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**Riga, 2022**

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Editorial Assistant  
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Layout  
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## Oral presentations

### BASIC MEDICAL SCIENCE

#### Co-Culture Approaches with Organoids of the Human Exocrine Pancreas

**Parfejevs Vadims**<sup>1</sup>, Goluba Karīna<sup>1</sup>, Kunrade Līga<sup>1</sup>, Pleiko Kārlis<sup>1</sup>, Jēkabsons Kaspars<sup>1</sup>, Vilmanis Jānis<sup>2</sup>, Pčolkins Andrejs<sup>3</sup>, Terjajevs Igors<sup>4</sup>, Riekstiņa Una<sup>1</sup>

<sup>1</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

<sup>2</sup>Surgery Clinic, Pauls Stradins Clinical University Hospital, Riga, Latvia

<sup>3</sup>Department of Abdominal and Soft Tissue Surgery, Riga East Clinical University Hospital, Riga, Latvia

<sup>4</sup>Traumatology Center, Hospital of Traumatology and Orthopaedics, Riga, Latvia

**Background.** There is an unmet need for therapies to treat pancreas-related conditions like diabetes, exocrine pancreatic insufficiency and cancer. Recently, protocols to establish human pancreatic organoids (hPO) containing progenitor-like cells have been developed. hPOs offer new ways to model pancreatic disorders and study the aspects of development and regeneration of this organ. Organoid cultures can be further complicated by integrating other cell types that are present in the pancreatic stroma.

**Aim.** The aim of our work is to establish adult hPOs from healthy and tumor tissue, co-culture them with mesenchymal cells and neural crest-derived glia to study the interaction of exocrine pancreas with stromal components.

**Methods.** hPOs were established from donor tissue material. Primary and commercial human Schwann cells (SC) and mesenchymal stromal cell lines were used for co-culture with pancreatic organoids. hPOs and co-culture constructs were characterized using immunofluorescence in gel sections and using whole-mount approaches.

**Results.** We report successful derivation of normal and tumour hPOs, as well as primary human SC cultures. hPOs express various markers of the exocrine pancreas including CK19, SOX9, PDX1, CDH1, and PTF1 $\alpha$ . SCs and mesenchymal cells are identified in co-cultures by vimentin expression. Both cell types survive in various co-culture set ups and media formulations. Unlike other cells tested, SCs form network-like structures around pancreatic organoids. Additionally, SCs support growth of organoids in depleted co-culture medium.

**Conclusion.** Successful hPO derivation and co-culture with SCs and mesenchymal cells offers opportunity to study the role of the stromal components in pancreatic deficiencies and physiology.

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## Validation of the GC Vitamin D Binding Protein Gene rs7041 and rs4588 Genetic Variations on the Association with Bronchial Asthma in Latvians

Trapiņa Ilva<sup>1</sup>, Paramonova Natalia<sup>1</sup>, Pļaviņa Samanata<sup>1</sup>, Rumba-Rozenfelde Ingrīda<sup>2</sup>, Sjakste Nikolajs<sup>1,2</sup>

<sup>1</sup>Genomics and Bioinformatics, Institute of Biology of the University of Latvia, Riga, Latvia

<sup>2</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

**Background.** Bronchial asthma (BA) is a chronic inflammatory, genetically complex, heterogeneous disease. Vitamin D is a nutrient and hormone that plays an important role in the pathogenesis of various allergic diseases, such as asthma and food allergy. Vitamin D acts through binding to a specific Vitamin D Binding Protein which is involved in vitamin D transport and storage. Genetic variants rs7041T/G and rs4588C/A of the GC (Vitamin D Binding Protein) gene have been studied as potential risk factors for vitamin D deficiency and were found to alter vitamin D metabolism (Ganz AB et al., 2018).

**Aim.** To identify the potential association of GC (rs7041 and rs4588) gene variations with bronchial asthma in Latvian children.

**Methods.** The case/control group included 148 children diagnosed with asthma and 253 individuals without asthma and any other autoimmune and chronic disease/condition. The GC (rs7041 and rs4588) were genotyped by restriction enzyme site polymorphism on BA main and sex-specific association. Statistical analysis was performed with SPSS.25 Statistical Package.

**Results.** In both BA and Latvian population cohorts, both SNPs genotyping call rate was 100%, and the markers were found to be in the HWE ( $p > 0.05$ ). Statistical analysis revealed a significant association with BA for both GC loci studied (rs4588,  $p < 0.01$  and rs7041,  $p < 0.05$ , respectively), for common alleles and for homozygotes involving common alleles. The heterozygote genotypes CA (rs4588) and GT (rs7041) and rare allele genotypes TT (rs7041) were found to be clinical protective factors in the BA cohort (OR=0.53, CI 95% [0.35–0.80]), OR=0.59, CI 95% [0.37–0.95] and OR=0.49, CI 95% [0.31–0.77], respectively). A sex-specific protective nominal effect ( $p < 0.01$ ) was found for the rare allele genotypes TT (rs7041) in affected women.

**Conclusion.** We present evidence that the GC (rs7041 and rs4588) may contribute to the risk of bronchial asthma in Latvian children, and thus plan to analyse the interaction of this polymorphism with the clinical characteristics of BA in future studies.

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## Meta- and Bioinformatics Analysis of GC Vitamin D Binding Protein Gene Polymorphisms as Possible Molecular Markers for Multiple Sclerosis in Latvian Population

Leonova Elina<sup>1,2</sup>, Trapiņa Ilva<sup>1</sup>, Pļaviņa Samanta<sup>1</sup>, **Paramonova Natalia**<sup>1</sup>

<sup>1</sup>Genomics and Bioinformatics, Institute of Biology of the University of Latvia, Riga, Latvia

<sup>2</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

**Background.** Vitamin D acts as a hormone and plays an important role in pathogenesis of different immunity related diseases, such as multiple sclerosis. Vitamin D acts through binding to a specific vitamin D binding protein (DBP), which is expressed in a variety of tissues. GC (Vitamin D Binding Protein) gene is genetically very polymorphic, but its health implications, if any, have not been studied. Genetic variants rs7041T/G and rs4588C/A of the GC gene have been also studied as potential risk factors for vitamin D deficiency. The GC rs7041 genotype was found to alter vitamin D metabolism.

**Aim.** To determine the prevalence of GC (rs7041 and rs4588) genetic polymorphisms in Latvian population and to evaluate its possible functionality in order to analyse their applicability as molecular markers.

**Methods.** Genotyping of 253 DNA samples of Latvian population representatives was made using allele specific PCR and restriction enzyme site polymorphism method. Literature and sequence data on GC gene polymorphisms were analysed using meta-analysis and bioinformatical tools for DNA and RNA secondary structure, DNA bending and transcription factor binding sites.

**Results.** All the studied SNPs demonstrated allele-dependent alternative secondary structures. Differential structures of DNA and/or RNA were found. Marked differences in simulated DNA curvature and bendability depending on allele were observed.

In the Latvian population, the minor allele frequency (MAF) of rs7041 and rs4588 corresponds to 52% and 38% and prevails in comparison with the general European population (43% and 25%, respectively). There is information on their associations or linkage with different diseases in different populations.

**Conclusion.** Meta and bioinformatic analysis of selected rs7041T/G and rs4588C/A of CG vitamin D binding protein genes illustrate the potential of using them as possible molecular markers by genotyping in association study.

Interactions of these polymorphisms with the GC gene methylation status and vitamin D levels in various disease cohorts in Latvians are planned in future studies.

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## Population Genetic Screening Reveals Congenital Myotonia as the Most Frequent Neuromuscular Disorder in Latvia

Lāce Baiba<sup>1,2</sup>, Stāvulis Jānis<sup>1</sup>, Mičule Ieva<sup>1,2</sup>, Ķēniņa Viktorija<sup>2,3</sup>, Strautmanis Jurgis<sup>4</sup>, Zdanoviča Anna<sup>1</sup>, Kleina Elfa<sup>1</sup>, **Inashkina Inna<sup>1</sup>**

<sup>1</sup>Latvian Biomedical Research and Study Centre, Riga, Latvia

<sup>2</sup>Medical Genetics Clinic, Children's University Hospital, Riga, Latvia

<sup>3</sup>Rare Disease Centre, Riga East Clinical University Hospital, Riga, Latvia

<sup>4</sup>Neurology Clinic, Children's University Hospital, Riga, Latvia

**Background.** Neuromuscular disorders (NMD) refer to a wide range of diseases, caused by deficits in the motor unit and characterised by progressive muscle weakness as the predominant condition. These diseases can be both inherited and acquired. The reported average prevalence of individual inherited neuromuscular disorders in the world is 3.7–4.99 per 10 000 inhabitants. This number varies greatly after applying population-wide studies for selected populations.

A retrospective study of NMD patient group throughout the years 2008–2020 confirmed spinal muscular atrophy and dystrophinopathies as the most common childhood onset NMDs, as well as facioscapulo-humeral muscular dystrophy type 1 and limb girdle muscular dystrophy as the most frequent molecularly confirmed diagnosis for adult-onset NMD patients. Unexpectedly, non-dystrophic congenital myotonia was also detected in similar frequency as the previously mentioned relatively frequent NMDs.

**Aim.** The objective of our study was to calculate the allelic frequencies and theoretical prevalence for recurrent genetic variants of the most common NMDs diagnoses in the population of Latvia.

**Methods.** Allelic frequencies of common disease-associated variants in unrelated individuals were obtained from the Genome Database of Latvian population.

**Results.** The carrier frequency of CAPN3, FKRP, SPAG11, and HINT1 gene reoccurring variants in the population of Latvia were within the range of the data, reported by other European countries. The carrier frequency of CLCN1 gene variant c.2680C>T (p.Arg894Ter) reaches 2.11 %.

**Conclusion.** The high allelic frequency of CLCN1 gene variant c.2680C>T, in conjunction with data on the already identified patients, makes congenital myotonia the most frequent neuromuscular disorder in our population, therefore suggesting introduction of its direct testing in patients with relevant clinical symptoms.

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## Citrulline, D-Lactate and Intestinal Fatty Acid Binding Protein Levels in Rat Plasma Using Rat Mesenteric Ischemia Model

Silavniece Marta<sup>1</sup>, Makrecka-Kūka Marina<sup>2</sup>, Bahire Ksenija Lūcija<sup>1</sup>, Jēkabsons Kaspars<sup>1</sup>, Jansone Baiba<sup>1</sup>, Volrāts Olafs<sup>1</sup>, Muceniece Ruta<sup>1</sup>

<sup>1</sup>University of Latvia, Riga, Latvia

<sup>2</sup>Latvian Institute of Organic Synthesis, Riga, Latvia

**Background.** Acute mesenteric ischemia is one of the most severe diagnostic and therapeutic vital emergencies. The clinical picture is nonspecific, dominated by acute abdominal pain. At present, no early biological marker is commonly used in clinical practice for diagnostic purposes. Among the biological blood markers that have shown a diagnostic interest, there are the two stereoisomers of lactate (D and L), intestinal fatty acid binding protein (I-FABP), which is a marker of enterocyte necrosis, citrulline, a marker of enterocyte mass and several others. The early diagnosis of intestinal ischemia remains a challenge.

**Aim.** The aim of the current study was to study the levels of citrulline, D-lactate and I-FABP in rat plasma under mesenteric ischemia conditions.

**Methods.** Rat plasma samples were collected from sham-operated animals (control) and at different ischemia's time intervals – 30, 60, 90 and 120 min. Concentration of citrulline was assessed according to the corresponding kits' manufacturer BioVision, Inc. (Milpitas, California, USA) instructions and fluorescence was measured at Ex/Em 535/587 nm. Level of I-FABP was measured using ELISA kit (Abbexa, Houston, USA) and optical density (OD) read at 450 nm. Concentration of D-lactate was assessed using colorimetric Sigma-Aldrich kit (St. Louis, MO, USA) and absorbance measured at 565 nm using a Tecan Infinite 200 PRO plate reader and i-control software.

**Results.** Level of plasma citrulline was significantly decreased in all ischemia time intervals, reaching 1.77-fold decrease after 120 min, compared with that in sham-operated rat plasma. D-lactate level was increased gradually in time course and after 120 min. it reached 2-fold increase vs control. I-FABP level was increased in all measurement intervals, whereas there was significant intensification of the increase after 120 min, reaching 4.4-fold increase vs control and almost 2-fold, compared with that after 90 min. However, inter rat fluctuations of the biomarker levels in one group of the rats were also observed.

**Conclusion.** The biomarker levels in rat plasma during mesenteric ischemia periods were significantly changed in comparison with the corresponding levels in control rat plasma. However, search for more specific biomarkers underline the effort that needs to be done in the acute mesenteric ischemia biological diagnosis.

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## CDKN2A/CEP9 Fluorescence *in Situ* Hybridization and Expression of p16 and p53 in Patients with Oropharyngeal Squamous Cell Carcinoma – Pilot Study

Tatičeka Margarita<sup>1,2</sup>, Nevidovska Kristīne<sup>1,2</sup>, Sperga Māris<sup>1</sup>

<sup>1</sup>Pathology Centre, Riga East Clinical University Hospital, Riga, Latvia

<sup>2</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

**Background.** Oropharyngeal squamous cell carcinoma (OPSCC) is a cancer of the middle part of the pharynx. Eighth-edition TNM classification separates OPSCC into two types: HPV-positive and HPV-negative. Precise HPV status determination is in favour of adequate therapy for patients.

The CDKN2A (Cyclin-Dependent Kinase Inhibitor 2A) gene is located on chromosome 9. CDKN2A codes two tumour suppressors: p16, which activates retinoblastoma (Rb) family proteins and p14arf, which activates tumour p53 suppressor. Alterations of the 9p21 locus include the tumour suppressor gene CDKN2A.

HPV-positive tumours tend to have p53 degradation, pRb inactivation with resulting p16 upregulation, but HPV-negative tumours tend to have p53 mutation and downregulation of p16. p16 immunostaining is used as a surrogate marker for detecting transcriptionally active HPV. p53 immunostaining is used as a surrogate for mutational analysis in carcinomas of multiples sites.

**Aim.** The aim of the study is to evaluate the association between p16 and p53 expression and CDKN2A/CEP9 fluorescence *in situ* hybridization (FISH) results in patients with OPSCC.

**Methods.** Archive search was done to identify patients with primary diagnosed OPSCC in 2021 in the Riga Eastern Clinical Hospital. Within the pilot-study total 12 cases with informative tissue samples on biopsies were enrolled in the study. Immunohistochemistry for p16 and p53, and CDKN2A/CEP9 FISH were performed for all cases.

**Results.** A strong and diffuse pattern of p16 immunostaining was observed in 6 cases; a negative p16 pattern was observed in 6 cases. In all HPV-positive OPSCC cases p53 immunostaining was positive in some tumour cells. Five of six HPV-negative OPSCC cases were negative for p53 (null expression); one case was strong and diffuse positive for p53. CDKN2A homozygous and heterozygous deletions are present both in HPV-negative and HPV-positive OPSCC. None of the cases present CDKN2A gene amplification. None of the cases present a normal CDKN2A pattern.

The results obtained are intermediate and will be supplemented in the future.

### Conclusion.

- 1) IHC p16 status does not reflect the presence of CDKN2A gene amplification.
- 2) IHC p53 expression does not reflect the presence of CDKN2A gene amplification.
- 3) Both HPV-positive and HPV-negative OPSCC have CDKN2A deletions.

**Acknowledgements.** The authors declare the absence of conflict of interest.

## The Effect of Electronic Cigarette Aerosol on Rat Testis

Popova Tetiana<sup>1</sup>, Gubina-Vakulik Galina<sup>1</sup>  
<sup>1</sup>Kharkiv National Medical University, Kharkiv, Ukraine

**Background.** Electronic cigarettes were recommended as a safer alternative to conventional cigarettes. They have become increasingly popular among adolescents. The impact of electronic cigarette aerosol on the organs of the reproductive system has not been fully assessed yet.

**Aim.** The aim of this study was to assess microscopic changes in seminiferous tubules of rats exposed to electronic cigarette aerosol.

**Methods.** A total of 20 ten-week-old male WAG rats were randomized into 2 groups of 10 animals each as follow: group 1: each animal in this group was exposed to the fresh airflow for 15 min per day, during 90 days; group 2: each rat was exposed to the electronic cigarette aerosol for 15 min per day, during 90 days. Electronic cigarette aerosol exposures were carried out by using the Boyarchuck chamber operating in a one-pass mode with the aerosol feed controlled externally by a metering pump. Electronic cigarette liquid was composed of propylene glycol/glycerin 50/50 (by volume fraction), 6 mg/ml nicotine, flavours: ethyl maltol and sucralose. Procedures involving the animals and their care followed the European Convention for the Protection of Vertebrate Animals used for Experimental and other Scientific Purposes. Paraffin-embedded testis were cut in 5  $\mu\text{m}$  and stained with hematoxylin and eosin.

**Results.** The qualitative and quantitative disorders of spermatogenesis were found in the testes of group 2 compared to group 1. The histological changes included a decrease in the diameter of the tubules, epithelial thickness, loosening of the germinal epithelium, appearing of cellular debris in the lumen of the tubules and fragmented nucleus pyknotic cells. The diameter of the tubules in group 2 was significantly reduced  $\text{Me}=203.5$  [197.6; 212.2]  $\mu\text{m}$  compared to group 1  $\text{Me}=238.2$  [236.1; 241.4]  $\mu\text{m}$  ( $p=0.007$ ). The thickness of the spermatogenic epithelium was  $\text{Me}=39.2$  [36.3; 41.6]  $\mu\text{m}$  significantly less than in group 1  $\text{Me}=63.4$  [61.2; 65.1]  $\mu\text{m}$  ( $p=0.004$ ).

**Conclusion.** The rat spermatogenesis is affected by electronic cigarette aerosol exposure. It resulted in a reduction of spermatogenesis and acceleration of testes' degeneration.

**Acknowledgements.** The authors declare the absence of conflict of interest and confirm that no funding has been received for the study.

## Phenotypic Diversity of Multidrug-Resistant *Pseudomonas Aeruginosa* and *Acinetobacter Baumannii*

Sproģe Dana<sup>1</sup>, Lozda Daniela<sup>1</sup>, Līduma Iveta<sup>1,2</sup>

<sup>1</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

<sup>2</sup>Microbiology Laboratory, Hospital of Traumatology and Orthopaedics, Riga, Latvia

**Background.** *Pseudomonas aeruginosa* and *Acinetobacter baumannii* are major pathogens that cause nosocomial infections globally. There also are increasing reports of multidrug resistance in these gram-negative bacteria. These bacteria frequently acquire multiple resistance mechanisms, like beta-lactamases, target-site modifications and efflux pumps, leaving less available treatment alternatives, therefore imposing an extensive burden on public health and healthcare systems worldwide.

**Aim.** To evaluate clinical strains of *Acinetobacter baumannii* and *Pseudomonas aeruginosa* for phenotypic antimicrobial resistance variation, and to determine multidrug-resistance rate of bacterial isolates.

**Methods.** Microorganisms were determined from surgical samples by BBL™ Crystal™ system, antibiotic susceptibility test of isolates was performed by Bauer-Kirby™ disc diffusion test and ETM-test. Data were obtained from the laboratory information system and isolated bacterial strains were typed according to antibiograms. Data processed using MS Excel 2019.

**Results.** Summarizing the results, in 2021, of the total 3856 clinical isolates 1.99% (n=77) were *Pseudomonas aeruginosa* and 1.14% (n=44) were *Acinetobacter baumannii*. *A. baumannii* isolated strains were most commonly resistant to β-lactam/β-lactamase inhibitor – 70.45% (n=31) whereas *P. aeruginosa* resistance was 41.55% (n=32). No resistance was observed to colistin in both strains. Among *P. aeruginosa* isolates multidrug-resistance was detected in 29.87% (n=23). Out of the 44 *Acinetobacter baumannii* isolates 70.45% (n=31) were multi-drug resistant. In this research were identified 10 *P. aeruginosa* phenotypes, of which MDR were 7 and from determined 9 different *A. baumannii* phenotypes, 8 were MDR.

### Conclusion.

1. Multidrug-resistance rates were more common among *A. baumannii* strains 70.45%.
2. The most frequently determined MDR phenotype out of *P. aeruginosa* isolates was phenotype IX (n=7, 9.09%).
3. The most frequently determined MDR phenotype out of *A. baumannii* isolates was phenotype IV (n=9, 20.45%).
4. *P. aeruginosa* isolates showed most common resistance to β-lactam/β-lactamase inhibitor 41.55%.
5. *A. baumannii* isolates showed most common resistance to β-lactam/β-lactamase inhibitor 70.45%.

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## Optimization of the 3-Dimensional Cell Culture Model of Colon Adenocarcinoma

Michel Olga<sup>1</sup>, Geneja Magdalena<sup>1</sup>, Gołdyn Elżbieta M.<sup>1</sup>, Gos Michalina<sup>1</sup>, Rossowska Joanna<sup>1</sup>

<sup>1</sup>Ludwik Hirszfeld Institute of Immunology and Experimental Therapy, Polish Academy of Sciences, Wrocław, Poland

**Background.** Cancer cell lines are most commonly cultivated as cell monolayers, and in that form, they have become a valuable tool for studying cell biology and anticancer treatments. However, this model is also burdened with disadvantages, such as the lack of a tissue architecture or alterations in cell genotype and phenotype, unlimited access to oxygen, nutrients, and signalling molecules, leading to different responses when compared to observations *in vivo*. Therefore, the role of 3-dimensional (3D) cell cultures is increasingly being recognized as a model much more faithfully reflecting rough conditions prevailing in the tumour microenvironment. However, cultivating reproducible and measurable microtumours is a complex task, requiring optimization.

**Aim.** The current study aimed to compare various methods of obtaining 3D cell cultures, identify their advantages and disadvantages, and finally, indicate the most suitable method for obtaining measurable and stable colon adenocarcinoma spheroids.

**Methods.** A murine colon adenocarcinoma MC38 cells were used as a model to assess two types of 3D cell culture: hanging drop and culture in non-adhesive plates. The latter was tested in two variants: i) commercially available pre-coated plates (BIOFLOAT™, FaCellitate); ii) 96-well polystyrene plates self-coated with the Anti-Adherence Rinsing Solution (STEMCELL Technologies). We optimized the culture conditions. Additionally, in both models, we verified the influence of the additional methylcellulose in a culture medium on the formation and stability of cancer spheroids. Spheres were photographed using an Olympus IX81 fluorescent microscope and measured with the Olympus cellSens and Fiji software. GraphPad Prism 9 software was used for graphs and statistical analysis.

**Results.** The hanging drop method allowed to obtain repeatable spheres but was adequate only for short-term culture. Pre-coated plates were effective for the formation of spheres which could be maintained for up to one month. Culture on plates self-coated according to manufacturer's recommendations appeared to be non-sufficient for the production of stable spheres. However, we managed to alter the protocol to enhance its efficacy. Methylcellulose addition had a positive effect on sphere stability.

**Conclusion.** Both methods allowed for the formation of cancer spheres, however, the application of pre-coated plates with the addition of methylcellulose was the most effective method to obtain stable, well-formed MC38 spheroids.

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## PHARMACY

### Antioxidant Fatty Acids of *Peganum Harmala*

Nasibova Tohfa<sup>1</sup>, Garaev Eldar<sup>1</sup>, Zeynalova Gulnar<sup>1</sup>, Gafarova Dostu<sup>1</sup>, Huseynova Nazila<sup>1</sup>,  
Ismayilova Shahnaz<sup>1</sup>

<sup>1</sup>Azerbaijan Medical University, Baku, Azerbaijan

**Background.** In the human body, oxidation affects cell membranes and other components, such as DNA, and cellular proteins. Oxygen metabolism leads to the formation of free radicals. These unstable molecules damage other cells by stealing electrons from molecules. Overloading the body with free radicals can over time lead to heart and liver disease, various cancer types such as malignancies of the mouth, oesophagus, stomach, and bowel. Antioxidant substances can play a role in preventing these problems by neutralizing the free radicals. The plant world is rich in antioxidants. In addition to vitamins and minerals, the fatty acids in plants have antioxidant effects.

