-2+ BrC patients that were submitted to Trastuzumab at IPO-PORTO.

Results: Our results show that HER-2+ (non-luminal) tumours display higher ANXA1 protein expression than luminal B (HER-2+) tumours. Additionally, patients whose tumours exhibit ANXA1 expression display shorter disease specific survival.

Conclusion: ANXA1 might be a promising biomarker for Trastuzumab resistance in HER-2 positive (non-luminal) BrC patients.

MORPHOLOGICAL ANALYSIS RESULTS OF USING THE STEM CELLS THERAPY OF CORNEA DAMAGES IN EXPERIMENT

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Introduction: Different types of cornea damages are widely spreaded all over the world and leads to the poor economic and social outcomes. Existing methods of treatment have list of limitations, however the stem cells therapy is very perspective nowadays.

Aim: The aim of study was to conduct the morphological analysis and to determine the efficiency of stem cells treatment of cornea burn in experience.

Methods: During research 20 rabbits were taken. The alkaline burn was modulated. During treatment antibiotics and lubricants were used both to the right (experimental) and left (control) eye, but stem cells were applicate only to the right eye.

Results: In experimental slides on the 5th day epithelium irregular regeneration and connective tissue edema were founded. In the control slides a massive defect of the epetilium and inflammation were noticed. On the 14th day, in experimental slides sings of cornea vessels fullness and complete epithelialization were found, which indicated active regeneration. In the control slides there were irregular regeneration and dystrophic changes in the epithelium. On the 30th day on the experimental slides irregular regeneration of the epithelium wasn't found, edema of connective tissue was observed. In the control slides regeneration also took place, but it was irregular in the form of thinning of the epithelium and its villous growths. Edema in the connective tissue was persisted.

Conclusion: The performed study allowed to define that using stem cells in the recovery gives good results, the structure of the cornea is approaching to normal. At the same time, treatment with traditional methods without using stem cells is accompanied by irregular regeneration and significant pathological changes. As result we can say, that cell therapy using mesenchymal cells is an important step in regenerative medicine of eye diseases.

THE EFFECTS OF DIETARY ANTIOXIDANT INTAKE IN WOMEN FERTILITY

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Introduction: Resveratrol and curcumin are sold as dietary supplements that benefit fertility. Resveratrol is a natural plant polyphenol widely present in grapes, wine and peanuts. Curcumin is a polyphenolic compound derived from Curcuma longa plant. Both compounds have been shown to exhibit antioxidant, anti-inflammatory and anticancer activities. Recent studies correlate these compounds with fertility, however its effects on human GC have not been describe yet. GC have a major role in estradiol and progesterone production and affect the reproductive cycle of women and, indirectly, interfere with oocyte quality and reproductive success.

Aim: Study the impact of Resveratrol and Curcumin on folliculogenesis.

Methods: COV434 cell line was treated with resveratrol and curcumin at different times (24-72 h) and concentrations (0,001–200 μ M). Viability and cytotoxicity were evaluated by MTT and LDH assays. Cell morphology was accessed by phase contrast microscopy, Giemsa and Höechst staining. Mitochondrial membrane potential was evaluated by fluorometry assay and reactive oxygen species generation by a fluorescent probe. Stress was induced using H2O2 and TBHP. Caspase activity was measured by luminescence.

Results: Both compounds induce a reduction in granulosa cell viability, in a concentration and time-dependent manner. After 48 hours, curcumin (5 μ M) induce a reduction of 24% in cell viability, whereas resveratrol induce similar effects but only after 72 h. Higher concentrations of either resveratrol or curcumin induce a more pronounced reduction on cell viability, though these effects are accompanied by LDH release and morphological alterations. Caspase 3/7 and 9 activities increase suggesting an apoptotic cell death. On the other hand, when COV434 cells are pre-treated during 72 h with lower doses of resveratrol and curcumin (0.001 μ M- 0.1 μ M), it presents a protective antioxidant effect, preventing both H2O2 and TBHP-induced stress.

Conclusion: At lower concentrations, resveratrol and curcumin present a protective effect against cell stress. However, at higher concentrations, these compounds induce apoptosis. Thus, although a healthy diet may be sufficient, moderate consumption of antioxidant supplementation might promote oocyte quality and optimize reproductive potential.

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LOCALLY ADVANCED SQUAMOUS-CELL CANCER OF THE ORAL CAVITY AND THE OROPHARYNX: EFFICACY OF THE PET/MRI IN GTV DELINEATION DURING RADIOTHERAPY PLANNING

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Introduction: Modern radiotherapy is based on different imaging modalities to appropriately determine GTV[1]. The first results indicate that PET/MRI[2] provides better accuracy than other methods in GTV delineation in head and neck cancer patients.

Aim: The objective of the study was to estimate the possibilities offered by FDG[3]-PET/MR in the GTV definition of primary tumours during radiotherapy planning in patients with locally advanced carcinoma of the oral cavity and the oropharynx.

Methods: A group of fifteen patients was included in the study. Based on standard diagnostic imaging evaluation (CT [4], ultrasound, MRI), patients were in clinical stages III or IV. The GTVs were delineated applying two different approaches. The first was a visual interpretation of CT (GTV-CT), MRI (GTV-MRI) and PET (GTV-PETvis) images - called "halo" method. Second, the quantitative automatic based on a determined threshold value: 20%, 30%, 40%, 50% of SUVmax[5] (maximum) and gaining: GTV-PET20%, GTV-PET30%, GTV-PET40%, GTV-PET50%. A statistical analysis of differences in obtained GTV values was performed. GTV-CT was used as a reference. The level of significance was p < 0.05.

Results: In 87% of GTV-MRI and 80% of GTV-PETvis volumes were larger than the reference GTV-CT. Primary tumour volumes obtained from GTV-PETvis (p = 0,0691) and GTV-PET30% (p = 0,8927) were the most closely correlated to the reference GTV-CT. Conversely, GTV-MRI (p = 0,0010), GTV-PET20% (p = 0,0409), GTV-PET40% (p = 0,0309) and GTV-PET50% (p = 0,0018) diverge significantly from the volumes based on CT images. The volumes obtained from PET images with the visual-based delineation method were inside the GTV-MRI contours in about 73% of cases. In 27% of cases, the increased FDG uptake was present outside the GTV-MRI boundaries.

Conclusion: The hybrid PET/MR is feasible in GTV delineation in patients with the oral cavity or oropharyngeal cancers and facilitates better precision of radiotherapy planning. Further studies on a wider population are required.

References:

[1] GTV - gross tumour volume

[2] PET/MRI - positron emission tomography/magnetic resonance

[3] FDG - fluorine-18-labeled fluorodeoxyglucose

[3] CT - computed tomography

[4] SUVmax - maximal standardized uptake value

DISCOVERY OF A MULTI-TARGET COMPOUND FOR ER+ BREAST CANCER: CHARACTERIZATION OF ITS BIOLOGICAL EFFECTS

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Introduction: Estrogen receptor-positive (ER+) breast cancer is the second related-cancer death in women worldwide. Estrogens, synthetized by aromatase, bind to ER α to promote growth of this type of cancer [1]. Therefore, the therapies used in clinic act either by inhibiting aromatase or by modulating ER α , although they can cause some adverse effects [2], reason why it is crucial to find novel therapeutic and safety approaches.

Aim: As aromatase and $ER\alpha$ have key proliferative roles in this type of cancer and $ER\beta$ has anti-proliferative action, our goal is to find multi-target compounds able to simultaneously inhibit aromatase, inactivate $ER\alpha$ and activate $ER\beta$.

Methods: Ligands of the three targets were collected from ChEMBL database and their features were evaluated, using ChemAxon software by the construction of molecular descriptors, in order to group them according to their similarity. Docking studies were performed and one potential multi-target compound (MT1) was selected to be studied in vitro. The anti-aromatase activity was evaluated by a radiometric and a GC-MS assay, using human placental microsomes studies. In a fibroblastic non-tumor cell line (HFF-1) and in an ER+ aromatase-overexpressing breast cancer cell line (MCF-7aro), it was explored the biological effects and characterized the mechanism of action.

Results: The aromatase inhibition studies showed that, unexpectedly, MT1 did not inhibit aromatase. Nevertheless, this compound induced a decrease in MCF-7aro cell viability, without affecting non-cancer cells. Using an ER α antagonist (ICI) and an ER β antagonist (PHTPP), it was possible to verify that the effects of MT1 on cells are ER α/β -dependent.

Conclusion: For the best of our knowledge, this is the first attempt to find multi-target compounds for ER+ breast cancer using this type of approach. We found MT1, which can act as a double-target compound by modulating $ER\alpha/\beta$. Although, MT1 was not able to inhibit aromatase, its study was crucial to pursuit structure-activity relationship studies.

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DIFFERENTIAL EXPRESSION OF CADHERINS IN BLADDER CANCER: ROLE IN EPITHELIAL MESENCHYMAL TRANSITION

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Introduction: Bladder cancer (BlCa) is the tenth most common malignancy worldwide. Although 70–80% cases display non-muscle-invasive bladder cancer (NMIBC) at the diagnosis, 50% of exhibit recurrences and some of which (5–25%) progress to muscle invasive disease (MIBC). Epithelial-Mesenchymal Transition (EMT) has been associated with BlCa progression and invasion. During EMT, epithelial cells lose cell-cell adhesion structures, change their polarity, and cadherins switch occurs. Indeed, type I cadherins, including E-, N- and P-cad deregulation have associated with cancer invasion and metastasis formation. Although, E-cad expression is associated with epithelial phenotype, N-cad and P-cad seem to be related to progression and advanced stages of bladder cancer. However, no solid data is still available regarding the progression from NMI to MI BlCa.

Aim: Investigate the role that these 3 cadherins might play in BlCa EMT and in invasive phenotype.

Methods: E, N and P-cads expression was assessed Western Blot (WB) in 7 bladder tumor cell lines and in 1 normal cell line to quantify. Furthermore, immunofluorescence assay allowed for the cellular distribution of the studied cadherins.

Results: E-cad and P-cad were found to be expressed in the same well differentiated BlCa cell lines, as well as, in the normal cell line. Conversely, N-cad was mostly expressed in less differentiated cell lines. Moreover, all cadherins were present at the cells' membrane confirming their involvement in cell-cell adhesion.

Conclusion: Our results suggest that in the studied cell lines E-and P-cad seem to be associated with an epithelial phenotype, whereas N-cad with a mesenchymal phenotype.

CLINICAL CHARACTERISTICS AND CORRELATION OF MARKERS WITH HISTOLOGICAL SUBTYPES IN BORDERLINE OVARIAN TUMOURS

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Introduction: Borderline ovarian tumours (BOT) are histologically defined by atypical epithelial proliferation without stromal invasion. They typically affect women in their thirties or forties and follow a more indolent clinical course compared to invasive ovarian cancer. They are associated with infertility and hormone replacement therapy (HRT). The majority of BOT histological subtypes are serous or mucinous.

Aim: To evaluate the common and distinctive features in clinical presentation of serous and mucinous BOTs.

Methods: We retrospectively identified patients treated at the University Medical Centre Maribor between 2009 and

2013 with histological diagnosis of BOTs. Patient data on clinical and pathological characteristics such as age, parity, HRT, invasive implants, histological subtype, uni or bilaterality of tumours, pre-operative diagnostics, type of surgical treatment and level of tumour markers (CA125 and CEA) were collected and analysed using descriptive statistics and non-parametric test (Mann-Whitney test).

Results: Of the 49 patients identified, 31 patients (63.3%) presented with serous, 15 (30.6%) with mucinous and 3 (6.1%) with another histological BOT subtype. Mean age at diagnosis of serous and mucinous BOT was 55 years and 52 years, respectively. In serous BOT, level of tumour marker CA125 ranged from 7–577 kU/L (SD 168.28) and CEA ranged from 0–7 ug/L (SD 1.80). In mucinous BOT, CA125 ranged from 15–38 kU/L (SD 12.16) and CEA ranged from 1–110 ug/L (SD 33.69). CEA showed statistically significant correlation with the mucinous histological type (p = 0.019), whereas no histological correlation was detected with CA125.

Conclusion: Raised levels of CEA correlate with mucinous BOTs, thereby predicting histological BOT subtype before histological diagnosis is available.

IMPROVEMENT OF AGE - RELATED OVARIAN INVOLUTION BY THE USE OF A NADPH - OXIDASE INHIBITOR

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Introduction: Advanced maternal age is related with higher infertility rates, pregnancy associated complications and progeny health issues. Behind these consequences is the ovary due to the progressive age-related loss of follicle number and oocyte quality, which appears to be related with a disruption of redox homeostasis that results in local oxidative stress (OS). OS is believed to increase tissue inflammation and fibrosis, thus affecting ovarian function and, ultimately, fertility.

Aim: This work aimed at evaluating if these features are age-related and contribute to tissue dysfunction, and whether specific antioxidant supplementation with a NADPH-oxidase inhibitor (apocynin) could ameliorate them.

Methods: Reproductively-young (8–12 weeks) or reproductively-aged mice (38–42 weeks) were employed. Aged mice were sub-divided into two groups, with one receiving apocynin (5 mM) in the drinking water for 7 weeks. Animals were sacrificed and ovaries collected. Picrosirius red, H&E and Sudan black staining were used for histological examination. Protein carbonylation, nitration and lipofuscin deposition were assessed by immunofluorescence. Collagens, matrix metalloproteinases (MMPs), MMP tissue inhibitors (TIMP), inflammation-related genes and miRNAs were quantified by qPCR. Statistical analyses were performed by ANOVA.

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Results: Ovarian structure was similar at both ages, but ovaries from reproductively-aged mice exhibited lipofuscin deposition, enhanced fibrosis and a significant age-related reduction in primordial and primary follicles when compared to younger animals. Markers of OS (protein carbonylation and nitration) were significantly increased with age. Likewise, mRNA levels of inflammation markers, collagens, MMPs and TIMPs were up-regulated. Expression of anti-fibrotic miRNA29c-3p was significantly reduced. Interestingly, apocynin ameliorated OS markers and normalized gene expression to levels similar to younger females.

Conclusion: These findings indicate that there is an age-related increase in OS that plays an important role in enhancing inflammation and collagen deposition, affecting ovarian function and female fertility. Its amelioration following apocynin supplementation, further emphasizes the role of OS in age-related ovarian involution.

FUNCTIONAL ANALYSIS OF PSMA-SPECIFIC CARS FOR PROSTATE CANCER IMMUNOTHERAPY

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Introduction: Worldwide, prostate cancer (PC) is known to be the third leading cause of cancer-associated deaths among elderly men. Clearly, there is a necessity for developing novel therapeutic modalities for this tumor. One of the recent advances in the field of cancer immunotherapy is based on the cancer-specific T and NK cells armed with chimeric antigen receptors (CARs).

Aim: In this study, we developed a series of CAR constructs targeting PC tumor marker (protein PSMA). These CARs were expressed in an NK cell line (YT) and primary T cells. Obtained CAR-T and CAR-NK cells were comparatively assayed for the cytotoxicity mediated by CARs having distinct organization of the spacer region.

Methods: We designed lentiviral constructs encoding a second-generation PSMA-specific CARs. The CARs either had IgG1- or CD8a-derived spacer regions or were hingeless. YT cell line and primary T cells were transduced with the constructs coding the CAR. Surface expression of CARs was assessed by flow cytometry. In vitro cytotoxic activity of obtained cells against target cells was measured by FACS and RTCA iCELLigence system.

Results: CAR-NK cells obtained expressed CARs at comparable high levels and we proved that in the context of NK cells the spacer region structure was crucial for cytotoxic activity in vitro: the highest level was observed for the hingeless version of the CAR. In case of primary CAR-T cells the level of CAR-positive cells was relatively low, despite this, CAR-T cells demonstrated pronounced cytotoxicity in vitro against target cells.

Conclusion: Thus, the PSMA-specific CAR designs assayed in the context of YT and primary T cells appear functional in vitro. Our study indicates that hingeless design is the best option for PSMA-specific CAR. We hope that our findings may serve as a platform for developing CAR-cell products for cell therapy of patients with PSMA-positive prostate cancer.

INVESTIGATING THE ROLE OF CD44V6 AS A MODULATOR OF CHEMOTHERAPY RESPONSE IN GASTRIC CANCER CELLS: DEVELOPMENT OF STUDY MODELS

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Introduction: Gastric cancer (GC) is the 5th most common cancer and 3rd with highest mortality. Most GC patients are diagnosed at advanced stages of disease, being chemotherapy the standard treatment. At this disease stage, treatment response is poor and the overall survival is only ~1 year. Therefore, finding predictors of therapy response is crucial. CD44 gene undergoes extensive alternative splicing, giving rise to many isoforms of a cell surface adhesion protein. CD44v6-containing isoforms are rarely expressed in normal tissues, and de novo expression is found in many types of cancer, including GC. Our preliminary data indicates that CD44v6-containing isoforms confer chemoresistance to GC cells.

Aim: We aim to understand whether exon-v6 is, itself, the responsible for increased CD44v6-associated chemoresistance in GC.

Methods: Two GC cell lines, endogenously expressing CD44v6-containing isoforms, were edited to selectively remove exon-v6 by CRISPR/Cas9 (permanent inhibition) or by Morpholino Antisense Oligonucleotides (PMO) (transient inhibition). For both approaches, cells were transfected, puromy-cin-selected (in CRISPR/Cas9) and its DNA and RNA genotyped by PCR-sequencing. CD44v6 inhibition was assessed by RT-PCR.

Results: CRISPR/Cas9 stable clones and PMO-transient clones were generated successfully. Genotyping demonstrated that exon-v6 was selectively, permanently and homozygously deleted in five CRISPR/Cas9 clones and depleted in two PMO clones for 48 hours. RT-PCR for PMO-transient clones confirmed CD44v6 inhibition while maintaining total CD44 expression. All edited clones maintain the reading frame, with exon-v6 being spliced out. Long-range PCR in cDNA from edited clones confirms the production of novel and shorter CD44 transcripts which are under characterization.

Conclusion: We successfully generated isogenic cells expressing endogenous CD44 v isoforms that specifically lack exon-v6 by CRISPR/Cas9 and PMO. These cell lines constitute an indispensable tool to understand the role of CD44 exon-v6 as a chemoresistance modulator in GC and redefine anti-CD44v6 containing isoforms-based therapy.

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THE MAIN METABOLITES OF CYCLOPHOSPHAMIDE, 4-HYDROXYCYCLOPHOSPHAMIDE AND ACROLEIN, ARE CARDIOTOXIC AT RELEVANT CLINICAL CONCENTRATIONS

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Introduction: Chemotherapeutic and immunosuppressive regimens commonly include cyclophosphamide, a nitrogen mustard alkylating agent. However, cyclophosphamide clinical application is limited by its induced cardiotoxicity. The underlying molecular mechanism of cyclophosphamide-induced heart toxicity is not fully understood, but the extent of drug's metabolism may be a key player.

Aim: The objective of this study was to evaluate the cytotoxicity of cyclophosphamide (100 to 10000 μ M) and two of its main metabolites, 4-hydroxycyclophosphamide (1 to 25 μ M) and acrolein (5 to 100 μ M) in AC16 cells, a human cardiomyocyte cell line.

Methods: The experiments were performed in two different states of differentiation: a differentiated (DMEM/F12 medium + 2% horse serum) and a proliferative (DMEM/F12 medium + 12.5% fetal bovine serum) state. The tetrazolium-based colorimetric (MTT) and the neutral red (NR) uptake assays were performed at different time-points (24, 48 and 72 h).

Results: In differentiated cells, cyclophosphamide only caused cytotoxicity at 7500 μ M (or higher) in both tests at 24 h, while in the proliferative state, it induced toxicity at concentrations higher than 5000 μ M . That cytotoxicity was time-dependent. Differentiated cells were very vulnerable to 4-hydrox-ycylophosphamide as a 1 μ M concentration induced toxicity at 24 h (only in the MTT assay), whereas cytotoxicity in cells in the proliferative state was only observed after 5 μ M, in both tests. For concentrations higher than 15 μ M in the MTT test, acrolein displayed a significant toxicity at 24 h in differentiated cells, whereas in proliferating cells, cytotoxicity was only displayed at 25 μ M. Overall, differentiated cells were more sensitive to cyclophosphamide metabolites.

Conclusion: Our study shows that the main cyclophosphamide metabolites, 4-hydroxycyclophosphamide and acrolein, exert a cardiotoxic effect within a scope of clinically relevant concentrations, while cyclophosphamide is cytotoxic at relatively high concentrations. This reinforces the idea of the key role of metabolization in cyclophosphamide-induced cardiotoxicity.

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DOXORUBICIN-INDUCED CYTOTOXICITY IN RAT CARDIOMYOBLAST-DERIVED CELL LINE

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Introduction: Anthracyclines such as doxorubicin are effective chemotherapeutic agents, however, their widespread clinical use is limited by their well-known cardiotoxic effect. Due to a significant improvement in the survival of cancer patients, the long-term side effects and complications of various anti-tumor therapies are becoming more emphasized. Therefore searching for substances capable of reducing the cardiotoxic effects of doxorubicin is of great importance.

Aim: Our aims were to establish a model of doxorubicin cardiocytotoxicity in rat cardiomyoblast-derived cell line and use this model for screening potential protective drugs.

Methods: To investigate doxorubicin-induced cytotoxicity, two days old cell cultures were treated with various concentrations of doxorubicin (75-1200 ng/mL) for 24 hours. At the end of the treatment period cell viability was measured by two different methods, calcein and MTT assays. The degree of oxidative stress was determined by DHE assay.

Results: The used concentrations of doxorubicin resulted in significant decreased cell viability in calcein $(24,5 \pm 8,5)$ and MTT (49 ± 17) assay too. Doxorubicin induced dose-dependent oxidative stress in rat cardiomyoblast-derived cell line.

Conclusion: Rat cardiomyoblast-derived cell line is a suitable model for testing potential protective agents against doxorubicin-induced cardiocytotoxicity.

MODIFICATION OF SURFACE WETTABILITY FOR MICROFLUIDIC BIOANALYSIS

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Introduction: Traditional diagnostics frequently require access to expensive laboratorial equipment, large quantity of reagents and are time-consuming, all critical parameters for efficient early treatment. Microfluidic based Point-Of-Care (μ F-POC) devices[1], where micro/nanoscale fluidic channels and chambers are integrated with biosensor technologies, are seen as promising tools for simple, fast and cost-effective bioanalysis.[2] However, the wettable nature of common materials used in microfluidics, such as glass and PDMS (polydimethylsiloxane), can lead to unwanted biofouling.[3]

Aim: Consequently, for microfluidics to reach its full potential as a robust tool for μ F-POC while using these materials, the control of surface wettability is critical.

Methods: In this work we used room temperature Chemical Vapor Deposition (CVD) to access its ability to tailor the wettability of glass and PDMS surfaces. This is done by exposing the surfaces to 6 mL of FDTS (perfluorodecyltrichlorosilane) under vacuum ($p = -0.78 \pm 0.09$ atm) for 2, 10, 20, 30 and 50 min.

The evaluation of the surface wettability modification (SWM) consisted on the measurement of contact angles (CA) of 6 mL droplets of phosphate-buffered saline solution (PBS) under controlled atmosphere. Images were obtained with a CMOS camera through backlight illumination and processed with ImageJ software plus LBADSA plugin.

Results: PDMS surfaces revealed no significant alteration in contact angle while glass, initially hydrophilic (CA ~20°), showed an hydrophobic tendency (CA ~60°) just after 30 min CVD. This behavior results from the covalent bond formed between the Si from trichlorosilane groups (–SiCl3) present in FDTS molecules with OH groups and subsequent interaction of the hydrophobic heavily fluorinated tails from FDTS with PBS. This explains the increase of the CA, detected only in modified glass surfaces.

Conclusion: This simple methodology was proven very efficient for SWM of glass towards microfluidic devices for bioanalysis.

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EXPERIMENTAL ADVICES FOR FORMAZAN-BASED METABOLIC VIABILITY ASSAY

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Introduction: When in vitro studies are performed the correct assessment of viable cells number is an essential output for a wide variety of medical studies in oncology, toxicology or pharmacology. Several viability assays have been developed for such evaluations (e.g., resazurin, LDH, ATP tests), the methyl tetrazolium salt (MTS) based assay being one of the most used metabolic test. The number of viable cells is measured by colorimetric dosing of the soluble formazan produced by MTS mitochondrial reduction via NADPH/NADH.