**Aim.** One of the plants worth studying in this regard is *Peganum harmala*. A good amount of seed oil is obtained from this plant, and these fatty acids have a valuable antioxidant effect. The purpose of the study is to research the composition and antioxidant properties of *P. harmala* seed oil.

**Methods.** Powdered seeds were placed on the Soxhlet system and extracted with n-hexane. The resulting yield of oil was 13%. To carry out the qualitative and quantitative analysis of fatty acids, the obtained oil was processed by the FAME (Fatty Acid Methyl Ester) method. Methanolic sodium hydroxide was added to 0.5 ml of oil. After the methanol evaporation, the reaction has been neutralized with sulfuric acid, n-hexane has been added to the mixture and dehydrated with sodium sulphate. In the final stage, the hexane layer was separated from the solution. Upon completion of this process, the last hexane sample was transferred to Gas Chromatography for analysis. For antioxidant evaluation, seed oil sample diluted in toluene were combined with a toluene solution of DPPH (2,2-Diphenyl-1-picrylhydrazyl) and incubated for 30 minutes. The decrease in absorption was measured at 515 nm against a blank of pure toluene without DPPH. Finally, the calculation process of the results was realized.

**Results.** According to the results, the most predominant fatty acids in *P. harmala* oil were linoleic acid with 57% and oleic acid with 30%. As for the results of the antioxidant analysis, the percentage of inhibition was equal to 78.45%. This number represents a high result in general and especially for fatty acids.

**Conclusion.** The widespread prevalence of the plant, normal fatty acid yield, and the effectiveness of antioxidant properties constitute a great reason for the therapeutic evaluation of *P. harmala* oil.

**Acknowledgements.** The authors declare the absence of conflict of interest.

## Comparative Analysis of Quantitative and Qualitative Composition of Phenolic Compounds and Antioxidant Activity Between Different Genotypes of *Vaccinium Vitis-Idaea* L.

Akelan Lijana<sup>1</sup>, Raudonė Lina<sup>1, 2</sup>

<sup>1</sup>Department of Pharmacognosy, Lithuanian University of Health Sciences, Kaunas, Lithuania

<sup>2</sup>Laboratory of Biopharmaceutical Research, Institute of Pharmaceutical Technologies, Laboratory of Biopharmaceutical Research, Kaunas, Lithuania.

**Background.** *Vaccinium vitis-idaea* L. is characterized by a variety of phytochemical compounds, which determine anti-neoplastic, anti-inflammatory, and strong antioxidant activity. These therapeutic effects and antioxidant potential are usually associated with high levels of phenols and flavonoids. According to research data, the predominant flavonoids in the leaves and fruits of *Vaccinium vitis-idaea* and *V. vitis-idaea* var. *leucocarpum* are arbutin, 2-O-caffeoylarbutin, rutin, quercetin, isoquercetin, (+)-catechin, (-)-epicatechin, quercitrin, avicularin. Furthermore, proanthocyanidins B1, B2, B3, C1, A1, A2 predominate in leaves and fruits. The results of this study provide new insights into the quantitative composition and antioxidant activity of individual phenolic compounds between different genotypes.

**Aim.** The purpose of this study was to identify *Vaccinium Vitis-idaea* L. and var. *leucocarpum* quantitative composition and antioxidant activity of leaves and fruits.

**Methods.** Baranava forest in Švenčionys district was chosen for collecting leaves and fruits of *V. vitis-idaea* var. *leucocarpum* and *V. vitis-idaea*. The collection of these leaves and fruits in their natural habitat was performed in August 2020. The spectrophotometric ABTS method was used to determine the total antioxidant capacity. The DMAC colorimetric method was used to determine proanthocyanidins. The HPLC method was used to determine composition of phenolic compounds.

**Results.** Proanthocyanidin content was the highest in *V. vitis-idaea* leaves – (46.23±9.98 EE mg/g). The fruits of *V. vitis-idaea* were determined with significantly higher amounts 15.49±3.05 of proanthocyanidins mg/g than *V. vitis-idaea* var. *leucocarpum* – 15.49±3.05 mg/g and 3.62±0.69 mg/g, respectively. The content of total identified proanthocyanidins was the highest in *V. vitis-idaea* leaves and fruits – (20917.22 mg/g.). The total amount of determined flavonoids in the leaves and fruits of *Vaccinium vitis-idaea* L. – 46420.56 mg/g was significantly higher than in *V. vitis-idaea* var. *leucocarpum* leaves and fruits (38838.67 mg/g). The predominant compounds in the phenolic profiles were arbutin in leaves and fruits of *V. vitis-idaea* and *V. vitis-idaea* var. *leucocarpum* – quercetin-HMG-rhamnoside was determined only in *Vaccinium vitis-idaea* leaves and fruits (257.61±150.13 mg/g and 35.86±13.73 mg/g), respectively.

**Conclusion.** The phenolic content and antioxidant activity is highly genotype dependent. The raw materials of *V. vitis-idaea* L. were determined with greater amount of flavonoids and antioxidant activity compared to *V. vitis-idaea* var. *leucocarpum*. Individual phenolic compounds, such as quercetin, proanthocyanidin A2 and isoquercetrin were determined in higher amounts in leaves and fruits of *V. vitis-idaea* var. *leucocarpum* compared to *V. vitis-idaea*.

## Variation of Antioxidant Activity and Total Proanthocyanidins Content in *Calluna Vulgaris* from Wild Cenopopulations

Kaunaitė Vytautė<sup>1</sup>, Raudonė Lina<sup>1,2</sup>

<sup>1</sup>Department of Pharmacognosy, Lithuanian University of Health Sciences, Kaunas, Lithuania

<sup>2</sup>Laboratory of Biopharmaceutical Research, Institute of Pharmaceutical Technologies, Kaunas, Lithuania

**Background.** *Calluna vulgaris* is the only member of the genus *Calluna* belonging to the family *Ericaceae*, which is distributed in North Africa, North America, Australia, British Isles, New Zealand and Iceland. The plant material is used for treating urinary tract diseases, rheumatism, arthritis, eczema, wounds. Various pharmacological effects have been reported such as anti-inflammatory, antiseptic, antioxidant, antiviral, genoprotective, cytotoxic, antiproliferative, cardioprotective, hepatoprotective and expectorant. Besides the aforementioned biological effects, they have been described as a preventive agent in cases of increased anxiety, irritability and sleep disturbances. High content of phenolic compounds such as proanthocyanidins, phenolic acids, flavonoids serves as the basis for its beneficial effect.

**Aim.** The aim of the current study was to determine antioxidant activity and total proanthocyanidins content of *Calluna vulgaris* aboveground parts collected in natural habitats in Lithuania.

**Methods.** Aboveground parts of *Calluna vulgaris* were collected from 10 different habitats at the beginning of the flowering period. The extracts were prepared using 0.2 g of dry matter and 20 mL of 70% ethanol. The content of total proanthocyanidins compounds in plant extracts was determined by spectrophotometric method using DMCA reagent and total antioxidant capacity – by ABTS assay.

**Results.** The results have shown that the highest and the lowest amounts of proanthocyanidins was determined in Sutkai village edge of forest and Ežerėlis (Kaunas municipality) forest –  $8.6 \pm 0.38$  mg/g and  $5.3 \pm 0.53$  mg/g, respectively. The greatest radical scavenging activity –  $1896.4 \pm 118.79$   $\mu\text{mol/g}$ ,  $1799.5 \pm 99.9$   $\mu\text{mol/g}$  were determined in Sutkai village (Šakiai municipality) and Tauragė regions edges of forests, respectively. The lowest antioxidant capacity was determined in Druskininkai and Varėna forests –  $1375.8 \pm 179.69$   $\mu\text{mol/g}$  and  $1345.7 \pm 179.34$   $\mu\text{mol/g}$ , respectively. Consequently, proanthocyanidins content and antioxidant activity are higher in outskirts than in forests.

**Conclusion.** The total amounts of proanthocyanidins in *Calluna vulgaris* raw materials and antioxidant activity vary significantly depending on the habitat peculiarities.

## Patterns of Direct Oral Anticoagulant Prescriptions in Latvia: A Retrospective Analysis of Electronic Records

Gavrilova Anna<sup>1,2</sup>, Latkovskis Gustavs<sup>3,4</sup>, Urtāne Inga<sup>1</sup>

<sup>1</sup>Rīga Stradiņš University, Riga, Latvia

<sup>2</sup>Red Cross Medical College of Riga Stradiņš University, Riga Latvia

<sup>3</sup>University of Latvia, Riga, Latvia

<sup>4</sup>Pauls Stradiņš Clinical University Hospital, Riga, Latvia

**Background.** Direct oral anticoagulants (DOACs) such as rivaroxaban, dabigatran, edoxaban, and apixaban, are used to decrease the risk of ischemic stroke and other embolic events. Consumption of this pharmacologic group increased 6.55 times in five years (2014–2018) in Latvia. Drug therapy should be safe and effective, but prescribing and dispensing errors prevent achieving the goal.

**Aim.** This study aimed to identify the prescribing and dispensing challenges of DOACs.

**Methods.** This retrospective study was performed, using the Latvian National Health Service electronic prescription database. The data repository was queried to retrieve prescription information on specific DOACs: rivaroxaban, dabigatran, edoxaban, and apixaban. We analysed the data from March 1 to November 31, 2020. Each prescription record covered anonymised information regarding patients' demographic data, prescribed drug description, and dispensed drug.

**Results.** In total, 58643 individual DOAC prescriptions of 26852 unique patients were analysed. Patients' mean age was 71.7±13.0 years, and 75.1% (n=20168) persons were 65 years or older. Rivaroxaban was the most prescribed DOAC (44899 prescriptions in 20802 patients), followed by dabigatran (8727 in 4033 patients), edoxaban (4743 in 2407 patients), and apixaban (274 in 98 patients). Around half (n=29580) of all prescriptions were with reimbursement. The diagnosis was not indicated in 20 439 prescriptions, but most common (n=32 459, 55.4%) prescribing purpose for DOACs therapy atrial fibrillation and flutter (I48). For this diagnosis, DOACs were most frequently prescribed by general practitioners (GPs) (n=29335, 90.1%), followed by cardiologists (n=1691, 5.2%), physician's assistants (n=320, 1.0%) and internists (n=315, 1.0%). In this prescription subcategory, specialists advised to divide the dose of the drug form (for example, 0.33 tablets or 0.5 capsules) in 366 (1.1%) prescriptions. Additionally, one daily capsule/pill was recommended in 15.0% (n=840/5587) of dabigatran and 32.5% (n=13/40) of apixaban prescriptions, and most of such prescription were made by GPs: in 91.1% (n=765/840) and 100% (n=13/13) of cases, respectively. In general, patients did not dispense one in ten (n=7483/58643, 12.8%) prescriptions at a pharmacy, but prescriptions with reimbursement were 3.55 times more likely to be fully or partly dispensed. The pharmacist or pharmacist's assistant dispensed DOAC at another dosage than prescribed in 2.9% (n=1880/64128) of dispensing times.

**Conclusion.** Inconsistencies were discovered between medicine prescribed by a physician and received by a patient at pharmacy in almost 3% of cases. Practical solutions are needed to reduce the risk of prescribing and dispensing errors. The target audience for practice enhancements is GPs, pharmacists, and pharmacist's assistants.

## Physiologically Based Metformin Pharmacokinetics Model of Mice and Scale-up to Humans for the Estimation of Concentrations in Various Tissues

Kurlovics Janis<sup>1,2</sup>, Zake Darta Maija<sup>1,3</sup>, Zaharenko Linda<sup>3</sup>, Komasilovs Vitalijs<sup>1</sup>, Klovinis Janis<sup>3</sup>, Stalidzans Egils<sup>1</sup>

<sup>1</sup>Institute of Microbiology and Biotechnology, University of Latvia, Riga, Latvia

<sup>2</sup>Division of Pharmaceutical Chemistry and Technology, University of Helsinki, Helsinki, Finland

<sup>3</sup>Latvian Biomedical Research and Study Centre, Riga, Latvia

**Background.** While metformin is the primary drug for type 2 diabetes treatment and a promising candidate for other disease treatment, the significant interindividual variability in therapy efficacy and pharmacokinetics has been observed, leading to the administration of an unnecessary overdose or an insufficient dose. There is a lack of data regarding the concentration–time profiles in various human tissues that limits the understanding of pharmacokinetics and hinders the development of precision therapies for individual patients.

**Aim.** The aim of the current study was to combine in vitro data with metformin concentration distribution data in mice tissues and human intestine cell culture experiments, to develop a whole-body mechanistic Physiologically based pharmacokinetics (PBPK) model for humans.

**Methods.** Models were developed in COPASI (COmplex PATHway Simulator) simulation software. Generic PBPK models for mice and humans were built in the form of ordinary differential equations. The model structure consists of the remainder, heart, fat, muscle, brain, lungs, stomach, liver, portal vein, venous and arterial plasma, and red blood cells compartments defined as independent one compartment organs, while kidney and small intestine were developed as multicompartiment organs to describe physiological processes by more detailed approach. The model was then adapted for humans, and the unknown parameters were estimated using clinical datasets—a dataset from Zaharenko et al. (2016) following a 500 mg PO dose.

**Results.** Most tissues have a half-life ( $t_{1/2}$ ) similar to plasma (3.7h) except for the liver and intestine with shorter  $t_{1/2}$  and muscle, kidney, and red blood cells that have longer  $t_{1/2}$ . The highest maximal concentrations ( $C_{\max}$ ) turned out to be in the intestine (absorption process) and kidney (excretion process). It was found that no body fluid at its maximum concentration contains more than 2% of absorbed metformin. At maximum the metformin amounts reach different fractions of absorbed metformin: 33% (66 mg) in muscle 29% (58 mg) in intestine, 17% (34mg) in kidney, 8.5% (17mg) in liver, 5% (10mg) in remainder and 4% (8mg) in adipose after following a 500mg PO dose. The metformin concentration peaks of other tissues were below 2%.

**Conclusion.** The developed PBPK model predicts the drug's tissue distribution and characterises some underlying differences in the individual responses to metformin therapy.

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## Proximity Ligation for *in Vitro* Aptamer Target Protein Identification

Pleiko Karlis<sup>1,2</sup>, Tambet Teesalu<sup>2,3,4</sup>, Una Riekstina<sup>1</sup>

<sup>1</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

<sup>2</sup>Laboratory of Precision- and Nanomedicine, Institute of Biomedicine and Translational Medicine, University of Tartu, Tartu, Tartu, Estonia

<sup>3</sup>Cancer Research Center, Sanford Burnham Prebys Medical Discovery Institute, La Jolla, USA

<sup>4</sup>Center for Nanomedicine and Department of Cell, Molecular and Developmental Biology, University of California, Santa Barbara, USA

**Background.** Proximity labelling in combination with mass-spectrometry proteomics has been used for protein-protein interaction. The method is also routinely used for RNA-binding protein determination and characterization. However, until now proximity labelling has not been used to identify protein targets for ssDNA or RNA aptamers.

**Aim.** This study aims to develop a proximity ligation-based method to identify protein target for triple-negative breast cancer cell line MDA-MB-231 binding aptamer using proximity labelling method followed by mass-spectrometry proteomics.

**Methods.** Seq36 aptamer or Ctrl aptamer conjugated to biotin was incubated with streptavidin-conjugated horseradish peroxidase (HRP). The prepared aptamer-HRP complex was added to MDA-MB-231 cells. After incubation supernatant was removed and tyramide-AlexaFluor555 reagent was added. The reaction was stopped after 2 min. Proximity labelling reaction was characterized using flow cytometry. Tyramide-biotin was used for target identification instead of tyramide-AlexaFluor555 and proteins were pulled down using streptavidin magnetic beads. Eluted proteins were run on a PAGE gel, stained using silver ion staining and the band of interest was cut out and analysed using mass spectrometry. Mass spectrometry identified proteins with >2 peptides identified were sorted based on signal intensity. Common contaminant proteins were excluded from the analysis.

**Results.** After the exclusion of contaminant proteins and proteins with <2 peptides, transmembrane integrin proteins  $\alpha 3$  and  $\beta 1$  were identified as two proteins with the highest signal intensity in PAGE gel band-of-interest. Intensity of integrin  $\beta 1$  was 766 times lower and integrin  $\alpha 3$  was not detected in control samples.

**Conclusion.** Mass spectrometry data provide convincing evidence of integrin protein heterodimer  $\alpha 3\beta 1$  being the target for Seq36 aptamer. Results must be further validated to confirm successful use of proximity ligation for aptamer target identification.

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## Site-Specific Contrast Media Side Effects

Sauer Natalia<sup>1</sup>, Karłowicz-Bodalska Katarzyna<sup>2</sup>

<sup>1</sup>Faculty of Pharmacy, Wrocław Medical University, Wrocław, Poland

<sup>2</sup>Department of Industrial Pharmacy, Faculty of Pharmacy, Wrocław Medical University, Wrocław, Poland

**Background.** Iodinated and gadolinium-based contrast media are used daily in most radiology practices such as computer tomography (CT) and magnetic resonance (MR). There is an urgent need to analyse the adverse effects of contrast media to increase the knowledge of the safety profile.

**Aim.** The paper aims to analyse the side effects of iodinated and gadolinium-based contrast media on different sites of the body.

**Methods.** This study used the database of spontaneous reports of AEs from the Regional Centre of ADRs monitoring in Wrocław (RCMADR). The number of reports of adverse reactions related to contrast agents was 124. Each report contains information about patient demographics, the profession of the person reporting (physician-specialty, pharmacist), route of administration (oral, intravenous, intramuscular, external), AEs, suspected drugs and concomitant drugs, patient outcomes, results of causality assessment, and report centres. Reported diagnoses were coded using the International Classification of Disease (ICD-10). ADRs were coded according to the Medical Dictionary for Regulatory Activities (MedDra) terminology and were coded to extract standardized generic names according to the Anatomical Therapeutic Chemical (ATC) classification.

**Results.** 30.30% of adverse effects reports were related to Iomeprol (Jomeron), 23.81% came from using Iopramide (Ultravist), 12.55% from Gadobutrol (Gadovist), 11.69% from Gadobenic Acid (Multihance), 9.09% from Ioversol (Optivay), 5.19% from Iodixanol (Visipaque), 3.46% from Iohexol (Omnipaque), 3.46% from Gadoteric Acid (Dotarem) and 0.43% from Gadoteridol (Prohance). Most of the reported adverse reactions of contrast agents were related to disorders of the skin and subcutaneous tissue (65.44%, n=174). 12.50% of adverse reactions were connected with respiratory disorders (n=34), 6.99% with vascular (n=19), 5.15% with gastrointestinal (n=14), 4.04% with nervous system (n=11) and 2.94% with general disorders (n=8). The fewest side effects came from eye and cardiac disorders.

**Conclusion.** Skin disorders, such as rash, itching and hives are the most common side effects among patients using both iodine and gadolinium-based contrast media. Iodine-based contrast agents are characterized by similar organ toxicity. Conversely, gadolinium-based contrast agents are more diverse – some of which show tissue specificity, like gadobutrol for the gastrointestinal system or gadodiamide for the respiratory tract. Clinicians should consider the differences in the prevalence of their application. This study shows that it is possible to choose the most optimal contrast agent for patients with specific organ-site problems to omit the possible complications.

## Long-Term Activity Assessment in the Voluntary Running Wheel in Mice Model of Ischemic Stroke

Ābola Agate<sup>1</sup>, Dzirkale Zane<sup>1</sup>, Jeļisejevs Ilja<sup>1</sup>, Upīte Jolanta<sup>1</sup>, Jansone Baiba<sup>1</sup>

<sup>1</sup>Department of Pharmacology, Faculty of Medicine, University of Latvia, Riga, Latvia

**Background.** Stroke is one of the major causes of death and disability worldwide. Ischemic stroke is a heterogeneous disease caused by the reduced blood flow and energy supply to the brain, which triggers multitude of pathophysiological processes, including on daily activity. PhenoMaster wheel running is used to assess voluntary physical activity in rodents. It preferably suits to study circadian (24-hour cycle) activity. There is a lack of scientific knowledge about post-stroke recovery level in a long-term period, e.g., several months after the stroke.

**Aim.** The aim of the current study was to evaluate the activity in voluntary running wheels in mice during day and night hours for a period of six months after the stroke surgery.

**Methods.** Stroke was induced by occlusion of the right middle cerebral artery using the intraluminal filament technique in C57BL/6HNSd male mice. Mice were divided in two groups: sham and stroke (fMCAo). Mice were placed within individual PhenoMaster cages (one mouse per cage). Voluntary running behaviour was observed 60, 120 and 180 days after fMCAo or sham surgery. Voluntary running wheel activity (the total run distance, run time, run attempts, the longest run distance) were detected by the TSE PhenoMaster mouse phenotyping system. The experimental data were analysed with Graph Pad Prism software.

**Results.** Total covered distance, time spent in the wheel, number of running episodes, and the longest run episode in the voluntary running wheel was increased during the night-time on day 60 after surgery for both sham and fMCAo mice. This increase for fMCAo mice was more pronounced compared to sham animals. On a test day 180, sham mice showed a similar activity pattern as on day 60, but fMCAo mice were less active in the voluntary running wheel.

**Conclusion.** The increased activity observed during night-time in the voluntary running wheel for sham mice is consistent with the natural behaviour of mice, while fMCAo activity shifted during testing periods (60 days after operation to 180 days), indicating disturbed natural behaviour which could be a stroke consequence.

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## The Effect of St. John's Wort (*Hypericum Perforatum L.*) on Catalase Activity in Mouse Organs

Tamkevičius Mantas<sup>1</sup>, Liekis Arunas<sup>2</sup>, Kubiliene Asta<sup>1</sup>, Sadauskiene Ilona<sup>2</sup>

<sup>1</sup>Department of Analytical and Toxicological Chemistry, Faculty of Pharmacy, Lithuanian University of Health Sciences, Kaunas, Lithuania

<sup>2</sup>Neuroscience Institute, Lithuanian University of Health Sciences, Kaunas, Lithuania

**Background.** St. John's wort, botanically known as *Hypericum perforatum L.* is a widespread medical herb widely used in Lithuania and all over the world. The aerial parts of the plant are rich in antioxidants such as flavonoids, carotene and vitamin C. Although the plant is well known for its anti-inflammatory, antidepressant, antimicrobial, antiviral and antioxidant effects, the studies for its capability to reduce oxidative stress in the brain are sparse. Though antioxidant properties of some phenolic compounds of St. John's wort have been proved to be effective *in vitro*, absorption of these compounds from the gastrointestinal tract, the further metabolism, tissue uptake and possibility to pass blood-brain barrier still remains unclear. There is also insufficient knowledge about the further fate of these compounds, depending on the dose and the mode of entry into the body.

**Aim.** The present study aimed to elucidate possible protective effects of *Hypericum perforatum L.* extract in alleviating the toxicity of aluminium on catalase (CAT) activity in mice brain and liver.

**Methods.** The experiments done on BALB/c laboratory mice. The CAT activity in mice organs homogenates determined spectrophotometrically. Results expressed as the mean  $\pm$  SEM.

**Results.** Results showed that aluminium decreases CAT activity in the liver and brain of mice by 13.91% and 88.42%, respectively, compared to the control group. Meanwhile, the influence of St. John's wort extract on enzyme activity was versatile. In the liver, *Hypericum perforatum L.* extract reduced CAT activity by 19.48% in comparison with control mice. The effect of the extract of St. John's wort for CAT activity in aluminium-treated mice liver was practically minimal. The effect of St. John's wort extract on CAT activity in the liver of aluminium-treated mice was practically minimal, i.e., equal to the control level (5.21% difference not statistically reliable). However, the effects of St. John's wort extract could be clearly seen in the brains. The extract decreases catalase activity by 74.53%, compared to control. But administration of St. John's wort extract to the aluminium group showed a large increase in CAT activity (78.51% higher than in the aluminium group).

**Conclusion.** *Hypericum perforatum L.* extract itself may reduce CAT activity in the brain and liver of mice. However, it can increase CAT activity in the brain and liver of the aluminium group, thus reducing the peroxidation induced by aluminium ions.

## Protective Effect of Zinc Against Nickel-Induced Adverse Effects in Brain of Mice

Šulinskienė Jurgita<sup>1,2</sup>, Bernotienė Rasa<sup>1,2</sup>, Naginienė Rima<sup>1</sup>

<sup>1</sup>Neuroscience Institute, Lithuanian University of Health Sciences, Kaunas, Lithuania

<sup>2</sup>Department of Biochemistry, Medical Academy, Lithuanian University of Health Sciences, Kaunas, Lithuania

**Background.** The nervous system is one of the major targets of nickel, as this metal crosses the blood-brain barrier and accumulates in the brain. Ni competes with redox active metals, reducing the activities of the enzymes of the antioxidant system, thus causing oxidative stress. Although redox inert zinc isn't an antioxidant in the true sense of the word, its deficiency is associated with increased free radical generation and weakened response to oxidative stress. The scientific data indicates the ability of Zn to reduce lipid peroxidation, enhance the capacity of the antioxidant system and suggests potential antagonism with Ni.

**Aim.** The aim of the present study was to evaluate the antioxidant defense capabilities of Zn on Ni induced brain oxidative damage of mice. To assess oxidative status of the brain, contents of reduced glutathione (GSH) and metallothionein (MT) were measured.

**Methods.** Mice were randomly assigned into 3 metal exposure groups plus a control group which received i.p. injections of saline. Mice of Ni and Zn exposure groups received an i.p. injections (once a day) of corresponding amounts of NiCl<sub>2</sub> and ZnSO<sub>4</sub>. Mice of the Zn+Ni exposure group were i.p. injected with ZnSO<sub>4</sub> and after 20 min with NiCl<sub>2</sub> solutions in corresponding doses.

**Results.** Our results have shown that single and repeated Ni<sup>2+</sup> administration significantly decreased the contents of GSH in the brain of mice – by 20% and 30% respectively. ZnSO<sub>4</sub> administration did not seem to affect content of GSH at either period of exposure, however the injection of Zn<sup>2+</sup> 20 minutes prior to the NiCl<sub>2</sub> administration has returned GSH concentration to the level of control at both periods of exposure (p<0.05). Brain MT concentrations were increased by 30% after a single exposure to Ni<sup>2+</sup> just as after single Zn<sup>2+</sup>+Ni<sup>2+</sup> exposure (p<0.05), however, MT concentration in the brain of once Zn<sup>2+</sup>-treated group of mice remained at control level. Repeated NiCl<sub>2</sub> administration increased brain MT content by 36%; repeated exposure to ZnSO<sub>4</sub> raised MT level by 121%, while Zn pre-treatment 20 minutes prior to the NiCl<sub>2</sub> administration increased MT concentration by 80%, comparing to the control group (p<0.05).

**Conclusion.** The exposure to Ni has significantly reduced content of GSH and increased level of MT after both single and repeated NiCl<sub>2</sub> administration. Zn<sup>2+</sup> pre-treatment has provided protective effect against Ni<sup>2+</sup>-induced GSH depletion at both exposure periods, however, MT levels after single and prolonged both metal administration remained increased.

## GASTROENTEROLOGY, NUTRITION, GASTROINTESTINAL ONCOLOGY & MICROBIOTA

### The Impact of the Nordic Diet on Fatigue in Mild and Moderate Ulcerative Colitis Patients

Girgensone Ginta<sup>1</sup>, Birka Ilze<sup>1,2,3</sup>, Anspuka Līva<sup>3</sup>, Šantare Daiga<sup>3</sup>

<sup>1</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

<sup>2</sup>Pauls Stradiņš Clinical University Hospital, Riga, Latvia

<sup>3</sup>Institute of Clinical and Preventive Medicine, University of Latvia, Riga, Latvia

**Background.** Nearly 50% of patients with ulcerative colitis (UC) suffers from fatigue. This burdensome symptom causes limitation of daily activities therefore affecting patients' quality of life. The Nordic diet (ND) has been associated with anti-inflammatory effects and may positively affect the symptoms of UC, including fatigue.

**Aim.** The aim was to evaluate if the ND improves the symptoms of fatigue in patients with mild and moderate UC.

**Methods.** Patients with mild and moderate UC from Latvia were included and then evaluated at week 0, 6 and 10. At the first visit, patients were consulted by a nutritionist and recommendations on the ND was given. The activity of UC was evaluated with faecal calprotectin (FC) and partial Mayo score (pMS). Fatigue level (FL) and fatigue impact (FI) on daily activities was evaluated with inflammatory bowel disease – fatigue (IBD-F) questionnaire. At every visit the patient's body mass index (BMI), FC, pMS and IBD-F scores were registered. The adherence to the ND was evaluated with the ND score which was calculated as described by Bjørnarå et al., 2015. All data were collected and then analysed using IBM SPSS 2.0 and Microsoft Excel. Statistical significance was assessed using Related-Samples Wilcoxon Signed Rank Tests. Differences of  $p < 0.05$  were considered as statistically significant.

**Results.** Overall, 13 patients were included – 10 females, 3 males. The median age was 37 years (IQR 31.0–45.0 years). Mild UC was present in 6 patients, but moderate in 7. The mean duration of disease was 7.6 years ( $SD \pm 5.7$ ). There was a statistically significant difference in the ND score ( $p = 0.01$ ), BMI ( $p = 0.04$ ) and FI on daily activities ( $p = 0.01$ ) between 1<sup>st</sup> and 2<sup>nd</sup> visit. The mean ND score changed from 3.8 points at 1<sup>st</sup> visit, to 6.0 points at 2<sup>nd</sup> visit. Mean BMI at 1<sup>st</sup> visit was 28.0 kg/m<sup>2</sup>, but at 2<sup>nd</sup> - 27.4 kg/m<sup>2</sup>. FI changed from 31.2 points at 1<sup>st</sup> visit to 16.4 points at 2<sup>nd</sup> visit. No statistically significant difference in FL between 1<sup>st</sup> and 2<sup>nd</sup> visit was noticed. There was no statistically significant difference in the ND score, BMI, FL and FI between 2<sup>nd</sup> and 3<sup>rd</sup> visit, nor between 1<sup>st</sup> and 3<sup>rd</sup> visit.

**Conclusion.** When followed, the ND is associated with reduction of BMI and improvement of FI on daily activities. Further studies are needed to evaluate the changes of FL.

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## Gastrointestinal Symptoms and Their Association with Metabolic Compensation, Duration of Diabetes and Faecal Calprotectin in Patients with Type I Diabetes Mellitus: Preliminary Data

Būmane Renāte<sup>1,2</sup>, Ivanova Santa<sup>1,2</sup>, Senkāne Silva<sup>3</sup>, Fedulovs Aleksejs<sup>1</sup>, Zaļizko Poļina<sup>1,2</sup>, Sokolovska Jeļizaveta<sup>1</sup>

<sup>1</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

<sup>2</sup>Pauls Stradiņš Clinical University Hospital, Riga, Latvia

<sup>3</sup>Statistics Unit, Riga Stradiņš University, Riga, Latvia

**Background.** Various gastrointestinal symptoms are associated with diabetes. Recent studies showed that gastrointestinal symptoms in patients with type I diabetes are associated with poorer quality of life and glycaemic control. However, the pathophysiology of gastrointestinal disorders in type I diabetes is not sufficiently clear.

**Aim.** The aim of this study was to analyse the frequency of upper and lower gastrointestinal (GI) symptoms in patients with type I diabetes (T1DM), as well as its association with haemoglobin A1c (HbA1c), duration of diabetes and faecal calprotectin.

**Methods.** Data of 112 patients from “LatDiane: Latvian Diabetic Nephropathy Study” were analysed. Patients with T1DM (N=73) completed a GI symptom questionnaire and HbA1c, calprotectin was detected. Subjects without diabetes (controls, N=39) were included in the study to compare GI symptom prevalence and the level of faecal calprotectin.

**Results.** 73 with T1DM (mean age 42.22±11.39 years) and 39 controls (mean age 37.64±8.18 years) were enrolled. 24 participants or 32.9% had good compensation of diabetes (HbA1c≤7 %) and 49 participants (67.1%) had poor metabolic compensation (HbA1c>7%). The mean HbA1c among participants was 8.14±1.72%. Median diabetes duration was 23.05±12.03 years. Upper GI symptoms were more frequent in patients with T1DM compared with controls (49.2 vs 33.5%, p=0.892), in particular – loss of appetite (15 vs 2.6%), abdominal pain (12.3 vs 10.3%), dysgeusia (9.6 vs 2.6%). The overall prevalence of lower GI symptoms was also higher in T1DM subjects (78.3 vs 43.8%, p=0.171). The study did not find statistically significant difference in the prevalence of GI symptoms between patients with good and poor metabolic control. The percentage of subjects showing elevated faecal calprotectin (>50 µg/g) were higher among subjects with diabetes (9.1%) than controls (2.8%) (p=0.416). The proportion of calprotectin positive individuals was higher in the microalbuminuria and macroalbuminuria group compared to controls, but the difference was not statistically significant. GI symptoms were not strongly associated with diabetes duration (p=0.220) and elevated faecal calprotectin (p>0.05).

**Conclusion.** In our study, there was no strong association between GI symptoms and HbA1c, levels of faecal calprotectin and duration of diabetes. GI symptoms and elevated faecal calprotectin were more frequent in T1DM compared with controls. It is likely that elevated faecal calprotectin in T1DM is related to the development of diabetic nephropathy, however, to ascertain that, further research is needed.

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## Current Smoking Associated with Precancerous Gastric Lesions “Missed” by Serologic Pepsinogen Testing

Razuka-Ebela Danute<sup>1,2</sup>, Polaka Inese<sup>2</sup>, Parshutin Sergei<sup>2</sup>, Ebela Inguna<sup>1</sup>, Daugule Ilva<sup>1,2</sup>, Santare Daiga<sup>1,2</sup>, Sjomina Olga<sup>2</sup>, Herrero Rolando<sup>3,4</sup>, Park Jin Young<sup>3</sup>, Leja Marcis<sup>1,2</sup>

<sup>1</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

<sup>2</sup>Institute of Clinical and Preventive Medicine, University of Latvia, Riga, Latvia

<sup>3</sup>International Agency for Research on Cancer, Lyon, France

<sup>4</sup>Agencia Costarricense de Investigaciones Biomedicas, Fundacion INCIENSA, San Jose, Costa Rica

**Background.** Serum pepsinogen (Pg) is the best non-invasive method of assessing gastric mucosal status. The sensitivity and specificity of Pg as a marker for precancerous gastric lesions has shown variable results.

**Aim.** To investigate factors associated with false negative pepsinogen (Pg) results in detecting gastric precancerous lesions.

**Methods.** Serum pepsinogen was measured and upper endoscopy with histology was performed for participants aged 40–64 within the “Multicentric randomised study of *Helicobacter pylori* eradication and pepsinogen testing for prevention of gastric cancer mortality: the GISTAR study”. Participants were classified as ‘increased risk’ if they had gastric atrophy or intestinal metaplasia on biopsy in a pattern concurrent with increased gastric cancer risk (according to the MAPS guideline), or dysplasia, with the rest deemed as ‘average risk’. Cases with ‘increased risk’ histology not identified by serum PgI/PgII  $\leq 2$  and PgI  $\leq 30$  ng/mL were considered false negative and analysed by smoking status, presence of *H. pylori*, gender and age. ROC was calculated for PgI and Pg I/II ratio and evaluated using AUC.

**Results.** Out of a total of 1210 participants, 367 (30.3%) had ‘increased risk’ histology, of which 160 (43.6%) were false negative. False negatives were more likely to be current smokers than former and never smokers (21.7% vs 10.7%,  $p < 0.001$ ), men (17.5% vs 9.7% women,  $p < 0.001$ ), and those positive for *H. pylori* (16.3% vs 8.7% negative,  $p < 0.001$ ). *H. pylori*-negative current smokers had substantially lower sensitivity when using pre-existing cut-offs for both PgI/II and PgI. *H. pylori*-positive current smokers had significantly lower sensitivity when using the pre-existing cut-off for PgI.

Sensitivity, specificity (%), 95% CI and area under ROC curve for pre-existing Pg cut-off values for detecting precancerous gastric lesions

	Pg I/Pg II $\leq 2$	Pg I $\leq 30$ ng/mL
All participants	65.38 (60.25–70.27); 87.12 (84.67–89.30); 0.82	62.64 (57.44–67.62); 81.56 (78.78–84.12); 0.75
Current smokers <i>H. pylori</i> -positive	52.00 (37.42–66.34); 87.04 (79.21–92.73); 0.76	32.00 (19.52–46.70); 91.67 (84.77–96.12); 0.63
Current smokers <i>H. pylori</i> -negative	32.26 (16.68–51.37); 93.33 (83.80–98.15); 0.68	38.71 (21.85–57.81); 86.67 (75.41–94.06); 0.68

**Conclusion.** The ability of serum Pg testing to detect gastric precancerous lesions was lower among current smokers and the relationship was modified by *H. pylori* presence.

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## Gastrointestinal Symptoms and Faecal Calprotectin Level in Patients with Type 1 Diabetes and Diabetic Kidney Disease

Fedulovs Aleksejs<sup>1</sup>, Tzivian Lilian<sup>1</sup>, Puzirevska Irēna<sup>1</sup>, Folkmane Inese<sup>1,2</sup>, Zaļizko Poļina<sup>2</sup>, Sokolovska Jeļizaveta<sup>1</sup>

<sup>1</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

<sup>2</sup>Pauls Stradiņš Clinical University Hospital, Riga, Latvia

**Background.** Gastrointestinal symptoms have been previously associated with chronic kidney disease, but their association with progression of diabetic kidney disease in type 1 diabetes (T1D) is little studied.

**Aim.** To evaluate the association between the intensity of gastrointestinal symptoms and the level of faecal calprotectin between patients with stable and progressive diabetic kidney disease and T1D.

**Methods.** 74 patients with T1D and 39 healthy participants were included. Questionnaire on gastrointestinal symptoms included 17 questions about pain, discomfort, impaired bowel movement such as diarrhoea and constipation. Faecal calprotectin was measured by Elisa. Progression of diabetic kidney disease was defined as estimated glomerular filtration rate (eGFR) decline  $\geq 2.5$  ml/min/year or increase albuminuria stage over the last 3–6 years. Statistical analysis was done in the SPSS 22 program

**Results.** The mean age in the T1D group was  $42.3 \pm 15.2$  years and in the control group  $37.3 \pm 10.6$  years. In the T1D group, the mean diabetes duration was  $23.1 \pm 12.2$  years, the mean HbA1c was  $8.2 \pm 1.9\%$ , and the prevalence of progression of kidney disease was 17.6% ( $n=13$ ). Groups of progressors and non-progressors did not differ in age, anthropometric measures, the prevalence of cardiovascular hard endpoints compared to non-progressors. Progressors had longer T1D duration ( $p=0.04$ ); higher prevalence of arterial hypertension ( $p=0.08$ ); severe retinopathy ( $p=0.010$ ); end-stage renal disease ( $p=0.029$ ), and previous gastrointestinal surgery ( $p=0.02$ ). Gastrointestinal symptom score demonstrated high validity in the T1D group (Cronbach's  $\alpha=0.82$ ) and in the control group (Cronbach's  $\alpha=0.78$ ). The mean value of gastrointestinal symptom score did not differ between T1D and controls ( $p=0.39$ ) and between progressors and non-progressors ( $p=0.77$ ). However, in the progressor group, 53.9% of participants noted that they had bowel movement disorders ( $p$  versus non-progressors= $0.010$ ). The level of calprotectin did not differ between progressors mean  $45.8 \pm 83.9$  and non-progressors mean  $23.4 \pm 53.3$  ( $p=0.17$ ), and between healthy mean  $11.5 \pm 17.2$  and cases mean  $27.5 \pm 59.8$  ( $p=0.81$ ). However, calprotectin level correlated statistically significantly with transglutaminase IgA ( $r=-0.252$ ;  $p=0.041$ ), GFR ( $r=0.255$ ;  $p=0.038$ ), T1D duration ( $r=0.239$ ,  $p=0.051$ ) in patients with diabetes.

**Conclusion.** Patients with T1D and progressive diabetic kidney disease have a higher prevalence of diarrhoea and constipation, and a history of gastrointestinal surgery. However, these factors were not associated with an increase in faecal calprotectin level in our study.

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## SURGERY, TRAUMATOLOGY & ORTHOPAEDICS

### Digital Planning Method Efficiency in Total Cementable Hip Arthroplasty

Rozenbergs Krišs<sup>1</sup>, Vecumniece Lauma<sup>1</sup>, Anastasija Miščurina<sup>1</sup>, Kalnbērzs Konstantīns<sup>1,2</sup>

<sup>1</sup>University of Latvia, Riga, Latvia

<sup>2</sup>Hospital of Traumatology and Orthopaedics, Riga, Latvia

**Background.** The amount of hip arthroplasty procedures increases yearly and preoperative planning is a crucial part of this procedure.

**Aim.** The aim was to determine the efficiency of digital planning method usage in total cementable hip arthroplasty.

**Methods.** A retrospective study performed at the Hospital of Traumatology and Orthopaedics in Riga, Latvia between October 2021 and January 2022. Study includes 104 randomly selected patients who did undergo total cemented hip arthroplasty surgery in 2020. Patients' radiological pelvic radiographs digital planning was made using Hectec digital planning mediCAD software and later compared to used prosthetic implant size. Data was analysed using IBM SPSS software. Descriptive statistics, as well as One-Sample Chi-square test were used to analyse the results. The significance level was set at  $p < 0.05$ .

**Results.** In total, 104 randomly selected patients met the inclusion criteria. As a result, 51 women and 53 men were analysed. In a total of 78.8% ( $\chi^2(1, N=82)=34.6, p < 0.001$ ) cases, the implanted acetabular component was either exact match or within  $\pm$  one size difference from digitally planned in anterior-posterior view. In a total of 71.2% ( $\chi^2(1, N=74)=18.6, p < 0.001$ ) cases the implanted femoral component was either exact match or within  $\pm$  one size difference from digitally planned in anterior-posterior view. There is statistically significant association between the patient hospitalization diagnosis and femoral components accuracy from preoperative digital planning ( $\chi^2(1, N=104)=6.05, p=0.014$ ) determined using Pearson-Chi-Square Test.

**Conclusion.** For over 70% preoperative digitally planned femoral and acetabular size is within  $\pm 1$  size of implanted components size. Preoperative digital planning is an effective method to determine the possible size of acetabular and femoral components in total hip arthroplasty procedure.

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# Hip Joint Periprosthetic Infection Treatment with Temporary Cemented Endoprosthesis – 10-Year Single Institution Experience

Repša Lauris<sup>1,2</sup>

<sup>1</sup>Hospital of Traumatology and Orthopaedics, Riga, Latvia

<sup>2</sup>University of Latvia, Riga, Latvia

**Background.** Periprosthetic joint infection is one of the most devastating complications in total hip replacement surgery. Standard worldwide approved treatment strategy is two-stage revision. At the first stage, surgery meticulous debridement and all implant removal is performed. Afterwards, on average after 6 weeks, the second stage surgery is done – repeated debridement and endoprosthesis implantation.

**Aim.** The aim of the study was to evaluate 10-year experience of our treatment method – a single-stage revision using temporary cemented prosthesis in the first-stage revision

**Methods.** 203 patients were enrolled in the study within 2010–2019. The analysis was performed on the basis of medical records, radiological and microbiological findings.

**Results.** 203 patients with hip joint periprosthetic infection were treated within 2010–2019 by 15 surgeons. Surgical approaches in the majority of cases were anterolateral, minority was lateral and posterior. No preferences regarding surgeons' tactics were taken into account. 80% (N=163) of all patients were treated using temporary prosthesis in first stage revision, 20% (N=40) were treated with implant removal at the first stage and reimplantation of cement spacer or no-spacer. Infection treatment success rate in the endoprosthetic group was 90% (N=139), in the no-endoprosthesis group 72% (N=28). Fistula, which is contraindication for one-stage revision, was present in 37% (N=60) of patients undergoing temporary prosthesis implantation, it was not a negative factor for infection eradication. 56% (N=91) from patients with temporary prosthesis no second stage revision was necessary. The most common reasons for second stage revision was Pain – 17% (N=28) and Instability – 14% (N=23). –Microbiological findings were similar to other authors' publications – *St. Aureus* 34%, *St. Epidermidis* 19%, *Gram-* 10%, *Streptococcus* 7%, others 15% unknown 15%. In cases of severe acetabulum bone defects, a more likely method of no-implant usage was chosen. Femur periprosthetic fracture was an indicator for more-likely secondary revision surgery. BMI>40, immunosuppression (HIV, oncological disease), radiation therapy are associated with worse prognosis regarding one-stage infection eradication. Treatment method preference was determined by the surgeon.

**Conclusion.** Temporary cemented endoprosthesis is a good method of choice for hip-joint periprosthetic infection treatment with good success rate regarding infection eradication, good functional results, in 60% of cases secondary revision surgery was not necessary.

**Acknowledgements.** The author declares the absence of conflict of interest.

## Evaluation of Tumour Extent Based on Upper Endoscopy, Computer Tomography and Pathohistological Results in Patients With Operable Gastric Cancer

Flaksmanis Artūrs<sup>1</sup>, Ivanovs Igors<sup>1,2</sup>, Belusa Anastasija<sup>1,3</sup>

<sup>1</sup>Riga East Clinical University Hospital, University of Latvia, Riga, Latvia

<sup>2</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

<sup>3</sup>University of Latvia, Riga, Latvia

**Background.** Gastric cancer is the 5<sup>th</sup> commonly diagnosed cancer in the world. Surgical therapy is the golden standard for gastric cancer treatment. Current management is mostly based on patient health condition, pre-operative upper endoscopy, and computer tomography (CT).

**Aim.** The aim of the study is to compare tumour size based on pre-operative endoscopy and CT with tumour size on post-operative pathohistological examination in patients with gastric cancer and review the difference in tumour size, location and following management.

**Methods.** Retrospective case-controlled study was done in Riga East Clinical University Hospital (Latvia) from 2017 to 2021. Sixty-four patients with confirmed cancer underwent total or subtotal gastrectomy. Patients with diffuse gastric cancer were excluded from this study. All patients had pre-operative endoscopy and CT. Pre-operative tumour size and location based on CT scans and endoscopy results was compared with post-operative tumour size and location based on pathohistological data. The data were considered coincident if the tumour size on pathohistological examination and the tumour size determined on endoscopy or CT did not differ by more than 10%.

**Results.** In total, 64 patients with gastric cancer were included in the study (35 males [54.7%] and 29 females [45.3%]). In 58 cases (90.6%), tumour size based on CT scan did not match the pathohistological results ( $p=0.001$ ). Tumour size on CT was less than tumour size on pathohistological examination in 71.9% – with the median deviation 5 mm [IQR 0–41.75]. In 18.8% it was greater – the median deviation 45 mm [IQR 37.5–67.5]. In 6 cases (9.4%) tumour size was coincident with tumour size on pathohistological examination. Endoscopy was performed in 61 cases (95.3%) because in 3 cases (4.7%) patient had an emergency surgery, without previous endoscopic examination. Only in 23 cases tumour size was mentioned in endoscopic protocol. Of them, in 22 cases (95.6%) tumour size did not coincident with pathohistological data ( $p=0.001$ ). In 17 cases (73.9%), tumour size according to endoscopy results was smaller than tumour size on pathohistological examination – with the median deviation 20 mm [IQR 10–30], and in 5 cases (21.7%) tumour size was larger – the median deviation 30 mm [QR 17.5–90]. Only in 1 case (4.3%) endoscopic tumour size was coincident with the pathohistological data.