Aim: We aimed to quantify the influence of phenol red from MTS culture medium on the viability assay results due to its possible interference with the absorbance signal acquisition.

Methods: Human CaCo-2 colorectal adenocarcinoma cells were cultured in 24-well plates starting from the same seeding cell concentration. Culture media with (P+) and without (P-) phenol red mixed with MTS (MTS:medium = 1:6) were added to the monolayer after 24, 48, 72 h of growth; the plates were incubated for another 1, 2, 3 or 4 h. The quantity of formazan was measured by absorbance at 490 nm using a standard plate reader.

Results: In spite of the contribution of phenol red to the absorbtion, lower absorbance values for P(+)-medium were obtained when compared to P(-) one regardless of MTS mix incubation time. Higher signals for formazan were observed for both P(+) and P(-)-media for longer incubation times. In case of small number cell cultures, minimum 2 h incubation time is required to obtain a formazan signal out of the background.

Conclusion: Our study revealed that the phenol red of standard culture medium may interfere with the formazan Absorption and experimental precautions should be taken when MTS data are analysed: 2 h incubation time is mandatory for good formazan signal and the comparison of MTS results is possible only when the same MTS mix medium is used.

UNCOVERING THE ROLE OF DYNAMIC PROTEIN LIN28A IN MOUSE PLURIPOTENT STEM CELLS AND EMBRYOS

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Introduction: Pluripotent stem cells (PSCs) are derived from the inner cell mass of blastocyst-stage embryo. They have the potential to differentiate into cells of all three germ layers and are also capable of self-renewal. Although PSCs were established nearly 40 years ago, the molecular regulatory mechanisms to safeguard pluripotency remain elusive.

Aim: One of the earliest identified developmental regulators are let-7 miRNAs, required for developmental timing. A highly conserved RNA-binding protein LIN28 has been in focus as a regulator of let-7 biogenesis and thus one of the central post-transcriptional regulators of cell fate. Contradicting studies aimed to uncover LIN28A/B mechanisms to repress let-7 biogenesis. Its function to block let-7 has been primarily proposed in the cytoplasm, but it is imperative that LIN28A is predominantly nucleolar protein in early blastocyst.

Methods: To gain insight into the protein's localization and details of LIN28/let-7 switch during the early embryonic development, we generated LIN28A-eGFP mESC cell line using CRISPR/Cas9 approach and observed LIN28A cytoplasmic accumulation upon the exit of naïve pluripotency. This led us to investigate if and at what point does such translocation affect biogenesis of let-7 miRNA. Next, we endogenously targeted NLS sequence to LIN28A genomic loci and forced fusion protein LIN28A-NLS to exclusively reside in the nucleus.

Results: We surprisingly observed that developmental LI-N28A translocation is essential to drive the exit of naïve pluripotency. Furthermore, in vivo tetraploid complementation assay in mouse embryos confirmed that the gain of cytoplasmic LIN28A function is essential for embryonic gastrulation. However, since LIN28A-NLS embryos are arrested in development without noticeable differences in let-7 levels, it leads us to believe there is a vital, still unclear function of cytoplasmic LIN28A concerning the breakdown of pluripotency.

Conclusion: Collectively, this demonstrates that LIN28A functions as a molecular 'gatekeeper', regulating the pluripotency transition in vivo and in vitro independent of let-7 biogenesis repression.

TO TREAT DIABETES WITH A SCALPEL? DUODENO-JEJUNAL OMEGA SWITCH SURGERY (DJOS) AND ITS IMPACT ON SELECTED INCRETINS IN HELD ON DIET SPRAGUE – DAWLEY RATS

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Introduction: GLP-1 and GIP are metabolic hormones released from alimentary system into cardiovascular system in response for nutrition intake, thus ameliorating insulin release in response for glucose. GLP-1 also promotes β -cells in pancreas, while suppressing glucagon secretion at the same time. What is more it improves peripheral insulin sensitivity.

Aim: To assess GLP-1 and GIP levels in Sprague – Dawley rats considering different dietary patterns.

Methods: Study involved 56 seven week old male rats. 8 weeks prior to the surgery. 28 rats were given high-fat, high sugar diet (HFS) to induce obesity, while another 28 were fed with a control diet (CD). After this time half of each group underwent DJOS surgery, while the other half underwent SHAM (placebo) surgery. In DJOS firstly the transection of duodenal bulb was performed, then suturing of the distal part of transected duodenum was conducted. The small intestine was measured and the incision was made at its 1/3 of its total length. Then, end-to-side anastomosis was made connecting bulb and loop of selection. For next 8 weeks half of each operative group was kept on the same diet as before. And the other half had it switched. GLP-1 and GIP were measured in periods both before and after operation.

Results: Significant changes of Δ GLP-1 (p < 0,05) were found in each DJOS group when compared to SHAM. Reversely Δ GIP-1 was significantly decreased in DJOS in comparison with SHAM except CD/CD (p < 0,001).

Conclusion: DJOS protocol has crucial impact on changes in incretin levels. Achieved results suggest improvement of both insulin secretion and sensitivity, thus allows to suggest a new way of diabetes treatment. Nevertheless, presence of CD at any point lead to significantly better results.

PROTEIN TRANSLATION IN SPERMATOZOA: NEW EVIDENCES

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Introduction: Spermatozoa are highly differentiated haploid cells originated through a sequence of mitotic and meiotic divisions – the spermatogenesis. During this process, spermatozoa undergo major structural and functional changes at the nuclear and cytoplasmic levels. Because of these changes, the silencing of the gene expression is widely accepted in mammalian spermatozoa. A new perspective emerged when de novo protein synthesis was shown to occurs in sperm cells under capacitation conditions, opening the discussion to established dogma.

Aim: The main objective of this work is to characterize and evaluate the translational activity that may occur in mammalian spermatozoa.

Methods: To achieve this goal a bioinformatic and experimental approach was performed.

Results: Bioinformatic analysis revealed the existence of 315 translation-related proteins present in spermatozoa. Simultaneous analysis of the biological processes and cellular compartments associated with each protein led to the identification of 31 translation exclusive-proteins. Additionally, the PPI network analysis reveals that 315 overlapping proteins are strongly connected and related to each other. Also, the enrichment analysis of PPI network, for biological processes and cellular compartment, evidenced the strong association to processes translation-related process and a preferential location in cytoplasmic and mitochondrial regions.

The SUnSET technique unequivocally established the existence of translational activity through the incorporation of puromycin into the nascent polypeptide chains. A decrease in puromycin incorporation was observed with the use of mitochondrial and cytoplasmic translational inhibitors, which leads us to believe the coexistence of both forms of translation in spermatozoa.

Conclusion: Together, these results evidenced the existence of translational activity in mammalian spermatozoa.

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UNCOVERING THE ROLE OF THE INTESTINAL STEM CELL MARKER MEX3A IN COLORECTAL CARCINOGENESIS

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Introduction: Intestinal epithelial homeostasis is ensured by a population of intestinal stem cells (ISCs). Among the different ISC markers described, LGR5 (a Wnt/b-catenin pathway target) is the most well-established. Lgr5+ cells have been shown to serve as the cell-of-origin for malignant intestinal lesions. We demonstrated that the RNA-binding protein MEX3A is associated with higher expression of LGR5 in cancer cell lines. More recently, we showed that MEX3A function is critical to maintain Lgr5+ cells as Mex3a knockout (KO) mice show impaired intestinal self-renewal.

Aim: The main objective of the current work is to evaluate the putative functional impact of MEX3A in colorectal carcinogenesis.

Methods: We are using human colorectal cancer (CRC) cases, cell lines, and genetically-modified CRC mouse models (Apclox14/+, KrasLSL-G12D, Apclox14/+;KrasLSL-G12), to characterize Mex3a expression and its association with specific cell-lineage markers using mRNA in situ hybridization, immunohistochemical, western blot and real-time PCR methodologies. Moreover, we are establishing new strains by combining these mouse models with the Mex3a KO.

Results: We observed that Mex3a expression is significantly increased in human CRC cases when compared to adjacent normal colonic mucosa. Interestingly, Mex3a expression is strikingly increased both in early focal adenomatous polyps and malignant lesions developed in the Apclox14/+ mice and particularly in the Apclox14/+;KrasGLSL-G12 animals. This is accompanied by higher Lgr5 mRNA levels and loss of differentiation markers. Moreover, we observed in CRC cell lines treated with small molecules activating (CHIR99021) or inhibiting (IWP-2) the Wnt signalling that MEX3A protein expression is modulated by the pathway. This response does not appear to be transcriptionally-mediated. Assays are currently ongoing to determine within a context of Wnt activation the effect of MEX3A modulation in cell proliferation, apoptosis and chemotherapy drug (5-FU) resistance.

Conclusion: For now, we can conclude that MEX3A expression is positively associated with the development of benign and malignant colorectal lesions.

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REGULATORY T CELLS CHARACTERISATION IN MURINE TUMOURS

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Introduction: The suppression of the tumour immune microenvironment may be critical for tumour cells to escape immune response. Tumour-infiltrative regulatory T cells (ti-Tregs) are present in several tumour types and induce immune tolerance. For this reason, they are correlated with poor prognosis. It is known that there are two different lineages of regulatory T cells (Tregs), based on where they originate: natural Tregs (nTregs) generated in thymus; and peripheral Tregs (pTregs) produced in the periphery through conversion from CD4+ T effector cells (Teff). The recruitment and activity of tiTregs are poorly understood due to the controversial use of the markers Neuropilin-1 and Helios to distinguish these two populations.

Aim: Our aim is to evaluate the origin of Tregs at the tumour site. To achieve that, we will compare T cell receptor beta (TCR beta) sequences between Teff and Tregs to observe if they share a common origin or if they originate from distinct clones.

Methods: Upon collection of 15 mouse tumours from the small intestine and colon, we sorted two cell populations: Teffs (CD4+, CD3+, FoxP3-) and Tregs (CD4+, CD3+, FoxP3+, CD25+). Finally, we sequenced the TCR beta by Next Generation Sequencing (NGS) from both populations and compared the data.

Results: In terms of immune infiltrate, we observed a heterogeneous number of CD4+ T cells at the tumour site, ranging between 1.3 to 2.8% of total cells. In the CD4+ population, between 10 to 22 % were Tregs.

Conclusion: In this study, we hope to better understand the relationship between cancer and the immune system in order to unveil targeting of other immune targets as potential applications in immunotherapies.

MITOCHONDRIAL DYNAMICS IN THYROID CANCER: UNRAVELLING THE ROLE OF DRP1

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Introduction: Mitochondria produce most cell energy through OXPHOS and adapt their function and structure through the action of mitochondrial fission and fusion regulatory proteins, providing adequate number of mitochondria to support growing and dividing cells. In opposition, cancer cells are more prone to metabolising glucose by glycolysis, even in the presence of O2. Our group demonstrated that DRP1 – a fission protein - is overexpressed in oncocytic thyroid cancer (TC).

MAPK signalling pathway is frequently activated in TC and, interestingly, BRAF (a key MAPK protein) activation was associated with DRP1 higher expression, suggesting a synergistic effect of both pathways.

Aim: We aim to assess the functional relevance of DRP1 and to understand the interaction between mitochondrial fission and MAPK signalling in TC.

Methods: We assessed the effects of Mitochondrial division related protein 1 inhibitor (Mdivi-1) and Dabrafenib – BRAF inhibitor – on cell viability, apoptosis and cell cycle in four TC cell lines – TPC1, C643, 8505C and XTC-1. Moreover, we evaluated their effects on downstream signalling targets through Western Blot.

Results: Our data demonstrate that Mdivi-1 decreases cell viability in a dose-dependent manner in all cell lines, and Dabrafenib decreases the cell viability in TPC1 and 8505C. Mdivi-1 induces apoptosis in all cell lines, except the oncocytic cell line XTC-1, where effects are minimal. Dabrafenib's effect is lower than Mdivi-1's in all cell lines, excluding XTC-1. Mdivi-1 increases the number of cells in G1 phase, in TPC1, whereas Dabrafenib does not affect cell cycle. Additionally, Mdivi-1 affects DRP1 phosphorylation and Dabrafenib inhibits ERK phosphorylation in 8505C, but not in TPC1.

Conclusion: Mdivi-1 seems to inhibit cell survival, and DRP1 phosphorylation may be implicated in this phenomenon. The differences observed with Dabrafenib could probably be due to BRAFV600E mutation in 8505C.

As future work, we will assess how these drugs could affect mitochondrial morphology, ROS levels and mitochondrial activity.

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MICRORNA-30A, MICRORNA-30C AND MICRORNA-204 DOWNREGULATED LEVELS AS PREDICTORS OF WORSE PROGNOSIS IN CLEAR CELL RENAL CELL CARCINOMA

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Introduction: Renal Cell Carcinomas are the most lethal urological cancers and clear cell renal cell carcinoma (ccRCC) carries worse prognosis compared to other common histological subtypes[1–2]. Currently, there is no recommended screening test for ccRCC early detection[3]. MicroRNAs have been described as deregulated in different types of malignancies[4], including ccRCC[5–6]. For their biological properties, these molecules show potential as diagnostic and prognostic biomarkers, and, thus, might improve ccRCC patient's clinical management.

Aim: Evaluate the diagnostic and prognostic value of deregulated microRNAs in ccRCC.

Methods: A series of 250 primary ccRCC diagnosed at IPO-Porto were enrolled, after patients' informed consent. Additionally, 28 renal normal tissues (RNT) served as controls. RNA was extracted using Trizol reagent. cDNA synthesis specific for miRNAs followed by RT-qPCR were performed for expression quantification.

Results: Using TCGA database microRNA significantly downregulated (P < 0.05) in ccRCC were identified, from which 3 microRNAs – microRNA-30a, microRNA-30c and microRNA-204 - were selected for independent validation in an IPO-Porto's cohort. All the tested microRNAs showed significantly lower levels (P < 0.05) in ccRCC compared with RNT. MicroRNAs expression downregulation associated with clinicopathological features, specifically metastatic dissemination and recurrence for microRNA-30a (P = 0.0482 and P = 0.0057, respectively) and microRNA-204 (P = 0.0025 and P = 0.0022, respectively). MicroRNA-30c downregulation associated with higher Fuhrman grade (P < 0.0001). Lower microRNA-30a, microRNA-30c and microRNA-204 expression levels associated with shorter time to relapse (P = 0.0457, P = 0.0180 and P = 0.0240, respectively), in univariable analysis. Combining the expression levels of all tested microRNAs in a panel, both higher clinical stage and Fuhrman grade as well as panel low expression levels independently predicted for shorter disease-specific survival (DSS) (HR = 3.338 P < 0.0001, HR = 2.611 P = 0.025 and HR = 0.395 P = 0.022 respectively, in multivariable analysis.

Conclusion: Clinical management of ccRCC patients faces many challenges, being the lack of a biomarker with prognostic value a major one. Henceforth, we present a panel of three microRNAs that might help to overcome this major health issue.

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DNA METHYLATION PANEL IN LIQUID BIOPSIES FOR DETECTION OF THE TWO MAJOR CANCERS IN MALES

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Introduction: Lung (LC) and Prostate (PCa) cancers are the two most incident cancers in males worldwide. The high false-positive rate of the current screening methods for these

cancer types is still a limitation, leading to overdiagnosis and consequently, overtreatment. Thus, due to the negative impact in health system's management and men's quality of life of these methods, the development of new and effective screening methods is urgently needed.

Aberrant DNA methylation is related with cancer development and is thought to precede the emergence of the malignant phenotype. Furthermore, DNA methylation of cancer related genes can be detected in circulating cell-free DNA (ccfDNA), representing a valuable minimally invasive tool for early cancer detection.

Aim: To develop a minimally invasive methylation-based test for simultaneous early LC and PCa detection in males, using liquid biopsies (LB).

Methods: CcfDNA was extracted from LB samples of 102 LC and 121 PCa patients. Additionally, LBs from 136 asymptomatic donors were used as control samples. After, sodium-bisulfite modification and whole-genome amplification, promoter methylation levels of 5 genes were assessed by multiplex qMSP. Biomarkers' diagnostic performance was evaluated (Ethics approval IPOPFG-CES 120/2015).

Results: A "PanCancer" panel (3 genes) detected simultaneously the two most incident cancers in males with 65% sensitivity and 72% specificity. Additionally, a "CancerType" panel (2 genes) discriminated the most probable location with a specificity over 97%, although with limited sensitivity.

Conclusion: DNA methylation-based testing in liquid biopsies might be clinically useful for LC and PCa screening in males, improving patient compliance and reducing healthcare costs.

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METFORMIN AND SIROLIMUS AS NEW TREATMENT OPTIONS IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA

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Introduction: Acute lymphoblastic leukemia (ALL) is the most common neoplasia in childhood characterized by an impairment of proliferation and/or differentiation of immature lymphoid cells. In general, the treatment of childhood ALL is successful with 5-year overall survival rates approaching 90%. However, relapse occurs in 15–20% cases and about 2–3% of ALL patients are refractory to primary therapy. ALL pathogenesis is complex and involves mTOR pathways, which constitu-

tive activation promote cellular growth, survival and autophagia regulation. The mTOR pathway can be inhibited directly through mTORC1 inhibition or indirectly by AMP-activated protein kinase (AMPK) activation.

Aim: This study aimed to assess the effects of sirolimus (SIR), an mTOR inhibitor, and metformin (MET), an AMPK activator, in three in vitro models of ALL.

Methods: B-ALL (697 and KOPN-8) and T-ALL (CEM) cell lines were incubated with SIR and MET in monotherapy. Metabolic activity was evaluated by resazurin assay. Cell death was assessed by optic microscopy (May-Grünwald-Giemsa) and flow cytometry (FC; Annexin V/7-AAD). Cell cycle was evaluated by FC (IP/RNase). The statistical analysis was performed, considering a significance level of 95%.

Results: Our results show that SIR and MET decrease metabolic activity in a time, dose and cell line dependent manner. CEM were the most sensitive cells to SIR and KOPN-8 cells show higher sensitivity to MET. After 72 h of incubation, IC50 of SIR was 1.4 μ M for CEM, 3.6 μ M for 697, and 8 μ M for KOPN-8 cells, while IC50 for MET was 6 mM for KOPN-8, 8 mM for CEM and 11.5 mM for 697 cells. Both drugs induced cell death by apoptosis. SIR also induced a cytostatic effect inducing cell cycle arrest in G0/G1 phase.

Conclusion: In conclusion, our results suggest that both, SIR and MET, may be potential new therapies in ALL. However, the therapeutic efficacy may depend on the ALL subtype.

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REPRODUCTIVE EFFECTS OF BISPHENOLS - ARE BPA ANALOGUES SAFER ALTERNATIVES?

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Introduction: Every day we are exposed to countless environmental contaminants, including endocrine disrupting chemicals (EDCs), which may be partly responsible for the rising incidence of infertility. [1] Bisphenol A (BPA) is one of the most ubiquitously distributed EDCs, coming its human exposure mainly from the diet due to the leaching from canned and packed foods. This EDC possesses estrogenic and anti-androgenic activities and has been detected in various biological matrices, including placental tissue, and thus, it may impact human endocrine function and fertility [2,3]. Growing global awareness has led international food safety authorities to demand its replacement by other bisphenols, as bisphenol AF (BPAF), whose effects in human health, including reproductive health, are unknown.

Aim: Assess the effects of an extensively distributed bisphenol (BPA) and of an alternative, presumably safer, BPA analogue (BPAF) in endometrial stromal cells, using environmentally relevant concentrations reflective of both acute and chronic human exposures.

Methods: Human immortalized endometrial stromal cell line St-T1b was used. Cell viability was assessed by the MTT/LDH assays, while cell proliferation was evaluated using SRB assay and cell cycle analysis, by flow cytometry. Cell morphology studies were conducted, namely Giemsa and Hoechst stainings. Caspase -3/-7 activity was assessed. Alterations in the expression of estrogen receptors alpha and beta were measured by western blot analysis.

Results: Both bisphenols showed contrasting effects. Drastic results were obtained for BPAF, which revealed dose-dependent anti-proliferative effects, exhibiting typical apoptotic features and alterations in the expression of estrogen receptors.

Conclusion: BPAF demonstrated hazardous characteristics not revealed by BPA, showing that the replacement of harmful EDCs by poorly studied structural analogues is a dangerous conduct, potentially causing a negative impact on human reproductive health. We believe that this study allows to clarify the consequences of human exposure to EDCs.

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HISTOPATHOLOGICAL PATTERN OF PRIMARY BONE TUMOURS IN CHILDREN - A 10-YEAR RETROSPECTIVE STUDY

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Introduction: Previous epidemiological studies have highlighted that primary bone tumours are relatively rare in contrast to other neoplasms. Nevertheless, the frequency of these tumours seems to rise when it comes to young people. Every so often, the patients might experience potentially devastating repercussions.

Aim: Our research aimed to establish the histopathological pattern of primary bone tumours diagnosed in a paediatric pathology department considering epidemiological data and the background reported in other studies.

Methods: The retrospective study is based on the medical records of 106 patients diagnosed with primary bone tumours at the "St. Mary" Emergency Hospital for Children in Iasi, Ro-

mania between 2009 and 2018. We analyzed the distribution according to age, sex, anatomical location and histopathological diagnosis. All the data were compiled due to SPSS 18.0 using adequate analysis.

Results: Over a period of 10 years, we identified 74 malignant tumours (69,8%) and 32 benign tumours (30,2%). The majority of our patients were diagnosed with osteosarcoma (OS), particularly children in the second decade of life (86,2%). The cases below 10 years old were considered to be rare (13,9%). The male to female ratio was 1.4:1 and the femur was the most frequently involved bone while the distal femoral metaphysis was the most relevant anatomical location, being followed by the humerus, fibula and the pelvis.

Conclusion: The results of our study regarding the distribution according to age, sex and anatomical sites are strikingly similar to previous reports in the medical field. The most frequent histological type was osteosarcoma, which generally occurs in males aged between 10 and 17 years. The pathologic examination of tumour samples is compulsory for the final diagnosis that guides the appropriate treatment according to the histological type.

Physiology & Immunology

EVALUATION OF THE SEROPROTECTION AGAINST HEPATITIS B AFTER VACCINATION IN LABORATORY STAFF MEMBERS

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Introduction: According to Global Hepatitis Report 2017 of the WHO 3,5% of the overall population lived with chronic Hepatitis B in 2015, most of them born before vaccination was widely available. Despite increasing coverage with three-dose Hepatitis B vaccine from 1% in 1990 to 84% in 2015 (Global Hepatitis Report 2017. World Health Organization), several publications (Gerlich 2013; Van Den Ende et al. 2017) report about seroprotection rates below 80% after vaccination.

Aim: The aim of the study was to evaluate the seroprotection of staff members of the Joint Laboratory of Pauls Stradiņš Clinical University Hospital against Hepatitis B and to find possible correlations with age and years since vaccination.

Methods: In 23 Hepatitis B vaccinated staff members of the Joint Laboratory of Pauls Stradiņš Clinical University Hospital the antibody-titer against Hepatitis B was detected (ARCHITECT anti-HBs, Architect systems). According to WHO recommendations a titer above 10mU/mL was considered to indicate seroprotection. In 20 cases where according data was provided statistical analysis regarding correlations between age or years since vaccination and titer or immunity was performed using SPSS.

Results: Out of 23 vaccinated staff members 7 (30%) presented without seroprotection against Hepatitis B. Even though the median years since vaccination of the immune staff members were 5 years less (immune: 10 years, not immune: 15 years) no significant correlation between age or years since vaccination and titer or seroprotection was found. **Conclusion:** The percentage of non-immunized subjects was with 30% unexpectedly high. Taking into account the everyday confrontation with potentially infectious material underlines the importance of control of the efficiency of Hepatitis B vaccination. The absence of significant correlations could also be explained by the small sample size.

THE THERAPEUTIC EFFECT OF CHRONIC SILDENAFIL SUPPLEMENTATION IN THE ZSF1 OBESE RAT MODEL OF HEART FAILURE WITH PRESERVED EJECTION FRACTION

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Introduction: Heart failure with preserved ejection fraction (HFpEF) is a syndrome with complex pathophysiology that already accounts for more than 50% of HF cases [1]. However, regarding their treatment, there are still no evidence-based therapeutic strategies. Although decreased protein kinase G (PKG) activity was proposed as a potential therapeutic option [2], results from randomized clinical trials with type-5 phosphodiesterase inhibitors (PDE5i) were discouraging [3]. Whether specific subgroups of HFpEF patients may benefit from PDE5i remains to be defined.

Aim: Our aim was to test chronic sildenafil (SIL) therapy in the young male ZSF1 obese rat model of HFpEF with severe hypertension and metabolic syndrome.

Methods: Sixteen-week-old male ZSF1 obese rats were randomly assigned to receive SIL 100 mg.Kg₁.d₁ dissolved in drinking water (ZSF1 Ob SIL, n = 8), or placebo (ZSF1 Ob PL, n = 8). We also evaluated healthy Wistar-Kyoto that served as control group (WKY, n = 8). Four weeks later animals underwent peak and endurance effort tests, haemodynamic evaluation under anaesthesia, aortic ring preparation and myocardial ATP quantification.

Results: ZSF1 Ob PL rats showed systemic hypertension and increased aortic and LV end-diastolic stiffness, with preserved ejection fraction compared to WKY. We also observed a decrease of their endurance capacity, as assessed by total workload and peak O2 consumption. In addition, LV ATP levels were also decreased. Chronic SIL treatment significantly attenuated hypertension and decreased aortic and LV stiffness, enhancing effort tolerance and restoring LV energetic resources.

Conclusion: Our results showed that chronic treatment with SIL effectively attenuated hypertension, preserved LV end-diastolic function and aortic vascular compliance, as well as improved endurance effort test performance. In conclusion, chronic SIL therapy has beneficial cardiovascular effects in this young male with poorly controlled comorbidities animal model of HFpEF, which support the implementation of clinical trials with PDE5i in HFpEF patient subgroups with similar features.

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EXAMINATION OF LEARNING CAPABILITIES ON MAM-E17 SCHIZOPHRENIA RAT MODEL IN PREPUBERTY, PUBERTY, AND ADULTHOOD

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Introduction: The widely accepted MAM-E17 schizophrenia rat model is based on the neurodevelopmental theory of the disease. In rats, the 17th embryonal day (E17) is critical in the development of the cortico-limbic circuits. Methylazoxymethanol-acetate (MAM) treatment on E17 leads to schizophrenia-like symptoms.

Aim: The aim of the experiments was the examination of cognitive skills of MAM-E17 rats in radial arm maze (RAM) test in prepuberty, puberty, and adulthood.

Methods: The examinations were performed on offsprings of pregnant dams injected intraperitoneally with MAM (or saline) on E17. The RAM apparatus composed of 8 arms, 4 of them contained reward (food). During conditioning phase the rats were placed into the apparatus for several days to find the rewards and learn their positions. Once the performance of the rats stopped improving, the location of the rewards was changed (reverse conditioning). The number of entries into the arms were registered and the errors of the rats were analyzed by two-way ANOVA.

Results: Entry into non-rewarding arms (ErrorI) or into the already visited arms (ErrorII) was enhanced by MAM-treated rats in the reverse paradigm in all age-periods. During conditioning, number of ErrorI and ErrorII was elevated only in puberty. In the reverse phase, empty arms which were rewarded in the conditioning phase (ErrorIII) were visited more frequently by the MAM-treated rats.

Conclusion: There was no significant group difference in the conditioning paradigm concerning Error I and II, reflecting appropriate learning capabilities and working memory of MAM-treated rats. By contrast, in reverse paradigm an elevated number of Error I and II was detected in MAM-E17 rats in each age-periods. This can indicate both long-term and working memory deficit. Presumably the deficient performance of MAM-E17 rats in reverse conditioning can be assigned to diminished behavioral flexibility and confusing effect of the new arrangement. Error III indicates perseveration.

C-REACTIVE PROTEIN AS A BIOMARKER IN NEWBORNS WITH CONGENITAL HEART DISEASE

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Introduction: Increased C-reactive protein (CRP) and inflammation are associated with congenital heart disease (CHD) in children and can be used to predict its complications.

Aim: The aim of this study was to evaluate CRP levels in newborns and determine whether inflammation has a role in CHD in this age group.

Methods: Data from 79 control and 49 CHD newborn patients was interrogated for a relationship between CRP and CHD subtypes. Within the CHD patients, the relationship between CRP, cardiac biomarkers and clinical parameters was also examined.

Results: CRP median concentration was significantly lower in CHD patients (0.20 mg/L) when compared to controls (0.50 mg/L) (p < 0.001). There was no significant difference in CRP levels between cyanotic CHD and acyanotic CHD (p > 0.999). Levels of creatinine kinase-MB were significantly higher in the cyanotic CHD group than in the acyanotic CHD group (4.80 vs. 3.8 ng/dL p = 0.049). CRP levels were increased in patients with O2 saturation $\leq 85\%$, however the correlation analysis was not significant between these parameters. CRP was not significantly increased in patients that underwent cardiac surgery. CRP correlated significantly with myoglobin (rho = 0.425 p = 0.003) and troponin I (rho = 0.476 p = 0.001).

Conclusion: Our results suggest that that myocardial strain- or hypoxia-driven inflammation is not established at the neonatal age. However, inflammation might be still be linked to early myocardial lesion or dysfunction, reflected by the correlation between CPR and myocardium injury biomarkers.

CRP levels were not associated with disease, disease subtypes, or with requirement for surgery, indicating that CRP is not a suitable biomarker for CHD at the neonatal age. It is still uncertain if CRP is involved in the pathophysiology or if it is a marker of severity of CHD. More studies are needed to determine from what age onwards could CRP be useful as a biomarker in CHD.

THE ROLE OF BEWO-DERIVED INTERMEDIATE-SIZED EXTRACELLULAR VESICLES IN REGULATORY T CELL DIFFERENTIATION

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Introduction: Regulatory T cells (Treg) are key players in the maintenance of immunotolerance during human pregnancy. The local cytokine milieu and HSPE1 have an impact on de novo Treg differentiation. The number and functional activity

of these cells are critical, however, the differentiation of these cells in the context of pregnancy is not fully understood. Extracellular vesicles (EVs) are lipid bilayer enclosed structures containing proteins and miRNAs, being recognized as important players of intercellular communication.

Aim: To examine the possible role of trophoblastic-derived EVs in their target CD4+ cells.

Methods: BeWo trophoblastic cell line was used as a model system. We isolated BeWo-derived intermedier-sized EVs by differential centrifugation (iEVs) and characterized the EV preparations according to the MISEV2018 guideline. For a deep molecular characterization, we applied omics approaches to describe the protein and miRNA content by mass spectrometry and next-generation sequencing, respectively.

Results: We identified 76 proteins in iEVs. STRING-based analysis showed that 36 proteins had immunoregulatory function and 30 proteins were involved in cell differentiation including the HSPE1 protein (validated by flow cytometry and immunodot analysis). The miRNA sequencing resulted in 517 miRNAs. The molecular function analysis identified cell differentiation as a main process that is triggered by the miRNA cargo. Additional in silico analysis showed that cell differentiation was mediated by signal transduction through the downregulation of interleukin 6 receptor (IL6R, GO:0005138) (padj = 0.02). Twenty one miRNAs target the IL6R through gene silencing of IL6ST and ERAP, including the hsa-miR-92a-3p (18170 \pm 5221 RPM), hsa-miR-520f-3p (5274 \pm 1002 RPM), hsa-miR-25–3p (5065 \pm 838.8 RPM), hsa-miR-519d-3p (3703 \pm 1261 RPM) and hsa-miR-26b-5p (1348 \pm 363.3 RPM).

Conclusion: Based on our preliminary results, we propose that the trophoblast-derived iEV-associated protein and miRNA cargo may orchestrate CD4+ T cell differentiation towards a regulatory phenotype.

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EFFECTIVENESS OF VOLUNTARY EXERCISE IN THE MECHANISM OF ACCELERATION OF COLONIC HEALING IN MICE WITH EXPERIMENTAL COLITIS. MEDIATING ROLE OF IRISIN AND ADIPONECTIN

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Introduction: Remarkable increase in the prevalence of Inflammatory Bowel Disease (IBD) comprising Crohn's disease and ulcerative colitis has been recently observed in countries characterized by,westernized" lifestyle. The cross talk between myokines released from exercising skeletal muscle such as irisin and adipokines such as adiponectin released from adipose tissue has been implicated in the pathogenesis of IBD. Besides pharmacotherapy, the physical acitivity has been proposed as additional therapy in IBD, however, the exact mechanism underlying its beneficial action remains unknown.

Aim: We attempted to investigate the influence of voluntary exercise (wheel running) on the course of experimental colitis including colonic blood flow (CBF), the expression of mRNA for proinflammatory cytokines in mesenteric fat and plasma levels of these markers, as well as plasma irisin and adiponectin concentrations.

Methods: Fifty mice fed standard diet (SD) and high-fat diet (HFD) were used in the study. After 6 weeks of exercise the experimental colitis was induced by intrarectal administration of 2,4,6-trinitrobenzenesulfonic acid.

Results: The colitis was aggrevated in HFD fed sedentary mice as manifested by a significant increase of mucosal damage, the decrease in CBF and a significant increase in the levels of proinflammatory markers such as TNF- α , IL-6 and leptin. These changes were accompanied by the reduction in plasma levels of irisin and adiponectin. These effects observed in HFD sedentary mice were reversed in voluntary- exercising mice because the index of mucosal damage and the plasma cytokine proinflammatory status were significantly decreased while the CBF and the plasma levels of adiponectin and irisin were significantly increased.

Conclusion: We conclude that a voluntary physical activity exerts beneficial effect on the course of colitis in mice fed HFD by mechanisms involving increase in the CBF and upregulation of protective and anti- inflammatory irisin and adiponectin resulting in healing acceleration of colonic mucosa.

RELATIONSHIP BETWEEN SINGLE NUCLEOTIDE POLYMORPHISM AND AN INCREASED PREDISPOSITION TO ACHILLES TENDON RUPTURE. A GENETIC STUDY

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Introduction: Achilles tendon (AT) rupture is a very serious injury and requires long-term treatment. It may be a consequence of physical activity or may occur at rest. Nevertheless, genetic factors might be associated with a higher susceptibility for tendinopathy. Single nucleotide polymorphisms (SNPs) of matrix metallopeptidase 1 (MMP1), matrix metallopeptidase 3 (MMP3), as well as COL5A1, and COL12A1 genes may have an impact on the tendon's biomechanical properties.

Aim: The aim of this study is to evaluate the relationship between the defined SNPs and the biomechanical features of the AT, analysed by the stress test.

Methods: The study involved 50 ATs acquired from 25 male patients. The DNA was extracted using Xpure Genomic Mini. Primer3Plus computer software was utilised to design the PCR primers of 5 DNA variants: rs970547, rs240736 in COL12A1, rs12722 in COL5A1, rs1799750 in MMP1 and rs3025058 in MMP3. The PCR products underwent single base extension reactions, were purified with FastAP Thermosensitive Alkaline Phosphatase and analysed on a Genetic Analyzer. The biomechanical analysis involved the AT's separation into 3 subtendons and evaluation using the INSTRONâ tension testing machine. The stiffness was assessed in terms of its Young's modulus and calculated from the strain curves.

Results: The genetic and biomechanical analysis revealed a strong correlation between the SNPs and greater endurance of the AT's in terms of the rs240736 and the rs1799750 polymorphisms. Moreover, some association was noticed in variant rs3025058, however its significance was imprecise and requires further research. The remaining SNPs did not provide any statistically significant evidence for the association. **Conclusion:** There is a significant correlation between SNPs and biomechanical features of the AT. Data included in this study could be combined with data on other musculoskeletal injuries in a cross-phenotype meta-analysis to find SNPs associated with musculoskeletal injuries in general and enable improving patient care.

DOES TASTE PREFERENCE CHANGE IN PATIENTS AFTER COLORECTAL CANCER SURGERY?

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Introduction: Enhanced Recovery After Surgery (ERAS) protocol, which is widely used in colorectal surgeries, comprises nutrition as a key component. Changes in food preferences are often reported as reasons for patients not tolerating full oral diet in the early postoperative period. However, little data is available about short term changes in taste after surgery.

Aim: We aimed to evaluate short-term changes in taste preference after colorectal surgeries.

Methods: Between April 2018 and April 2019, 63 patients who underwent colorectal surgeries were included. Patients who developed clinical complications requiring restriction of oral intake after surgery or withhold their consent were excluded from the study. In the end, 46 patients were included. In all of them the 16-item ERAS Protocol was applied. Using 10-points Numeric Rating Scale (1–10) patients completed questionnaire and rated flavoured standardized liquids' taste and food images for the 6 group of taste (sweet, umami, sour, spicy, bitter and salty) preoperatively and on the first postoperative day. Data were analysed with Statistica 13.0 PL.

Results: Analysed group consist of 46 patients (19 females, 27 males). Mean age was $61 \pm 11,75$ years old. Changes in rating of flavoured liquids were revealed only in bitter sample (1-horrible, 10-very tasty; 4 [3–5] vs. 5 [3–7], p < 0,05). There were also changes in ratings for spicy food image, patients marked it as less appetizing after surgery(1 - not appetizing, 10 - very appetizing, 7 [5–8] vs. 5 [3–8], p < 0,05). There were no statistically significant results in the ratings of other liquids or images.

Conclusion: The study showed that although colorectal surgery does not influence patients' taste perception, it quickly decreases theoretical desire to eat certain types of food. No changes in all the individual tastes, with the exception of bitter, in the postoperative period were observed. The topic requires further analysis.

URINARY MIRNA-21 AS POTENTIAL BIOMARKER OF INTERSTITIAL FIBROSIS AND TUBULAR ATROPHY (IFTA) IN KIDNEY TRANSPLANT RECIPIENTS.

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¹Department of Transplantation Medicine, Nephrology and Internal Medicine, Medical University of Warsaw, Warsaw, Poland; ²Department of General and Transplantation Surgery, Medical University of Warsaw, Warsaw, Poland **Introduction:** Chronic renal allograft dysfunction (CAD) is a major limiting factor of long-term graft survival. The greatest hallmarks of progressive CAD are interstitial fibrosis and tubular atrophy (IFTA).

Micro RNAs (miRNAs) are small endogenous, regulatory RNAs consisting of about 19–25 noncoding nucleotides, which have been involved in many immunological processes including inflammation and fibrosis. Particularly, miR-21 seems to be strongly associated with renal pathogenesis regarding tubulointerstitium.

Aim: The aim of this study was to evaluate urinary miR-NA-21 expression levels and assess their application in the prospective evaluation of renal allograft function.

Methods: The expression levels of miRNA-21 were quantified in urine of 24 kidney recipients with biopsy proven IFTA (IFTA I: n = 10; IFTA II: n = 8; IFTA III: n = 6) and 7 kidney recipients without IFTA by real-time quantitative PCR. Urine samples were collected at the time of protocolar biopsies which were performed 1 or 2 years after kidney transplantation. MiRNA-191 was used as reference gene for miRNA-21 expression levels normalization. Correlations between the clinicopathological parameters and the level of expression of miRNA-21 were evaluated.

Results: MiRNA-21 was significantly up-regulated in IFTA III group compared to IFTA 0 group (p = 0.04; Dunnett's test). There was significant correlation between expression levels of miRNA-21 and serum creatinine (r = -0.52, p = 0.003) as well as eGFR (r = 0.45; p = 0.01).

Conclusion: MiRNA-21 is associated with the renal allograft dysfunction and severe IFTA. Therefore, it could be considered as potential diagnostic, non-invasive biomarker for monitoring of renal graft function.

DESCRIPTION OF HISTOCHEMICAL PROPERTIES OF NIPPLE – AREOLAR COMPLEX IN BREAST, USING MODIFIED MOVAT'S PENTACHROME METHOD

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Introduction: Integumentary system is composed of skin and its' regional specializations, which include structure located in the middle of the breast: nipple - areolar complex.

This complex is composed of raised region of tissue on the surface of the breast with 10 - 15 openings of lactiferous ducts – nipple (mamilla), and peripheral discoid structure which is separated from the rest of the thin skin with areolar limbus – areola.

Aim: The aim of this work was to use modified Movat's pentachrome method to mark and describe the structure and histochemical properties of areolar region of breast and the surrounding skin, with special review of distribution and qualitative properties of collagen and elastic fibers, as well as smooth muscle cells and mast cells.

Methods: The research was based on the unaltered tissue samples of breast areola and surrounding skin, excised from 10 amputates of breast from female patients with mammary gland carcinoma. The samples were stained with modified histochemical Movat's pentachrome.

Results: The number and the diameter of smooth muscle bundles in breast areola declines from perimammillary region towards periphery of samples, however with presence of solitary, narrow bundles even 1 cm peripherally to areola limbus. Fibroelastic components of reticular dermis are relatively constant between perimammillary region and sample periphery. Mast cells are located in the perivascular space and also in parts of reticular dermis surrounding bundles of smooth muscle cells.

Conclusion: Modification of Movat's pentachrome method, used for staining of nipple-areola complex, gives the widest range of histochemical results and visualization of tissue structures.

SERUM IRON PARAMETERS AS POSSIBLE INDICATORS OF HIV+ PATIENTS PREMATURE AGING

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Introduction: The human immunodeficiency virus (HIV) is one of the most complex virus which attacks CD4+ lymphocytes. It has been found that HIV leads to accelerated aging in the population, but the causes that lead to it have not yet been clarified. The development of AIDS is accompanied by an increasing iron accumulation in macrophages, microglia, endothelial cells, brain white matter, muscle and liver, so the question arises as to whether this disorder is one of the possible factors leading to premature aging due to HIV infection in humans.

Aim: The aim of this paper was to determine iron metabolism parameters and, by comparing with alredy established biomarkers of aging determine, whether certain parameters of metabolism of iron could be indicators of biological aging of the organism.

Methods: In this cross section study, 48 patients older than 18 years, who are HIV+ and who have been using at least 12 months of combined antiretroviral therapy (cART: 2NRTIs+N-NRTI or 2NRTIs+PI) have been included. RTL (relative telomere length) was estimated by Real-time PCR. Iron metabolism parameters are determined using the Biosystem Photometer BTS-330 (Barcelona, Spain) according to the manufacturer's recommendations.

Results: We found a statistically significant correlation between the serum iron concentration and the relative length of the telomere (p = 0.034) and the statistically significant relationship between transferrin saturation and the relative length of the telomere (p = 0.031).

Conclusion: In this paper, we have shown that the concentration of serum iron and the transferrin saturation level are iron metabolism parameters that can be considered as biomarkers of aging.

ANGIOTENSIN II-INDUCED CONTRACTION OF THE COLON: A STUDY IN AN EXPERIMENTAL MODEL OF INFLAMMATORY BOWEL DISEASE

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Aim: To explore a putative role of purinergic receptors on Ang II-induced contraction of the colon of control and TNBS-induced rats.

Methods: Protocols were approved by institutional and national competent authorities. Male Wistar rats (8 to 12 weeks-old) were rectally instilled with TNBS (20 mg/rat in a 30% ethanolic solution) or used as controls. After 7–8 days, the rats were euthanized, and three segments of the colon were mounted longitudinally in organ baths: proximal colon (PC, without macroscopic lesion), upstream distal colon (UDC, upstream the macroscopically lesioned area) and terminal distal colon (TDC, downstream the macroscopically lesioned area). Isometric responses to Ang II were obtained in the absence and presence of caffeine (300 μ M) or suramin (100 μ M) to block of adenosine and ATP receptors respectively. Paired Student's t test was used for statistical analysis.

Results: Neither caffeine nor suramine changed Ang II-induced contraction of either segment of the colon mechanisms (p > 0.05 for all).

Conclusion: Ang II-induced contraction of the rat colon is not mediated by activation of purinergic receptors neither in control nor in TNBS-induced rats.

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COMPARISON OF METABOLIC AND HORMONAL CHANGES IN IDIOPATHIC AND NON-IDIOPATHIC PREMATURE OVARIAN INSUFFICIENCY

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Introduction: Currently premature ovarian insufficiency (POI) is a challenging disease, with limited knowledge of hormonal and metabolic profiles.

Aim: This study determined metabolic and hormonal differences between women with the idiopathic POI and non- idiopathic POI caused by well-known reason.

Methods: One hundred two women with POI were enrolled to one of the following groups: 1) idiopathic POI (n = 81) and 2) non-idiopathic POI (n = 51). Hormones (including estradiol, testosterone, follicle-stimulating hormone -FSH), lipidogram and both glucose, and insulin levels indicated during oral glucose tolerance test (OGTT) were marked in all women.

Results: The two groups did not differ regarding age, body mass index (BMI), FSH and estradiol levels. In the idiopathic POI group, we noticed lower total cholesterol (by -7.8%), tri-glycerides (by -28.5%) and low-density lipoprotein cholesterol (by -9.7%) than non-idiopathic POI group. In contrast to women idiopathic POI, women with well-known cause of POI, had 2.2 – times higher baseline insulin levels (15.75 vs 7.05). **Conclusion:** Our study showed that women with idiopathic POI have favorable lipid profile than woman with non-idiopathic POI what may have beneficial effect on cardio-vascular system.

ENDOCAN, A NOVEL ENDOTHELIAL DYSFUNCTION BIOMARKER, IS ASSOCIATED WITH VENTRICULAR DYSFUNCTION, INFLAMMATION AND WORSE HEMODYNAMICS IN HUMAN ACUTE HEART FAILURE

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Introduction: Acute heart failure (AHF) remains a major health problem, bearing high mortality and morbidity rates. Recent studies suggest that inflammation and endothelial dysfunction contribute to the development and progression of AHF. Endocan is a proteoglycan synthesized and secreted by the activated vascular endothelium. Although endocan is increasingly being recognized as an endothelial dysfunction biomarker, its role in AHF has seldom been investigated.

Aim: To evaluate serum endocan in human AHF and to determine its correlation with cardiac dysfunction/injury, inflammation and systemic hypoperfusion in human AHF.

Methods: This study is approved by the Health Ethics Committee of CHSJ. Patients with diagnosis of AHF (n = 11) and cardiogenic shock (CS) (n = 9) were included and blood samples were collected at days 1–2 (admission), days 3–4 and days 5–7. Blood donors were used as controls (n = 10). Serum endocan and myeloperoxidase (MPO) were measured with ELISA kits. Ventricular dysfunction was assessed by echocardiography and systemic B-type natriuretic peptide (BNP), high-sensitivity troponin I, C-reactive protein (CRP) and lactic acid were evaluated using automated analyzers.

Results: Endocan and MPO were significantly increased in both AHF and CS patients [endocan, ng/mL, controls: 1.9 ± 0.3 ; AHF: 8.8 ± 3.7 ; CS: 0.0 ± 3.8 , p < 0.01 (AHF) or p < 0.001 (CS) vs controls; MPO, ng/ml, controls: 115.6 ± 18.9 ; AHF: 349.4 ± 57.7 ; CS: 461.4 ± 121.8 ; p < 0.01 (AHF and CS) vs controls]. Lactic acid was significantly higher in CS than in AHF patients (5.99 ± 1.91 vs 1.86 ± 0.27 mmol/L, p = 0.027). Endocan was significantly positively correlated with BNP (r = 0.51, p = 0.006), MPO (r = 0.420, p = 0.001) and lactic acid (r = 0.55, p = 0.024). Moreover, when patients were stratified according to ejection fraction (EF), endocan (ng/mL) significantly increased in line with the degree of EF impairment (preserved/mildly impaired: 2.4 ± 0.6 ; moderately impaired: 9.8 ± 2.5 ; severely impaired: 18.4 ± 4.2 ; p = 0.014, preserved/mildly impaired vs severely impaired).

Conclusion: Endocan is significantly associated with the deterioration of ventricular function, inflammation and worse hemodynamics in human AHF.