**Conclusion.** In most cases, tumour size measured on pre-operative endoscopy and CT was smaller than tumour size on final pathohistological examination. This fact should be taken in consideration when planning treatment tactics and surgical therapy.

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# Comparison of Functional and Radiological Results Between Total Shoulder Arthroplasty with Global Icon and Global Unite Implants

Vugulis Rihards<sup>1,3</sup>, Zadorožnijs Sergejs<sup>2</sup>, Vugulis Aigars<sup>4</sup>

<sup>1</sup>Hospital of Traumatology and Orthopaedics, Riga, Latvia

<sup>2</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

<sup>3</sup>University of Latvia, Riga, Latvia

<sup>4</sup>Department of Hand Surgery, Hospital of Traumatology and Orthopaedics, Riga, Latvia

**Background.** Shoulder arthroplasty is one of the surgical treatments for degenerative osteoarthritis. Modern technologies provide constant development and diversity of endoprostheses. When replacing a patient's joint with an artificial implant, it is important to choose the type of prosthesis that suits best to the condition, fulfills daily activities, needs, and, most importantly, achieves the best postoperative results.

**Aim.** Compare the effectiveness of Global Icon Stemless implant and Global Unite Stemmed implant by evaluating the clinical and radiological results a year after the surgery.

**Methods.** The study included 25 patients who underwent shoulder arthroplasty with Global Icon Stemless implant and Global Unite Stemmed implant. Only patients with pre-operative diagnosis of osteoarthritis were included. In the study, patients were evaluated by Constant-Murely score before the surgery and a year after surgery to assess clinical improvements. Data were gathered and evaluated using SPSS IBM Statistics 22 software.

**Results.** 12 patients' shoulder joints were replaced with Global Icon implant and 13 patients' shoulder joints were replaced with Global Unite implant. The average age of patients in Global Icon group was 52.8 years; SD=2.57, and 61.1 years; SD=1.64 in Global Unite group.

The average pre-operative total CMS for Global Icon patient group was 25.08; SD=2.15, while the average total score for Global Unite was 24.07; SD=1.61.

A year after the surgery, the average CMS for Global Icon patients was 74.18 points; SD=1.97, while Global Unite average total score was 58.6; SD=3.26.

**Conclusion.** Regardless of patient's age, Global Icon Stemless shoulder prosthesis delivers more effective short term clinical results than Global Unite stemmed shoulder prosthesis. As a result of radiographic analysis, signs of bone reabsorption without clinical manifestations were observed in one case in each study group.

## Hip Shape Abnormalities Leading to Osteoarthritis

Džeriņš Andris<sup>1,2</sup>, Studers Pēteris<sup>1,2</sup>

<sup>1</sup>Joint Laboratory of Traumatology and Orthopaedics, Riga Stradiņš University, Riga, Latvia

<sup>2</sup>Hospital of Traumatology and Orthopaedics, Riga, Latvia

**Background.** Currently, we have poor results in predicting the onset and preventing progression of hip osteoarthritis (OA). A theory proposed by Murray suggests that most of the OA cases are caused by subtle abnormalities of the hip joint, which have not been previously recognized.

**Aim.** To analyse the frequency and characteristics of hip joint anatomical abnormalities, that could be associated with OA development based on radiographic measurements and statistical shape modelling.

**Methods.** 150 pelvic radiographs of unilateral hip OA patients (Arthritis group) and 70 patients with a non-OA underlying disease or injury (Control group) admitted to the Hospital of Traumatology and Orthopaedics during the period from 2018 to 2021 were examined. Predefined radiographic parameters characteristic for Cam-type impingement (alpha angle, pistol grip deformity), Pincer-type impingement (lateral centre edge angle, acetabular depth, crossover sign), acetabular index, femoral head diameter, femoral neck width, neck-shaft angle was measured and assessed using the Impax-Orthopaedic-Tools 3.0.2.3 program. A statistical shape model was built using the BoneFinder 1.3.4 program which detects and sets 75 landmark points on the proximal femur and acetabulum in AP pelvic radiographs to analyse the shape variations between the two groups. The obtained data were statistically analysed by the IBM SPSS 23 program.

**Results.** Increased alpha angle ( $>50^\circ$ ) ( $p<0.001$ ), Pistol grip deformity ( $p<0.001$ ) (characteristic for Cam deformity) and centre-edge-angle less than  $25^\circ$  ( $p<0.001$ ), acetabular index  $>47^\circ$  ( $p=0.012$ ) (characteristic for acetabular dysplasia) was significantly more prevalent in the Arthritic group. From radiographic signs characteristic for Pincer-type impingement, only acetabular protrusion was significantly more prevalent in the Arthritis group ( $p=0.02$ ). The overall variation of the hip joint was divided into 10 modes. Patients with hip osteoarthritis had significantly higher scores of shape modes 1, 2, 4 and 6 ( $p=0.002$ ;  $p=0.01$ ;  $p=0.02$ ;  $p=0.03$ ) indicating flattened head-neck junction, non-spherical femoral head, prominent acetabular posterior wall, and a larger femoral head.

**Conclusion.** While FAI is a common radiographic finding in OA patients, only Cam-type impingement was significantly associated with OA. Not only severe forms but also mild degrees of dysplasia present an important risk factor for OA. Statistical shape modelling is a promising method which analyses the overall shape variance. Better understanding of shape variations and their origins could offer new methods to predict and prevent hip OA in the future.

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## CARDIOVASCULAR AND REGENERATIVE MEDICINE

### Intrahospital Outcomes After True Coronary Bifurcation Stenting

**Bolsteina Eva**<sup>1</sup>, Laduss Arnis<sup>1,3</sup>, Camane Evija<sup>1,3</sup>, Podolsky Ilya<sup>1</sup>, Erglis Andrejs<sup>1,3</sup>, Trusinskis Karlis<sup>2,3</sup>, Latkovskis Gustavs<sup>1,3</sup>, Sondore Dace<sup>1,3</sup>, Narbutė Inga<sup>1,3</sup>, Dombrovska Kristine<sup>3</sup>, Dombrovskis Andis<sup>3</sup>, Briede Ieva<sup>1,3</sup>, Lismanis Aigars<sup>3</sup>, Rudzitis Ainars<sup>1,3</sup>, Jegere Sanda<sup>1,3</sup>, Kumsars Indulis<sup>1,3</sup>

<sup>1</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

<sup>2</sup>Faculty of Medicine, Riga Stradiņš University, Riga, Latvia

<sup>3</sup>Latvian Centre of Cardiology, Pauls Stradiņš Clinical University Hospital, Riga, Latvia

**Background.** Percutaneous coronary intervention (PCI) for bifurcation disease is known to be technically challenging and has historically been associated with lower procedural success rates and worse clinical outcomes than non-bifurcation lesions.

**Aim.** The aim of the current study was to evaluate intrahospital outcomes of patients who underwent PCI for bifurcation lesions involving the main vessel and a side branch with a diameter above or equal to 2.5 mm.

**Methods.** A cohort retrospective analysis of the ongoing Coronary Bifurcation Treatment Registry in Latvian Centre of Cardiology (PCI performed from 01.01.2017. to 30.03.2021.). Study population was divided into two groups: provisional single-stenting (1-stent) and systematic double-stenting (2-stent). Intrahospital complications rates were compared between groups.

**Results.** A total 519 patients with true bifurcation were included in this study. 428 patients in 1-stent group and 91 in 2-stent group. Procedural complications were perforation (1-stent 0% (n=0) vs 2-stent 1.1% (n=1), p=0.175), side branch occlusion (1-stent 2.1 % (n=9) vs 2-stent 1.1 % (n=1), p=0.527), no reflow phenomenon (1-stent 0.2% (n=1) vs 2-stent 0% (n=0), p=0.165). Intrahospital complications were cardiogenic shock (1-stent 0% (n=0) vs 2-stent 1.1% (n=1), p=0.175), early stent thrombosis (1-stent 0% (n=0) vs 2-stent 1.1% (n=1), p=0.176), periprocedural myocardial infarction (1-stent 4.2 % (n=18) vs 2-stent 4.4 % (n=4), p=0.938), all cases were NSTEMI. Creatine kinase-MB levels 24h after PCI were measured in 173 patients. Creatine kinase-MB mean levels – 1-stent 7.4 ng/ml, 95% CI [4.1;10.2] vs 2-stent 10.5 ng/ml, 95% CI [2.4;18.6], p=0.017. Creatine kinase-MB levels more than 3 times above upper normal limit (1-stent 5 % (n=7) vs 2-stent 11.5 % (n=3), p=0.733). Creatine kinase-MB levels more than 5 times above upper normal limit (1-stent 6 % (n=9) vs 2-stent 4 % (n=1), p=0.367.

**Conclusion.** Intrahospital complication rate in the treatment of true coronary bifurcation lesions was low. There was one case of early stent thrombosis in systematic double-stenting technique group. Creatine kinase-MB levels 24h after PCI were higher in systematic double-stenting technique group.

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## Characteristics of Lipoprotein(a) Levels in Patients Included in the Latvian Registry of Familial Hypercholesterolemia

Ļesterovičs Georgijs<sup>1,2,3</sup>, Šaripo Vita<sup>1,2,3</sup>, Meiere Rūta<sup>1,2,3</sup>, Tērauda Elizabete<sup>1,2,3</sup>, Kriššcūne Annija<sup>2</sup>, Skudriņa Gunda<sup>2,3</sup>, Gilis Daiņus<sup>1,2,3</sup>, Ērglis Andrejs<sup>1,2,3</sup>, Latkovskis Gustavs<sup>1,2,3</sup>

<sup>1</sup>Latvian Institute of Cardiology and Regenerative Medicine, University of Latvia, Riga, Latvia

<sup>2</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

<sup>3</sup>Pauls Stradiņš Clinical University Hospital, Latvian Centre of Cardiology, Riga, Latvia.

**Background.** Lipoprotein(a) [Lp(a)] is determined as a risk factor for atherosclerotic cardiovascular disease. High Lp(a) levels may mimic familial hypercholesterolemia (FH) and may additionally increase risk of major cardiovascular events.

**Aim.** The aim of this study was to determine prevalence of elevated Lp(a) levels in patients with suspected or established FH in Latvia and analyse potential differences in FH diagnostic subgroups.

**Methods.** This was a retrospective analysis of patients included in the Latvian Registry of Familial Hypercholesterolemia. Patient groups were defined according to Dutch Lipid Clinic Network Criteria (DLCNC) for FH diagnosis in probands. In this analysis we included probands with definite, probable, or possible FH. Relatives of probands with definite or probable FH who had LDL-C above 95<sup>th</sup> percentile (and therefore established FH diagnosis) were also included. Patients with DLCN <3 points or high triglyceride level, and relatives with LDL-C <95<sup>th</sup> percentile were excluded.

**Results.** Among 1026 patients of the Registry, 887 met the inclusion criteria. Lipoprotein(a) had been measured in 255 (28.8%) patients, and the median [interquartile range, IQR] was 29.2 [10.0–95.0] mg/dL. Elevated levels defined as Lp(a) >50 mg/dL were found in 106 (41.6%) patients. Very high (>100 mg/dL) and extremely high (>180 mg/dL) levels were measured in 63 (24.7%) and 16 (6.3%) patients, respectively. The highest recorded Lp(a) was 442 mg/dL. No significant differences in Lp(a) levels were found among the patient subgroups according to the diagnostic likelihood of FH (all  $p > 0.05$ ; Table). There was, however, a trend towards lower Lp(a) in patients with a higher FH likelihood.

**Conclusions.** High Lp(a) levels are very common in hypercholesterolemic patients with suspected or established FH, but there seems to be no association with phenotypic likelihood of FH diagnosis. Thus, measurement of Lp(a) should be strongly considered in all patients with high cholesterol levels with or without FH.

Table. Lp(a) levels in patient subgroups.

	Definite (n=38)	Probable (n=74)	Possible (n=120)	Relatives (n=23)
Lp(a) mg/dL, median [IQR]	24.2 [11.0–118.9]	24.1 [9.1–115.1]	36.7 [11.3–80.5]	34.5 [7.3–71.5]
Lp(a) >50 mg/dL, n (%)	14 (36.8%)	30 (40.5%)	52 (43.3%)	10 (43.5%)

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## Effect of Inclisiran on Lipid Profile at 3 Month Follow-Up: First Clinical Experience in Latvian Centre of Cardiology

Trušinskis Kārlis<sup>1,3</sup>, Kokina Baiba<sup>1,3</sup>, Lapšovs Māris<sup>1</sup>, Karantajere Mairita<sup>2,3</sup>, Knoka Evija<sup>1,3</sup>, Caunīte Laima<sup>1,3</sup>, Jēgere Sanda<sup>2,3</sup>, Narbutė Inga<sup>2,3</sup>, Mintāle Iveta<sup>2,3</sup>, Roze Rūdolfs<sup>2,3</sup>, Sondore Dace<sup>3</sup>, Kumsārs Indulis<sup>2,3</sup>, Ērglis Andrejs<sup>2,3</sup>

<sup>1</sup>Rīga Stradiņš University, Riga, Latvia

<sup>2</sup>University of Latvia, Riga, Latvia

<sup>3</sup>Pauls Stradiņš Clinical University Hospital, Riga, Latvia

**Background.** Lipid accumulation is the cornerstone of atherosclerotic cardiovascular disease. The most emphasized risk factor is low-density lipoprotein cholesterol (LDL-C), with therapeutic target <1.4 mmol/l in very high cardiovascular risk patients. Statins are the standard of hypolipidemic therapy, nevertheless, treatment goal is not always achievable with highest tolerated dose, highlighting implication for new medications. Inclisiran is a small interfering ribonucleic acid (RNA) molecule, inducing degradation of messenger RNA of proprotein convertase subtilisin/kexin type 9 (PCSK9) and interfering its translation in hepatocytes. Subsequently, LDL receptor degradation is decreased, leading to reduction in circulating LDL-C.

**Aim.** To evaluate effect of inclisiran on plasma lipid profile (total cholesterol (TC), LDL-C, high-density lipoprotein cholesterol (HDL-C), triglycerides (TG), non-HDL-C and remnant cholesterol) after 3 months.

**Methods.** Very high cardiovascular risk patients, not achieving LDL-C target on maximally tolerated statin therapy, undergoing percutaneous coronary intervention in the Latvian Centre of Cardiology were enrolled. Baseline demographic and medical data was acquired. Participants received subcutaneous inclisiran injection (284 mg), concomitantly taking statin and/or ezetimibe. 3-month follow-up was conducted, including plasma lipid profile and the second inclisiran injection. Data was analysed using MS Excel and SPSS Statistics software.

**Results.** Outcomes of 23 patients have been analysed. Significant reduction by 25.5% in TC ( $4.35 \pm 0.90$  vs  $3.24 \pm 0.84$  mmol/l,  $p < 0.001$ ), by 47.6% in LDL-C ( $2.75 \pm 0.94$  vs  $1.44 \pm 0.90$  mmol/l,  $p < 0.001$ ) and by 25.0% in TG ( $1.76 \pm 0.90$  vs  $1.32 \pm 0.68$  mmol/l,  $p = 0.037$ ) was established. Tendency for HDL-C increase by 5.56% was observed, nevertheless, without statistical significance ( $1.26 \pm 0.37$  vs  $1.33 \pm 0.35$  mmol/l,  $p = 0.188$ ). Significant decrease in non-HDL-C by 36.6% was established ( $3.22 \pm 1.06$  vs  $2.04 \pm 0.90$  mmol/l,  $p < 0.001$ ), whereas remnant cholesterol was reduced by 9.6% without statistical significance ( $0.52 \pm 0.47$  vs  $0.47 \pm 0.21$  mmol/l,  $p = 0.887$ ). 13 patients (56.5%) achieved LDL-C target after 3 months. 65.2% of patients ( $n = 15$ ) had baseline LDL-C  $\leq 2.9$  mmol/l. In this group, statistically significant reduction in TC by 21.5% ( $3.86 \pm 0.60$  vs  $3.03 \pm 0.52$  mmol/l,  $p < 0.001$ ), LDL-C by 47.7% ( $2.22 \pm 0.33$  vs  $1.16 \pm 0.48$  mmol/l,  $p < 0.001$ ), non-HDL-C by 40.3% ( $2.95 \pm 0.65$  vs  $1.76 \pm 0.44$  mmol/l,  $p = 0.002$ ) and increase in HDL-C by ( $1.23 \pm 0.41$  vs  $1.37 \pm 0.39$  mmol/l,  $p = 0.047$ ) was determined. There was no significant difference in TG level, reduced by 27.6% ( $1.81 \pm 1.05$  vs  $1.31 \pm 0.62$  mmol/l,  $p = 0.069$ ), and remnant cholesterol with decrease by 12.7% ( $0.55 \pm 0.53$  vs  $0.48 \pm 0.23$  mmol/l,  $p = 0.894$ ). In this group, 66.7% of patients ( $n = 10$ ) achieved LDL-C goal.

**Conclusion.** Inclisiran effectively improved lipid profile in patients with established atherosclerotic cardiovascular disease. LDL-C lowering of 47.6% within 3 months is similar with observed inclisiran effectiveness in clinical trials.

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## Sea Buckthorn Seed Oils as a Novel Omega 3 Source for Coronary Heart Disease Patients with Residual Risk

Mintale Iveta<sup>1,2,3</sup>, Erglis Kristaps<sup>3</sup>, Zuzans Ralfs<sup>1,2</sup>, Romanovska Aija<sup>3</sup>, Erglis Martins<sup>1,2</sup>, Bajare Iveta<sup>2,3</sup>,  
Dzerve Vilnis<sup>1,2,3</sup>, Erglis Andrejs<sup>1,2,3</sup>

<sup>1</sup>Latvian Centre of Cardiology, Pauls Stradiņš Clinical University Hospital, Riga, Latvia

<sup>2</sup>University of Latvia, Riga, Latvia

<sup>3</sup>JSC "SISTEMU INOVACIJAS", Jaunmārupe, Latvia

**Background.** Coronary heart disease (CHD) remains a paramount cause of death in Latvia and worldwide. Despite the availability of preventive therapies, CHD events still occur because of residual risk. Lifestyle management is particularly important, and so are the most recent treatment strategies to reduce residual risk. Omega 3, obtained from fish oil, is a long-standing, approved treatment for secondary prevention.

**Aim.** To determine whether sea buckthorn oils (containing high amount of plant Omega 3) could improve risk profile in CHD patients with residual risk, defined by clinical conditions as obesity, hypertension, dyslipidaemia, elevated C-reactive protein and uric acid levels.

**Methods.** 25 CHD patients with optimal treatment were included in the trial in Latvian Cardiology Centre. Body mass index, blood pressure, heart rate were measured, analysis were taken – lipid profile, glucose, C-reactive protein and uric acid. 2 sea buckthorn capsules were prescribed per day for 3 months.

After 1 month, patients were questioned about possible side effects and sensations. After 3 months, patients were observed – possible adverse events, change of medication, vital parameter measurements and body mass index were recorded. Efficacy of the treatment was evaluated.

**Results.** All 25 patients were adherent to the treatment. There were no side effects, the tolerability was good. One patient was hospitalised with worsening of heart failure, in 2 hypertensive patients' medication was changed, in 4 patients the dose of statins was increased.

Significantly improved level of uric acid ( $p < 0.05$ ). No significant changes in other parameters, but with a tendency to improve for blood pressure, lipid profile, glucose and C-reactive protein levels.

**Conclusion.** The supplementary treatment with sea buckthorn seed oils seems promising for decreasing residual risk in CHD patients. A larger number of participants is needed to strengthen the hypothesis of efficacy of plant-derived Omega 3 in high-risk patients.

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## Correlation of Inflammation, Lipidogram and Haematological Readings in Chronic Heart Failure Patients

Gujytė Greta<sup>1</sup>, Mongirdienė Aušra<sup>1</sup>, Laukaitienė Jolanta<sup>1,2</sup>

<sup>1</sup>Cardiology Clinic, University Hospital, Lithuanian University of Health Sciences, Kaunas, Lithuania

<sup>2</sup>Department of Biochemistry, Lithuanian University of Health Sciences, Kaunas, Lithuania

**Background.** Neutrophils take part in maintaining of pro-inflammatory state. HF pathogenesis differences in chronic heart failure (CHF) patients with reduced ejection fraction (HFrEF) and HF with preserved ejection fraction (HFpEF) remain to be investigated.

**Aim.** The aim of the current study was to determine differences in complete blood count, C-reactive protein (CRP) concentration and lipidogram between chronic HF patients with an absence/presence of myocardial infarction (MI) history and preserved/reduced EF.

**Methods.** We separated the patients (n=266) according to CHF phenotype: 1) HFrEF patients (n=149) into groups according to presence of MI: no MI (n=91) and with MI (n=58); 2) CHF without MI according to left ventricular ejection fraction (LVEF): LVEF $\geq$ 50%, n=117; LVEF<50%, n=91. All readings were taken from the patients' medical histories.

**Results.** MCHC was lower and RDW-CV was higher in the lower EF group without MI (337.32 (10.60) and 331.46 (13.13), p=0.004; 13.6 (11.5–16.9) and 14.7 (12.6–19.1), p=0.001). In the group according to LVEF without MI lymphocyte count correlated with RDW-CV ( $r_s=-0.223$ ; p=0.032) and body mass index ( $r_p=0.186$ , p=0.032). RDW-CV and monocyte count correlated with NT-proBNP and serum creatinine ( $r_s=0.358$ , p=0.034;  $r_s=0.424$ , p<0.001 and  $r_s=0.354$ , p=0.012;  $r_s=0.205$ , p=0.018 respectively). CRP (6.9 (1.46–62.97), 7 (1–33.99), p=0.012) was higher and HDL concentration was lower (0.96 (0.44–2.2), 0.92 (0.56–1.97), p=0.010) in HFrEF with MI in comparison with the group without MI. LVEF correlated with MCHC and RDW-CV ( $r_s=0.273$ , p=0.001;  $r_s=-0.404$ , p<0.001). HDL cholesterol concentration was lower (0.96 (0.44–2.2); 0.92 (0.56–1.97), p=0.010) in the HFrEF with MI group. Uric acid concentration correlated with PLR and LMR ( $r_s=0.321$ , p=0.032;  $r_s=-0.341$ , p=0.023). A correlation between CRP and MCHC ( $r_s=0.262$ , p=0.008) was observed.

**Conclusion.** The higher pro-inflammatory condition was in HFrEF in comparison with HFpEF. HDL inverse correlation with monocyte count and percentage could show relation between the low-grade inflammation and lipid metabolism in HFrEF. Both MCHC and RDW-CV may be relevant in assessing the chronic HF patients' condition.

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## Association of Mineralocorticoid Receptor Gene NR3C2 Polymorphism rs4635799 with Acute Myocardial Infarction

**Braukyliene Rima**<sup>1</sup>, Aldujeli Ali<sup>1</sup>, Maciulevicius Laurynas<sup>1</sup>, Jankauskaite Darija<sup>1</sup>, Jurenas Martynas<sup>1</sup>, Unikas Ramunas<sup>1</sup>, Zabiela Vytautas<sup>1</sup>, Baksyte Giedre<sup>1</sup>, Gustiene Olivija<sup>1</sup>, Lesauskaite Vaiva<sup>1</sup>, Simonyte Vaiva<sup>1</sup>, Zaliaduonytė Diana<sup>1</sup>

<sup>1</sup>Lithuanian University of Health Sciences, Kaunas, Lithuania

**Background.** The NR3C2 gene encodes the mineralocorticoid receptor (MR). MR has pathological roles not only in classical MR epithelial target organs like kidney and colon but also in non-epithelial tissues like heart and vascular smooth muscle cells and endothelial cells. No data are currently available on the impact of NR3C2 rs4635799 polymorphism on acute myocardial infarction (AMI).