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DEVELOPMENT OF AN ANTIGEN DELIVERY PLATFORM BASED ON AIP56

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Introduction: Bacterial AB toxins are potent virulence factors possessing a bi-modular structure. They comprise a catalytic A domain targeting eukaryotic cells' components and a B domain that binds cell surface receptors and translocates the A domain to the cytosol. AIP56 (Apoptosis Inducing Protein of 56 kDa) is an AB toxin with great biotechnological potential, due to catalytic activity towards NF-kB p65 and a specificity for mouse and human most relevant antigen presenting cells (APCs). Replacing its catalytic domain with an antigen may turn AIP56 into a potent antigen delivery platform to the cytosol of APCs. Several uncharacterized toxins with homologous AIP56's B domain were identified and may be used as alternative shuttles, circumventing any eventual immunogenic reaction against the shuttle.

Aim: Currently used strategies for antigen-toxin fusion rely on genetic engineering and heterologous expression/purification of the recombinant fusion. Indeed, the delivery of beta-lactamase and Diphtheria catalytic domain to the cytosol of APCs has been already achieved in our lab by genetically fusing those moieties to AIP56's B domain. However, genetic fusion of antigens to toxins may have downsides such as rendering instable chimeras.

Methods: In the present project, we developed a novel and flexible antigen delivery platform based on the B domain of AIP56 as shuttle using Sortase A mediated reactions and the SpyCatcher-Spytag system to bind a proof-of-concept antigen as beta-lactamase, which provides an easy read-out through FRET.

Results: Moreover, competition assays using AIP56 and the aforementioned uncharacterized toxins were performed in a mouse-immortalized bone marrow macrophages cell line and analyzed through flow cytometry, showing that these toxins share AIP56's receptor and could be used as alternative vehicles.

Conclusion: This proof-of-concept demonstrates that AIP56 has potential for antigen delivery into the cytosol of APCs, eventually stimulating a cytotoxic T lymphocyte-mediated response, much needed to potentiate vaccination strategies against cancer and intracellular pathogens.

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PERCENTAGE REPRESENTATION OF BROWN AND WHITE ADIPOSE TISSUE IN VISCERAL AND SUBCUTANEOUS DEPOTS IN THREE DIFFERENT RODENT SPECIES

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Introduction: Morphometric analysis and the determination of percentage representation of different adipocyte types can be of great importance when studying the function of adipose tissue.

Aim: To determine and compare the percentage of brown (BAT) and white (WAT) adipose tissue in visceral and subcutaneous depots in laboratory mice (NMRI strain), Syrian golden hamster (Mesocricetus auratus) and laboratory rat (Wistar strain).

Methods: The study involves twelve experimental animals, divided by species into three groups of four individuals (two male and two female). After the sedation of animals, transcardial perfusion fixation was carried out, adipose tissue from nine regions were isolated, and further fixed and dehydrated. The sections were stained with hematoxylin-eosin and immunohistochemical mitochondrial marker COX IV. The preparations were photographed and morphometrically analyzed. Obtained results were processed with one-way ANOVA and MANOVA statistical tests.

Results: Histological analysis revealed qualitative similarity of BAT and WAT between species, with the exception of mice with white adipocytes of a smaller diameter. Brown adipocytes of all three species were positive for mitochondrial marker COX IV. Statistical analysis of total BAT and WAT tissue present on histological slides showed that there was no significant difference between species and sexes within species. In all three species, WAT completely fulfills inguinal, mesenteric, retroperitoneal and epididymal/periovarial regions, while axillary, subscapular, interscapular and perirenal regions are made of mixed BAT and WAT. Comparing the presence of BAT between species, a significant difference was found, depending on the adipose tissue region in which BAT is located.

Conclusion: Determination of percentage of BAT and WAT in healthy mice, hamster and rat species in different fat depots can set the basis for further development of experimental models of metabolic disorders and obesity.

DIVING-RELATED CHANGES IN FLOW-MEDIATED DILATION

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Introduction: Endothelial dysfunction is considered to be one of the most prominent risk factors in the development of decompression sickness – one among the most frequent diving-related complications. Vascular endothelial function can be determined by a non-invasive method, estimating the arterial flow-mediated dilation (FMD).

Aim: The aim of this study was to compare the pre-dive and post-dive values of FMD and observe the diving-induced changes in the endothelium-dependent vasodilator function.

Methods: Twelve male divers were recruited for this study, who performed a single-dive at a depth of 18 m with a 47-min bottom time and two-minute ascent to surface without any decompression stops. Endothelium-dependent vasodilator function of the brachial artery was assessed pre-dive and post-dive using a rapid inflation and deflation blood pressure cuff and a vascular ultrasound system with the belonging computer software. The measurements included the baseline diameter, peak diameter, time to peak diameter, shear rate and the absolute and relative values of FMD. Kolmogorov-Smirnov test and RM-ANOVA test were used to process all the data.

Results: Statistically significant (p < 0.05) decrease was observed in the absolute and relative values of FMD post-dive, paralleled with the same changes in shear rate. Post-dive baseline diameter, peak diameter and time to peak diameter showed no statistically remarkable changes ($p \ge 0.05$).

Conclusion: There are significant changes in the endothelium-dependent vasodilator function of the brachial artery related to SCUBA diving, and we suppose that these modifications are result of the cumulative effects of different diving-related factors, first of all hyperoxic and hyperbaric conditions, which lead to the damage of the endothelial function, presumably by modifying the bioavailability of nitrogen monoxide.

THE INFLUENCE OF THE TYPE OF TRAINING ON ANTHROPOMETRIC CHARACTERISTICS AND BIOCHEMICAL PARAMETERS IN ATHLETES

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Introduction: Athletes represent a specific population enrolled with active and intensive systemic physical activity, which is leading to a series of adaptations in organism, organs, tissues and cells. Depending on the type and intensity of physical activity, exercising can be divided into dynamic and static or aerobic and anaerobic, respectively. Skill sports are consistent of sports with low static and low dynamic component so they cannot be classified as aerobic neither as anaerobic sports. Meanwhile, power sports are consistent of sports with high static component and are classified as anaerobic.

Aim: Evaluation of the influence of the type of training on anthropometric characteristics and biochemical parameters between skill sports and power sports.

Methods: In this study participated 70 male athletes, divided into two groups of sports: skill sports (auto racing, motor sports, shooting, archery, golf and bowling, n = 42, mean age 24.8 ± 5) and power sports (weightlifting, bodybuilding and wrestling, n = 28, mean age 26.1 ± 3,9). The following parameters were measured: anthropometric (body height, body mass, body mass index-BMI, percentage of muscles, percentage of body fat-%BF, body surface) and biochemical (glycaemia, cholesterol, triglycerides, urea, creatinine, hemoglobin, hematocrit, aspartate-aminotransferase-AST, alanine-aminotransferase-ALT, total plasma proteins, serum iron, total and direct bilirubin).

Results: Body mass, BMI and percentage of muscles were significantly higher in the group of power sports, while %BF was significantly higher in the group of skill sports. As it con-

cerns biochemical parameters, creatinine and urea were significantly higher in the group of power sports, while total plasma proteins, hemoglobin and hematocrit were significantly higher in the group of skill sports. Other measured parameters were not of statistically significant difference.

Conclusion: Noticed differences in measured parameters can be explained by the specific influence of different type of training/sports on organism, leading to adaptive changes in an-thropometric and biochemical parameters.

THC IMPAIRS 2-ARACHIDONOYLGLYCEROL METABOLIC ENZYMES IN PLACENTAL EXPLANTS

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Introduction: Cannabinoids are compounds produced by the Cannabis sativa, being Tetrahydrocannabinol (THC) its major psychoactive substance. Cannabis consumption has been increasing for recreational or medical use and also during gestation, where it is associated with low birth weight, prematurity and intrauterine growth retardation. However, the underlying biochemical mechanisms are unknown.

Aim: Our group has previously described the impact of THC on anandamide (AEA) placental homeostasis. In this work we explore THC actions upon the other major endocannabinoid, 2-arachidonoylglycerol (2-AG), whose levels are crucial for placental development.

Methods: Term placental explants were exposed to 10–40 μ M of THC for 24 and 72 h. The 2-AG synthetic enzyme diacylglycerol lipase (DAGL) and the degrading enzymes monoacylglycerol lipase (MAGL) and alpha beta hydrolase domain 12 (ABHD12) expression was analyzed by western blot and qRT-PCR.

Results: THC impaired the expression of 2-AG metabolic enzymes, being the results dependent on time of exposure. At 24 h, it was verified an increase in both DAGL and MAGL expression at 40 μ M. With 72 h of treatment, DAGL expression was unaffected, while MAGL decreased with the studied concentrations. Moreover, an increase in ABHD12 expression with 40 μ M of THC was observed at 72 h.

Conclusion: It is known that endocannabinoids have an essential role in placental development. THC impaired 2-AG metabolic enzymatic machinery. The alterations are dependent on time of exposure, being dramatically altered at 72 h. Surprisingly, while DAGL levels were not affected, MAGL expression was strongly diminished and the new player ABHD12, for the first time detected in placental tissues, took over its role in 2-AG degradation. As consequence of THC impact, 2-AG levels disturbance, may explain some of the negative effects in pregnancy related to cannabis consumption.

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THE IMPACT OF TREATMENT ON ADULT PATIENTS WITH COMMON VARIABLE IMMUNODEFICIENCY: SINGLE CENTER EXPERIENCE

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Introduction: Common Variable Immunodeficiencies (CVIDs) represents the most common, symptomatic primary immunodeficiency in adults.

Aim: To compare the impact of transfer from intravenous (IVIG) to subcutaneous administration of immunoglobulins (SCIg) on the quality of life and symptoms in case series of patients suffering from CVID.

Methods: Eleven CVID patients, five females and six males, treated at the single center were analyzed. Lymphoproliferative phenotype with splenomegaly and lymphadenopathy was in 6/11 cases, autoimmune phenotype was observed in 3/11 patients. Initially all patients received IVIG, while two years ago five patients were transferred to SCIg administration. Clinical phenotype, trough levels of serum immunoglobulins, were assessed in the whole group, while the quality of life was estimated in nine available patients using questionnaire designed in 2016 specifically for CVID patients (CVID QoL). After initial CVID QoL evaluation two years ago, five patients that had transferred to SCIg administration had been rechallenged to the same questionnaire.

Results: No matter the route of immunoglobulin administration, all cases had a serum through levels between 6–8 g/l, except the patient with lymphoproliferative phenotype, massive splenomegaly and weight loss whose immunoglobulin level was below 5 g/l. All cases except one with immune thrombocytopenia suffered from recurrent chronic sinusitis and occasional diarrheal syndrome, while one of them suffered also from recurrent pneumonias due to bronchiectasis. Patients who had passed from IVIG to SCIg administration maintained serum through levels within a same range. CVID QoL questionnaire revealed no difference in emotional, gastrointestinal and skin symptom dimensions results among patients. Patients receiving SCIg that were rechallenged to the same CVID QoL questionnaire had improved the fear of therapeutically adverse effects, fear of infection and need for isolation.

Conclusion: Transferring CVID patients from IVIG to SCIg route of administration had no influence on disease status but insignificantly improved some aspects of the quality of life.

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CHANGES OF GLYCOGEN CONTENT IN HEART OF EXPERIMENTAL DIABETIC RATS AND ADMINISTRATION OF MELATONIN

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Introduction: Diabetes may cause myocardial cell damage and eventually lead to the development of diabetic cardiomyopathy (DCM). The main characteristics of DCM include oxidative

stress, cardiac hypertrophy, apoptosis, myocardial fibrosis and impaired cardiac function. Melatonin, a potent antioxidant agent, is essential for glucose homeostasis and regulation.

Aim: Therefore, the aim of the present study was to investigate the effects of melatonin against DCM in a rat model of diabetes and the possible mechanism.

Methods: The experiments were carried out on 24 sexually mature male albino rats with the body mass – (0,18 - 0,20) kg. Alloxan diabetes was evoked via injecting with a 5% solution of alloxan monohydrate intraperitoneally in a dose of 170 mg/ kg of body weight (b.w.). The animals were divided into three subgroups: 1) control group; 2) diabetic rats; 3) diabetic animals which were introduced the melatonin preparation intraperitoneally in a dose of 10 mg/kg of b.w. at 8 a. m. daily during 7 days starting with a 5th day after the injection of alloxan. The splitting of heart muscle tissue with 30% solution of KOH, followed by the addition of ethanol and cooling, precipitate of glycogen has fallen. Glycogen content.

Results: We have established reduction of glycogen in the heart muscles of diabetic animals by 20% compared with the control. Such changes are likely occurred because of a decreasing in revenues of glucose in heart muscle tissue and inhibition of its use. According to our research, week daily administration of melatonin to diabetic rats at 10 mg/kg of b.w. normalized heart muscle glycogen content.

Conclusion: The positive impact of melatonin probably mediated by improved of glucose utilization due to increased capture of tissues and activating major enzymes of gluconeogenesis.

ANALYSING PROTEOME DATA FOR DROSOPHILA MODELS OF HUMAN PRIMARY CILIARY DYSKINESIA

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Introduction: Primary ciliary dyskinesia (PCD) is a rare genetic disorder that affects motile cilia. Defective cilia cannot clear mucus from airways, resulting in recurrent respiratory tract infections. Approximately 40 gene mutations associated with PCD have been identified to date. Dynein motors are responsible for cilia motility and must be preassembled in the cytoplasm before being transported to the cilium. This process requires dynein axonemal assembly factors (DNAAFs), although their mechanism of action remains unclear.

Aim: To confirm the role of CG17669, Wdr92 and CG6980 as DNAAFs and explore their biochemical function.

Methods: We analysed proteomic data from three Drosophila mutants, CG17669, CG6980 and Wdr92, with mutations in genes that encode either known or suspected DNAAFs. We hypothesised that analysing the differences in protein levels among Drosophila bearing mutations in DNAAFs would clarify the biomolecular mechanisms involved in dynein assembly.

Results: The subsequent enrichment analysis of differentially expressed proteins appears to confirm the roles of the investigated proteins as DNAAFs, although their mechanisms of action and the pathways in which they are involved remain unknown.

Conclusion: Our findings showed that dynein assembly is the primary function of these three proteins and, for the first time, provides evidence that CG6980 works as a DNAAF.

Porto Biomedical Journal

WOMEN WITH PREMATURE OVARIAN INSUFFICIENCY VERSUS POSTMENOPAUSAL WOMEN: HORMONAL AND METABOLIC PROFILES

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Introduction: Little is known regarding the hormonal and metabolic status among women with premature ovarian insufficiency (POI) in comparison to women after menopause.

Aim: This study evaluated differences in sex hormones, glucose metabolism and lipid profile in postmenopausal woman depending on the age ranges in which the menopause had occurred.

Methods: In this retrospective case-control study two hundred fifty women were assigned to one of the following groupswith: 1) POI, age below 40 yrs (n = 101), 2) early menopause, age beteen 40–45 yrs (n = 49) 3) postmenopausal, age over 45 yrs (n = 78). Sex hormones (including estradiol and testosterone), lipid profiles, glucose and insulin levels marked during oral glucose tolerance test (OGTT) were determined among all participants.

Results: The final analysis included 228 women. Women with POI (aged 29.6 - 6.9) had lower body mass index (BMI) than early- and postmenopausal women (-8.8% and -8.4%, respectively). The three groups did not differ regarding follicle stimulating hormone (FSH), estradiol (E2) and testosterone concentrations. In the POI group we observed lower total cholesterol (TC) levels when compared to the postmenopausal group (-10.4%) and lower low-density lipoprotein cholesterol (LDL-C) in contrary to both early and postmenopausal groups (-16.7% and -16.3% respectively). Post hoc analysis revealed that postmenopausal group had higher fasting plasma glucose levels than women with POI (+19.3%) and women with early menopause (+31.1%). In contrast to the early and postmenopausal group, women with POI had higher insulin levels after 60 (+30.2% and +21.7% respectively) and 120 minutes (+45% and +29.3% respectively) of OGTT.

Conclusion: In contrast to early- and postmenopausal participants, women with premature ovarian insufficiency had better lipid profile expressed by lower both TC and LDL-C levels. However, they represented worse glucose and insulin metabolism. Our data shows evidence that women with POI, alongside postmenopausal women, are at risk of abnormal metabolic profile.

Public Health & Medical Informatics

THE INJURIES OF THE NECK'S INTERNAL STRUCTURES IN CASES OF SUICIDE BY HANGING-ANALYSIS OF THE TYPES AND THE FREQUENCY

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Introduction: Suicidal death by hanging is caused by an asphyxia secondary to mechanical compression of the main blood vessels of the neck. It can result in various mechanical injures of neck's internal structures. Evaluation of them may be useful in forensic investigation. Nonetheless, there is a discrepancy in the literature concerning a frequency of the particular injuries.

Aim: The objective of the study is to determine the frequency and types of the internal neck injures associated with the suicide by hanging.

Methods: There were 1373 cases of suicide by hanging in the archives of the Department of Forensic Medicine of Jagiellonian University in Cracow between 2008–2018. 1294 of them had documented full forensic autopsies, which were analyzed in terms of types of internal neck injuries and their locations.

Results: We found 1082 cases with the internal injures of the neck (83,88 %), 1036 with the hemorrhages in the sternocleidomastoid muscle (80,37%), 141 cases of thyroid cartilage fracture (10,91%), 131 cases of hemorrhage in other internal parts of the neck (10,13%), 88 cases of hyoid bone fracture (6,81%), 16 cases of the carotid artery damage (1,24%), 16 cases of vertebrae fractures (1,24%), 7 cases of sternocleiodmastoid muscle rupture. The cases with the hyoid bone fracture were significantly older than the other cases (51,89 vs 47,22 p < 0,05). The hyoid bone and the thyroid cartilage fractures were independent of each other (p < 0,05).

Conclusion: The internal injures of the neck associated with hanging are very common but the occurrence of the particular injuries is widely diversed. The low prevalence of cartilage and bone fractures may indicate that causing death asphyxia is secondary to compression which is generated only by the gravity associated with the body weight. A higher frequency of the hyoid bone fractures in older people is probably due to the bone degeneration process associated with aging.

PATIENTS' ASSESSMENT OF TREATMENT BURDEN IN ATRIAL FIBRILLATION

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Introduction: Oral anticoagulation (OAC), using either vitamin K antagonists (VKAs) or non-VKA OAC (NOACs), is the cornerstone of thromboprophylaxis in atrial fibrillation (AF). Safety and efficacy of OAC strongly depend on adherence to treatment. Whereas several determinants of good adherence have been described, patients' perception of OAC-related treatment burden (TB), which could significantly influence the adherence, is largely unknown (hence, neglected by physicians).

Aim: Using a 7-item questionnaire, which has been validated among patients with chronic conditions (but not AF), we investigated the TB in AF patients.

Methods: A single-centre, prospective study included consecutive adult AF patients seen during May 2019. Patients voluntarily and anonymously answered the questionnaire; their demographic and disease-related data were retrieved from medical records; TB was calculated as a sum of points (range 0–10) assigned by patients to each of the questions (maximum score = 170).

Results: Of 179 patients (mean age 65.8 \pm 9.6 years, 56.4% males), n = 166 (92.7%) were taking an OAC (n = 89, 49.7% VKA). The mean number of comorbidities and concomitant drugs was 2.66 \pm 1.74 and 6.13 \pm 2.52, respectively. Total TB was 32.74 \pm 26.11, being greater in patients on OAC (33.03 \pm 27.13) than in those not on OAC (29.08 \pm 21.05). Among patients on OAC, the highest TB was related to medications other than OAC (5.44 \pm 8.04), followed by arranging the

appointments (4.40 \pm 4.05), paperwork (4.11 \pm 4.13) and OAC itself (4.02 \pm 7.14). Notably, total TB was significantly lower in patients on NOAC (25.38 \pm 20.50) than in those on VKAs (37.58 \pm 29.19), p = 0.001.

Conclusion: Our study is the first to report on TB in AF patients. Given the key importance of adherence to OAC for effective stroke prevention in AF patients, identifying total TB and addressing its main drivers should be integral part of holistic management of AF patients. Further research is needed to confirm whether our finding can be translated to other AF cohorts.

MODULATORY EFFECT OF THE INFLAMMATORY POTENTIAL OF DIET ON THE RELATIONSHIP BETWEEN AIR POLLUTION AND ASTHMA IN CHILDREN: EVIDENCE FROM A CROSS-SECTIONAL STUDY

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Introduction: Inhalation of fine particulate matter (PM) can cause systematic inflammation and oxidative stress, which may further aggravate the development and progression of asthma. Although nutritional intake of fatty acids and antioxidants may attenuate some effects of fine PM, the role of overall dietary intake has not been studied.

Aim: To investigate possible modulatory effects of dietary inflammatory potential on the association of indoor air pollution and childhood asthma-related outcomes.

Methods: In a sample of 501 children (48.1% males, aged 7 to 12 years) from 20 local schools located in city of Porto, Portugal, we evaluated airway reversibility (post-bronchodilator spirometry), exhaled nitric oxide levels, atopy (skin-prick testing) and current symptoms (breathing difficulties and irritative cough). A dietary inflammatory index (DII) was calculated based on information collected through a parental-reported 24-hour recall questionnaire, and participants were categorized as having an anti-inflammatory or pro-inflammatory diet. Concentrations of indoor PM2.5, PM10, ultrafine particles, carbon dioxide, ozone and nitrogen dioxide were measured to assess indoor air quality. Generalized linear mixed models were used to investigate the proportion of effects explained by the exposures to PM2.5 and PM10.

Results: After adjustments for age, sex, body mass categories, atopy, exposure to tobacco and maternal smoking during pregnancy the exposure effect of PM2.5 and PM10 levels on children with asthma was higher for those having a pro-inflam-

matory diet, being the odds ratios, respectively, 1.42 (95% CI: 1.01 to 2.16), and 1.30 (95% CI: 1.03 to 1.68), compared to those having an anti-inflammatory diet.

Conclusion: These findings suggest that the quality of diet might affect the association of indoor pollution and lung function in children, highlighting the relevance of children's diet as a potential protective factor to pollutants exposure in childhood asthma.

ANALYSIS OF CO-OCCURING ILLNESSES WITHIN THE DECEASED HOMELESS POPULATION IN KRAKOW

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Introduction: The topic is often discussed in medical community, although no research on the homeless population has been previously conducted in our academic centre. As death causes in this population may differ from the general population, we believe our analysis may be considered as potential background for further research in this field.

Aim: Aim of the study was to analyse most frequent causes of death of the homeless and accompanying diseases to observe possible analogies and create a database for future record, as well as determine problems with identifying an unequivocal cause of death.

Methods: Data was collected from archives of Forensic Medicine Department of Jagiellonian University Medical College from years 2014–2017, with the lack of permanent residency as a main inclusion criterion. 203 corresponding cases were recorded (M = 184, F = 14, mean age 58,5 +/- 29,5 years, 32 unspecified). Collected data include time and cause/s of death categorised to 10 groups, presence of hepatocirrhosis or steatosis, pneumonia and ethanol presence in blood and urine. Cases were analysed year by year and overall. Calculations were made using Excel.

Results: The most common causes of death were acute ethanol intoxication (16,3%), injuries (15,3%) and suicide (4,9%). For 68 autopsies (33,4%) causes of death could not be clearly defined. Hepatocirrhosis/steatosis appeared in 65,5% of cases. Ethanol was found in 127 samples (62,6%). Tests were not performed in 21 cases (10,3%). Moreover, ethanol co-occurred with 88 cases of hepatocirrhosis/steatosis (66,1%), which accounts for 43,3% of all subjects, but it was not found in 29 cases (21,8%) of liver pathologies. Pneumonia was present in 66 cases (32,5%), 22 cases found during winter months.

Conclusion: Ethanol presence co-occuring with hepatocirrhosis/steatosis suggests alcohol abuse. Time of the year impacted the amount of pneumonia cases. Difficulty in identifying a single death cause brings attention to the problem and its complexity which needs future resolving.

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ASSOCIATION BETWEEN POLYTHERAPY AND FRAILTY: FINDINGS FROM SHARE

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Introduction: Frailty is a complex geriatric syndrome resulting in decreased physiological reserves, which has attracted increasing interest as it is associated with increased vulnerability for adverse health outcomes. Frail people are more likely to polytherapy, which increases adverse drugs reactions, falls, use of healthcare services and mortality.

Aim: This study aimed to analyze the relationship between polytherapy and frailty in a large database, Survey of Health, Ageing and Retirement in Europe (SHARE), in people aged 50 and over.

Methods: In this cross-sectional analysis, we used data from participants from Wave 6 of SHARE. Polytherapy was defined as taking five or more medications, and frailty was assessed using a version of Fried's Phenotype operationalized to SHARE. Association of polytherapy and frailty with age and gender data was also assessed.

Results: From 68,231 participants, we selected participants that answered questions related to age, gender, polytherapy and frailty, yielding a total of 46,433 participants (68.9 \pm 9.6 years old, 56.7% female). Prevalence of polytherapy, prefrailty and frailty in this population was of 26.7%, 46.6% and 9.8% respectively. Polytherapy prevalence in prefrail and frail individuals was of 30.8% and 59.8%, respectively. Prefrail men and frail women were more prone to polytherapy. Polytherapy increases along ageing groups within prefrail and frail individuals, with exception of frail individuals aged 85 years or more. In prefrail individuals, Czech Republic was the country with highest level of polytherapy (43.7%) and Greece the one with the lowest level (21.1%). In frail individuals, Portugal had the highest (74.2%) and Greece the lowest (49.3%) prevalence of polytherapy.

Conclusion: Our results suggest that polytherapy and frailty are highly prevalent conditions. Prefrail individuals are 2 times and frail individuals 4 times more prone to polytherapy comparing with robust ones. Patient centered interventions are required to reduce polytherapy and to prevent/mitigate frailty.

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THE FREQUENCY AND LOCATION OF SIMON'S BLEEDING- ANALYSIS OF SUICIDE CASES BY HANGING

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Introduction: Hanging is the most common type of suicide and is associated with various marks on deceased person's body. Simon's bleeding is a vital sign of hanging and it is a type of hemorrhage localized on ventral surface of the intervertebral disks of the lumbar part of spine.

Aim: The objective of the study is to determine the frequency and location of Simon's bleeding and its association with age, gender and neck injuries.

Methods: There were 1373 cases of suicide by hanging in the archives of the Department of Forensic Medicine of Jagiellonian University in Cracow between 2008–2018. 94,25% of them had documented full forensic autopsies and were analyzed in terms of occurance of Simon's bleeding and other hanging related injuries.

Results: We found 159 cases with the Simon's bleedings overall (12,34%), 114 (71,70%) in the lumbar spine, 21 (13,21%) cases in the thoracic spine, 3 (1,89%) cases with Simon's bleeding in the thoracolumbar spine, 1 case in cervical spine and 20 (12,58%) cases where location wasn't specified. The cases with Simon's bleeding were strongly correlated with internal neck injuries (the absence of internal neck injuries plus Simon's bleeding 6,19% vs. the presence of internal neck injuries plus Simon's bleeding 13,57%, p < 0,05). Simon's bleeding was also correlated with younger age (medium age of suicides with Simon's bleeding 36,53 vs. medium age of suicides without Simon's bleeding 49,10).

Conclusion: The intervertebral haemorrhages associated with hanging occur quite frequently and there is a correlation between them and several factors, such as age and internal neck injuries. In our study the frequency of Simon's bleeding was much lower (12,34%) than in literature (40-50%). According to literature Simon's bleeding occurs with traumatic elongation of spinal column which correlates with our finding of coincidence between internal neck injuries and intervertebral haemorrhages.

NUTRITIONAL HABITS AND BMI AMONG POLISH TEENAGERS IN MALOPOLSKA

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Introduction: A balanced diet is fundamental to healthy growth and development of children and adolescents. Inappropriate eating habits lead to overweight and obesity which increase a risk for cardiovascular and other chronic diseases in the older age.

Aim: The aim of the study was to analyze the prevalence of increased body mass and nutrition habits in a sample of Polish teenagers.

Methods: A questionnaire was used to survey teenagers from randomly chosen first and second classes of middle schools in Malopolska in 2015–17. This study is a part of the Malopolska Cardiovascular Preventive Intervention Study – M-CAPRI.

Results: The study involved 3753 junior high school students (49.9% females) at the mean age of 14.1 ± 0.7 years. Body

weight and height were reported by 91.2% of respondents. Most of them (66.2%) had a normal BMI (5-85 percentile): 60.3% of males (M) vs 72.1% of females (F), p < 0.001; 5.9% of teenagers were underweight (<5pctl), 10.5% were overweight (85-95 pctl)(9.1% F vs 11.9% M, p = 0.002) and 8.6% were obese (>95 pctl)(5.6% of F vs 11.7% M, p < 0.001). The highest percentage of teenagers (44.2%) admitted to eating 3-4 meals a day. Most respondents (56.1%; 60.9% M vs 51.3% F; p < 0.001) reported to eat breakfast every day, while 15.1% (12.6% M vs 17.6% F, p < 0.001) reported not to eat breakfast at all. Vegetables were eaten daily by only 22.5% teenagers (19.2% M vs 25.8%F, p < 0.001) while 4.3% (35.8% males vs 44.8% females, p < 0.001) consumed fruits every day. Most teenagers admitted to eat fast food once or less a week (77.7%, 78.1% M vs 77.3%F, p = 0.012). Only 13.7% respondents consumed sweets less often than once a week, while 21.9% (19.5% M vs 25.5% F, p < 0.001) did it daily. Most responders drank 71.5% (82%) M vs 61%F, p < 0.001) drank soft drinks it at least once a week.

Conclusion: Increased body weight and unhealthy dietary habits are important epidemiological problem among Polish teenagers.

CAMPYLOBACTER SPP. IN CHICKEN BROILERS: FROM FARM TO MEAT

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Introduction: Campylobacteriosis has been the most commonly reported food-borne infection in Europe since 2005[1]. Poultry farming is the main source of this bacteria to humans (food chain) and to the environment (manure).

Aim: To study the evolution of Campylobacter contamination between the broiler farm and packaged meat in an important Portuguese broiler producer.

Methods: The productive cycle of 19 intensive farmed chicken meat lots was studied by collecting samples in the three main stages:

i) primary production at the farm level (faeces);

ii) slaughtering process (neck skin);

iii) commercial distribution (packaged breast fillets).

Detection, identification and enumeration of Campylobacter spp. was performed following cultural methods (ISO 10272-2:2017), multiplex PCR and qPCR.

Results: At the farm, 58% of the flocks were positive, with a contamination level of 6.2×10^{6} UFC/g. However, combining molecular findings, 95% of faecal samples were positive. After slaughtering the prevalence remained unchanged (58% positivity), albeit the contamination level of chilled carcasses had decreased to 3.7×10^{4} UFC/g (neck skin). Campylobacter was detected in 4 out of 19 packed breast fillets analysed; none of the positive samples was contaminated with more than 100 UFC/g. C. jejuni was the predominant species on fecal and neck skin samples, while C. coli was most frequent in meat.

Conclusion: The high prevalence of Campylobacter in chicken broiler flocks is worrisome. Public health concerns pro-

pelled European Union to establish a maximum contamination level of 1000 CFU/g (neck skin of chilled carcasses)[2]. Results of our investigation revealed that compliance with this hygiene criteria could be difficult without effective biosecurity measures at the farm level. Unfortunately, efficient vaccines and probiotics are currently unavailable. Interestingly, prevalence levels of Campylobacter decreased down the line: at the market level, only four meat samples were positive, displaying a low number of cultivable bacterial cells and no C. jejuni was recovered from those samples.

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HOW EHEALTH SYSTEMS MIGHT IMPROVE TREATMENT OUTCOMES IN BARIATRIC SURGERY?

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Introduction: Obesity begins to escalate into one of the biggest health problems in the XXI century. Conservative treatments, based only on a proper diet and physical activity, without the support of an interdisciplinary team of specialist does not bring satisfactory results in patient's condition

Aim: The main research hypothesis is that prolonged continuous monitoring of bariatric patients in the perioperative period, supported by efficient algorithms of medical data interpretation and harmonized with medical advice, contributes to better weight loss and reduction of comorbidities

Methods: A prospective clinical trial, case-control without randomization, patients were recruited from among bariatric patients qualified for surgical treatment of morbid obesity. The study group consisted of patients continuously monitored during a 6-month period along with typical follow-up visits, and a control group (20 patients, both men and women) of retrospective patients who were not included in the follow-up program but only participated in scheduled follow-up visits at 1 and 6 months postoperatively. In order to collect data during the trial, a dedicated system consisting of a patient communication center, data transfer module, electronic patient records, central data management and data repository. The proposed monitoring system was equipped with a web application that was used for processing, viewing and storing patient data

Results: Our survey results show that continuous monitoring of the treatment process through a mobile system, foreseen by a specialist and continuous graphical presentation of the results through graphs, leads to better treatment outcomes in the form of weight loss in more than 90% of cases

Conclusion: Constant monitoring and successive motivational alerts to continue treatment contribute to obtaining better treatment effects in the studied bariatric group, i.e. body weight and a reduction in symptoms of comorbidities. The results obtained will help to develop a prototype platform for monitoring of bariatric patients.

Acknowledgements:

eHealth, bariatric surgery

THE CURSED SOLDIERS- GUNSHOT WOUNDS ANALYSIS

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Introduction: In Poland the topic of II World War is still vivid and research are still in progress. As a consequence in october 2018 The Institute of National Remembrance- Commision for the Prosecution of Crimes against the Polish Nation exhumate 12 sets of remains of Polish soldiers today known as "the Cursed Soldiers". They were sentenced to death by the communist government of Poland in 1947–1949 as a result of membership in anti-communist Polish resistance movement. The cause of death in most cases was attributed to a gunshot head injury. In our research we focused on reconstruction of damaged skulls and bones with gunshot injury and to find characteristic features necessary to victim's identification.

Aim: To reconstruct damaged bones, investigate the dry bone damage and methods of execution

Methods: This study is focused on the examination of twelve cases, exhumed in October 2018. The majority of the skulls was highly damaged and required complete reconstruction followed by the analysis of trajectory of gun shots. The dry bone study revealed multiple lesions in the skulls and bones of appendicular skeleton as humerus, tibia and pelvic bone. The skulls were additionally inspected to determine the entrance and exit holes.

Results: Post-mortem reconstruction allowed to confirm the characteristics of firearms injuries, which included the approximate number of projectiles and their trajectory. The study revealed that in the majority of the cases execution by gunshot to occipital or temporal bone had been performed. Althought there were a few exceptions such as frontal or multiple headshots. Moreover in some cases the results of the research enabled us to establish the soldiers identity. Shooting distance and the weapon's characteristics were unable to determine.

Conclusion: Our results verify, that in the described cases soldiers were executed by various types of gunshot.

THE AWARENESS AND KNOWLEDGE ABOUT HEART FAILURE IN POLAND - LESSONS FROM THE HEART FAILURE AWARENESS DAY AND INTERNET SURVEYS

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Introduction: Heart failure (HF) is a life-threatening condition which affects up to 2% of contemporary populations. Generally, it is a chronic and progressive disease, however in many cases it can be prevented or treated. Nevertheless, effective control of this disease requires HF awareness of symptoms in the society. **Aim:** The aim of the study was to assess the level of HF knowledge in the Polish population.

Methods: The questionnaire concerning knowledge about HF prepared by the Competence Network HF under the patronage of the European Heart Failure Association of the ESC, was used. The survey included 534 contributors who formed three groups: medical students (MS) – 198 (37.1%), HF Awareness Day participants (HFDP) – 134 (25.1%) and other (OP) – 202 (37.8%).

Results: Study groups differed in terms of gender, age and level of education. As predicted, MS achieved the highest score (22.5 [20.0–24.0]), compared to HFDP (20.0 [17.0–22.0], P < 0.001) and OP (19.0 [16.0–21.0], P < 0.001). Knowledge on typical HF symptoms was alarmingly low in each of the analyzed groups – dyspnea (MS – 96.0%, HFDP – 78.4%, OP - 74.6%), ankle edema (MS–79.8%, HFDP–50.6%, OP–32.2%), body weight gain (MS–14.1%, HFDP–17.2%, OP–4.5%). By multivariate model medical education (b 3.372, 95% CI 2.738–4.005) and own illness or having relatives or friends with HF (b 0.654, 95% CI 0.066–1.242) independently affected the score of HF awareness questionnaire.

Conclusion: The basic knowledge on HF in Poland is not sufficient. It is moderately better among MS. Further campaigns improving HF awareness are necessary.

THE IMPACT OF ANATOMY COMPUTER-ASSISTED LEARNING TRAINING AND COMPUTER LITERACY ON MEDICAL STUDENTS PERFORMANCE

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Introduction: Anatomy education is facing increasing challenges. This context is contributing to the introduction of new pedagogical approaches, such as computer-assisted learning (CAL). This approach provides insight into students' learning profiles and features that are correlated with anatomy knowledge acquisition.

Aim: The objective of this study was to understand the influence of anatomy CAL training on academic performance as well as to characterize the students' computer literacy and computer usage.

Methods: A total of 671 medical students attending Musculoskeletal (MA) and Cardiovascular Anatomy (CA) courses, were distributed in three groups (MA Group, CA Group, MA + CA Group). Students' computer literacy and attitudes towards computer-based learning were assessed through the Computer-based learning questionnaire. Multiple linear regression models evaluated the association between students' characterization variables and their anatomy academic performance.

Results: The use of computer and internet for pedagogical purposes was ubiquitous among the study participants, while the students presented positive attitudes towards e-learning, considering that CAL favors learning process. Musculoskeletal and Cardiovascular Anatomy academic performance in both MA Group (r = 0.761, p < 0.001) and MA+CA Group (r = 0.786, p < 0.001) and in both CA Group (r = 0.670, p < 0.001) and MA+CA Group (r = 0.772, p < 0.001) respectively, showed a large positive correlation with the number of CAL training sessions. Multiple linear regression models were used, showing an association between the amount of CAL training and anatomy academic performance.

Conclusion: CAL training in anatomy has a positive dose-dependent effect on Anatomy academic performance. The inclusion of these platforms in anatomy learning process contributes to a better understanding of students' learning profiles, individual features, and academic background contribute to the optimization of the learning process.

MAPPING GEOGRAPHICAL PATTERNS AND HIGH-RISK AREAS FOR SEXUALLY TRANSMITTED INFECTIONS IN PORTUGAL – A RETROSPECTIVE STUDY BASED ON THE NATIONAL EPIDEMIOLOGICAL SURVEILLANCE SYSTEM

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Introduction: Sexually transmitted infections (STIs) continue to be a global public health problem, with some reports evidencing recent increases in STIs occurrence [1,2]. Examining their spatial distribution can help establishing more targeted public health strategies to control these infections.

Aim: To describe the spatial patterns of chlamydia, gonorrhoea and syphilis infections and identify high-risk and low-risk areas across Portuguese municipalities.

Methods: STIs notifications (2015–2017) were obtained from the National Epidemiological Surveillance System (SINAVE). Crude and age-sex adjusted notification rates were calculated at municipality-level and smoothed using the Empirical Bayesian estimator. Moran's I and Local Moran's I were computed to assess spatial autocorrelation and identify high- and low-risk areas. Correlation between STIs spatial patterns was measured using Pearson correlation coefficient. Geodaâ was used for spatial statistics and ArcGIS for mapping.

Results: There were 4819 STIs notifications between 2015 and 2017. Chlamydia, gonorrhoea and syphilis accounted for 15.3%, 33.2% and 51.6% of the notifications, respectively. Most of the cases were men - 66.1%, 88.8%, 75.1% - and mean age was 29.9 (SD 10.6), 30.1 (11.6), 41.0 years (16.3), for chlamydia, gonorrhoea and syphilis, respectively. Heterosexual contact was the commonest form of STIs acquisition. The national notification rate for chlamydia was 2.4 /100,000 inhabitants, for gonorrhoea 5.2 /100,000 and, for syphilis, 8.0

/100,000. STIs were strongly clustered in space, with Moran's I ranging from 0.670 for chlamydia to 0.406 for syphilis (p < 0.001). STIs rates were consistently higher in Porto and Lisbon metropolitan area and surrounding municipalities, whereas the lowest-risk municipalities were located in inner North, Centre and Alentejo. The spatial patterns of the three STIs were significantly correlated, particularly chlamydia and gonorrhoea (r = 0.845, p < 0.001).

Conclusion: STIs are clustered in Portuguese metropolitan areas and affect disproportionally more men and younger people, suggesting that these communities and demographic groups should be targeted for effective STI prevention and control.

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TREAD MARKS, TRAUMATIC AMPUTATIONS AND TRAUMATIC STRIAE- FORENSIC ANALYSIS OF MARKS ON DECEASED PEDESTRIANS

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Introduction: Car accident may leave various marks on pedestrians' bodies. These marks can be associated with velocity of a car or help identify it. Our study investigates three types of marks associated with car accidents: traumatic striae, traumatic amputations and tread marks. According to forensic literature, their occurrence is common in particular types of motor vehicle accidents and provides information about speed of the car and the mechanism of impact.

Aim: Objectives of the study are to determine frequency of rare marks associated with vehicle accidents and to evaluate their potential significance.

Methods: There were 665 cases of dead pedestrians in archives of the Department of Forensic Medicine of Jagiellonian University in Cracow in years 2007–2017. Most, but not all of them, had documented photographs and were analysed in terms of types of marks and their locations.

Results: We found 7 cases with tread marks (1.05%), 22 with traumatic amputations (3,3%) and 17 cases of traumatic striae (2,56%). 12 striae were located in inguinal regions, we found 4 stretch marks located in lower abdomen, in one case both types of stretch marks were present. We found 10 cases of upper and 12 of lower limb amputations. Tread marks were located on head (1 case), upper limb (2), trunk (1), Back (1),

lower limb (1) in one case tread marks were located on the back and a lower limb.

Conclusion: All of the investigated marks are very rare. Often it is hard to determine if it is a tread mark, because several other marks can imitate them. Distinction between traumatic amputation and amputation caused by running over limb may also be problematic. Striae on lower abdomen were present only among female pedestrians, they may be associated with undergone cesarean section but we need further investigation to check this hypothesis.

EARLY OUTOME PREDICTIONS IN PATIENTS WITH TBI: COMPARISON OF CT PREDICTION SCALES

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Introduction: Computer tomography (CT) is an essential tool in diagnosing and treating traumatic brain injury (TBI). Marshall CT classification, Rotterdam and Helsinki CT score were developed as prediction outcome scales by computing TBI CT abnormalities.

Aim: The aim was to determine which one is the most accurate and has the best grading discriminatory power in determining the early outcome.

Methods: This study included 1006 consecutive TBI patients who underwent CT head scan. Each score was calculated, then compared in terms of their performance and accuracy in predicting patients' early outcome (by using Glasgow outcome scale-GOS). Area under the curve (AUC) was used as the discriminatory power of each system while the statistical correlation was the instrument of comparison between two scales.

Results: The areas under the curve (AUCs) indicated that all scoring systems had similarly high discriminative power in predicting early death/early unfavorable outcome (Marshall, AUC = 0.86 vs. Rotterdam, AUC = 0.82 vs. Helsinki, AUC = 0.84). Correlation between the scores is decreasing in the following order: Marshall vs. Rotterdam grading, r = 0.78, Marshall vs. Helsinki, r = 0.62 and Rotterdam vs Helsinki, r = 0.51, respectively

Conclusion: All classifications have similarly predictive power for early outcome, but even greater discrimination results could be obtained if GCS and ISS were incorporated in the calculation. Helsinki CT score is the least predictable of the all three. Marshall's CT classification has at least the same prediction power as the newer scoring scales. Rotterdam system, having the high predictability and also including characteristic like subarachnoid hemorrhage, should be scale of choice.

DO HIV POSITIVE PATIENTS HIT THERAPEUTIC TARGETS?

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Aim: The aim of the study was to estimate cardiovascular risk in HIV infected patients and to evaluate achieving therapeutic goals as recommended by Polish AIDS Society (PTN AIDS).

Methods: Retrospective analysis of cardiovascular risk factors of 210 patients of the Acquired Immunodeficiency Outpatient Clinic in Lodz was performed based on medical records. Lipid parameters were analysed, Atherogenic Index of Plasma was calculated with: AIP = Log(TG/HDL). A, B and C group affiliation was determined with the use of CDC classification.

Results: 210 HIV positive patients included in the study were: 79% men in mean age 42 ± 10 years.

Patients were divided into two groups of cardiovascular risk based on the PTN AIDS recommendations; high–89.5% patients-group 1 and very high 10.5% patients-group 2. The average LDL level in the group 1 patients was 104.55 ± 32 mg/dl(LDL < 100 mg/dl achieved by 49.04% patients without hypolipemic treatment and 41.94% on lipid lowering drugs). Other lipid parameters: HDL-47.7 \pm 15 mg/dl, TG-138.2 \pm 69 mg/dl and AIP- 0.45 \pm 0.3. In the group 2 mean LDL level was 98.05 \pm 21 mg/dl (LDL < 70 mg/dl achieved by 33.3% patients without hypolipemic treatment and 7.69% on lipid lowering drugs). Other lipid parameters: HDL-42 \pm 17 mg/dl, TG-182.8 \pm 121 mg/dl, AIP-0.64 \pm 0.4 mg/dl.

8 patients experienced cardiovascular incidents. Mean age during cardiovascular incident was 42.3 ± 10 years. The average LDL in those patients is 94.6 ± 25 mg/dl. None of them has recommended LDL.

The patients of clinical category C (symptomatic AIDS) turned to have the highest TG level (p < 0.05) and the lowest HDL level (p < 0.05) and thus the highest AIP (p < 0.05) of all CDC groups.

Conclusion: Most of HIV patients in our study do not reach therapeutic LDL. Interestingly the reachability is worse in patients on lipid lowering therapy. HIV patients from CDC classification groups differ significantly from each other and group C has the most atherogenic plasma.

Surgery

CHRONIC RHINOSINUSITIS: ACUTE EXACERBATION IN PATIENTS AFTER ENDOSCOPIC SURGERY

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Introduction: Chronic rhinosinusitis (CRS) is an inflammatory disease of paranasal sinuses which includes symptoms such as mucopurulent drainage, nasal obstruction, facial pain or decreased sense of smell. The acute exacerbation of CRS (AECRS) occurs as an abrupt worsening of a patient's condition. AECRS is frequently caused by bacterial infection.

Aim: The aim of this study is to identify the most frequent microorganisms that cause AECRS after functional endoscopic sinus surgery (FESS) and determine the most effective treatment.

Methods: A group of 776 adult patients admitted to the Department of Otolaryngology JUMC between 2015 and 2017 were analyzed retrospectively. Symptoms of CRS (according to EPOS criteria) were present within all patients. All of them underwent FESS. Pathological secretion for microbiological tests was collected from the middle nasal meatus or directly from the sinuses. Symptoms of bacterial infections were examined during following appointments.

Results: 152 patients (19,59%) presented symptoms of bacterial infection in the first six months after FESS. During that period of time 83 (54,6%) patients were treated with an empiric antibiotic therapy (EAT) with success in 35 cases, 15 (18,07%) patients were lost to follow-up. A targeted antibiotic treatment (TAT) was implemented in 94 cases, 52 (71,23%) patients were treated successfully, 21 of them were lost to follow-up. The effectiveness of targeted antibiotic treatment is statistically significantly higher compared to empiric approach (p = 0,025). A total of 210 bacterial species were found. The most common bacteria were: Staphylococcus aureus (SA) (35,71% - MRSA: 2,86%), Pseudomonas aeruginosa (PA) (12,86%) and Escherichia coli (EC) (10,95%).

Conclusion: A TAT is more effective than an EAT thus it is always worth collecting swabs to identify a factor that caused AECRS. In the meantime, in case of clinical indications an empiric antibiotic therapy can be used. The most common bacteria that occurred in a current study was SA, PA and EC.