**Aim.** To assess the relationship between the genetic polymorphisms rs4635799 of NR3C2 and AMI.

**Methods.** 314 patients diagnosed with acute myocardial infarction and 140 patients without coronary artery (CA) stenosis during CA angiography were enrolled. Patients admitted from April 2018 and November 2020 at Hospital of Lithuanian University of Health Sciences due to AMI with no previous history of acute coronary syndrome and previous revascularization were prospectively enrolled. The genotypes of the group were compared with the control group's (n=140) genotypes. Single-nucleotide polymorphism (SNP) of NR3C2 gene (rs4635799) was evaluated using real-time PCR.

All of the statistical analyses were performed with SPSS 23.0 software (SDSPSS, Chicago, IL, USA). The variables were expressed as the median (interquartile range) or mean and standard deviation (M (SD)) and a percentage (number). Chi-squared, and logistic regression tests were used for analysis.

**Results.** Ischemic heart disease risk factors such as age (M – 64.8 (SD – 11.3) vs M – 64.7 (SD – 12)), gender (male N (%), 203 (64.4) vs 82 (58.6)), hypertension ((N (%), 284(91.0) vs 129 (90.2)), diabetes mellitus (N (%), 43(18.3) vs 23 (16.4)), body mass index (kg/m<sup>2</sup> median [25–75%], 27.7 [25.1–31.1] vs 28.9 [24.9–33.3], family history of heart attacks (N (%), 36 (11.5) vs 24 (17.3)) showed no significant differences between the AMI and reference groups. However, smoking patients were more frequently prone to AMI than the patients without CA stenosis (p=0.000). There were more patients with AMI in the TT genotype group, than control group patients (51.9% vs 19.4%, p<0.05). In contrast, there were more reference group patients than acute MI in the TC and CC genotype groups (53.2% vs 32.1% and 27.3 %vs 16%, p<0.005, respectively). The genetic polymorphisms rs4635799 of NR3C2 were significantly associated with increased AMI rate [OR 1.969, 95% CI: 1.211–3.203, p=0.006] in Lithuanian patients.

**Conclusion.** The genetic polymorphism rs4635799 of NR3C2 was significantly associated with an increased AMI rate.

## How to Reduce the Residual Cardiovascular Risk: Focus on Phytosterols

Ērglis Kristaps<sup>1,2</sup>, Dzērve Vilnis<sup>2</sup>, Romanovska Aija<sup>1</sup>, Jēgere Sanda<sup>1,2</sup>, Mintāle Iveta<sup>2,4</sup>, Kalviņš Ivars<sup>1,3</sup>, Jakobsons Ēriks<sup>1,2</sup>, Ērglis Mārtiņš<sup>1,2</sup>, Romanovska Beatrise Lūcija<sup>1,2</sup>, Ērglis Andrejs<sup>1,2,4</sup>

<sup>1</sup>JSC "Sistēmu inovācijas", Rīga, Latvia

<sup>2</sup>Institute of Cardiology and Regenerative Medicine, University of Latvia, Riga, Latvia

<sup>3</sup>Latvian Institute of Organic Synthesis, Riga, Latvia

<sup>4</sup>Pauls Stradiņš Clinical University Hospital, Riga, Latvia

**Background.** While statins are the treatment of choice for lowering low-density lipoprotein cholesterol (LDL-C) in the majority of patients, many patients retain a high CVD risk despite achieving the recommended LDL-C targets with statins (residual risk). This 'residual risk' is mainly due to elevated triglyceride (TG) and low high-density lipoprotein cholesterol (HDL-C) levels. Phytosterols as natural components of vegetable oils have received particular attention because of their capability to lower serum cholesterol levels in humans resulting in a significant reduction in the risk of heart disease. Given that  $\beta$ -sitosterol is the most abundant phytosterol and that  $\beta$ -sitosterol exhibits a similar oxidation pattern as that of cholesterol in terms of oxidation products, they are important constituents of our daily diets.

**Aim.** To find the most effective  $\beta$ -sitosterol extraction protocol using supercritical fluid extraction with CO<sub>2</sub> technology from sea buckthorns seeds harvested in Latvia.

**Methods.** After juice pressing the sea buckthorn press cake was freeze-dried (residual moisture content – 3.99%). Sea buckthorn seeds (SBS) were separated (using vibrating sieves and compressed air) and grinded (particle size: 0.80–1.20 mm). SBS was extracted using supercritical fluid extraction with CO<sub>2</sub>. Five different samples were obtained by changing the temperature (40–50°C), CO<sub>2</sub> flow rate (70 or 80 kg/h) and humidity (2, 3 or 4%).

$\beta$ -sitosterol extraction yield together with omega 3,6,9 fatty acids extraction yield were the main indicators of extraction efficiency.

### Results.

Table: Extraction yield of  $\beta$ -sitosterol and omega 3,6,9 in different SBS oil samples

	001	002	003	004	005
	Yield %				
omega 3	32.9±1.6	33.6 ±1.7	32.8±1.6	33.2±1.7	32.4±1.6
omega 6	36.4±1.8	36.3±1.8	35.8±1.8	36.0±1.8	35.4±1.8
omega 9	16.6±1.5	16.5±1.5	16.8±1.5	16.6±1.5	17.2±1.6
$\beta$ -sitosterol	27.99 mg/g±4.4	29.30 mg/g±5.7	27.56 mg/g±4.2	27.75 mg/g±5.5	31.54 mg/g±4.4

All the samples show the stable extraction yield of omega fatty acids, as well as  $\beta$ -sitosterol. However, the sitosterol extraction rate of the sample 05 is superior compared to the other attempts.

**Conclusion.** The most effective extraction yield of  $\beta$ -sitosterol can be achieved by pressure in extractor 150 bar, temperature 40°C, CO<sub>2</sub> flow rate of 80 kg/h and solvent to feed ratio 50:1. Resulting in average 2.9%  $\beta$ -sitosterol content in extracts which is one of the highest results at this moment according to published scientific literature.

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## Comparison of Two Preparation Methods for Platelets Rich Plasma on Treatment of Knee Osteoarthritis: Platelets/Leukocytes Count Measurement and Clinical Outcome Evaluation

Shalha Loay<sup>1</sup>, Goncars Valdis<sup>1,2</sup>

<sup>1</sup>University of Latvia, Riga, Latvia

<sup>2</sup>Hospital of Traumatology and Orthopaedics, Riga, Latvia

**Background.** The fact that platelet's  $\alpha$ -granules degranulation releases numerous essential growth factors has been used in treatment of degenerative osteoarthritis (OA).

Platelet-rich-plasma (PRP) is a centrifuged blood-derived product created to describe plasma presenting platelet level higher than that related to peripheral blood.

**Aim.** Compare the preparation methods of the PRP using separating gel versus PRP without the separating gel in the treatment of knee OA monitoring the platelets count and clinical outcome.

**Methods.** Twenty knee OA patients were divided into two groups with 10 patients in each group. The preparation of PRP from 8 ml venous blood was performed. On group one we use regular tubes, on group two tubes with separator gel. One ml of PRP was used to analyse Platelets/Leucocyte count and the rest was injected in the knee joint cavity. Patient's outcome and response to the PRP treatment were evaluated using KOOS score.

**Results.** The differences founded in age and gender distribution, as well as blood platelets and leukocyte count were not significant.

The mean platelets level in PRP prepared with regular tubes was  $141.2 \times 10^9/L$  ( $p < 0.05$ ) whereas the separator gel group had mean platelet level of  $98.4 \times 10^9/L$  ( $p < 0.05$ ).

The leukocyte level in the PRP prepared with separator gel tubes had a mean of  $0.1 \times 10^9/L$  ( $p = 0.3$ ), while in the group with regular tubes it was  $2.6 \times 10^9/L$  ( $p < 0.05$ ).

The separator gel group had a mean KOOS score of 60 ( $p = 0.06$ ) before treatment and in one month follow up of 67 ( $p < 0.05$ ) and the patient with regular group had initial KOOS score of 59 ( $p = 0.06$ ) and in one month follow-up was 65 ( $p < 0.05$ ).

**Conclusion.** There was a higher platelet outcome using tubes without separator gel.

The leukocyte level was lower by using tubes with separator gel.

We found that there was no a significant difference in clinical outcome measured by KOOS and adverse events between both groups.

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## Real-Time Lactate Production Monitoring in Bioreactor System by Multi-Channel Photometric Device

Jakobsons Eriks<sup>1,2</sup>, Eihentale Alma<sup>2</sup>, Rupaine Beatrise Lucija<sup>1</sup>, Erglis Kristaps<sup>1,2</sup>, Erglis Martins<sup>1</sup>, Romanauska Aija<sup>1</sup>, Muiznieks Indriķis<sup>2</sup>, Erglis Andrejs<sup>1,2</sup>

<sup>1</sup>JSC "Sistēmu inovācijas", Jaunmārupe, Latvia

<sup>2</sup>Institute of Cardiology and Regenerative Medicine, University of Latvia, Riga, Latvia

**Background.** The advanced therapy medicinal product development drives research towards more cost-effective, time and labour-effective human cell cultivation methods. The large-scale cell expansion bioreactor systems are applied to achieve significant cell yields. Bioprocess automation, process traceability and quality control are the major challenging issues in the field. The glucose consumption and lactate production dynamics in cultivation media are main parameters used to control bioprocess. So far, glucose consumption and lactate production in cultivation media are measured by biochemical analysis or electrochemical sensors that are time consuming and direct sample acquisition can result in bioreactor system contamination. To resolve these aspects, this study is focusing on development of optical devices for real-time lactate level monitoring without direct contact with cultivation media.

**Aim.** The aim of the current study is to evaluate optical device ability to monitor lactate concentration during adherent cell cultivation in a bioreactor system for large-scale cell expansion.

**Methods.** Prototype of the lactate monitoring device was based on multi-channel photometry. Light beams from at least one light source were targeted upon cultivation media passing through translucent tubes. Afterwards, scattered light was captured with multiple photodetector channels. Signals from photodetectors were filtered electronically, amplified and repeatedly filtered to differentiate signal components that are afterwards transmitted to microprocessor to digitalise the signal and to proceed with mathematical filtering, correction and recognition algorithms. Based on mathematical analysis and physically related signal variety, lactate concentration in culture media was calculated.

An automated bioreactor system constructed by the research team was applied for evaluation of device performance. Cultivation medium samples were collected, and concentration of lactate determined by biochemical analyser. Obtained data were compared with device readings.

**Results.** The real-time monitoring device readings of lactate concentration changes in cultivation media were compared with biochemical analyser readings at same time points. The obtained data show that device readings reach precision of  $\pm 0.08$  mmol/l in a lactate range of 0–16 mmol/l.

**Conclusion.** The principle of multi-channel photometry can be applied for real-time lactate production monitoring without direct contact to cultivation media.

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## Cell Expansion Process Automation by Application of Real-Time Glucose and Lactate Monitoring Device

Jakobsons Eriks<sup>1,2</sup>, Eihentale Alma<sup>2</sup>, Rupaine Beatrise Lucija<sup>1</sup>, Erglis Kristaps<sup>1,2</sup>, Erglis Martins<sup>1</sup>, Romanauska Aija<sup>1</sup>, Muiznieks Indriks<sup>2</sup>, Erglis Andrejs<sup>1,2</sup>

<sup>1</sup>JSC "Sistēmu inovācijas", Jaunmārupe, Latvia

<sup>2</sup>Institute of Cardiology and Regenerative Medicine, University of Latvia, Riga, Latvia

**Background.** The cell expansion bioreactor systems are applied to achieve significant cell yields utilised for development of advanced therapy medicinal products or for research purposes. The bioprocess automation can optimise cell cultivation operations, expenses and quality. The real-time glucose and lactate concentration monitoring device was developed in previous stages of study and utilised as a part of bioreactor automation system.

**Aim.** The aim of the current study is to evaluate the cell cultivation process automation performance.

**Methods.** The automated bioreactor system constructed by the research team was applied to evaluate the cell cultivation process. Disposable transfusion bioreactor kit with silicone tubing was installed. The real-time glucose and lactate concentration monitoring device was integrated in the cultivation media circulation loop. The cell culture was seeded, and consumption of glucose and production of lactate were monitored. The cell cultivation process was stopped by reaching the end of the logarithmic growth phase.

**Results.** The maximum average consumption of glucose reached 207.2 mg/d, and the minimum consumption – 14 mg/d. The maximum average production of lactate reached 111 mg/d, and the minimum – 6 mg/d respectively. The average cultivation media used for feed during the cultivation cycle reached 497.2 ml. The maximum daily cultivation media feed/overflow reached 97% of total volume in the system. The average time to reach the end point of a bioprocess was 16 days. The evaporation ratio did not exceed 1% of total media used in the bioreactor. All the performed trials reached acceptance criteria. No bacterial contamination was observed during cell cultivation.

**Conclusion.** No significant deviations between all trials were observed. Further studies will be focused on different cell lines and cultivation patterns.

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## Clinical Outcome of Hip and Knee Joint Early Osteoarthritis Treatment Using Bone Marrow Derived Mononuclear Cells on Three-Year Follow-Up

Alpe Kristians<sup>1</sup>, Goncars Valdis<sup>1,2</sup>, Jakobsons Eriks<sup>1,3</sup>, Erglis Andrejs<sup>1,3</sup>, Kalnberzs Konstantins<sup>1,2</sup>

<sup>1</sup>University of Latvia, Riga, Latvia,

<sup>2</sup>Hospital of Traumatology and Orthopaedics, Riga, Latvia,

<sup>3</sup>Pauls Stradiņš Clinical University Hospital, Riga, Latvia

**Background.** Evaluate the clinical symptom changes on patients with hip and knee stage II–III osteoarthritis after treatment with bone marrow-derived mononuclear cell (BMNC) intra articular injection in a period of 3 years.

**Aim.** To evaluate derived mononuclear cell intra articular injections into the knee and the hip joint osteoarthritis to observe changes in symptoms after a dose of bone marrow-derived mononuclear cell intra-articular injection over a 36-month period.

**Methods.** The group of 59 patients with early OA on 66 hip and knee joints get the intraarticular injection of BMNC. The Knee OA group consists of 32 patients and 34 knee joints. The mean age  $53.96 \pm SD$  14.15 years, 16 males, 16 females, Kellgren–Lawrence grade: II – 16, III – 18. The Hip OA group of 27 patients and 32 hip joints were analysed. The mean age  $58.1 \pm 10$  15 males, 12 females, Kellgren–Lawrence grade: II – 20, III – 12. The average nucleated cell count used in the Knee group was  $45.56 \pm 34.94 \times 10^6$  and  $53.35 \pm 41.57 \times 10^6$  in the Hip group. The patients were evaluated using KOOS and Harrys Hip Score before and at 6, 12 and 36 months.

**Results.** No adverse effects after the BM–MNC injection were observed. At the 12 months, all subscale results had improved as compared to the starting point on 33 (97%) Knee joints and 29 (90%) Hip joints.

Over the period, we observed clinical outcome distribution of Knee and Hip OA patients in three subgroups:

1) No increase of OA signs – 17 (50%) of Knee and 16 (50%) Hip joints still had clinical improvement without other additional treatment.

2) Mild increase of OA signs additional treatment with intra-articular injections of hyaluronic acid and PRP used – 8 (23.5%) Knee and 4 (12.5%) Hip joints.

3) Severe increase of osteoarthritis signs – the Total Joint Arthroplasty performed on 9 (26%) Knee and 12(37.5%) hip joints.

### Clinical Score results

Time point	No. of Knee Joints	KOOS total Mean $\pm$ SD	Number of Hip Joints	HHS total Mean $\pm$ SD
Before	34	61.6 $\pm$ 15.0	32	73.65 $\pm$ 10.79
6 <sup>th</sup> month	34	78.7 $\pm$ 12.2	32	86.68 $\pm$ 10.82
12 <sup>th</sup> month	34	76.9 $\pm$ 13.3	32	86.97 $\pm$ 11.33
36 <sup>th</sup> month	17	91.99 $\pm$ 9.04	16	90.53 $\pm$ 5.28

**Conclusion.** After a 3-year period, 50% of patients with Knee and Hip Joint early OA treated with BMNC injection showed clinical improvement or were nearly symptom-free without any additional treatment.

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## Assessment of Three-Dimensionally Printed Polycaprolactone Tissue Scaffold Fabrication Protocols

Jakobsons Ēriks<sup>1,2</sup>, Rupaine Beatrise Lūcija<sup>1</sup>, Ērglis Kristaps<sup>1,2</sup>, Kļava Juris<sup>3</sup>, Ērglis Andrejs<sup>1,2</sup>

<sup>1</sup>Cell Transplantation Department, Pauls Stradiņš Clinical University Hospital, Riga, Latvia

<sup>2</sup>Institute of Cardiology and Regenerative Medicine, University of Latvia, Riga, Latvia

<sup>3</sup>Institute of Solid State Physics, University of Latvia, Riga, Latvia

**Background.** Properties of polycaprolactone (PCL) are poorly studied from the perspective of three-dimensional (3D) bioprinting, and it is essential to evaluate material application potential. Three-dimensional printed tissue models could contribute to study novel approaches to tissue regeneration and treatment strategies. Application of 3D printing technology could make it possible to fabricate biologically compatible tissue – personalized transplants.

**Aim.** The aim of study stage is to evaluate PCL scaffold printing protocols developed in previous stages of study.

**Methods.** The scaffolds were designed by computer-aided design (CAD) in Simplified 3D software. The combined thermoplastic/bioink extrusion system was utilized to fabricate tissue scaffold models. The system was developed in first stage of this study. The scaffold molten were printed on glass slide, after cooling they were removed and printing quality was assessed.

**Results.** Printing qualities were assessed by series of scaffold fabrication. Architecture of all printed scaffolds was the same – two-layer grid, 6 mm diameter, tread width 100 μm, space between grids 50 μm, density of grid filling 33%, dimension of strut 100 μm, outside perimeter layer width 400 μm and outside perimeter support ring. Total construct diameter – 12 mm.

PLC extrusion temperature was +130°C, molten bed temperature +10°C, PLC tread laminating speed was 4, 6 and 8 mm/s. The printing chamber ambient temperature was set to +20°C, air humidity was 50–60%.

In each series, 50 samples were printed (total n=150). Most scaffold deformations were observed in series with 8 mm/s laminating speed – 28% of samples did not reach acceptance criteria. Series with 4 mm/s laminating speed – 20% and series with 6 mm/s laminating speed – 4% of samples did not reach acceptance criteria, respectively.

**Conclusion.** Applied extrusion temperature and molten bed temperature minimize condensate forming while tread is positioned. Observed deformation of samples was related to PLC tread torsion, shrinkage, and cooling during positioning.

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## INFECTIOUS DISEASES AND PULMONOLOGY

### Rhinosinusitis and Its Impact on Bronchial Reactivity in Allergic and Non-Allergic Adults

Ievina Marta<sup>1,2</sup>, Strazda Gunta<sup>1,2</sup>, Mukans Maksims<sup>3,4</sup>, Taivans Immanuel<sup>1</sup>

<sup>1</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

<sup>2</sup>Pauls Stradiņš Clinical University Hospital, Riga, Latvia

<sup>3</sup>Riga Stradiņš University, Riga, Latvia

<sup>4</sup>Aiwa Clinic, Riga, Latvia

**Background.** Bronchial asthma (BA) is one of the most common non-communicable diseases in the world, and its provoking factors are still being studied. Rhinosinusitis is one of the factors that can affect development of asthma. RS patients with asthma may be at increased risk of exacerbations, poorer disease control, and more frequent hospitalizations.

**Aim.** To evaluate the relationship between rhinosinusitis and increased bronchial reactivity in patients with different BA phenotypes in Latvian adults.

**Methods.** The data were collected and statistically analyzed on 4038 adults who underwent bronchoprovocation test (BPT) to exclude possible asthma diagnosis at the Centre for Lung Disease and Thoracic Surgery at the Pauls Stradiņš Clinical University Hospital at time period from 2014 to 2020.

**Results.** 69.2% of women and 30.8% of men participated in the study. The diagnosis of BA was confirmed in 1030 women and 383 men. Patients with allergies are more likely to be diagnosed with BA at an earlier age. The median age of patients with allergic asthma was 44 years for women and 34 years for men, and 55 years for women and 45 years for men in the non-allergic BA group. The difference between the groups was shown to be statistically significant ( $p < 0.001$ ). RS is more common in allergic individuals ( $p < 0.001$ ), with no significant gender differences. In cases of proven BA, RS was found in 48% of allergic patients and 33% of non-allergic patients, with no significant gender difference ( $p = 0.893$ ,  $p = 0.276$ ). In the case of RS, BPT is more often positive (40% with RS vs 32% without RS,  $p < 0.001$ ). In 80% of cases, RS is not treated, and treatment decreases with age. In the treated and untreated RS groups, the bronchial response was induced at the first dose of MCH and gradually decreased, but no statistically significant difference was found between the groups ( $p = 0.063$ ).

**Conclusion.** Increased bronchial reactivity is significantly more common in allergic and non-allergic patients with rhinosinusitis. This type of association is most common in young women with allergies. In practice, more attention should be paid to the symptoms of rhinosinusitis, which indicate an increased risk of developing bronchial asthma. Adequate treatment of rhinosinusitis in both patients with and without allergies could improve the situation. Further research of bronchial reactivity and the factors that affect it is still needed.

**Acknowledgements.** The authors declare the absence of conflict of interest.

## Airwave Oscillometry for Monitoring of COVID-19 Pneumonia

Grima Laura<sup>1</sup>, Jurka Normunds<sup>1</sup>, Strazda Gunta<sup>1</sup>, Taivans Immanuels<sup>1</sup>

<sup>1</sup>University of Latvia, Riga, Latvia

**Background.** Airwave oscillometry (AO) is a non-invasive method for investigation of lung mechanics. Interstitial inflammation characteristic for COVID-19 pneumonia (CVP) changes the mechanical properties of lungs which manifest in different ways including the reduction of lung dynamic compliance.

**Aim.** The aim of the study was to find out if lung mechanics data measured with AO associated with other data used to characterize the severity of lung damage, like CT score or oxygen demand, and whether AO could be used as a tool for monitoring the course of CVP.

**Methods.** In the study were enrolled 34 CVP patients who gave written consent for such examinations. The study was approved by ethics committee of Pauls Stradiņš Clinical University Hospital. During the hospital stay and 3 months after the discharge from hospital repeated measurements of lung mechanics were performed with portable device Tremoflo-100 (Thorasys, Canada). During the examination, patients performed one-minute-long tidal breathing through the instrument

**Results.** Among all Tromoflo-100 indices – R5, R5-20, X5, RF and AX, the last two showed the most relevant differences between disease stages. They are presented in the table below. Resonance frequency (RF) measured during hospital stay was elevated to 175%, but Area X – to 492% of predicted value 3 months after the discharge from hospital mean values were significantly lower (see p values in the table), but still did not reach the predicted levels.

0 vs 3 mo	Resonance frequency (RF%)			P vs 3 mo	Area X (AX%)			P vs 3 mo	n
	Mean	M-95%	M+95%		Mean	M-95%	M+95%		
0	175	164	185		492	405	599		70
3	130	109	152	0.0004	212	103	435	0.0003	17

Correlation analysis also was performed between AO indices and CD score, body mass index (BMI), patients age, blood CRO and ferritin levels, duration of hospital stay and patients' oxygen demand (FiO<sub>2</sub>). Significant correlations were found between the last two. The highest significance show RF expressed as % of predicted and AX % pred. RF correlated to FiO<sub>2</sub> with R=0.498 and p=0.0000004, but AX% with r=0.502.

**Conclusion.** Lung mechanical properties measured by AO are changed significantly in COVID-19 pneumonia. The changes persist up to three months and even more after the discharge from the hospital. The duration of post-COVID changes correlate to their severity during the acute phase of the disease. In contrast to expectation, AO indices do not correlate significantly with CT score. This fact may be explained by the major impact of airways in AO examination compared to CT that mostly characterize the changes in lung parenchyma.