A STUDY OF GLENOID CAVITY MORPHOLOGY AND AN ATTEMPT TO ESTABLISH INDIAN REFERENCE VALUES

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Introduction: Restoration of gleno-humeral kinematics using morphometry is elementary for successful shoulder surgery. 1, 2, 3 Indian reference values for glenoid morphology is lacking. 4,5,6,7,8,9,10,11,12,13,14

Aim: To study and compare with Indian literature, size and shape of glenoid cavity in 82 adult dry human scapulae (38 right, 42 left). To propose Indian reference for glenoid morphometry.

Methods: Inclusion - 82 unpaired (38-right 44 left) ossified, dry, unbroken adult human scapulae.

Exclusion - Damaged glenoidal end, healed fractures.

Digital vernier calliper to measure superior-inferior glenoid (SI), anterior-posterior glenoid (AP1), anterior-posterior glenoid (AP2) diameters and calculate glenoid cavity index (GCI). Shape assessment, using impressions.

Indian reference by pooling data from 12 Indian studies. Standard statistical tools for calculations. R plots for graphs.

Results: Mean SI diameter 33.81 ± 2.91 , 33.91 ± 2.80 . Mean AP1 23.14 ± 2.14 , 23.05 ± 2.25 .

Mean AP2 16.14 \pm 2.06, 15.47 \pm 2.15 (right and left in mm respectively).

GCI 66.59% right 69.09% left, mean 67.92 %.

On right pear and oval shape equal. Pear majority in left. Inverted comma least.

Derived reference Indians: SI 34.63 ± 3.9 , 32.29 ± 3.6

AP 1 24.87 ± 2.7, 24.07 ± 2.6, AP 2 17.51 ± 1.7, 17.28 ± 1.82 (right and left respectively).

Conclusion: Compared data with studies across major Indian regions. SI was similar to half of the Indian studies on right while rest were high. On left, majority had higher values.

AP1-1/3 each Indian studies were similar, higher and lower bilaterally.

AP2, majority of Indian values were higher than our study. Mean GCI of 67.92% was comparable.

Similar to Indian studies, in right pear and oval were almost equal, pear dominated left and inverted comma the lowest.

High light: Attempt to prepare Indian reference for first time.

Limitations: Absence of gender/age specificity and lack of multimodality cadaver dissection.

Suggestion: Pan Indian representative study using 3D model of scapula that can improve the prognosis of shoulder arthroplasty patients.15,16

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IMPACT OF BARIATRIC SURGERY TYPE ON QUALITY OF LIFE - A 10 YEAR FOLLOW-UP

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Introduction: According to WHO estimates in 2016, more than 1.9 billion people were overweight and 650 million were obese worldwide. Excessive body weight leads to many comorbidities such as type 2 diabetes, CAD or neoplasms. Currently, surgical treatment is considered as the only permanent way to lose weight for patients with morbid obesity.

Aim: The aim of this study was to compare the two most popular types of bariatric surgery: laparoscopic sleeve gastrectomy (LSG) and laparoscopic Roux-en-Y gastric bypass (LRYGB) in terms of their impact on the weight loss and quality of life.

Methods: Sixty-five people diagnosed with obesity participated in this study. Thirty-four of them were treated with LSG and thirty-one qualified for LRYGB. 89% of qualified patients suffered from hypertension, while 52% of them were diagnosed with type 2 diabetes mellitus. Quality of life was assessed using the MA QoL Questionnaire II and SF-36 Questionnaire in three time points: before, one-year and 10 years after the surgery. Bariatric effects (like WL, EWL, EBMIL) were measured at the same time points.

Results: Among patients who underwent LSG surgery, the average Percent Excess Weight Loss (%EWL) after one year was 58.65%, while in 10 years it dropped to 52.15%. In the group where LRYGB was performed, %EWL after one year was 57.67%, whereas after 10 years its value remained at roughly the same level (57.15%). Both treatments resulted in more than 50% of %EWL, but the effects of the LRYGB are more stable. Improvement of quality of life was observed in both types of treatments, however, it was more significant in patients qualified for LSG.

Conclusion: LRYGB is a technique that provides stable weight loss. However, LSG results in greater improvement in the quality of life. The outcomes of the surgery are more satisfying in short-term observation.

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PREOPERATIVE HEMOGLOBIN AND URIC ACID LEVELS AS PREDICTORS OF ACUTE RENAL INJURY IN CARDIAC SURGERY

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Introduction: Acute renal failure associated with cardiac surgery is a significant postoperative complication, with a frequency of 9–39% according to studies. Acute renal failure after and due to surgery is the second most common cause of acute renal failure in intensive care units. In those patients in whom it was necessary to use some form of therapy to replace renal functions, there is a three times greater risk of developing the final stage of chronic renal failure. The mortality rate in patients with renal replacement therapy is 40–70%, and is directly dependent on the number of acute renal failure events during hospital treatment.

Aim: To investigate the importance of preoperative hemoglobin and uric acid as a predictors of the development of acute renal failure in postoperative period in cardiac surgery patients.

Methods: The study covered a total of 118 patients, older then 18 years, who were classified into two groups. The first group consisted of patients who developed acute renal failure, so it was necessary to apply renal replacement therapy. The second, control group consisted of patients without postoperative complications in the form of acute renal failure according to AKIN and RIFLE criteria.

Results: A statistically significant difference exists between preoperative hemoglobin values; postoperative renal function parameters (urea, creatinine), acute inflammatory phase reactants (CRP and procalcitonin), CPK-MB isoenzymes; duration of the extracorporeal circulation and clamp of the ascendent aorta during cardiac surgery. The exception is preoperative uric acid levels, where there is no statistically significant difference between examined groups. There is a statistically significant correlation between the use of inotropic drugs and the development of acute renal failure.

Conclusion: There is a correlation between preoperative low hemoglobin values and postoperative occurrence of acute renal failure. There is no statistically significant correlation between preoperative values of uric acid and postoperative occurrence of acute renal failure.

DOES WOMEN'S VISION CHANGE DURING PREGNANT? CORNEA AND PREGNANCY

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Introduction: Pregnancy is a time of intense changes in a women's body, during which the hormonal system is being rebuilt. These changes also affect the organ of vision, which has been studied by many researchers.

Aim: The aim of this study was to compare the values of corneal keratometry parameters, central corneal thickness (CCT) and depth of anterior chamber (ACD) of healthy pregnant women before and after natural birth.

Methods: The observational study examined the eyes of 30 healthy women (60 eyes) aged 25 to 35 years old. The pregnant women underwent two physical examinations. one in the third trimester at 36th week of gestation, and at the end of 6th week after labour. Women with a twin pregnancy, with refractive error $> \pm 4,00$ D sph, with eye diseases and the history of eye surgeries were excluded from the study. In order to unify the research group only patients that delivered naturally were analysed. The patients underwent imaging examination of anterior segment of the eye using the Scheimpflug camera (Pentacam system). The following parameters were analysed: flat parameter (K1), steep parameter (K2), central corneal thickness (CCT), depth and angle of the anterior chamber. Results were obtained with statistical analysis using the t-student test.

Results: A decrease in CCT (p = 0.01) and decrease in values of the iridocorneal angle (p < 0.01) were observed in patients after delivery in comparison to values from examination in 36th HBD. Remaining parameters did not change.

Conclusion: Decreased values of central corneal thickness and iridocorneal angle may be associated with an rapid reduction of the level of sex hormones after childbirth. The evaluation of these parameters is important to the treatment of ophthalmic diseases during pregnancy such as glaucoma. A more detailed explanation of the variability of parameters of the cornea during pregnancy requires further research.

LAPAROSCOPIC CHOLECYSTECTOMY AS AMBULATORY SURGERY AT THE CLINIC FOR DIGESTIVE SURGERY, CLINIC CENTER OF SERBIA

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Introduction: Ambulatory Surgery represents operation or procedure performed on an outpatient basis in a facility which may be either free-standing or a suite inside the hospital and the patient is discharged on the same working day. Laparascopic cholecystectomia, because of its benefits compared to the open cholecystectomia, represents "gold standard" for the surgical treatment of gallbladder disease and can also be performed as an ambulatory intervention.

Aim: The aim was to determine the practice of Ambulatory Surgery of laparoscopic cholecystectomy in the Clinic for digestive surgery, CCS, during the 6-month period, from July to December 2018.

Methods: The sample was made of 201 patients who had Laparoscopic cholecystectomy, at the Clinical center of Serbia, during the 6-month period, from July to December 2018. The results were obtained with a descriptive and retrospective insight in the medical documentation of patients.

Results: The average age of patients was 50.92 years. Most of the patients in the period of this study were women (62.1%). Only 4 (1.99%) patients were discharged on the same working day and 41 (20.39%) patients stayed overnight. Most of them were discharged on the 2nd day (33.33%), but the maximum stay was 16 days. The reason for staying longer than 1 day was mostly because of the surgical drain (58.20%) and because of the rewinding and procedures (23.38%), as stated in the medi-

cal documentation. In 12.56% of cases the operation lasted less than 60 minutes, in 74.37% it lasted up to 120 minutes and in 13.06% of cases it lasted up to the maximum 215 minutes according to this research.

Conclusion: Looking at the reasons for the extended stay, we can conclude that most of them do not need hospitalization and that patients can come from home or other accommodation.

GIANT CARCINOMA OF THE FACE - SURGICAL TECHNIQUES AND RESULTS

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Introduction: The excision of giant carcinomas in the facial region most often results in a considerable soft tissue defect, which would need a surgical solution that would serve both functional and esthetic purposes.

Aim: This report is meant to provide insight into reconstructive surgery techniques that would cover such defects.

Methods: The report is based on 10 patients aged between 60 and 85 years, all of whom presented carcinomatous lesions with an on-going evolution lasting between 7 and 12 years. All of the lesions were proven to be nodular basal cell carcinomas. Each of them measuring between 5 and 7,5 cm, they presented various localization: 4 of them were placed in the external angle of the eye, one was situated in the glabellar region and extended to both eyes. In each case, the intervention performed consisted in complete excision (including the oncological limit restriction) and covering with local flaps (3 Mustarde flaps, 3 associations of frontal laps and 4 genian advancement flaps, one of which anchored in the zygomatic bone). All of the surgical interventions were performed in one operatory time, and only two of the patients required additional reinterventions, three months post-surgery. The purpose of these reinterventions was sectioning of the conjunctival flap to enhance eye protection.

Results: Every patient has had a timely and efficient recovery: the vascularization of the flaps was unproblematic and the long-term evolution was good, with full reintegration of the flaps and a pleasant esthetic result. None of the patients presented recurrences when evaluated, 18 months ulterior to the interventions.

Conclusion: The giant basal cell carcinoma, through its tendency to appear in the later decades of life and especially when it's placed in the facial region can be a real challenge for the surgeon. The importance of efficient excision and managing consecutive soft tissue defects can not be understated.

PRE-OPERATIVE GLYCATED HAEMOGLOBIN A1C LEVEL AS A POTENTIAL PREDICTOR OF 1-YEAR OUTCOMES IN PATIENTS WITH CRITICAL LIMB ISCHAEMIA TREATED WITH ENDOVASCULAR PROCEDURES IN THE COURSE OF DIABETES MELLITUS

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¹Students⁶ Scientific Group of Clinical Angiology, Jagiellonian University Medical College; ²Department of Angiology, Jagiellonian University Medical College **Introduction:** Peripheral arterial occlusive disease (PAOD) is a disease with worldwide increasing occurrence. Diabetic patients are greatly exposed on the risk of PAOD and its complications.

Aim: The aim of the study was to check the influence of preoperative HbA1C on the outcomes of patients with diabetes undergoing PAOD related endovascular treatment.

Methods: The study was conducted among 59 patients with PAOD referred from the diabetic foot outpatient clinic for endovascular treatment. They were included in oneyear observation based on follow-up visits in 1, 3, 6 and 12 months after angioplasty and divided into 2 groups basing on their preoperative glycaemia. The clinical condition of the lower limbs was assessed by use of the Rutherford classification, ankle-brachial index (ABI) and toe-brachial index (TBI). Changes in patients' quality of life (QoL) were also evaluated.

Results: Reintervention within 12 months were less frequent in patients with HbA1C≤8.0% than in HbA1C>8.0% patients (9.09% vs. 35.48%, p = 0.03). TBI of the treated limb was lower in patients with elevated than in patients with proper glycaemia at 6 month [0.2 (0.0–0.38) vs. 0.38 (0.31–0.46); p < 0.008] and 12 month follow-up [0.17 (0.0–0.27) vs. 0.32 (0.25–0.38); p < 0,001]. The rate of healed ulcerations after 6 months was higher in patients HbA1C≤ 8.0% (45.0% vs. 16.13%; p = 0.02) and they had significantly greater improvement of QoL.

Conclusion: Results of this study shows that preoperative level of glycaemia is an important factor for long-term prognosis in diabetic patients with PAOD. Elevated HbA1C level decreases significantly long-term improvement of QoL in DM patients undergoing endovascular treatment.

INDICATIONS, RESULTS AND COMPLICATIONS OF PRENATAL INTERVENTION IN LOWER URINARY TRACT OBSTRUCTION: OUR EXPERIENCE, LITERATURE REVIEW AND META-ANALYSIS.

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Introduction: The incidence of congenital urinary tract defects is approximately 0.5–1%. The spectrum of these defects extends from asymptomatic to severe ones leading to the end stage renal disease (ESRD). The indications for prenatal interventions are still controversial.

Aim: To assess indications, results and complications of vesicoamniotic shunting (VAS) and fetal cystoscopy (FC) for lower urinary tract obstruction (LUTO)

Methods: Electronic database MEDLINE, ScienceDirect and Mendeley were searched from their inception until December 2018 to select studies on indications and complications of prenatal management for treatment of LUTO. Two reviewers extracted independently English papers in a standardized manner. Randomized controlled trials, case control studies, observational studies and our cohort were included. Complex congenital anomalies and studies not reporting survival were excluded. The primary outcomes were prenatal and postnatal survival. The secondary outcomes were renal function at 6 months and number of complications associated with the procedures. Data were reported as odds ratio (OR) with 95% of confidence interval (CI).

Results: 6 articles with total of 257 fetuses were included. 84 fetuses had VAS and 82 had FC. In 78 fetuses no intervention was done and 13 were lost from follow up. Higher survival rate was in the VAS and FC groups than in the non-intervention group (OR4,33;95%CI2,24-8,40). The number of complications was higher in the VAS than in the FC group (OR1,26;95%CI0,71-2,26). Postnatal renal function on the short term was better in VAS and FC group than in non-intervention (OR1,21;95%CI0,40-3,70). FC showed better outcome than VAS (OR5,09;95%CI1,50-17,23). Indications for VAS and FC treatment were similar.

Conclusion: Prenatal interventions in the selected cases of LUTO might improve survival, and kidney function the short term. Otherwise there is a risk of serious complications, therefore they should be performed in strictly defined situation. Long term follow up is necessary to establish the role of the FC.

ISOBARIC OR HYPERBARIC BUPIVACAINE - FOR LOW DOSE SPINAL ANESTHESIA?

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Introduction: The use of low doses of local anesthetics reduces the most common complications, shortens hospitalization and recovery periods.

Aim: To compare dynamics of motor and sensory blockade during spinal anesthesia using low doses of isobaric or hyperbaric bupivacaine, also to evaluate the pain intensity, side effects and patient's comfort after knee arthroscopy.

Methods: In 2018–2019th the prospective research study was performed In Republican Vilnius University hospital. 20 patients participated, age range 38–70. Based on the baricity of bupivacaine in cerebrospinal fluid the participants were divided into two groups. For induction of the spinal anesthesia in the 1st group 7 mg of isobaric bupivacaine was injected for patients 165 cm in height (\pm 1 mg/5 cm)+10 µg phentanyl. In the 2nd group the same dose of hyperbaric bupivacaine with phentanyl was used keeping the patient on the affected side for 15 min after injection. All patients were examined using the Bromage scale [0–3] for motor function and a cold sample for sensory function at 15th min, then immediately and 30 min after surgery. Side-effects, patient's satisfaction [0–10] and pain intensity [0–10] during the postoperative period was registered.

Results: Groups homogeneity was confirmed. 80% – ASA II. Side-effects were observed for 25% (n = 5). The development of bradycardia requiring atropine treatment was more common in the isobaric bupivacaine group (p = 0.01). Only 1 patient had urinary retention, where hyperbaric bupivacaine was used. Patient's satisfaction (p = 0.129) and maximum postoperative pain scores (p = 0.496) between two groups had no statistically meaningful differences. Following spinal anesthesia with isobaric bupivacaine, statistically reliable shorter lengths of sensory (p = 0.003) and motor blockades (p = 0.001) were recorder.

Conclusion: Sufficient perioperative analgesia and high patient satisfaction is achieved, using 7 mg/165 cm (± 1 mg/5 cm) dose of isobaric or hyperbaric bupivacaine with phen-

tanyl for spinal anesthesia. Use of hyperbaric bupivacaine is related with longer motor and sensory blockade time, thus, priority for day-case surgery could be given to isobaric bupivacaine.

DEVELOPMENTAL PROGRESSION OF THE FETAL AORTIC ARCH AND ITS BRANCHES IN THE PERIOD FROM THE 4TH TO THE 7TH LUNAR MONTH

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Introduction: In prenatal and adult cardiovascular surgery and cardiology, knowledge about development of the aorta and great arteries is very important. The growth dynamics of these structures is essential for understanding of their morphological and functional characteristics.

Aim: The aim of this study was to determine the morphometric characteristics as well as developmental progression of the fetal aortic arch and its branches in the period from 4th to the 7th lunar month.

Methods: The study was performed on 51 preparation of the fetal heart with the aortic arch (AA) and its branches: brachiocephalic trunk - BT; left common carotid artery - lCCA; left subclavian artery - lSCA. Preparations were photographed and by using ImageJ program diameters of AA, BT, lCCA and lSCA were measured. Statistical analysis was done in program IBM SPSS Statistic ver. 20.0.

Results: All measured parameters showed statistically significant increasing in 7th lunar month (p < 0.05) and only ISCA had statistically significant increasing in 5th lunar month (p < 0.05), too. Pearson's correlation (r) was calculated between AA diameter and AA branches diameters. Between 4th and 6th lunar month r(AA/BT) showed decreasing (0.403 to -0,022) and in 7th lunar month it was 0.629. This coefficient showed increasing during all analysed months for ICCa; r(AA/ICCA) = -0,567 to 0.495. Between 4th and 6th lunar month r(AA/ISCA) showed decreasing (-0.015 to -0,095) and in 7th lunar month it was 0.466.

Conclusion: Absence of linear developmental progression of AA branches in comparison with AA, could be consequence of developmental differences between fetal regions. Constant increasing of r(AA/ICCA) indicates constant progression of head region development. Similarity of r values for the other two branches indicates differences in speed of fetal arms development. Positive r values for all three AA branches in 7th lunar month suggest the pronounced growth of all regions in the 3rd trimester.

A COMPARATIVE SYSTEMATIC REVIEW AND META-ANALYSIS OF PROSPECTIVE CONTROLLED TRIALS FOR THE EARLY-STAGE COMPLICATIONS BETWEEN SUBTOTAL AND TOTAL THYROIDECTOMY IN PATIENTS WITH BENIGN MULTINODULAR GOITRE

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Introduction: The best choice of Benign multinodular goiter (BMNG) treatment is surgery. However, the surgical method of BMNG is still controversial between Subtotal thyroidectomy (STT) and Total thyroidectomy (TT). The selected surgical method for BMNG should aim to eradicate the disease as well as to minimize postoperative complications.

Aim: We conducted this systematic review and meta-analysis to compare the postoperative length of hospital stay and the early-stage postoperative complications rate between STT and TT in patients underwent surgery for BMNG.

Methods: In March 2019, we searched PubMed, Scopus, Web of Science, and Cochrane Central Register of Controlled Clinical Trials with search terms including "Subtotal thyroidectomy", "Total thyroidectomy", and "Benign Multinodular Goitre". We included prospective controlled trials in which the population was patients with BMNG, the intervention was STT, the comparator was TT, and the outcomes were the postoperative length of hospital stay and the early-stage complications including; Hemorrhage, Hematoma, Temporary hypoparathyroidism, Permanent hypoparathyroidism, Wound infection, Permanent recurrent laryngeal nerve palsy, and temporary recurrent laryngeal nerve palsy. We excluded observational studies, conference abstracts, thesis, editorials, letters, reviews, and studies with data that were not sufficiently reliable for extraction. Data were extracted for study design, patient characteristics, risk of bias domains, and study outcomes. Fixed and random-effects models were used to generate pooled risk ratios (RRs) and 95% confidence intervals (CIs). The Analysis was done using RevMan software version 5. We could not asses the publication bias as only six studies were included. We assessed the risk of bias for the included studies using the risk of bias tool provided by Cochrane handbook for systematic reviews.

Results: We included six studies that enrolled 1471 patients with BMNG. Our analysis revealed a significant difference between the STT and TT regarding the length of hospital stay (MD -0.33, 95% CI [-0.56 - -0.10]; P = 0.005). There was no significant difference for most of the postoperative complications; Hemorrhage (RR 1.05, 95% CI [0.05 - 22.49]; P = 0.97), Hematoma (RR 1.24, 95% CI [0.38 - 4.04]; P = 0.72), Temporary hypoparathyroidism (RR 0.49, 95% CI [0.22 - 1.13]; P = 0.09), Permanent hypoparathyroidism (RR 0.46, 95% CI [0.15 - 1.47]; P = 0.19), Wound infection (RR 1.14, 95% CI [0.25 - 5.14]; P = 0.86), Permanent recurrent laryngeal nerve palsy (RR 0.63, 95% CI [0.19 - 2.12]; P = 0.46). However, there was a significant difference regarding the postoperative temporary recurrent laryngeal nerve palsy (RR 0.53, 95% CI [0.32 - 0.88]; P = 0.01).

Conclusion: There was no difference between the two procedures in all the assessed complications except for the length of hospital stay and the postoperative temporary recurrent laryngeal nerve palsy which were more prevalent with the TT procedure.

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THE FREQUENCY OF POSTOPERATIVE COMPLICATIONS IN DIFFERENT ASA PHYSICAL STATUS CLASSIFICATION GROUPS OF PATIENTS WHO UNDERWENT ENDOVASCULAR ANEURYSM REPAIR BECAUSE OF ABDOMINAL AORTIC ANEURYSM (AAA)

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Introduction: Myocardial injury after noncardiac surgery (MINS) is a common complication in adult patients undergoing noncardiac surgery and is an independent predictor of 30-day mortality. In opposition to myocardial infarction (MI), most patients with MINS do not present any ischemic symptoms or electrocardiographic abnormalities. The ASA physical status classification system (ASA) is used for assessing the fitness of patients before surgery.

Aim: The aim of our study was to determine the frequency of MINS, myocardial infarction (MI), acute kidney injury (AKI) and intra-hospital mortality incidents and its dependency on preoperative ASA score in patients undergoing endovascular aneurysm repair (EVAR).

Methods: The observational retrospective study was performed on medical records of 172 patients (82% men) undergoing EVAR in St. John Grande Hospital in Cracow. ASA score was obtained from anesthetic charts. Statistical analysis was performed with Kruskal-Wallis test and Chi^2 test as appropriate.

Results: For the statistical comparisons, AAA patients were divided into three groups depending on preoperative ASA score: ASA II – 16(9,3%) of patients), ASA III – 94(54,65%) and ASA IV – 62(36,05%).

MINS was detected in 52 of all patients (30,23%), while MI was diagnosed only in 3 (1,74%) of them, AKI occurred in 9 (5,23%) patients and intra-hospital death in 2 (1,16%).

There was statistically significant difference in MINS frequency between ASA groups (ASA II-IV, respectively): 0% vs 24,1% vs 44%, p = 0,02. No significant difference was found in the frequency of MI, AKI and intra-hospital mortality incidents between the study groups.

Compared groups varied depending on the prevalence of coronary artery disease (ASA II-IV, respectively: 0% vs 61,45% vs 86%, p < 0,01), history of MI or acute coronary syndrome (ASA II-IV, respectively: 0% vs 39,76% vs 68%, p < 0,01) and chronic heart failure (ASA II-IV, respectively: 0% vs 28,92% vs 72,00%, p < 0,01). The study groups were comparable regarding creatinine serum concentration, eGFR-MDRD level on admission and arterial hypertension prevalence.

Conclusion: The most common complication after EVAR is MINS, which is asymptomatic in most cases and rarely fulfills the universal definition of MI. The frequency of MINS incidents increases with higher class of ASA scale.

Therefore patients undergoing EVAR, especially with high ASA score, should be routinely tested for troponin levels after surgery.

UNDERSTANDING THE ANATOMICAL SIGNIFICANCE OF THE MENISCOFEMORAL LIGAMENTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: The knee features a complex system of ligaments. Two of the many elements are the posterior meniscofemoral ligament (pMFL) of Wrisberg, and the anterior meniscofemoral ligament (aMFL) of Humphry. Both meniscofemoral ligaments (MFLs) attach the posterior horn of the lateral meniscus to the lateral intercondylar aspect of the medial femoral condyle.

Aim: To perform a systematic review and summarize the plethora of clinical advancements made over the past two decades regarding the anatomy of the MFLs within the scope of arthroscopic surgery.

Methods: An extensive literature search of the major online databases was performed to evaluate all reported data on MFLs. No date or language restrictions were applied. Assessments of article eligibility and data extractions were both completed independently by two reviewers. There was strict adherence to the PRISMA guidelines.

Results: A total of 61 articles were included in the study. The overall pooled prevalence of aMFLs and pMFLs were 56.2% (95%CI: 46.7–65.4) and 71.0% (95%CI: 64.3–77.2) respectively. Both ligaments were more prevalent in cadaveric studies than in MRI studies. The aMFL was most prevalent in South America, while the pMFL was most commonly in Asia.

Conclusion: Despite the variability in recent results, the MFLs are much more prevalent, larger, and play a greater role in the stabilization of the knee than has been previously described. The shared features of the pMFL with the PCL are highlighted to necessitate the consideration of these ligaments in their valuable role supporting recovery after knee arthroscopic procedures. The high prevalence of MFLs generated a demand to elucidate their functionality and relevance in orthopedic management of the knee. An understanding of these ligaments may provide key insight for optimal management during treatment, particularly in discoid and torn menisci.

THE ACCESSORY PAROTID GLAND AND ITS CLINICAL SIGNIFICANCE: A META-ANALYSIS OF ITS PREVALENCE

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¹International Evidence-Based Anatomy Working Group, Krakow, Poland; ²Department of Anatomy, Jagiellonian University Medical College, Krakow, Poland **Introduction:** The accessory parotid gland (APG) is a collection of salivary tissue separate from the main parotid gland that may complicate parotidectomies, promote parotitis and serve as a potential site for benign and malignant lesions.

Aim: The aim of this study was to provide a comprehensive overview of the prevalence and anatomy of the APG.

Methods: An extensive search of the major electronic databases was conducted to identify all studies which reported relevant data on the APG. No date or language restrictions were applied. Data on the prevalence, side of occurrence and sex dimorphism of the APG were extracted and pooled into a meta-analysis.

Results: A total of 13 articles (n = 3,115 parotid glands) were included in the study. The overall pooled prevalence of an APG was 32.1% (95% CI: 21.2-44.0). It was more prevalent in cadaveric studies (35.8%) than in CT studies (21.5%), its prevalence was higher in Asia (33.8%) compared to North America (23.5%), and when present, it was most often unilateral (77.8%).

Conclusion: Considering the high reported prevalence of the accessory parotid gland in this meta-analysis, caution is recommended when planning and performing parotidectomies, investigating a possible cause of recurrence of sialadenitis, and its presence should be considered when differentiating cheek masses.

ORTHOPEDIC TREATMENT AND EARLY WEIGHTBEARING FOR BIMALLEOLAR ANKLE FRACTURES IN ELDERLY PATIENTS. QUALITY OF LIFE AND COMPLICATIONS

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Introduction: Conservative treatment of Weber's type B ankle fractures is essential in elderly patients. However, there is controversy surrounding post-reduction management of the fracture between the use of early weightbearing or traditional treatment with non-weightbearing for 6–8 weeks. There is limited evidence available regarding which rehabilitation regimen should be included.

Aim: The aim of this study was to compare the quality of life as well as the number of complications between the two types of intervention (weightbearing and non-weightbearing).

Methods: Prospective cohort study. The quality of life was analyzed through the SF-12 and the Barthel Index at 6 weeks, at one year and at two years. The mean age was 83 ± 3 years in the weghtbearing group and 82 ± 3 in the non-weightbearing group. In addition, the associated complications were analyzed.

Results: A total of 80 patients were divided into two groups: a control group of 37 patients (non-weightbearing) and an experimental group of 33 patients (weightbearing). A significant difference was observed in favor of early weightbearing in SF-12 both in the short and long term (52.9 ± 5.3 vs 64.9 ± 4.6 ; p < 0.001 and 69.8 ± 4.1 vs 81.0 ± 3.6 ; p < 0.001). Significant differences were also observed in favor of early loading with respect to the Barthel Index (54.3 ± 4.9 vs 64.2 ± 3.9 ; p < 0.001 and 70.6 \pm 4.2 vs 80.4 \pm 3.0; p < 0.001). There were no significant differences in the complication rate between the two groups.

Conclusion: Early weight bearing improves quality of life and functionality in elderly patients with Weber type B fracture, without increasing complications.

COMPARISON OF CEMENTED AND UNCEMENTED FIXATION HIP ARTHROPLASTY TECHNIQUE IN ONE-YEAR-LONG FOLLOW UP

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Introduction: Total hip replacement (THR) is one of the most frequent orthopedic surgery. In Poland the number of THR is rising every year. In 2017 the total number reached 56,688. The society is getting older and number of THR is supposed to grow proportionally.

Aim: The main aim of our study was to emphasize the advantages and disadvantages of both methods. We wanted to check different risk factors that cause complications. Furthermore, we wanted to categorized all patient by age, sex, and comorbidieties such as hypertension, diabetes mellitus type 2, osteoporosis.

Methods: The observational retrospective study with oneyear-long follow up was performed on medical records of 180 patients who underwent THR at the Department of Orthopedics of University Hospital in Kraków in 2017. To compare both groups we used Statistica program.

Results: The study group consisted of 180 patients in average age of $65,77 \pm 12,6$ years (male 52%). Uncemented fixation was performed in 137 cases, cemented in 33 and 10 by hybrid method.

Compilations (long lasting pain, fractures, limited mobility, infections) were observed in 11,6% and 18,2% of patients in uncemented and cemented group, but the difference was not statically significant (p = 0,47). Serious complications ended with reoperations was observed at 4,4% of all patients. Patients who underwent THR provided by uncemented technique were younger than those whose prothesis were inserted using cemented technique (63,28 ± 10,81 vs. 78,76 ± 8,88), p = 0.001). Additionally, their hospitalization remained shorter (5 vs. 7 days, p = 0,019).

Conclusion: Our outcomes suggest that younger patients undergo uncemented fixation and hospitalizations of this patients are shorter. It is essential to establish the best treatment for patient in every day clinic routine. What is interesting current-smoking patients faster were able to move because of cigarette requirement.

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THE COMPARISON OF EARLY POSTOPERATIVE OUTCOMES BETWEEN SANO MODIFICATION OF THE NORWOOD PROCEDURE AND MODIFICATION OF THE NORWOOD I PROCEDURE WITH BILATERAL PULMONARY ARTERY BANDINGS

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¹Medical University of Silesia in Katowice, Department of Pediatric Cardiac Surgery, John Paul II Upper Silesian Child Health Centre in Katowice **Introduction:** Hypoplastic left heart syndrome (HLHS) is a congenital condition of the heart in which the left side of the heart does not fully develop. Among others, the treatment options include Sano modification of the Norwood procedure and modification of the Norwood I procedure, in which the aortic arch was reconstructed with an extracellular matrix patch and bilateral pulmonary artery bandings.

Aim: The aim of this study is to assess the odds ratio and compare early postoperative complications of patients who undergo either of these procedures using propensity score matching (PSM).

Methods: The study group consisted of 38 pairs selected from 124 patients with HLHS diagnosis. Subjects in each pair differed in the type of procedure they underwent (either of the above) while they were similar in terms of sex, age, body mass, the occurrence of preoperative sepsis and past procedures. The chosen treatment method was not a matter of patients' classification to surgery but a method of choice during particular years.

The complications taken into consideration were: delayed sternal closure, the requirement of postoperative extracorporeal membrane oxygenation, reexploration due to bleeding, chest reexploration due to other reasons, peritoneal dialysis, abdominal drainage, circulatory and respiratory failure and early mortality up to 30 days.

Results: The study showed that after matching there were no differences in odds ratio between the procedures in observed endpoints beyond chest reexploration due to an inadequate pulmonary flow -which was significantly higher in Sano modification group (OR: 3.11; 95% CI:1.04–9.2; p = 0,041).

Conclusion: The retrospective comparison of both procedures showed that there were no significant differences in odds ratio in observed endpoints beyond chest reexploration-which was significantly higher in Sano modification group. Crucial for full assessment is similitude of the results after third- ending stage of palliative treatment in this patients.

SURGICAL TREATMENT OF FRACTURES OF THE ANKYLOSED SPINE

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Introduction: Progressive ankylosis of the spine is a hallmark of two distinct diseases: ankylosing spondylitis (AS) and diffuse idiopathic skeletal hyperostosis (DISH). Fractures in the ankylosed segments are often unstable because of the ossification of supportive and elastic soft tissues. These are more prone to dislocation with associated neurologic deficits. Also, clinical outcomes are worse in patients with ankylosed spine segments compared to the general population. New back pain in patients with AS or DISH should be assumed to be caused by a fracture until proven otherwise. This way, systematic assessment through clinical history and radiology imaging needs to be implemented and repeated for the first few weeks after a trauma, especially if the patient complains of indefinable pain or if neurological deficits are recorded. Treatment of spinal fractures in the ankylosed spine is controversial. There are several reports on non-surgical treatment describing it as safer compared to operative management due to the higher rates of morbidity and mortality of the later. However, more recent studies have shown better outcomes in surgically-treated patients with lower complication and mortality rates and higher chances of neurological improvement.

Aim: We aim to identify retrospectively surgically treated patients with an ankylosed spine who sustained a vertebral fracture. Our goal is to evaluate the main outcomes and complications.

Methods: We selected patients through the database of surgical interventions in the setting of fractures of an ankylosed spine segment between January 1st 2008 and June 30th 2018. We collected data from digital medical records. The parameters analyzed include hospital length of stay, Intensive Care Unit (ICU) admission, perioperative and postoperative complications as well as neurologic evolution.

Results: Fractures occurred in 14 patients with Ankylosing Spondylitis (82%) and 3 patients with Diffuse Idiopathic Skeletal Hyperostosis (8%). All patients were male and the mean age was 69 years. Fourteen fractures occurred after minor trauma (83%) from which 11 were due to falls from standing height or lower (65%). The cervical spine represents the majority of the levels involved (59%). Seven patients were admitted to the ICU (41%) and 11 suffered neurologic damage. There was improvement of the neurological status in less than 50% and there were great percentages of post-operative complications.

Conclusion: Patients with an ankylosed spine disease are at higher risk for vertebral fracture even after minor trauma and these are located predominantly in the cervical spine. The surgical treatment of these conditions is effective as it allows improvement of the patient's neurological status. However, they still present higher morbidity and mortality as well as increased post-op complications. Prevention of falls may drastically change patients' outcome, neurologic function and independence for daily activities.

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MORPHOMETRIC ANALYSIS OF THE INFRAORBITAL FORAMEN IN HUMANS

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Introduction: The position of the infraorbital foramen (IOF) has great importance in clinical practice. There is a wide spectrum of variations regarding to position of IOF or its number. Racial or variations between different populations are noted, too.

Aim: The aim of this work was to determine the morphometric characteristics of IOF in Serbian population.

Methods: Infraorbital foramina of 53 dry adult skulls (osteological collections from Faculties of Medicine in Nis and Novi Sad, Serbia) of undetermined gender were examined for variations in number and in relation to bony landmarks (infraorbital margin, maxillary alveolar margin, pyriform aperture) and midline of skull. Skulls are photographed with ruler and these four linear parameters were measured by using ImageJ software. Statistical analysis was performed in program IBM SPSS Statistic ver. 20.0.

Results: The infraorbital foramina were located at an average distance of 6.81 ± 1.69 mm below the infraorbital margin, 24.52 ± 3.10 mm from the median plane, 13.24 ± 2.80 mm from the lateral margin of the pyriform aperture, and 18.77 ± 7.30 mm above the maxillary alveolar border. Statistically significant difference in measured parameters between right and left side, was not noted. Two IOFs were noted in one skull on the right and in four skulls on the left side. In one skull there were two IOFs bilaterally.

Conclusion: There is variability in the position and anumber of the IOF. The mrgin of the pyriform aperture is not palpable in live patients. The level of the maxillary alveolar border differs from person to person depending upon their periodontal status. The infraorbital margin and the facial midline would be the most dependable references for locating the IOF. The observations made in this study should be useful for planning infraorbital nerve block or surgery around the IOF.

ARE PATIENTS WITH SCHMORL NODES MORE LIKELY TO DEVELOP LOW BACK PAIN? A META-ANALYSIS

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Introduction: Schmorl nodes (SN), defined as intervertebral disc's protrusions into neighbouring vertebrae, are common findings in radiographic images of the spine. Low back pain (LBP) is highly prevalent and potentially detrimental to quality of life disorder with varying and sometimes unclear etiology. The role of SN in pathogenesis of chronic LBP remains controversial.

Aim: To conduct meta-analysis on the prevalence of SN and determine its association with LBP.

Methods: Search through major electronic databases (PubMed, Embase, Web of Science - Core Collection, SciELO and BIOSIS) was performed to identify articles describing SN prevalence and its relationship to LBP. Data regarding SN prevalence in both LBP-affected and control group was extracted. The type of study (Xray/MRI) and country of origin were also included in the analysis.

Results: A total of 6 papers (n = 2504 patients) published in years 2001–2015 were considered relevant. Overall prevalence of SN in the whole study was 19.3% (95%CI:12.6– 27.0): 22.8% (95%CI:14.9–31.8) for LBP patients and 17.0% (95%CI:8.8–27.1) for asymptomatic group. Pooled odds ratio, calculated with usage of random effects model, equaled 1.45 (95%CI: 0.86–2.42, I-squared 76.39%), thus was statistically not significant.

Conclusion: Our meta-analysis showed that SN is a highly prevalent structure. The results indicated that there is no relationship between the presence of SN and LBP. Therefore the presence of SN on spine radiographs should not be regarded as satisfactory explanation for occurence of LBP. To our knowledge this is the first meta-analysis assessing the association of SN and chronic LBP.

SPECTRUM OF DISEASES LEADING TO ACUTE ABDOMEN IN GERIATRIC PATIENTS- AGE GROUP AND SEX DIFFERENCES

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Introduction: Acute abdomen is one of the most common reasons for emergency hospitalizations in surgical wards. Due to the aging of the population the number of elderly undergoing emergency surgeries is expected to increase.

Aim: Our aim was to identify the causes of emergency hospitalization in patients ≥ 65 years undergoing abdominal surgery depending on their sex and age.

Methods: Consecutive patients ≥ 65 years, requiring emergency abdominal surgery in 2010–2017 were enrolled into the study. Patients were divided into three age groups (65–70 years,

71–84 years and \geq 85 years) between which the frequency of particular reasons for hospitalization was compared.

Results: The study sample comprised 986 older patients (562 female, 424 male) with a median age of 76 (from 65 to 102). 25,9% patients had 65-70 years, 57,0% had 71-84 years and 17,1% had \geq 85 years. In the first and second age group the most frequent reasons for surgery were: acute cholecystitis, non-malignant ileus, colorectal cancer complications and acute appendicitis. In the oldest age group (≥ 85 years) the most common were colorectal cancer complications, acute cholecystitis, non-malignant ileus and complicated diverticulitis. Men were most frequently diagnosed with acute cholecystitis, colorectal cancer complications and non-malignant ileus. Among women the most common conditions were acute cholecystitis, non-malignant ileus and colorectal cancer complications. The following conditions were statistically more frequent in patients aged ≥ 85 than in younger patients: colorectal cancer complications (p = 0.041), complicated diverticulitis (p = 0,025), complicated peptic ulcer disease (p =0,023). The highest in-hospital mortality was reported for acute intestinal ischemia (57,1%), followed by pancreatic cancer complications (51,9%) and complicated peptic ulcer disease (44,8%).

Conclusion: The reasons for abdominal surgery in geriatric patients differ between age groups and while comparing men and women. In individuals aged 85 or more, complications of diverticulitis, peptic ulcer disease and colorectal cancer are significantly more common than in younger geriatric patients.

THE SIGNIFICANCE OF THE TRANSVERSE FACIAL ARTERY ANATOMY IN PLASTIC SURGERY PROCEDURES

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Introduction: The transverse facial artery (TFA) is the vessel that provides blood supply to the lateral face. In aesthetic and plastic surgery it is crucial to know the topographical anatomy of the lateral face, especially when it comes to the face lift flap and face transplant.

Aim: The aim of the present study was to assess detailed TFA morphometrical features.

Methods: One-hundred computed tomography head angiographies were analyzed. TFA numbers and origins were recorded bilaterally (200 cases). TFA diameters and lengths in addition to their positions in relation to neighboring vessels and the zygomatic arches were measured.

Results: TFA was present in 96% of cases (192/200, left = 97, right = 95). A single TFA was present in 95.3% and double TFAs were present in 4.7% of cases. In 91.7%, the TFA originated from the superficial temporal artery, and in 3.1%, it originated from the external carotid artery. One left TFA originated from the maxillary artery. The TFA was significantly longer on the right than on the left side (56.6 ± 26.0 versus 47.3 ± 22.2 mm; p = 0.03). The TFA mean diameter was 1.0 ± 0.4 mm (range: 0.4–2.2 mm) with no difference between face sides. TFA length correlated with its diameter (r = 0.46, p < 0.05). The TFA always originated below the zygomatic arch, and it should be found in the 8.8 mm wide area beginning 17.0 mm below the lower border of the zygomatic arch.

Conclusion: The TFA has a significant role in lateral face vascularization, and absence of this vessel is not very common.

EFFICACY OF IVF-ET IN PATIENTS WITH MYOMECTOMY AND EMBOLIZATION OF THE UTERINE ARTERIES

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Introduction: Leiomyoma rate in infertile women – 27%. In vitro fertilization-embryo transfer (IVF-ET) outcome in patients after different treatment is unclear.

Aim: To evaluate IVF-ET effectiveness after different treatment of fibroids.

Methods: Retrospective study of 158 case histories (2015–2017). Patients were divided into 3 groups depending on treatment: I – myomectomy (ME) – 72(40%), laparoscopy (Ls) – 44(61%), laparotomy (Lt) – 28(39%); II – uterine artery embolization (UAE) – 19(11%); III – control – 67(37%) patients with fibroids without treatment.

Results: Mean age in groups – 38.04 ± 0.37. Main infertility factors: tubal factor - 69%, low ovarian reserve - 15%. Fibroids location on anterior, posterior uterine wall, single fibroids, intramural and intramural-subserosal types prevailed. Leiomyomas size >40 mm in group I - 67%, in the rest - level didn't exceed 32%. Average IVF attempts number in control group: ≤35 years -1.59 ± 0.17 , ≥ 36 years -2.51 ± 0.24 ; in group I: 2.81 ± 0.45 and 4.07 ± 0.33 (p < 0.05). After UAE in comparison with ME number depended on age: ≤ 35 years – 2.5 ± 0.29 vs. 2.81 ± 0.45 (p>0.05), ≥ 36 years -2.77 ± 0.55 vs. 4.07 ± 0.33 (p < 0.05). IVF+ovarian stimulation was performed in 60, 74, and 66% of patients, sperm donation cycle - in 8, 5 and 6%, respectively, all the rest – IVF without stimulation. Good quality embryos was >58% in each group. Canceled ET: 5% (I), 21% (III). In group III transfer of one/two embryos - 46 and 33%, in I and II - single embryo transfer was performed 2 times more often. Effective IVF-ET was in 23(34%) patients of control group, in 12(52%) of them – after the first attempt. After Lt-ME – in 20(28%), 11(55%) of them conceived after \geq 4 IVF attempts; after Ls-ME - in 36(50%), 15(42%) of them after 2-3 attempts; after UAE in 11(58%), 6(54%) of them after 2–3 attempts.

Conclusion: Pregnancy rate after IVF-ET is 2 times higher both after ME and UAE than without treatment; IVF-ET effectiveness after ME is higher than after UAE.

THE IMPORTANCE OF MONITORING D-DIMER LEVELS IN PREDICTING THE RECURRENCE OF DEEP VEIN THROMBOSIS OF LOWER EXTREMITIES

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Introduction: Venous thrombosis is one of the most common diseases today. The occurrence of the postthrombotic syndrome and high mortality and recurrence rates reflect its large significance. Current research efforts are focused on detecting parameters that could estimate the risk of recurrence of this disease, and according to some researchers, D-dimer can be used for this purpose.

Aim: The aim of this study was to determine whether D-dimer monitoring is important in predicting the recurrence of deep vein thrombosis (DVT) of lower extremities.

Methods: The study was conducted on 92 participants who experienced one episode of DVT of the lower extremities. The values of D-dimer determined 2 months after the discontinua-

tion of oral anticoagulant therapy (OAK) were analyzed. Participants were classified into those who, during a two-year follow-up, experienced recurrence of DVT, and those who didn't. Based on the comparison of D-dimer levels with the cut-off value, participants were further classified into a group with high, and a group with normal D-dimer levels.

Results: There is a higher percentage of recurrence among participants who have experienced unprovoked, than among those who had provoked DVT. The results of logistic regression, with OR as a risk rate, after excluding the influence of confounding factors, indicate that D-dimer is not a significant predictor of DVT recurrence.

Conclusion: Results of our research indicate that monitoring D-dimer levels after discontinuation of OAK therapy is not a valid parameter in predicting DVT recurrence.

ISOKINETIC EVALUATION OF THE ISOLATED REPAIR OF THE SUPRASPINATUS MUSCLE AT 4 MONTHS

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Introduction: Double row arthroscopic rotator cuff repair has been the gold-standard for rotator cuff repair in the last few years. The supraspinatus is the most susceptible muscle to rupture in this context.

Aim: The aim of this study was to evaluate patients submitted to a double row arthroscopic repair of the rotator cuff with isokinetic tests, surface electromyography and Constant-Murley Score, and correlate these data with their clinical evolution four months after surgery.

Methods: Six patients with isolated and unilateral ruptures of the supraspinatus muscle, confirmed by MRI, were submitted to isokinetic dynamometry, surface electromyography and Constant-Murley functional Score. Injured and uninjured shoulder results were collected immediately before and four months after the surgery.

Results: Our results show improvements in isokinetic, strength and functional parameters.

Isokinetic results correlate well with functional and clinical scores and add value to the followup process. For the angular velocity of 90°/s in post-op, the angle at Peak Torque for the injured and uninjured limb was approximately the same (~42°). Electromyographic measurements provided valuable insight over the electrical activation of muscles of the shoulder girdle. After surgery, electromyographic measurements showed a lower normalized activation pattern for the injured and uninjured muscles, suggesting an increased efficiency in post-operative muscle function.

Conclusion: The performed surgery was effective. The selected four-month time frame is an important landmark to evaluate patients' recovery, since our data showed that most variables collected on the injured limb tend to evolve towards the values of the uninjured limb.

ACHILLES TENDON'S GRAFT CHARACTERISTICS FOLLOWING EXCESSIVE FREEZE-THAW CYCLES

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Introduction: Successful allograft surgery requires that graft has equal or greater biomechanical properties than of those tissues it is supposed to replace. The number of freeze-thaw (F/T) cycles might be a variant that influences the properties of the graft.

Aim: This study aimed to investigate the influence of the F/T cycles upon tendon graft biomechanical properties.