## Evaluation of Remdesivir Effectiveness in COVID-19 Patients in Latvian Centre of Infectious Diseases: Real Life Data

Mjasnikovs Dmitrijs<sup>1</sup>, Tolmane Ieva<sup>1,2</sup>, Orlova Marija<sup>2</sup>, Ivancenکو Ludmila<sup>2</sup>, Rozentale Baiba<sup>2</sup>

<sup>1</sup>University of Latvia, Riga, Latvia

<sup>2</sup>Latvian Centre of Infectious Diseases, Riga East Clinical University Hospital, Riga, Latvia

**Background.** In February 2020, WHO designated the disease COVID-19. Global spread of SARS-CoV-2 virus led to declaration of pandemic. More than 290 000 confirmed cases and >4 thousand deaths have been reported in Latvia. Several therapeutic agents have been approved for the treatment of COVID-19.

**Aim.** The aim of this study was to evaluate remdesivir efficacy in real life.

**Methods.** Analysis of 180 patient medical records who were hospitalized in Latvian Centre of Infectious Diseases in 2020. There were 145 patients in remdesivir group and 35 in control group. The authors analyzed demographic, clinical, laboratory characteristics at the hospital admission. P-values were calculated by Chi-squared, Wald-Chi square and Pearson Chi-Square test, Wilcoxon rank sum test, two-proportions z-test. All values calculated as median except when stated differently.

**Results.** Age for control and remdesivir group was 61 and 60, respectively. 34.3% in control group were female, 37.2% in remdesivir group. Day of admission for control group was the 7<sup>th</sup>, whereas the 8<sup>th</sup> – for remdesivir group. Lymphocytes 1.09  $\mu$ L for control, 0.83 for remdesivir (p=0.0079). Control LDH 380 U/L, remdesivir 355, p-value 0.5013. Control GFR 82 ml/min, remdesivir 86, p-value 0.6555. Control ferritin 782.9 mkg/L, remdesivir 909.6, p-value 0.4539. Control CRP 71.9 mkg/L, remdesivir 76.4, p-value 0.8349. Control HbA1C 7.1%, remdesivir 6.4, p-value 0.0101. Control d-dimer 0.52 mkg/L, remdesivir 0.57, p-value 0.6953. Control IL-6 45pg/mL, remdesivir 38.1, p-value 0.5354. Control procalcitonin 0.101 ng/mL, remdesivir 0.122, p-value 0.4876. Lowest SpO<sub>2</sub> for control and remdesivir group are 89 and 90%, respectively, p-value 0.6372. Coexisting conditions: 34.3% from control group and 56.6% from remdesivir group had hypertension (p-value 0.02938), 20% from control group and 15.2% from remdesivir group had congestive heart failure, p-value 0.6591. 17.1% patients from control group and 34.5% from remdesivir group were obese, p-value 0.07419. 20% and 16.6% patients from control and remdesivir group, respectively, had diabetes mellitus, p-value 0.8138. Both groups were statistically comparable. 54.3% (N=19) patients from control group had severe illness (defined as SpO<sub>2</sub> <90%), 47.6% (N=69) from remdesivir group. Remdesivir therapy was started on day 10. Length of hospitalization for control group was 10 days, 11 for remdesivir group, p-value 0.243. 9 patients (25.7%) from control group were admitted in ICU and 12 (8.3%) from remdesivir group, p-value 0.0040. Negative outcome (*exitus letalis*) for control group had 25.7% (N=9) patients, 9.7% (N=14) from remdesivir group, p-value 0.011.

**Conclusion.** Remdesivir was effective in reducing mortality, but not in reducing length of hospitalization.

**Acknowledgements.** The authors declare the absence of conflict of interest.

## The Profile of Hospitalized COVID-19 Patients

Mjasnikovs Dmitrijs<sup>1</sup>, Tolmane Ieva<sup>1,2</sup>, Orlova Marija<sup>2</sup>, Ivancenکو Ludmila<sup>2</sup>, Rozentale Baiba<sup>2</sup>

<sup>1</sup>University of Latvia, Riga, Latvia

<sup>2</sup>Riga East Clinical University Hospital, Latvian Centre of Infectious Diseases, Riga, Latvia

**Background.** As the ongoing COVID-19 pandemic engulfs the planet, it is essential to understand the factors associated with hospitalization.

**Aim.** The aim of the study was to investigate the clinical characteristics of hospitalized COVID-19 patients.

**Methods.** Analysis of 130 patient medical records who were hospitalized in Latvian Centereof Infectious Disease from 01.12.2020 to 31.12.2020.

**Results.** Out of 130 patients, 69 were male (53.1%) and 61 female (46.9%). The median age of patients was 64. Out of 130 patient hospital records, 117 had a specified day of the disease at which patients admitted to hospital, mode was the 8<sup>th</sup> day. All values are calculated as median at hospital admission except SpO<sub>2</sub>, Leukocytes 5.78  $\mu$ L (N=130), lymphocytes 0.97  $\mu$ L(N=128), ASAT 37 U/L (N=81), for females 32(N=35), for males 45(N=46). ALAT 30 U/L (N=127), for females 25 (N=59), for males 34 (N=68), LDH 310 U/L, potassium concentration 3.97 mmol/L (N=127) and sodium 135 mmol/L (N=128), creatinine 82 mmol/L, minimum 37, maximum 468 (N=128), for females 69.00 (N=60), for males 87.50 (N=68). GFR (MDRD) 81.00 (N=129), minimum 7, maximum 213, ferritin 655.0 mkg/L (N=119), minimum 16.02, maximum 8881.0, for females 382.50 (N=55), for males 920.15 (N=64), C-reactive protein 47.25 mg/L (N=128), troponin-t was 15.40 pg/mL (N=121), HbA1C was 6.47% (N=56), d-dimer 0.67 mkg/L (N=107), CD4 cell quantity  $0.329 \times 10^9$ /L (N=38), interleukin-6 32.80 pg/mL (N=51), procalcitonin 0.115 ng/mL(N=85). Out of 130 patients, 95 (73.1%) had pneumonia on x-ray. The lowest median SpO<sub>2</sub> measurement while being hospitalized was 91% (N=129). Patients had different coexisting conditions – 82 patients had high blood pressure (63.1%), 42 (32.3%) – coronary artery disease, 32 (24.6%) – obesity, 22 (16.9%) – diabetes mellitus, 22 (16.9%) – chronic kidney disease, 14 (10.8%) – COPD, whereas 2 (1.5%) patients had decompensation of diabetes mellitus, and one (0.8%) had multiple myeloma. The median length of stay at the hospital was 8 days, minimum 2 and maximum – 36. Only 2 (1.5%) people were transferred to intensive care unit. Out of all 130 patients, 113 (86.92%) were discharged from hospital, but in 17 (13.08%) cases there was a lethal outcome (*exitus letalis*).

**Conclusion.** Hospitalized patients had lowered lymphocyte, sodium, GFR, CD4 cell, SpO<sub>2</sub> levels, males had elevated ASAT, LDH, ferritin, CRP, troponin-t, HbA1C, d-dimer, IL-6, procalcitonin. The majority of patients had pneumonia on x-ray and high blood pressure. The median stay at the hospital was 8 days. In 13% of the cases there was a lethal outcome.

**Acknowledgements.** The authors declare the absence of conflict of interest.

## Impact of Type II Diabetes on Mortality Rate in Patients With COVID-19 – A Retrospective Study

Gorgadze Gigi<sup>1</sup>, Khachiashvili Gvantsa<sup>1</sup>, Gordeladze Marine<sup>2</sup>, Gabunia Luiza<sup>1</sup>, Jikia Nikoloz<sup>1</sup>, Jorbenadze Mariam<sup>1</sup>, Khmaladze Tamar<sup>1</sup>

<sup>1</sup>Faculty of Medicine, Tbilisi State Medical University, Tbilisi, Georgia;

<sup>2</sup>Department of Endocrinology, Tbilisi State Medical University, Tbilisi, Georgia

<sup>3</sup>Department of Medical Pharmacology, Tbilisi State Medical University, Tbilisi, Georgia

**Background.** Clinical course, severity and outcome of COVID-19 is often influenced by various pre-existing chronic conditions. According to the studies, type II Diabetes is one the most commonly identified comorbidities among patients with SARS-CoV-2 infection, often associated with increased risk of complications and mortality.

**Aim.** The aim of our study was to analyse the prevalence of type II diabetes as a comorbid condition in hospitalized patients with confirmed COVID-19, assess the average duration of the period in which they required inpatient care, and evaluate mortality rate.

**Methods.** We conducted a retrospective cohort study. The eligibility criteria were imposed that included PCR confirmed SARS-CoV-2 infection and hospitalization in the First University Clinic of Tbilisi State Medical University from 1 January 2021 to 31 December 2021. Based on these criteria, 4868 patients have been selected and their histories have been reviewed to identify the presence of type II diabetes. We studied the demographic data of these patients, hospitalization days and frequency of lethal outcomes.

**Results.** From 4868 patients, 9.7% (n=474) had a history of type II diabetes. 48.3% (n=229) of them were female, 51.7% (n=245) – male. Age of these patients ranged from 35 to 92, the mean age was 63.9 (SD=11.01). The period of hospitalization varied from 1 to 48 days, the mean – 12.7 days, Standard Deviation=9.38. Mortality rate in the overall 4868 hospitalized patients with COVID-19 was 5.6 % (n=273). The same value among patients with diabetes equals 10.3% (n=49). Out of the total of 273 patients that died from severe COVID-19, 17.9% (n=49) had type II diabetes. Relative risk =2.0278 (95% CI 1.5109–2.7215), p<0.0001.

Age range	Age distribution of diabetic comorbidity	Mortality
20–40	3% (n=14)	0
40–60	28.6% (n=136)	8.8% (n=12)
60–80	55.5% (n=263)	12.9% (n=34)
80<	12.9% (n=61)	26.2% (n=16)

**Conclusion.** Presence of type II diabetes in medical history increases the risk of severe COVID-19 and poor outcome. Proper attention should be given to insulin resistance state and control of glucose levels while managing patients with SARS-CoV-2 infection.

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## Methicillin Resistance in *Staphylococcus Aureus* Among Vilnius University Medical Students

Sinkevič Rafal<sup>1</sup>, Vosyliūtė Rūta<sup>1</sup>, Kirkliauskienė Agnė<sup>2</sup>

<sup>1</sup>Faculty of Medicine, Vilnius University, Vilnius, Lithuania

<sup>2</sup>Faculty of Medicine, Institute of Biomedical science, Vilnius University, Vilnius, Lithuania

**Background.** *Staphylococcus aureus* is frequently considered a colonizer but it is also able to cause life-threatening infections under favourable circumstances. Asymptomatic colonization is a crucial predisposing factor. Infections caused by methicillin-resistant *S. aureus* (MRSA) are usually difficult to deal with due to its virulence factors and resistance to a wide range of antibiotics. Medical students are believed to be a high – risk group that is a real threat to the patients.

**Aim.** This study aimed to assess the carrier rate of MRSA among medical students in Vilnius University and evaluate susceptibility patterns of isolated *S. aureus* strains to various other antimicrobial agents.

**Methods.** Bacterial culture samples for *S. aureus* carriage were obtained from the anterior nares and throat with sterile swabs between 2018 and 2020. Identification of *S. aureus* was based upon the growth, mannitol fermentation on phenol red-mannitol-salt agar, colony morphology on Columbia 5% sheep blood agar, the tube coagulase test results with rabbit plasma, DNase and latex agglutination tests, and microscopy. All *S. aureus* isolates were tested against various antibiotics using commercial discs according to EUCAST guidelines. Quality control was achieved by *S. aureus* ATCC 29213.

**Results.** 358 medical students were examined, 716 samples from nose and throat were taken.

This study included 31.6% (n=113) male and 68.4% (n=245) female respondents aged 18 to 25. Overall carriage prevalence was 42.2%, out of them 54.3% were identified as nose carriers and 27.2% – throat carriers. The antimicrobial susceptibility testing revealed that 42.8% of the isolated strains were susceptible to penicillin. Susceptibility to tetracycline, fusidic acid, erythromycin, clindamycin and norfloxacin were 96.9%, 99.4%, 93.1%, 93.7% and 98.7%, respectively. Only 38.4% of isolated *S. aureus* strains were sensitive to all antibiotics used in this study. Carriage of MRSA was not identified at all.

**Conclusion.** A considerable proportion of medical students revealed to be colonized by *S. aureus* with the most common site of carriage being the nose. Antimicrobial susceptibility studies revealed that 42.8% of the isolates were susceptible to penicillin, but as there were no resistant strains to mupirocin and rifampicin, any kind of restrictions in usage do not have to be introduced. MRSA carriers were not determined.

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# Importance of Clinical Pharmacogenetic-Pharmacokinetic Studies in Unravelling Determinants of Tuberculosis Treatment Outcomes: Findings and Implications in Latvia

Igumnova Viktorija<sup>1,2</sup>, Kivrāne Agnija<sup>1,2</sup>, Vīksna Anda<sup>2,3</sup>, Freimane Lauma<sup>1</sup>, Sadovska Darja<sup>1,2</sup>, Čapligina Valentīna<sup>1</sup>, Pahirko Leonora<sup>4</sup>, Ozere Iveta<sup>2,3</sup>, Norvaiša Inga<sup>3</sup>, Bogdanova Ineta<sup>3</sup>, Krams Alvilis<sup>3</sup>, Cīrule Andra<sup>3</sup>, Pugovičs Osvalds<sup>5</sup>, Grīnberga Solveiga<sup>5</sup>, Sevostjanovs Eduards<sup>5</sup>, Bandere Dace<sup>2</sup>, Ranka Renāte<sup>1,2</sup>

<sup>1</sup>Latvian Biomedical Research and Study Centre, Riga, Latvia

<sup>2</sup>Riga Stradiņš University, Riga, Latvia

<sup>3</sup>Centre of Tuberculosis and Lung Diseases, Riga East Clinical University Hospital, Upeslejas, Latvia

<sup>4</sup>Faculty of Physics, Mathematics and Optometry, University of Latvia, Riga, Latvia

<sup>5</sup>Latvian Institute of Organic Synthesis, Riga, Latvia

**Background.** Personalized medicine and therapeutic drug monitoring (TDM) strategies could be highly important to improve the effectiveness of anti-tuberculosis (anti-TB) therapy. Several drug-metabolizing enzymes exhibit genetic variations leading to deviations of plasma concentrations of anti-TB drugs, however, associations between genetic polymorphisms, metabolic ratio and treatment outcome are not entirely clear.

**Aim.** The aim of this study was to determine the predictors of treatment outcome by kinetic measurements of isoniazid (INH) and its major metabolite acetylisoniazid (AcINH) in blood plasma and genotyping analysis of two drug-metabolizing enzymes involved in the INH pharmacokinetic pathway.

**Methods.** Human DNA and plasma samples were obtained from TB patients (n=33) admitted to the Centre of Tuberculosis and Lung Diseases. Plasma levels of INH and AcINH were measured using Liquid Chromatography-Tandem Mass Spectrometry at 0, 2 h, and 6 h time points after medication administration. Patient N-acetyltransferase 2 (NAT2) phenotype (slow acetylator, SA; intermediate acetylator, IA) was assigned based on the obtained genotyping data using 7-SNP panel identification. Glutathion-S-transferase M1 class (GSTM1) class null/plus genotype assay was carried out by a comparative duplex PCR. Time-to-event analysis was applied to analyse time to sputum culture conversion (tSCC) denoted by treatment success. In each NAT2 subgroup, Cox proportional hazards model was used to estimate hazard rate ratios of treatment success time adjusted for INH/AcINH metabolic ratio (MR).

**Results.** Treatment was successful in 21 patients, 12 were considered as censored. The median tSCC was 65, 65, 56 and 112 days for IA/null, SA/null, IA/plus and SA/plus genotypes, respectively. The mean MR ( $\pm$ SD) was  $0.55\pm 0.14$ ,  $2.59\pm 0.96$ ,  $0.61\pm 0.14$  and  $2.66\pm 1.14$  for genotype groups. No statistically significant differences between cumulative probability curves of tSCC were observed ( $p=0.13$ ). In the Cox model for SA genotype, global log-rank  $p=0.004$  and concordance index was 0.76. The odds of SA/null carrier to achieve treatment success before SA/plus carrier was 5.65 (CI 1.09, 29.30),  $p=0.039$ ; probability of SA/null carrier to heal first was equal to 0.85. One unit increase of individual's MR lowers the odds of achieving treatment success prior to the individual with one-unit lower MR (HR 0.36, (CI 0.16, 0.85),  $p=0.019$ ); probability to heal first was 0.26.

**Conclusion.** Genotyping and TDM approach could be beneficial for implementation of personalised care for TB, and further research is needed to increase the level of evidence supporting dose adjustment strategies.

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## Assessment of Complete Blood Count-Derived Marker Association With Pulmonary Tuberculosis Severity and Treatment Response

Kivrane Agnija<sup>1,2</sup>, Igumnova Viktorija<sup>1,2</sup>, Viksna Anda<sup>2,3</sup>, Simanovica Ilze<sup>3</sup>, Ozere Iveta<sup>2,3</sup>, Pole Ilva<sup>3</sup>, Bandere Dace<sup>2</sup>, Ranka Renate<sup>1,2</sup>

<sup>1</sup>Latvian Biomedical Research and Study Centre, Riga, Latvia

<sup>2</sup>Riga Stradiņš University, Riga, Latvia

<sup>3</sup>Centre of Tuberculosis and Lung Diseases, Riga East Clinical University Hospital, Upeslejas, Latvia

**Background.** Recent studies have demonstrated the utility of non-specific baseline cell count-derived markers, including thrombocyte-lymphocyte ratio (TLR), neutrophil-lymphocyte ratio (NLR), and monocyte-lymphocyte ratio (MLR), in differentiating site and form of tuberculosis and predicting treatment outcome. Currently, newly diagnosed pulmonary tuberculosis (PTB) patients are subjected to a standard 6-month treatment regimen, and early identification of patients with severe PTB and increased risk of delayed treatment response would be beneficial.

**Aim.** To investigate the association of baseline TLR, NLR, and MLR with disease severity and treatment response in patients with newly diagnosed PTB.

**Methods.** The clinical data was extracted from medical records of otherwise healthy patients with active PTB (n=33) admitted to the Riga East Clinical University Hospital, Centre of Tuberculosis and Lung Diseases. The chest radiography findings were used to assess the severity of the disease before treatment initiation. Baseline markers were calculated using absolute cell counts ( $\times 10^9/L$ ) from complete blood count analysis of peripheral blood samples. Time to sputum culture conversion (tSCC) was available for 22 out of 33 patients and used as a treatment response marker. Data analysis was performed using IBM SPSS Statistics 25 software.

**Results.** Overall, patients with bilateral pulmonary lesions had significantly higher TLR, NLR and MLR than those with unilateral lesions (median 96 vs 176; 1.7 vs 3.3, and 0.3 vs 0.4, Mann-Whitney,  $p < 0.05$ ). The absence or presence of pulmonary cavitation resulted only in changes of MLR (median 0.3 vs 0.4, Mann-Whitney,  $p < 0.05$ ). TLR, NLR, and MLR fairly positively correlated with the number of affected lobes ( $\rho = 0.47$ ,  $\rho = 0.46$ , and  $\rho = 0.44$ ,  $p < 0.01$ ). When assessing treatment response among TB patients (n=22), the median tSCC was 53 days (IQR: 41–84). NLR was higher in patients with tSCC above 60 days from anti-TB treatment onset (median 2.5 vs 3.9, Mann-Whitney,  $p < 0.05$ ). Of all three markers, a fair positive correlation was observed solely between NLR and tSCC ( $\rho = 0.57$ ,  $p < 0.01$ ). A fair but insignificant correlation was found for TLR ( $\rho = 0.40$ ,  $p = 0.07$ ).

**Conclusion.** The selected baseline markers were associated with different chest radiological findings characterising the extent of PTB. Moreover, NLR appeared to be a promising prognostic marker of treatment response. Further studies are required to evaluate the performance of these markers for discrimination between different grades of PTB severity and for prediction of delayed tSCC.

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## ONCOLOGY

## The Role of Exosomal Proteins CD9, CD63 and DNA Mismatch Repair Proteins in Prostate Adenocarcinoma

Folkmanis Kristofs<sup>1</sup>, Junk Elizabete<sup>2</sup>, Merdane Evelina<sup>2</sup>, Eglitis Janis<sup>1</sup>, Folkmane Inese<sup>2</sup>, Folkmanis Valdis<sup>2</sup>, Jakubovskis Maris<sup>3</sup>, Ivanovs Igors<sup>4</sup>, Isajevs Sergejs<sup>5</sup>, Addali Mustapha<sup>6</sup>, Lietuvietis Vilnis<sup>3</sup>

<sup>1</sup>Department of Oncology, Faculty of Medicine, University of Latvia, Riga, Latvia

<sup>2</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

<sup>3</sup>Department of Urology, Riga East Clinical University Hospital, Riga, Latvia

<sup>4</sup>Department of Surgery, Faculty of Medicine, University of Latvia, Riga, Latvia

<sup>5</sup>Department of Pathology, Riga East Clinical University Hospital, Riga, Latvia

<sup>6</sup>Department of Urology, Kreisklinikum, Siegen, Germany

**Background.** Exosome and DNA mismatch repair (MMR) biomarkers could play an important role in cancer risk stratification and prognosis assessment. The gold standard for prostate cancer (PCa) diagnosis is biopsy and histopathological examination. Thus, the evaluation of exosome- and MMR biomarkers in parallel with standard existing diagnostics could be a more specific method.

**Aim.** To evaluate and compare the expression of exosomal biomarkers (CD9, CD63) and MMR in the tissue of patients with benign prostate hyperplasia (BPH) and PCa.

**Methods.** The study was retrospective. Altogether, 92 patients with PCa and 20 patients with BPH were enrolled. The exosome and MMR expression was analysed by immunohistochemistry. Follow up for each PCa patient lasted until disease progression and/or maximum of 5 years.

**Results.** A total of 112 patients were included in the study: 92 patients with PCa and 20 patients with BPH. Low-grade PCa was observed in 56 patients, and high-grade PCa in 36 patients. CD63 expression was significantly higher in patients with high grade PCa compared to low grade, 6.24 vs 1.57,  $p < 0.0001$ . Cancer PFS was significantly longer in patients with low CD63 expression compared to high CD63 expression, respectively 42.50 and 26.50 months [HR=1.73;  $p = 0.018$ ]. CD9 expression was significantly reduced in PCa compared to BPH: 1 vs 6  $p < 0.0001$ . Cancer PFS in patients with high CD9 expression was significantly longer than in patients with low CD9 expression: 43.00 vs 28.50 months, [HR=2.65;  $p = 0.016$ ]. MMR expression was absent in 10 patients (10.86%) from 92 PCa patients. Loss of MMR expression was in 8/36 (22.22%) of high-grade PCa patients and 2/56 (3.57%) of low-grade PCa patients. MMR were present in all cases of BPH. There was a negative correlation between MMR protein loss and PCa WHO 2016 grade groups (Rho=-0.25;  $p = 0.02$ ). Cancer PFS in patients with MMR deficiency was significantly shorter than in patients with maintained MMR expression, 22.00 and 60.00 months [HR=4.18;  $p = 0.0007$ ].

**Conclusion.** Prostate cancer is characterized by increased CD63 expression but decreased CD9 expression and loss of DNA mismatch repair protein compared to benign prostate hyperplasia tissues. The progression free survival is significantly longer in patients with low CD63 expression, but high CD9 expression and proficient MMR expression.

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## Thyroid Carcinoma (Part I): The Diagnostic Value and Management. One Single-Centre Retrospective Study 2019–2021

Pokšāne Diāna<sup>1</sup>, Fokins Vladimirs<sup>1,2</sup>, Rasa Ingvars<sup>2</sup>

<sup>1</sup>Rīga Stradiņš University, Riga, Latvia

<sup>2</sup>Riga East Clinical University Hospital, Riga, Latvia

**Background.** Ultrasound imaging and fine-needle aspiration (FNA) is the mainstay in evaluating thyroid nodules. There is a substantial lack of recent data on thyroid carcinoma.

**Aim.** This study aimed to determine the effectiveness of Green Corridor and to collect the data on the prevalence of thyroid carcinoma by FNA and after surgical intervention, and to compare both data, since the malignant result in the FNA is an indication for surgery.