Methods: The authors evaluated 12 Achilles Tendons (AT) from healthy patients which were immediately frozen following their collection. The samples were randomly assigned to one of 3 groups subjected to 1, 2 or 3 F/T cycles that included 1 week of deep freezing, followed by 6 hours of thawing at room temperature. Biomechanical tests were performed with a uniaxial tension testing machine (INSTRON[®]) using a load cell with a maximum capacity of 10 kN in standard atmospheric conditions. The elasticity of the AT samples was evaluated in terms of Young's modulus, derived from the strain curves. The Shapiro-Wilk test, t-tests, non-parametric tests and p of < 0.05 applied in the statistical analysis. The research protocol was approved by local Ethics Committee in accordance with the 1964 Declaration of Helsinki and its later amendments.

Results: Based on the stress-strain curves the researchers noted that Group I had the highest mean value of the Young's modulus (279.8 \pm 38.6 MPa), hence the highest elasticity. A statistically significant decrease between Group I and Group II (168.4 \pm 26.1MPa, p < 0.01) was observed. Group III had the lowest mean value of Young's modulus (119.8 \pm 26.6MPa), which was significantly lower than the values of Group I (p < 0.01) and Group II (p < 0.05).

Conclusion: The results from this study point out to the fact that repetitive F/T cycles diminish the biomechanical properties of the AT tendon grafts.

INFLUENCE OF INTRACRANIAL ARTERY TORTUOSITY ON RISK OF THE ANEURYSM RUPTURE.

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Introduction: Blood vessel tortuosity plays an important role in the development of aneurysms, but its influence on their rupture is yet to be checked.

Aim: In our study we decided to determine, whether tortuosity of cerebral arteries such as Anterior Cerebral Artery, Middle Cerebral Artery, Basilar Artery and Internal Carotid Artery might be related to risk of these arteries aneurysms rupture as well as to severity and treatment outcome of subarachnoid haemorrhage (SAH).

Methods: We retrospectively analyzed vascular anatomy of 395 patients with intracranial aneurysm. From patients' medical records we obtained their history including previous and current diseases and data about aneurysm from their Digital Subtraction Angiography imaging data. Presence of SAH was determined based on CT scan. Upon admission patients were assessed using Glasgow Coma Scale (GCS). Upon discharge patients were assessed using modified Rankin Scale (mRS). For each patients' imaging data we performed series of image transformation to track course of aneurysm feeding artery and calculated its Relative Length (RL), Sum of Angle Metrics (SOAM), Triangular Index (TI), Product of Angle Distance (PAD) and Inflection Count Metrics (ICM) using software of our own design.

Results: A total of 134 (33.92%) had ruptured aneurysm. These patients had significantly higher RL (0.59 ± 0.21 vs. 0.51 ± 0.22 ; p < 0.01) and significantly lower SOAM (0.28 ± 0.19 vs. 0.35 ± 0.22 ; p < 0.01), PAD (0.27 ± 0.18 vs. 0.33 ± 0.21 ; p < 0.01) and ICM (0.33 ± 0.21 vs. 0.25 ± 0.19 ; p < 0.01) of aneurysm feeding artery. Additionally, we found significant negative correlation between mRS upon discharge and TI (R = -0.248; p = 0.042).

Conclusion: Higher cerebral arteries tortuosity might be protective factor against their aneurysm rupture. It can also be protective against aneurysm growth and poor outcome after SAH.

THE EFFECTIVENESS OF MICROWAVE ENDOMETRIAL ABLATION IN WOMEN AT PRE- AND POSTMENOPAUSE WITH ABNORMAL UTERINE BLEEDING

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Introduction: The choice of treatment for the patients with abnormal uterine bleeding (AUB) and concomitant somatic pathology remains one of the most relevant problems in gyne-cology. 25–30 % of AUB are caused by recurrent endometrial hyperplasia, uterine myoma, adenomyosis.

AUB often requires repeated hysteroscopies, dilatation and curettage (D&C). Commonly used hormone therapy is contraindicated in many cases because of apparent somatic pathology; radical surgery treatment can be life-threatening.

Microwave endometrial ablation (MEA) has recently evolved in many countries due to its maximum atraumatic technique, low frequency of intra- and post-operative complications, short recovery period and high economic efficiency.

Aim: To assess the effectiveness and safety of MEA in women at pre- and post-menopause with AUB in the early and late postoperative period. To determine the criteria of MEA effectiveness.

Methods: The study involved 142 patients with AUB divided into 2 groups: 62 premenopausal and 80 postmenopausal women, that underwent 3D-ultrasound, D&C with histologic evaluation, MEA with obligatory hysteroscopy control.

MEA was performed under intravenous anesthesia using Microsulis Microwave Endometrial Ablation System (UK) with subsequent hysteroscopy via 'KARL STORZ' equipment (Germany).

Results: We determined clinical, hysteroscopic and 3D-ultrasound criteria of MEA effectiveness. Hysteroscopic image of "burned field" (small layers of coagulated tissues of light-brown color) supposes to be the criterion of effective MEA. It's absence may be an indication for repeated targeted ablation of intact endometrial fields.

Clinical criteria are: amenorrhoea of premenopausal patients, absence of the bloody discharge of postmenopausal patients.

We defined 3D-ultrasoud criteria allowing not only to elevate the effectiveness of ranking patients at pre-hospital stage, but also to assess the effect of MEA (only in conjuction with clinical and hysteroscopic criteria).

The full effect after MEA for premenopausal patients was achieved in 80,6 % cases, partial – in 11 %, absence of effect – in 8 %. Partial or absence of effect has been seen in patients with associated apparent adenomyosis and metabolic syndrome. Effectiveness of MEA at postmenopause was 100 %.

Conclusion: The criteria of effectiveness of MEA are determined.

Clinical results demonstrated that MEA is the safe and effective method that can be used as an alternative to hormone therapy and hysterectomy in the treatment of AUB at pre- and postmenopause, especially in women with apparent somatic pathology, excluding patients with apparent adenomyosis and metabolic disorders.

THE ANALYSIS OF COMPLICATIONS IN PATIENTS UNDERGOING LAPAROSCOPIC CHOLECYSTECTOMY IN CRACOW, POLAND

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Introduction: Laparoscopic cholecystectomy (LC) is the "gold standard" in the treatment of gallbladder diseases as it possesses many advantages over the open method. Despite its numerous benefits, choosing the laparoscopic method is not completely risk-free.

Aim: The aim of this study was to analyze complications seen in patients treated with LCs at the General Surgery Clinic of the 5th Military Hospital in Cracow, Poland between 2012 and 2017.

Methods: The study was a retrospective analysis of 1,073 participants operated using the LC technique. The study recorded both intraoperative and postoperative patient complications and the incidence and reason for conversion to the open method.

Results: Intraoperative complications (IOCs) were noted in 29 cases (2.7%). A statistically significant difference was found between the occurrence of IOCs and procedure mode (emergent vs elective) (p < 0.001), presence of peritoneal adhesions (p = 0.03), duration of surgery (p < 0.001), and patient's gender (p = 0.016). There were 38 (3.5%) conversions to the open method. No statistically significant difference between conversion and the surgeons experience (p = 0.252) was found. Postoperative complications (POCs) were noted in 43 cases (4.0%). A statistically significant difference was found between POCs and patient's age (p < 0.001), and presence of gallbladder empyema (p < 0.001).

Conclusion: After analysis of all IOCs, POCs, and conversions this study strongly suggests that LC is a relatively safe procedure. The occurrence of complications or conversions is not dependent on the surgeons experience and may occur at any point.

ENDOMETRIAL INFERTILITY FACTOR IN PATIENTS WITH OVARIAN ENDOMETRIOSIS

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Introduction: It is known that endometriotic ovarian formations (EOF) are often associated with infertility, which is directly due to impairment of the ovarian reserve (OR).

Aim: To assess the state of the endometrium, evaluating the OR, in patients with endometriosis-associated infertility.

Methods: 98 patients with infertility who were operated on EOF were included in the study. They were divided into two groups according to the degree of impairment of OR. I group consisted of patients (60) with altered OR, II group - patients (38) with unchanged OR.

Ultrasonography was performed using of transvaginal volumetric sensor with a frequency of 5 MHz in 3D mode.

Endometrial volume (V, cm3), thickness, vascularization (VI), flow (FI) and vascularization flow indexes (VFI) of vessels in the basal and parabasal endometrial zones were studied on the 5th day after ovulation (the implant window).

Results: The following values were obtained during the study: endometrial thickness values ranged from 6.1 to 7.0 mm in the I group and 8.5–14.2 mm in the II group, that is 1.7 times more compared to the I group.

Average endometrial volumes were 1.42 \pm 0,96 and 2.5 \pm 0,57 cm3 respectively, 1.7 times more in II group, p < 0.05.

In the vessels of the basal and parabasal zones of first group VI was $(1.25 \pm 2.37; 1.68 \pm 2.57)$, and in group II $(2.02 \pm 1.44, 4.22 \pm 2.04)$, respectively, which is significantly 2.5 times more in the arteries of the parabasal zone in II group (p < 0.05).

Comparing FI between groups was insignificant.

The VFI of the arteries in the parabasal zone in patients of group I (0.15 \pm 0.46) were significantly 2.9 times lower than in group II (0.44 \pm 0.48) (p < 0.05). In the arteries of the basal zone, the difference in VFI indices between groups was insignificant.

Conclusion: Studying blood flow of basal and parabasal vessels in the endometrial zone is an indicator of the state of the endometrium with endometriosis-associated infertility.

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EPIDEMIOLOGICAL AND MORPHOLOGICAL ANALYSIS OF VERTEBRAL AND CEREBRAL METASTASES OF PROSTATE CANCER DIAGNOSED IN THE LARGEST NEUROSURGERY HOSPITAL IN NORTHEAST ROMANIA

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Introduction: Adenocarcinoma of the prostate is the most common form of cancer in men and the second leading cause of cancer death. Metastasis occurs in approximately 18% of patients with prostate cancer, with the most frequent sites involving the skeleton, distant lymph nodes, liver and thorax.

Aim: We want to reveal the main features of the brain and vertebral metastases arising from the prostate cancer: the average age of the patients, time of occurrence after the primary diagnosis, topography, and anatomopathological appearance.

Methods: We included in this study 29 patients (15 with vertebral and 14 with cerebral metastases) who presented to the Neurosurgery Hospital Iasi from January 2017 to December 2018. The anatomopathological examination suggested a metastatic foci of prostate cancer.

Results: The average age of those with vertebral metastases was 74, and of those with cerebral metastases was 69. The time of occurrence after the primary diagnosis was, on average, 28 months for those with vertebral metastases and 31 months for those with brain metastases. Three patients (2 with vertebral and 1 with cerebral metastases) hadn't been diagnosted with prostate cancer before. Three patients had a solitary brain metastasis and eleven had multiple. The vertebral sites of metastases were thoracolumbar in 9 patients (60%), thoracal in 4 patients (26.66%) and lumbar in 2 patients (13.33%). In patients with vertebral metastases 6 well differentiated (40%), 5 moderately differentiated (33.33%) and 4 poorly differentiated carcinomas (26.66%) were identified. In patients with brain metastases, 8 carcinomas were moderately differentiated (57.14%), 4 were poorly differentiated (28.56%) and 2 were well differentiated (14.28%).

Conclusion: Brain metastases occurred in younger patients, but their time of development was longer. Metastases tended to be multiple in both locations. Moderately differentiated carcinoma was more frequent among brain metastases and well differentiated carcinoma was more frequent among vertebral metastases.

PROLONGED HOSPITALIZATION AFTER PROCTOLOGY SURGERY AT THE CLINIC FOR DIGESTIVE SURGERY, CLINICAL CENTER OF SERBIA

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Introduction: Ambulatory Surgery has been defined as any surgical procedure performed on the same day as patient presents to and is released from a facility. Proctology Ambulatory Surgery is safe and offers potential benefits. In world proctology interventions are done as Ambulatory Surgery or also known as one day surgery.

Aim: To analyze Ambulatory Proctology Surgery clinical practice and reasons for prolonged hospitalization in patients treated at the Clinic for digestive surgery, CCS.

Methods: The study included 133 surgical patients with proctology conditions: fissure, abscess, fistula, hemorrhoids, pilonidal sinus, hypertrophic papilla in a 6 months period (from July to December 2018). Data related to demographic charac-

teristics, type of operations and prolonged hospitalization were obtained with an insight in medical documentation of patients.

Results: In our cohort of respondents there were 63.9% men and 36.1% women. The mean age was 46 years. Local anesthesia was applied in 64 (48%) while the others had general anesthesia. 90 % of patients had ASA score 1 and 2. In most cases surgery lasted between 30 and 60 minutes (56.4%), while with the shorter duration (less than 30 minutes) was 36% of patients. We found that only 7 patients were discharged on the same day, and 44 in a period of one day. Hospitalization of 2 days had 25.5%, and with 3 days 21% of patients. Reasons for prolonged stay (61.6% patients) were rewinding (21), protocol (30), weekend (17), drain (6) and among 54 was no reason stated. There were no life-threatening reasons for prolonged stay.

Conclusion: Bringing out the consciousness about the Ambulatory Surgery is still an issue as well as the question of good preoperative preparation in patients. Analyzing reasons for prolonged hospitalization we came to conclusion that all that procedures can be done as outpatient.

ANALYSIS OF THE RESULTS OF TREATMENT OF THORACIC AORTIC ANEURYSMS AND DISSECTIONS BY THE TEVAR PROCEDURE WITH COVERAGE OF THE LEFT SUBCLAVIAN ARTERY

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Introduction: The gold standard method for descending aortic aneurysms and B-type dissection treatment is thoracic endovascular aortic repair (TEVAR). Due to the anatomy and technical limitations, in some cases coverage of the left subclavian artery (LSA) is necessary. Mostly, it does not cause symptoms requiring immediate intervention. Symptoms of subclavian steal syndrome or left upper limb ischemia can be treated with elective procedures.

Aim: Our aim was to analyse the incidence and severity of steal syndrome after the coverage of LSA and necessity of surgical treatment thereof.

Methods: 154 patients with thoracic aortic aneurysm and aortic dissection admitted to the Department of Vascular and Endovascular Surgery at John Paul II Hospital in Kraków, Poland, between 2014 - 2018 were included into analysis. Patients were divided into 2 groups based on the coverage of LSA. The groups were compared in terms of the urgency of the procedure, incidence of post-operative steal syndrome, other complications and reintervention rate.

Results: There were 113 (75%) urgent procedures. Elective patients were statistically older than the urgent (66.9 + -11.1 vs 61.8 + -14.9, p = 0.047). 39 patients (25%) had the LSA covered. Both groups had the same percentage of coverage of LSA (21% vs. 27%, p = 0.65). Overall, 7 (4,5%) patients experienced symptoms of steal syndrome - 1 (2.4%) in elective and 6 (5.3%) in urgent group (p = 0.92). In one case reintervention was necessary due to the symptoms of upper limb ischemia.

Conclusion: In case of TEVAR with LSA coverage, revascularization of the left subclavian artery may be postponed and performed depending on the observed symptoms. In the literature, there is still not enough data regarding the proper approach in such cases.

OUTCOMES AND COMPLICATIONS OF THE TREATMENT OF UNRUPTURED WIDE-NECK BIFURCATION ANEURYSMS WITH PCONUS DEVICE

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Introduction: Endovascular management of bifurcation aneurysms is a technical challenge for interventional radiologists. In our study we present our initial experience with the new pCONus device, which was used for wide-neck intracranial bifurcation aneurysms.

Aim: The objective of the study was to show the results of pCONus application in patients with unruptured bifurcation aneurysms.

Methods: A retrospective study was performed to analyze 6 male patients with unruptured aneurysms treated with the pCO-Nus device and coiling in 2017 in the angiological diagnostics and interventional radiology section of the Department of Radiology, University Hospital in Cracow. The mean age was 62.2 ± 10.2 years (range 49 - 74 years).

Results: Localisations of aneurysms were, as follows: basilar tip (33.3%, n = 2), anterior communicating artery (33.3%, n = 2)= 2), middle cerebral artery bifurcation (33.3%, n = 2). Mean volume of the aneurysms was $188.2 \pm 143.7 \text{ mm3}$. Immediately after the procedure, 4 of aneurysms were completely occluded (RROC I), while remaining 2 had residual neck (RROC II). Only 1 procedure (16.7%) had complications (thrombosis within both posterior cerebral arteries) that was successfully treated and the patient had only temporary neurological deficit after the procedure. Neurological status of remaining 5 patients remained unchanged. Mean hospitalization time was 3.5 ± 1.9 days, none of the patients died during the hospitalization. 4 patients had follow up examination (2 of them conventional angiography of the head and remaining two MR angiography of the head), which was performed averagely after 3.7 ± 3.1 months. There was only 1 recanalization of initially completely obliterated aneurysm, 2 remained properly occluded (RROC I), while 1 with initially residual neck turned out to be completely occluded after 6 months.

Conclusion: Use of pCONus device and coiling in widenecked bifurcation aneurysms provides good occlusion rates and is effective and safe.

RISK FACTORS OF 30-DAY MORTALITY IN PATIENTS WITH NON-VARICEAL UPPER GASTROINTESTINAL BLEEDING

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Introduction: Non-variceal upper gastrointestinal bleeding is serious clinical condition which remains one of the most common indications for hospital admission in emergency unit. Despite advancement in treatment non-variceal upper gastrointestinal bleeding is still associated with significant mortality.

Aim: The purpose of our study was to determine the predictive factors of 30-day mortality in patients with non-variceal upper gastrointestinal bleeding. **Methods:** The retrospective analysis included consecutive patients with non-variceal upper gastrointestinal bleeding between January 2011 to March 2019 in a single tertiary referral centre. We analysed association of demographical and clinical characteristics, endoscopic findings, blood transfusion, laboratory tests and presence of complications with 30-day mortality. Statistical analysis was performed with Statsoft STATISTICA v.13.

Results: We analysed 592 patients with non-variceal upper gastrointestinal bleeding, 64.2% male and 35.8% female, with a mean age 67.3 years (range 20–101). Most patients (73.3%) had at least one comorbidity and 38.3% of examined took at least one risky medication for upper gastrointestinal bleeding. 12.3% of them had a history of ulcer whereas 14.3% underwent upper gastrointestinal bleeding in the past. Rebleeding occurred in 12.7% of patients and 3.7% of them required surgical treatment. Mortality rate in the entire group was 10%.

Univariate regression analysis showed that presence of any comorbidity (p = 0.0433), renal disease (p = 0.0025), hemodynamic instability during admission (p < 0.0001), BUN \geq 40 mg/ dl (p = 0.0053), rebleeding (p = 0.0169), unconsciousness on admission (p = 0.0005) and necessity of surgical treatment (p = 0.0022) are significant factors. Multivariate logistic regression model showed that only presence of comorbidities (p = 0.0471), hemodynamic instability (p = 0.0056), unconsciousness on admission (p = 0.0471) and rebleeding (p = 0.0301) are independent predictors of 30-day mortality.

Conclusion: Presence of comorbidities, hemodynamic instability, unconsciousness on admission and rebleeding are the most significant predictive factors of 30-day mortality in patients with non-variceal upper gastrointestinal bleeding in analysed group of patients.

THE TREATMENT OF WIDE-NECKED BIFURCATION ANEURYSMS WITH THE USE OF PCONUS DEVICE AND ITS COMPLICATIONS. A META-ANALYSIS

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Introduction: Endovascular treatment of wide-necked bifurcation aneurysms represents a technical challenge for interventional radiologists. In order to achieve better results of the embolization, the pCONus device was developed.

Aim: The aim of the study was to summarize the overall safety and efficacy of the pCONus device in the treatment of wide-necked bifurcation aneurysms.

Methods: The major electronic medical databases were thoroughly searched to identify relevant studies. Data regarding the type of included studies, type of aneurysm and its localization as well as results and complications of the treatment were extracted from the eligible studies and included into a meta-analysis.

Results: A total of 9 studies (218 patients with 220 aneurysms) were included into the meta-analysis. The most common localization of treated aneurysms was the middle cerebral artery with the pooled prevalence estimate (PPE) of 45.3%. Significantly less often aneurysms were located on the anterior communicating artery (PPE 29.7%) and the basilar artery (PPE 15.1%). Immediately after the procedure, in 41.6% of patients, RROC I (complete obliteration of the aneurysm)

was observed. RROC II (residual neck) was present in 31.3% of patients, while RROC III (residual aneurysm) in 27.1% of patients. The results of short-term follow-up showed that the most frequently RROC I was observed - in 53.9% of cases. Less often, RROC II with PPE of 24.9% was seen, followed by the RROC III with PPE of 21.2%. PPE of intraprocedural complications was 15.2%.

Conclusion: The use of pCONus device with coiling in the treatment of wide-necked bifurcation aneurysms provides good occlusion rates and high safety.

DOES PREGNANCY INFLUENCE EYE PARAMETERS ? ASSESSMENT OF CHOROIDAL THICKNESS USING EDI-OCT BEFORE AND AFTER LABOUR DEPENDING ON THE WAY OF DELIVERY METHOD

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Introduction: Pregnancy is a period when metabolic, hormonal and hemodynamic changes occur in many systems and organs which also applies to the organ of vision. Pregnancy impact on the choroid remains unexplained. EDI-OCT is a new technique of image diagnostics that enables to assess parameters of the choroid that supplies 85% of blood to an eyeball.

Aim: The aim of this research work is to assess the morphology of choriocapillaris with EDI-OCT method in patients before and after delivery depending on the way of delivery method.

Methods: 45 patients (90 eyes) at the age of 27 to 35. EDI-OCT examination was conducted without mydriasis with the use of Heidelberg Spectralis OCT equipment. The examination was performed twice – in 36 HBD and 6 weeks after labour. Women with a multiple pregnancy, refraction error > \pm 4,00 D sph, eye diseases and the history of eye surgeries were excluded from the study. The measurements of choroid was conducted manually in nine locations, each time twice by two independent researchers (4 measurements in total), mean value was used to further statistical analysis. The results were analysed using Student's t-test.

Results: The results showed a statistically significant (p < 0,05) decrease of choroidal thickness in the subfoveal area and parafoveally: nasally and temporally. These changes are more noticeable in women after cesarean section in comparison to women after natural labour.

Conclusion: In the third trimester of pregnancy, the thickness of choroid decreases in comparison with the postpartum period. The phenomenon can be a result of blood flow redistribution to certain vital organs or vasoconstriction of choroidal vessels due to the increased a1 receptors activity during pregnancy. There is a need to conduct vast, multicenter research that would enable to explain the physiological grounds of this phenomenon.

PROLONGED HOSPITAL STAY IN PATIENTS AFTER INGUINAL HERNIA REPAIR IN AMBULATORY SURGERY AT THE CLINIC FOR DIGESTIVE SURGERY, CLINICAL CENTER OF SERBIA

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Introduction: Ambulatory Surgery, also known as Outpatient Surgery is that where the patient is discharged on the same working day. Surgical treatment of inguinal hernia is one of the Ambulatory Surgery procedures.

Aim: Analyzing Ambulatory Surgery clinical practice in patients with inguinal hernia and reasons for prolonged hospitalization at the Clinic for Digestive Surgery, Clinical Center of Serbia.

Methods: The study was carried out at the Clinic for Digestive Surgery, Clinical Center of Serbia and included patients who had inguinal hernia repair, in the period between July 2018 and January 2019. By insight into the anesthetic charts and computerized medical database of the patients, their demographic data, type of surgical intervention, comorbidities, duration of surgical intervention, length of postoperative stay in the hospital and ASA score were collected.

Results: The study included 175 patients aged 19 to 88, of which 12 were women, 6.86% and 163 men, or 93.14%. The

average age of patients was 59.45 years. In 35 (20%) patients were discharged on the same working day, 140 stayed in the hospital. 44.57% were discharged after one day and the longest stay was 9 days. Reasons for staying overnight were: unknown (64%), rewinding and surgical drain (18.86%), procedures (17.14%). In 24.57% of cases the operation lasted less than 60 minutes, in 83.43% it lasted up to 120 minutes and in 16.57% of cases it lasted up more than 2 hours. ASA (American Society of Anesthesiologists) scores in patients were: ASA 1 (22.29%), ASA 2 (53.71%), ASA 3 (24%). The price of general care per day is 1545 Serbian Dinars and prolonged hospitalizations cost 444960 Serbian Dinars (about 3772 €).

Conclusion: By analyzing the results, we think that because of many advantages of one.day surgery, including cost savings, the number of discharges during the same working day may increase.