**Methods.** The authors provided the single-centre real-world retrospective observational study (2019–2021). Authors analysed patients sent to physicians along the Green Corridor (code Z03.173) RECUH. After surgical interventions, we collected FNA data, treatment types, thyroid cancer types, and comorbidities. The data provided an indication of the number of malignancies cytologically – starting from Bethesda III (atypia of undetermined significance or follicular lesion of uncertain significance) – and histologically, comparison of their efficiencies and an analysis of the efficiency of the green corridor. The statistical analysis was conducted using IBM SPSS.

**Results.** The authors manually analysed medical records of 563 patients for 3 years, and thyroid cancer was confirmed in 153 patients (27.2%); women were 123 patients (80.4%). The average age was 53.5±14.3 SD years. 147 patients had surgical intervention (total thyroidectomy or hemithyroidectomy) and confirmed thyroid cancer histologically. Four patients (2.6%) had radiation therapy; two patients (1.3%) had palliative care due to an inoperable condition. FNA results of malignancy coincided with the histological analysis in 114 patients (77%). In 84 (73.7%) patients FNA results of malignancy types coincided with the histological analysis.

**Conclusions.** According to the Green Corridor, the distribution of patients has proven its effectiveness, taking into account its percentage as far as the disease is histologically confirmed. The fine-needle aspiration biopsy is the gold standard for malignancy diagnosis in thyroid cancer and has proven its high diagnostic value in combination with cost-effectiveness and minimal invasiveness.

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## Impact of COVID-19 Pandemic on the Proportion of Breast Cancer Admitted

Halturina Marija<sup>1</sup>, Hasnere Sigita<sup>1,2</sup>

<sup>1</sup>University of Latvia, Riga, Latvia

<sup>2</sup>Oncology Clinic, Pauls Stradiņš Clinical University Hospital, Riga, Latvia

**Background.** Breast cancer has been the most common and frequent cancer among women for several decades. Since the beginning of the COVID-19 pandemic in Latvia (March 2020), restrictions came into force in our country due to which scheduled visits to doctors and diagnostics were postponed.

**Aim.** The aim of the study is to analyse and compare the number of advanced breast cancer patients in the third and fourth stage before and after the COVID-19 pandemics. The years before being specified as 2018 and 2019.

**Methods.** 1758 patients were diagnosed with histologically proven stage 1–4 breast cancer between 2018–2021 in the Oncology Centre of Pauls Stradiņš Clinical University Hospital, their data were gathered from archives and subsequently retrospectively analysed. Patients were correlated to the year of their first histological biopsy confirming the diagnosis of breast cancer between 2018–2021. In the next step, the stage of the disease was established after computer tomography data analysis, which showed whether there were metastases and how much the cancer had spread to the lymph nodes.

**Results.** In 2018, the total number of diagnosed breast cancer patients was 452, of which 138 were diagnosed with stage 3 or 4, accounting for 30.53%. In 2019, the total number was 465, of which 161 were stage 3 or 4, accounting for 34.53%. In 2020, the total number was 409, of which 115 had stage 3 or 4, which is 28.12%. In 2021, the total number was 432, of which 154 were stage 3 or 4, accounting for 35.97%. The average of the percentage of advanced stages of cancer over four years is 32.31%. Standard deviation is 3.63%. P value for 2018 is 0.31, for 2019 – 0.26, for 2020 – 0.12 and for 2021 – 0.16.

**Conclusion.** According to the results of the study, the increase in the number of patients with the third and fourth stages of breast cancer was by several percent and average p value give evidence for our research hypothesis that the restrictions introduced in Latvia during the COVID-19 pandemic did not affect the diagnosis of breast cancer in 2021.

## Effects of Urinary Extracellular Vesicles from Prostate Cancer Patients on Transcriptomes of Cancer-Associated and Normal Fibroblasts

Keiša Laura<sup>1,2</sup>, Sadovska Lilite<sup>1</sup>, Zayakin Pavel<sup>1</sup>, Bajo-Santos Cristina<sup>1</sup>, Auders Jānis<sup>1,2</sup>, Jansons Juris<sup>3</sup>, Lietuviētis Vilnis<sup>3</sup>, Linē Aija<sup>1</sup>

<sup>1</sup>Latvian Biomedical Research and Study Centre, Riga, Latvia

<sup>2</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

<sup>3</sup>Riga Stradiņš University, Riga, Latvia

**Background.** Increasing evidence suggests that cancer-derived extracellular vesicles (EVs) alter the phenotype and functions of fibroblasts and trigger the reprogramming of normal fibroblasts into cancer-associated fibroblasts (CAFs).

**Aim.** The aim of the current study was to determine the effects of urinary EVs from prostate cancer (PC) patients and healthy males on the transcriptional landscape of prostate CAFs and normal foreskin fibroblasts.

**Methods.** Patient-derived prostate fibroblast primary cultures PCF-54 and PCF-55 were established from two specimens of PC tissues. EVs were isolated from urine samples of 3 patients with PC and 2 healthy males and used for the treatment of prostate fibroblast primary cultures and normal foreskin fibroblasts. The EV-treated fibroblasts were subjected to Ribonucleic acid (RNA) sequencing analysis.

**Results.** RNA sequencing analysis showed that the fibroblast cultures differed significantly in their response to urinary EVs. The transcriptional response of foreskin fibroblasts to the urinary EVs isolated from PC patients and healthy controls was very similar and mostly related to the normal functions of fibroblasts. On the contrary, PCF-54 cells responded very differently – EVs from PC patients elicited transcriptional changes related to the regulation of the cell division and chromosome segregation, whereas EVs from healthy males affected mitochondrial respiration. In PCF-55 cells, EVs from both PC-patients and controls induced the expression of a number of chemokines such as CCL2, CCL13, CXCL1, CXCL8, whereas pathways related to regulation of apoptotic signaling and production of cell adhesion molecules were triggered specifically by EVs from PC patients.

**Conclusion.** This study demonstrates that urinary EVs from PC patients and healthy controls elicit distinct transcriptional responses in prostate CAFs and supports the idea that EVs contribute to the generation of functional heterogeneity of CAFs. Moreover, this study suggests that the changes in the gene expression pattern in EV recipient cells might serve as a novel type of functional cancer biomarkers.

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## Effects of Exercise-Induced Extracellular Vesicles on Progression of Cancer

Auders Jānis<sup>1,2</sup>, Sadovska Lilite<sup>1</sup>, Zayakin Pavel<sup>1</sup>, Keiša Laura<sup>1,2</sup>, Kalniņa Zane<sup>1</sup>, Linē Aija<sup>1</sup>

<sup>1</sup>Latvian Biomedical Research and Study Centre, Riga, Latvia

<sup>2</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

**Background.** Increasing evidence suggests that regular physical exercise not only reduces the risk of cancer but also improves functional capacity, treatment efficacy and disease outcome in cancer patients. We hypothesized that exercise-induced extracellular vesicles (EVs) may directly interact with cancer cells and alter their behaviour and/or change the functional phenotype of circulating and tumour-infiltrating immune cells.

**Aim.** The aim of the study is to get an insight into the effects of exercise-induced EVs on the progression of cancer using a rat model of metastatic prostate cancer.

**Methods.** Plasma samples were collected before and after the exercise from rats subjected to regular forced wheel running exercise and sedentary rats. EVs were isolated using size exclusion chromatography and characterized by transmission electron microscopy and nanoparticle tracking analysis. RNA content of EVs was studied by RNA sequencing analysis. The effects of exercise-induced EVs on the progression of cancer were studied in a syngeneic orthotopic prostate cancer model in rats.

**Results.** We did not observe a consistent increase in the circulating EV levels after the exercise, however, the RNA sequencing analysis demonstrated substantial changes in the RNA content of EVs collected before and immediately after forced wheel running exercise, as well as differences between EVs from runners at resting state and sedentary rats. The major RNA biotype in EVs was mRNA, followed by miRNA and rRNA. Molecular functions of differentially expressed RNAs reflected various physiological processes including protein folding, metabolism and regulation of immune responses triggered by the exercise in the parental cells. Intravenous administration of exercise-induced EVs into F344 rats with orthotopically injected syngeneic prostate cancer cells PLS10, demonstrated reduction of the primary tumour volume by 35% and possibly – attenuation of lung metastases.

**Conclusion.** Our data provide the first evidence that exercise-induced EVs may modulate tumour physiology and delay the progression of cancer.

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## Therapy Outcome Depending on Clinical Features of Multiple Myeloma Patients in Pauls Stradiņš Clinical University Hospital From 2019 to 2020

Keiša Laura<sup>1</sup>, Bernāte Kristīne<sup>2</sup>, Auders Jānis<sup>1</sup>

<sup>1</sup>University of Latvia, Faculty of Medicine, Riga, Latvia

<sup>2</sup>Pauls Stradiņš Clinical University Hospital, Riga, Latvia

**Background.** Multiple myeloma (MM) is a clonal plasma cell proliferative disorder characterized by the abnormal increase of monoclonal paraprotein leading to evidence of specific end-organ damage. Analysing and determining prognostic factors may play a significant role that could help to define a prognostic model of disease development and apply the most optimal choice of further tactics.

**Aim.** The aims of this study were to collect data with typical demographic parameters, clinical, laboratory and radiological manifestations, specific therapy and to establish correlations to MM outcomes to determine prognosis and the optimal choice of treatment tactics.

**Methods.** 25 patients with multiple myeloma diagnosis between 2019 and 2020 at Pauls Stradiņš Clinical University Hospital (PSKUS) were included in this retrospective analysis. Clinical, laboratory, and radiological features were defined according to the criteria developed by International Myeloma Working Group.

SPSS was used to analyse data. To assess correlations, Spearman's rank correlation coefficient was used. Fisher's exact test and Mann-Whitney U test were used to analyse associations and statistically significant differences.

**Results.** We analyzed 25 symptomatic myeloma patients diagnosed between 2019 and 2020 at PSKUS. The mean age was 68 years (range: 44–78) and 60% were female. The distribution of disease subtypes was dominated by heavy chain disease with IgG prevalence (53%). The most common clinical manifestations of the disease were lytic bone lesions with pain syndrome (84%) followed by anaemia (56%) and renal failure (24%). The choice of therapeutic tactics was dominated by the CyBorDex (Cyclophosphamide/Bortezomib/Dexamethasone) scheme (64%), with an average number of 6 cycles. Increased creatinine and calcium levels after the first course of treatment indicate a more unfavourable outcome of the disease (24% ( $p=0.04$ ) and 4.8% ( $p=0.04$ ), furthermore, the trend towards worse outcome was indicated by urgent hospitalization 36.4 % ( $p=0.07$ ), lambda light chain disease ( $p=0.07$ ) and renal failure ( $p=0.3$ ). After therapy, a significant decrease in M gradient ( $p=0.007$ ),  $\beta_2$  microglobulin ( $p=0.03$ ) and serum IgG levels ( $p=0.001$ ) was observed, indicating the efficacy of the chosen treatment.

**Conclusion.** The most significant correlations towards worse outcome showed increased creatinine and calcium levels. Among end-organ damage factors, the presence of bone disease appeared to be the most useful factor predicting the prognosis of symptomatic myeloma patients treated with novel agents. These findings can be used to improve decisions concerning treatment tactics and sequentially improve the patient's quality of life.

**Acknowledgements.** The authors declare the absence of conflict of interest.

## FDG-PET/CT Use for Lymphoma Patients in Pauls Stradiņš Clinical University Hospital Cancer Clinic in 2018–2021

Miščurina Anastasija<sup>1</sup>, Vecumniece Lauma<sup>1</sup>, Rozenbergs Krišs<sup>1</sup>, Purviņa Velta<sup>1</sup>, Ūdre Sintija<sup>1</sup>, Pavlova Jeļizaveta<sup>1,2</sup>, Hasnere Sigita<sup>1,2</sup>

<sup>1</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

<sup>2</sup>Pauls Stradiņš Clinical University Hospital, Riga, Latvia

**Background.** Fluorodeoxyglucose positron emission tomography-computed tomography (FDG-PET/CT) is highly sensitive and specific for detecting the location of lymphoma-related uptake and distinguishing it from physiologic uptake. International guidelines recommend the FDG-PET/CT for initial lymphoma diagnosis, staging and treatment response assessment. In Latvia, PET/CT has become financially covered by the National Health Service only since the second half of 2018.

**Aim.** To analyse the changes of FDG-PET/CT use for lymphoma patients in clinical practice.

**Methods.** A retrospective study was conducted at the Pauls Stradiņš Clinical University Hospital Cancer Clinic. 176 patients, with histologically confirmed lymphoma in the time period from 2018 to 2021, were enrolled. Patient data, diagnosis, type of the lymphoma, stage, patients' functional status, histological analysis, performed imaging studies were studied. In addition, 15% of FDG-PET/CT were compared to contrast enhanced computed tomography (CECT), both of which had less than one month interval between. Data was processed using IBM SPSS Statistics 22.

**Results.** In 2018, 1% (N=4) of all lymphoma patients that year were evaluated by FDG-PET/CT, 20% of whom had Hodgkin's lymphoma (HL), 80% – non-Hodgkin's lymphoma (NHL). In the following years there were a significant increase in the use of FDG-PET/CT: in 2019 62% (N=37) of lymphoma patients were evaluated by FDG-PET/CT, in 2020 – 73% (N=33), in 2021 – 70% (N=40). In 2019–2021 17% of patients who were evaluated by FDG-PET/CT had HL and 83% – NHL, high-grade lymphomas were 70%, low grade – 30%. In 2018 40% of all FDG-PET/CT were done before therapy for staging purpose and 60% – after therapy to determine remission. Of all FDG-PET/CT, which were done in 2019–2021, 35% were done before therapy, 22 % – during therapy, 43% – after therapy.

Pearson-Chi-Square Test showed statistically significant association between patients' ECOG and grade of lymphoma – high grade lymphomas were more frequent in patients with higher ECOG score ( $\chi^2$  (4, N=118) =16.5, p=0.002).

15% of FDG-PET/CT were compared to patients CECT. In 75% of FDG-PET/CT additional disease lesions, which were not seen in CECT, were discovered.

**Conclusion.** FDG-PET/CT use for lymphoma in Latvia has become more frequent, since it became financially covered by the National Health Service, which brought lymphoma diagnostics in Latvia closer to international standards. FDG-PET/CT use before treatment helps to discover additional disease lesions, which may lead to alteration of disease staging and change in treatment strategy.

**Acknowledgements.** The authors declare the absence of the conflict of interest.

## Distribution Pattern of Barcelona Clinic Liver Cancer Classification Stages in Hepatocellular Carcinoma Patients Treated with Transarterial Chemoembolization

Šmidberga Beatrise<sup>1</sup>, Kratovska Aina<sup>1,2,3</sup>, Zdanovskis Nauris<sup>1,3</sup>, Zaiceva Veronika<sup>3</sup>,  
Mundeciems Andrejs<sup>3</sup>, Ivanova Patrīcija<sup>2,3</sup>, Ponomarjova Sanita<sup>1,3</sup>

<sup>1</sup>Faculty of Medicine, Riga Stradiņš University, Latvia

<sup>2</sup>Faculty of Medicine, University of Latvia, Latvia

<sup>3</sup>Department of Interventional Radiology, Riga East Clinical University Hospital, Latvia

**Background.** Barcelona Clinic Liver Cancer classification (BCLC) is the most frequently used staging system for patients with hepatocellular carcinoma (HCC). BCLC is subdivided in five stages (0, A, B, C, D). Treatment strategy is chosen according to BCLC stage. Transarterial chemoembolization (TACE) is the standard of care for BCLC stage B patients. Patients with stage 0 – A are usually addressed to ablation, open resection or liver transplantation, BCLC stage C – systemic chemotherapy, stage D – palliative management. Since introduction of BCLC, numerous studies have been performed for evaluation of TACE also in BCLC stages A, C and even D. It was clearly shown that in real world studies the management of HCC frequently deviates from the BCLC recommendations.

**Aim.** The aim of the study was to evaluate the BCLC stage distribution pattern in HCC patients treated with TACE.

**Methods.** This retrospective single centre study enrolled the patients with HCC who received drug-eluted bead TACE from 2020–2021 in tertiary care hospital. 77 patients were included into the study. All patients received TACE according to a multidisciplinary tumour board decision. The mean patient age, gender and BCLC stage was analysed. General performance status was analysed according to Eastern Cooperative Oncology Group (ECOG) classification. Data analysis was performed in MS Office Excel.

**Results.** The mean age – 68 years (range 52–91), men – 41 (53%), women – 36 (47%). ECOG performance status varied from 0–2. TACE was performed in 38% (n=29) with BCLC stage A, 40% (n=31) – stage B, 19% (n=15) – stage C, 2% (n=3) – stage D. In stage A 28% (n=8) had multinodular disease (2–3 nodules); 72% (n=21) had a single lesion. In stage C 27% (n=4) of patients had extrahepatic metastasis, which were managed with open surgery and 73% (n=11) had portal invasion. 2 patients classified into stage D due to failing liver function (Child-Pugh C), nevertheless, one of them had liver function improvement after medicamentous treatment.

**Conclusion.** The results of our study are consistent with literature data and support the real world findings, where TACE is most frequently applied to HCC BCLC stage B, but is also used in other HCC BCLC stages. This can be explained by variable centre dependent availability of other treatment modalities like liver transplantation and percutaneous ablation techniques. TACE clearly has an important role in the treatment of HCC as a solitary or combination therapy in each stage of HCC.

**Acknowledgements.** The authors declare the absence of conflict of interest.

## Breast Cancer Rate in Different Age Groups: A Single Tertiary Centre Perspective in 2020

Tiltiņa Lelde<sup>1</sup>, Enģele Ilze<sup>1,2</sup>

<sup>1</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

<sup>2</sup>Oncology Centre of Latvia, Riga East Clinical University Hospital, Riga, Latvia

**Background.** Breast cancer affects a large proportion of women worldwide, and while the incidence of breast cancer grows with age, cancer can also affect younger women (pre-screening age group women).

**Aim.** The aim of the study was to assess how many women in different age groups had a breast cancer diagnosis in 2020.

**Methods.** This is a retrospective study, based on data collected from medical databases at the Oncology Centre of Latvia. Altogether, the study included 954 women, who had a 'core' biopsy done of suspicion for breast cancer in 2020. Women in the study were divided into 3 different groups: pre-screening (below 50 years of age); screening (50–69 years of age) and post-screening (more than 69 years of age).

### Results.

1. The average age of women in the study was 61.
2. In total 954 women had 'core' biopsy done, of these women 700 were diagnosed with breast cancer.
3. Out of 223 women in the pre-screening age group, 54.26% of women were diagnosed with breast cancer.
4. Out of 446 women in the screening age group, 72.2% of women were diagnosed with breast cancer.
5. Out of 285 women in the post-screening age group, 90.18% of women were diagnosed with breast cancer.

**Conclusion.** Although the risk of having cancer up to the age of 50 is relatively low, there is still a significant number of women who are diagnosed with breast cancer in the pre-screening age group. Therefore, at least the physical examination of breasts is important for women in the pre-screening age group. For better and earlier detection of breast cancer, it is useful to combine physical examination with a further evaluation with sonography or mammography, if necessary.

**Acknowledgements.** The present study has received the approval of the ethics committee of the University of Latvia.

## Breast Cancer in Women at the Oncology Centre of Latvia in 2020

Tiltiņa Lelde<sup>1</sup>, Enģele Ilze<sup>1,2</sup>

<sup>1</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

<sup>2</sup>Riga East University Hospital, Oncology Centre of Latvia, Riga, Latvia

**Background.** Breast cancer is the most common oncological disease for women and one of the leading causes of death in Latvia and worldwide. Breast cancer has a very good recovery prognosis if detected in the early stages, however, the later the disease is detected, the lower the chance of curing cancer.

**Aim.** The aim of the study was to investigate how many women in 2020 were diagnosed with breast cancer, whether they were symptomatic or asymptomatic, and at what stage they were diagnosed.

**Methods.** This is a retrospective study, based on the data collected from medical databases records from 2020 at the Oncology Centre of Latvia. Data included histopathological results and pre-procedure clinical breast assessment of 954 women who had 'core' biopsy and 75 women who had stereotactic breast biopsy done in 2020.

### Results.

1. The mean age of women in the study was 61.
2. Of 954 women who had a 'core' biopsy done in 2020, breast cancer was detected in 700 of them (73.4%). Breast cancer was detected in 19 (25%) of 75 women in total who had stereotactic breast biopsy in 2020.
3. 252 women with breast cancer did not experience any breast cancer-related symptoms or the clinical assessments did not provide sufficient data thereof.
4. 30% of women were diagnosed with stage I breast cancer, 36% had stage II breast cancer, 22% – stage III breast cancer, 7% –stage IV breast cancer, whereas 0 stage cancer/*Cancer in situ* was diagnosed in very few cases.
5. 2 women who had a 'core' biopsy done, were diagnosed with metastasis from another primary cancer.

**Conclusion.** For a better outcome of therapy, it is important to diagnose breast cancer in the early stages. As the stage goes higher, the 5-year survival rate lowers, consequently, we must continue to educate women about the seriousness of the disease and promote our screening programs. Data of investigations for 2020 at the Oncology Centre of Latvia demonstrates that 22% of patients were diagnosed with stage III and 7% – with stage IV cancer – the rates which are unacceptably high according to Screening guidelines.

**Acknowledgements.** The present study has received the approval of the ethics committee of the University of Latvia.

## Comparative Study of NRAS and BRAF Mutation Status With Clinical and Histopathological Characteristics of Melanoma

Zablocka Tatjana<sup>1,2,3,5</sup>, Kreismane Madara<sup>4</sup>, Pjanova Dace<sup>4</sup>, Isajevs Sergejs<sup>1,2,5</sup>

<sup>1</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

<sup>2</sup>Riga East Clinical University Hospital, Riga, Latvia

<sup>3</sup>Pauls Stradiņš Clinical University Hospital, Riga, Latvia

<sup>4</sup>Latvian Biomedical Research and Study Centre, Riga, Latvia

<sup>5</sup>Hospital of Traumatology and Orthopaedics, Riga, Latvia

**Background.** Recent genomic classification subdivides melanoma into four subtypes based on the pattern of the most prevalent significantly mutated genes: mutant BRAF, RAS, NF1, and triple-WT (wild type). BRAF V600 mutations were recognized as the primary driver mutation in tumour progression of melanoma patients. Previous studies have shown that BRAF mutations correlated with primary tumour type and stage. However, conflicting conclusions on NRAS mutations in the natural course of non-metastatic melanoma, and their prognostic significance is still controversial.

**Aim.** The current study's objective has been to compare the NRAS and BRAF mutation status with clinical and histopathological characteristics of melanoma.

**Methods.** Altogether, 85 patients who underwent melanoma surgical treatment at the Riga East University Hospital at the stage IA-IIC from 2012 until 2017 were retrospectively enrolled in the study. The histopathological characteristics were assessed according to the current World Health Organization (WHO) and The American Joint Committee on Cancer (AJCC) 8<sup>th</sup> edition guidelines. The melanoma BRAF mutation status was assessed by digital droplet PCR (ddPCR) using BRAFV600 Screening Assay (*Bio-Rad*, USA). The NRAS E1 codons 12 and 13 mutations status was assessed by ddPCR.

Correlation of mutation status with clinical and pathological features was analysed by using Pearson X<sup>2</sup> together with the Log-logistic regression test to calculate statistical significance. Progression-free survival (PFS) was estimated with the Kaplan-Meier method with the log-rank test. Multivariate regression was analyzed using Cox proportional hazards model.

**Results.** The BRAF mutation was observed in 52 patients (61.2%). The BRAF mutation in melanoma correlated with Clark invasion level ( $p=0.045$ ), patient age ( $p=0.02$ ) and peritumoral lymphocytes ( $p=0.04$ ). However, the correlation between the disease stage, mitotic activity, ulceration, median tumour size and BRAF mutational status was not demonstrated.

NRAS mutation was observed in 9 patients (10.6%). NRAS mutation in melanoma correlated with Breslow thickness ( $p<0.0001$ ), disease stage ( $p=0.002$ ) and lymphovascular invasion ( $p=0.03$ ).

Our study showed that melanoma patients with BRAF mutation had a significantly better progression-free survival (PFS) than patients with NRAS mutation (hazard ratio, HR=4.2, 95% CI=2.8–10.4,  $p<0.0001$ ). However, in patients with concomitant BRAF and NRAS mutation the PFS was significantly worse compared to patients with only BRAF or NRAS mutation (respectively,  $p<0.001$  and  $p=0.02$ ).

**Conclusion.** Patients with NRAS mutation had a significantly worse prognosis compared to patients with BRAF mutation. NRAS mutational status should be routinely assessed in primary melanoma for risk stratification of disease progression.

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## PAEDIATRICS

### Joint Activities of Parents and Children in Family Aimed at Promotion of Children's Health

**Strazdiene Neringa**<sup>1</sup>, Strukcinskiene Birute<sup>2</sup>, Mickiene Raimonda<sup>1,3</sup>, Strukcinskaite Vaiva<sup>4</sup>,  
Darius Steponkus<sup>2</sup>

<sup>1</sup>Faculty of Social Sciences and Humanities, Klaipeda University, Klaipeda, Lithuania

<sup>2</sup>Faculty of Health Sciences, Klaipeda University, Klaipeda, Lithuania

<sup>3</sup>Department of Education, Klaipeda City Municipality, Klaipeda, Lithuania

<sup>4</sup>Faculty of Health Care, Vilnius University of Applied Sciences, Vilnius, Lithuania

**Background.** Parents and children's joint activities, collaboration and cooperation on family level are of importance for promoting children's health.

**Aim.** The aim of the study was to explore parents' opinion about the joint activities of parents and children in the family, which help to promote children's health.

**Methods.** Altogether 303 parents who have primary school age children and live in the Western Lithuania were enrolled in the survey. Chi-square and Mann-Whitney tests were applied.

**Results.** The study showed that the majority (64.1%) of parents prepare healthy food together with their children very often (16.2%) and often (47.9%). Parents with university degree more often prepare healthy food with children ( $U=9858.5$ ;  $p=0.025$ ). 32% of parents very often and 55.4% – often discuss healthy lifestyle and hygiene with their children. Regarding boosting the physical health of children (activities in water, air, sun etc.), 15.5% of parents do this with their children very often, 41.3% – often, and 35.6% – sometimes. Urban respondents engage in these health-improving activities with their children more frequently ( $\chi^2=10.488$ ;  $df=4$ ;  $p=0.03$ ).

24.8% of parents very often and 55.4% – often actively spend time with their family. 8.6% of parents exercise and enjoy sports with their children very often, 24.4% – often. 13.5% of parents travel and use recreation and tourism services together with the family very often, 29.0% – often. Urban respondents more often actively spend time and exercise together with family ( $U=9522$ ;  $p=0.017$ ). 22.1% of parents very often create a common agenda with their children, 52.5% – often.

**Conclusion.** The study revealed that parents make considerable efforts to organize and conduct joint activities with their children in order to develop healthy lifestyle attitudes and promote health of primary school age children.

More than a half of the parents very often and often prepare and consume food together with their children in the family based on the principles of a healthy and balanced diet. However, nearly a third of families do this sometimes, rarely or never. Parents often talk to their children and discuss healthy lifestyle and hygiene. However, families do not sufficiently engage in health-improving activities together with their children. Although the majority of parents spend time actively with their children very often and often, only a third of the parents exercise and enjoy sports together with their children, and less than a half of the respondents travel and use recreation and tourism services together with the family.

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## Prolonged Recovery in Children With Acute Appendicitis Due to a Previous SARS-Cov-2 Infection

Vansevičienė Idilė<sup>1</sup>, Dekerytė Inga<sup>1</sup>, Krunkaitytė Ugnė<sup>1</sup>, Lukošiuūtė-Urbonienė Aušra<sup>1</sup>, Malcius Dalius<sup>1</sup>, Barauskas Vidmantas<sup>1</sup>

<sup>1</sup>*Paediatric Surgery Department, Lithuanian University of Health Sciences, Kaunas, Lithuania*

**Background.** The COVID-19 pandemic has resulted in severe cases of respiratory compromise in adults. Although children were thought to be asymptomatic or only slightly affected by the virus, a pronounced course of disease due to the SARS-Cov-2 virus has been identified – Paediatric multisystem inflammatory syndrome (MIS-C), affecting multiple organ systems and showing different features from the COVID-19 infection in adults. However, with one of its main symptoms being gastrointestinal, it has presented paediatric surgeons worldwide with the question if acute appendicitis is a differential diagnosis to MIS-C or whether it can be a part of it.

**Aim.** Our aim was to present acute appendicitis cases with paediatric multisystem inflammatory syndrome (MIS-C), to give recommendations how to spot a possible MIS-C and what treatment options to consider.

**Methods.** We analyzed 6 patients, admitted to the Paediatric Surgery Department at the Hospital of Lithuanian University of Health Sciences from 7 January to 23 March 2021 with acute appendicitis, that had a prolonged and complicated recovery after standard treatment, who were later confirmed to have MIS-C.

**Results.** All presented patients were treated with antibiotics and five were operated. All patients were found to have a deteriorating condition and increase in inflammatory markers despite treatment, and were found to have MIS-C, with all of them having positive Immunoglobulin G for SARS-COV-2.

**Conclusion.** During the COVID-19 pandemic, even with clear signs of acute appendicitis, MIS-C must be considered in children with known recent exposure to COVID-19 or in patients where surgical and antibiotic treatment does not improve the condition and/or other organ system involvement is noticed and must be treated accordingly.

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## Indicators Affecting the Treatment of Burn Wounds of Paediatric Patients: A Retrospective Analysis

Budzyńska Julia<sup>1</sup>, Koziół Ilona<sup>1</sup>, Leśniewska Magdalena<sup>1</sup>, Korzeniowski Tomasz<sup>2,3</sup>, Surowiecka Agnieszka<sup>3</sup>

<sup>1</sup>Medical Simulation Student's Research Society, Department of Didactics and Medical Simulation, Medical University of Lublin, Lublin, Poland

<sup>2</sup>Chair and Department of Didactics and Medical Simulation, Medical University of Lublin, Lublin, Poland

<sup>3</sup>East Center of Burns Treatment and Reconstructive Surgery, Medical University of Lublin, Łęczna, Poland

**Background.** Burns are one of the most common injuries to children after traffic accidents and interpersonal violence. They are one of the leading causes of death in children under 4 years old and 85% of them are caused by hot liquids. Burn wounds in children require a quick and comprehensive treatment process due to the lower mass of adipose tissue, especially less muscle mass, and much softer and thinner skin.

**Aim.** The aim of this study was to retrospectively analyze paediatric patient cases and determine the impact of burn characteristics on the selection of treatment management and outcomes.

**Methods.** This retrospective study identified 55 paediatric patients (39 boys and 16 girls) with burns hospitalized in 2019. Cases were analyzed for age, sex, burn area, total number of days of hospitalization, and wound care.

**Results.** The age range was 1 to 15 years. The average age was 3.75 years. The most commonly burned area of the body was the trunk, upper limb, and lower limb. As many as 71% of patients suffered boiling water burns. Hospitalization ranged from 2 to 29 days, respectively. It averaged 11.95 days. The percentage of body surface area burned ranged from 0.5% to 35%, respectively. Injuries to the upper limb were most commonly associated with contact burns ( $p=0.01$ ), while the hand was most commonly injured by contact with boiling water ( $p=0.04$ ). Necrectomy was the main method of wound care in burned children (94.5%). A specific relationship was noted for head burns ( $p<0.001$ ). The Mann-Whitney U test showed correlations between the transplant performed and the age of the child ( $p=0.04$ ). The performance of the transplant affected the duration of hospitalization ( $p<0.001$ ). It was also noted that transplantation was more common when the foot was burned ( $p=0.01$ ), and when the child was burned by a flame ( $p=0.04$ ). Time to hospitalization was influenced by the presence of perineal ( $p=0.01$ ) and lower limb ( $p=0.02$ ) burns.

**Conclusion.** Burns are a common injury to children around age 3. The primary management of burns is excision of necrotic tissue and skin grafting, which should be performed promptly. The age of the child and the location of the burns influenced the overuse of the treatment procedure. Performance of graft, upper limb and perineal burns prolonged the length of hospitalization.

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## Assessing Quality of Life in Children with Atopic Dermatitis

Gedroviča Jūlija<sup>1</sup>, Ozola Jana<sup>1</sup>, Rumba-Rozenfelde Ingrīda<sup>1</sup>

<sup>1</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

**Background.** Atopic dermatitis (AD) is a chronic, allergic skin inflammation condition that is common mostly among children. AD significantly affects everyday life of patients and their families, and shows a high impact on clinical care especially during exacerbation.

Determining children's quality of life is one of the key factors which helps to assess their health condition. Therefore, for children with AD quality of life assessment is particularly important.

Analysing the quality of life of children with AD enables finding problems which were given less attention and to find solutions which may help to improve clinical care.

**Aim.** The aim of the research is to assess and analyse quality of life in atopic dermatitis patients using CDQLI (The Children's Dermatology Life Quality Index) questionnaire.

**Methods.** 100 people with AD between 0–18 years were involved in the research. The participation was voluntary. The survey was conducted on social media networks (Facebook, Twitter, etc.).

The main method for data collection was CDQLI (The Children's Dermatology Life Quality Index) questionnaire for quality of life measurement.

The data was collected and analysed by using Microsoft Excel and SPSS programs.

**Results.** We analysed 100 questionnaires. The average age of the children was  $5.64 \pm 4.02$  (0–18) years, 53% (n=53) were female, 47% (n=47) – male.

55% (n=29) of females and 62% (n=29) of males enrolled in the research had a period of exacerbation of AD. 45% (n=24) of females and 38% (n=18) of males had a period of remission.

The mean quality of life index of children with AD during the research did not exceed  $9.56 \pm 6.5$  (with maximum possible score 30).

The average life quality index of children with AD in the exacerbation period was  $11.5 \pm 6.36$ , in remission –  $6.9 \pm 5.7$  ( $p < 0.05$ ). When analysing the average quality of life score children were divided into groups by gender. According to the applied Mann-Whitney U test, no statistically significant differences between females and males were found in the exacerbation stage ( $p = 0.342$ ), as well as in the remission period ( $p = 0.098$ ).

**Conclusion.** The data show that AD affects the quality of life in all groups of cases. Quality of life was significantly higher in the remission period, but gender did not affect the quality of life. To better understand the role of AD in a respondent's life, in further research the number of respondents should be increased.

## Multisystem Inflammatory Syndrome in Children Associated with COVID-19 Characteristics in Children in Latvia

Bloha Milāna<sup>1</sup>, Rumba-Rozenfelde Ingrīda<sup>1</sup>

<sup>1</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

**Background.** Multisystem inflammatory syndrome in children is a rare potentially life-threatening condition that was described for the first time in April 2020. It develops in <1% of children and adolescents under 21 years of age, who have a laboratory evidence of COVID-19. The most common symptoms are persistent fever, lasting more than 24 hours, gastrointestinal and mucocutaneous manifestations. (Dufort et al. 2020)

**Aim.** To analyse MIS-C characteristics in children in Latvia.

**Methods.** 33 patients with diagnosed MIS-C were included in the retrospective study. The data were taken from Children's Clinical University Hospital and were statistically analysed in IBM SPSS Statistics.

**Results.** Overall, 33 participants were included in this study – 45.5% (n=15) girls and 54.5% (n=18) boys. The mean age was 9.06±4.28 (min=1, max=17) years. 36.4% were children aged 12–17; 36.4% – 1–6 years; 27.2% – 7–11 years old. Only 2 patients had comorbidity before MIS-C occurred – one boy had obesity, the other – Asperger's syndrome.

The mean treatment time in hospital was 14,33±5.58 (min=7, max=39) days. Boys were treated on average 0.31 days longer than girls (p>0.05). 55% (n=18) of them were initially treated in the ICU – 7 girls and 11 boys, i.e., 46.7% of girls and 61.1% of boys.

100% of children had fever >24 hours. Gastrointestinal manifestations were observed in all participants, furthermore, vomiting in 55%; abdominal pain – 61%; diarrhoea – 65%. One girl had reactive pancreatitis, but one boy – reactive gallbladder wall thickening. Mucocutaneous manifestation occurred in 94%: maculopapular rashes – in 74%; swelling of hands and feet – 24% with a higher prevalence in boys (p<0.0001.); nonexudative conjunctivitis – 32%; scleral injections – 45%. Peripheral lymphadenopathy was diagnosed in 30% with the most common localisation in submandibular and cervical groups.

Renal involvement developed in 30%. Cardiovascular system was affected in all patients: hypotension in 90%; myocarditis – 18% with a higher prevalence in boys (p<0.0001); rhythm disorders – 93%; conduction disorders – 39%. In 61% was diagnosed valvular regurgitation with most common localisation in tricuspidal and mitral valves; dilatation of coronary arteries was observed only in one patient. Nervous system was affected in 48%: 0.03% had syncope; 13% were presented with dizziness and 42% with headache. Respiratory system was involved in 32%, and half of them required oxygen therapy.

**Conclusion.** The data obtained, in general, are similar to international studies, but children in Latvia were more likely to have hypotension and arrhythmias, whereas myocarditis was less common. Typical comorbidities are slightly less common in our children.

## Isolated Cleft Palate is Not Always Multifactorial Disease

Pajusalu Sander<sup>1,2,3</sup>, Livčāne Diāna<sup>1</sup>, Grīnfelde Ieva<sup>4,5</sup>, Akota Ilze<sup>4</sup>, Mauliņa Ieva<sup>4</sup>, Barkāne Biruta<sup>4</sup>,  
Stāvusis Jānis<sup>1</sup>, Iņāškina Inna<sup>1</sup>, **Lāce Baiba**<sup>1</sup>

<sup>1</sup>Latvian Biomedical Research and Study Centre, Riga, Latvia

<sup>2</sup>Department of Clinical Genetics, Institute of Clinical Medicine, Faculty of Medicine, University of Tartu, Tartu, Estonia

<sup>3</sup>Department of Clinical Genetics, United Laboratories, Tartu University Hospital, Tartu, Estonia

<sup>4</sup>Cleft, Lip and Palate Centre, Institute of Stomatology, Riga Stradiņš University, Riga, Latvia

<sup>5</sup>Medical Genetics Clinic, Children's Clinical University Hospital, Riga, Latvia

**Background.** Isolated cleft palate is a congenital anomaly caused by the failure of secondary palate fusion process, which is anatomically distinct from the primary palate development. Formation of secondary palate starts around the seventh gestational week and continues up to the 12<sup>th</sup> gestational week, meanwhile, primary palate formation is already finished by seventh/eight weeks (Mossey et al. 2009). CP is more common in females contrary to CLP, which is more frequent in males, and this aspect is constant across all populations (Mossey and Modell 2012). The manifestation of CP severity varies, it can be classified as unilateral or bilateral, complete, or incomplete, and a submucous form of cleft palate. European congenital anomaly registry EUROCAT study revealed that in 18% cases cleft palate was associated with other congenital anomalies, and in 27% cases CP is one of the symptoms in recognized genetic syndromes. CP and CLP accompanying other major congenital anomalies are referred to as syndromic forms, and, similarly, CP and CLP not connected with major congenital anomalies are non-syndromic types (Calzolari et al. 2007). Human Phenotype Ontology database currently lists 857 disease associations with a cleft palate, which includes monogenic diseases with known or unknown etiology, chromosomal aberrations, imprinting disorders and embryofetopathies.

**Aim.** The aim of the current study was to identify Mendelian disorders in patients with isolated non-syndromic cleft palate.

**Methods.** A total of 30 patients with isolated CP were analyzed by whole genome sequencing.

**Results.** Six pathogenic or likely pathogenic variants were discovered in OMIM genes – *MAPK1*, *TBX22*, *COL2A1*, *FBN1*, *PCGF2*, *KMT2D*, associated with cleft palate. Pathogenic copy number variations were not identified.

**Conclusion.** 20% of patients with cleft palate have pathogenic/likely pathogenic variants in OMIM genes. Based on our results, we propose that all newborns with orofacial clefts should undergo genetic testing, at least with an appropriate gene panel for CLP; only after negative results, and where there is no suggestive family history or additional clinical symptoms (which validate the requirement for additional exome or genome-wide investigations), should a multifactorial risk prediction percentage be provided for families.

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## Assessment of Olfactory Dysfunction in Children After COVID-19 Infection

Pūķe Anda<sup>1,2</sup>, Kupica Ligita<sup>1,2</sup>

<sup>1</sup>Rīga Stradiņš University, Riga, Latvia

<sup>2</sup>Children's Clinical University Hospital, Riga, Latvia

**Background.** Olfactory dysfunction (OD) is a recognized symptom of COVID-19 infection. Majority of patients recover their olfaction within weeks, however, OD may persist in some patients. Olfactory training is proposed as a simple method to recover olfaction.

**Aim.** The aim of the study was to assess olfactory-related symptoms and results of olfactory training in children with OD after COVID-19 infection.

**Methods.** A prospective study was carried out in Children's Clinical University Hospital Otorhinolaryngology Outpatient Clinic. Children with complaints of OD after laboratory-confirmed COVID-19 infection were enrolled in the study. The exclusion criteria were adenoid hypertrophy with upper airway obstruction, inflammation in nasal cavity, bilateral obstruction of nasal passages, OD before COVID-19 infection and previously performed olfactory training. Patients were asked about specific symptoms related to OD. Ear, nose and throat examination and olfactory testing with internationally approved 12 odour identification tests was performed. At least 10 correct answers out of 12 were considered normal. Patients carried out an olfactory training programme by smelling defined scents – lemon, rose, clove and eucalyptus. Each scent was smelled for 20 seconds twice a day for a month. After completion of the olfactory training, patient inquiry and olfactory test was repeated.

**Results.** 15 children were enrolled in the study, 3 (20%) boys and 12 (80%) girls. The median age was 14 years (from 6 to 17 years). The mean duration of symptoms before the first visit was 3 months. 9 (60%) children reported hyposmia, 5 (33%) – parosmia, 2 (13%) – phantosmia, 3 (20%) – hypogeusia and 7 (47%) – dysgeusia. 10 children performed the olfactory training for a whole month. 6 children (60%) reported improvement of their symptoms. The mean score in the 12 odour identification test was 8.2 (the median 8.5) correct answers on the first visit and 9.7 (the median 10) correct answers 1 month after the olfactory training ( $p < 0.05$ ).

**Conclusion.** These are preliminary data of OD in children after COVID-19 infection. Most frequent olfactory related symptoms after COVID-19 infection in children were hyposmia, dysgeusia and parosmia. Olfactory training could facilitate recovery of olfaction after COVID-19 infection. Further research is needed to obtain data from a larger patient population.

**Acknowledgements.** The authors declare the absence of conflict of interest.

## Association Between Infant Anaemia and Their Feeding Practice, Length Velocity and Atopic Dermatitis in the First Year of Life

Vecumniece Lauma<sup>1</sup>, Rozenbergs Krišs<sup>1</sup>, Miščurina Anastasija<sup>1</sup>, Purviņa Velta<sup>1</sup>, Kārklīņa Daiga<sup>1,2</sup>, Kupča Sarmīte<sup>1</sup>, Rumba-Rozenfelde Ingrīda<sup>1</sup>  
<sup>1</sup>Faculty of Medicine, University of Latvia, Riga, Latvia  
<sup>2</sup>Ella Šatalova Family Physician's Practice, Riga, Latvia

**Background.** Iron deficiency anaemia is the most frequent nutritional deficiency in infants which may be associated with inappropriate complementary food introduction. Insufficient nutrient intake negatively affects infant general health. Screening for anaemia is recommended at 9 to 12 months of age. Capillary blood hemoglobin express test provides a quick and minimally invasive diagnosis of anaemia.

**Aim.** The aim of the study was to evaluate the impact of infant feeding practice to capillary hemoglobin level at 12 months of age, and the impact of capillary hemoglobin level to length velocity and atopic dermatitis at the first year of life.

**Methods.** Data was collected from a family physician's practice database (*smartmedical*). We analysed: infant gender, capillary hemoglobin level at the age of 12 months, length and weight at birth, 1 and 6 months, feeding practice in the first 6 months of life and atopic dermatitis in the first 12 months of life.

**Results.** Half of the participants had anaemia (<11.0 g/dL), with equal gender distribution. Results show that 100% formula-fed infants had normal capillary hemoglobin level, anaemia is more often seen in breast-fed (55.6%) and mixed-fed (50%) infants, but statistically non-significant due to the small study group. Spearman's rho correlation shows significant positive correlation between capillary hemoglobin level and length velocity in the first 6 months ( $r=0.49$ ,  $p=0.009$ ). In Pearson-Chi-Square Test the moderate anaemia group showed significantly frequent atopic dermatitis in their first 12 months of life ( $\chi^2=8.786$ ,  $p=0.012$ ).

**Conclusion.** Breast-fed infants are at higher risk of anaemia and prevalence of atopic dermatitis in the first year of life is significantly associated with moderate anaemia. Therefore, breast-fed infants need to be supplemented with iron-rich solids before 6 months of age, complete nutrient intake is essential in infant growth velocity in their first 6 months of life.

**Acknowledgements.** The authors declare the absence of conflict of interest.

## Vitamin D and Total IgE in Childhood Bronchial Asthma in Latvian Population

Tapīņa Sandra<sup>2</sup>, Paramonova Natalia<sup>1</sup>, Trapiņa Ilva<sup>1</sup>, Pļaviņa Samanta<sup>1</sup>, Ļeņonova Elīna<sup>1</sup>, Rumba-Rozenfelde Ingrida<sup>2</sup>, Sjakste Nikolajs<sup>1,2</sup>

<sup>1</sup>Laboratory of Genomics and Bioinformatics, Institute of Biology, University of Latvia, Riga, Latvia

<sup>2</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

**Background.** Bronchial asthma (BA) is a chronic inflammatory, genetically complex, heterogeneous disease. Vitamin D is a nutrient and hormone that plays an important role in the pathogenesis of various allergic diseases. Low circulating vitamin D levels have been associated with risk of asthma, atopic dermatitis, and elevated total immunoglobulin E (IgE), therefore it may represent a marker of other factors that may lead to increased asthma prevalence and severity.

**Aim.** To determine the relationship between measured vitamin D levels and total IgE (allergy marker) in a cohort of children with BA in the Latvian population.

**Methods.** The cohort of examined patients included 55 children diagnosed with asthma, recruited on the basis of the Riga 1<sup>st</sup> Hospital, polyclinic “Bruņinieku” and medical institution Gārša Inese medical practice in paediatrics (Valmiera). Vitamin D and IgE levels in blood serum were determined by means of enzyme-linked immunosorbent assay (ELISA). Statistical analysis was performed with SPSS.25 Statistical Package.

**Results.** Vitamin D level was determined in fifty-five children with asthma (29 females, 53%); data on IgE level were obtained from thirty-one serum samples. The median vitamin D level in the investigated disease cohort was 29 ng/mL (range of 6.39–56.56, the mean of 29.02±10.79) and did not differ by gender. Deficient levels of vitamin D (<20 ng/ml) were detected in 25% of BA patients, and only in one case it was critically low (<12 ng/ml). The median IgE level was 69.54 IU/mL (range of 0.02–139.12). There is no statistically significant correlation ( $r=-0.14$ ;  $p=0.46$ ) between vitamin D and IgE levels. The level of vitamin D is statistically significantly ( $p<0.05$ ) associated with vitamin supplementation in BA patients.

**Conclusion.** In our group of children with asthma, no correlation was found between the level of vitamin D and IgE. The cause-and-effect relationship between vitamin D, asthma, and allergy should be further clarified. Vitamin supplementations have a positive effect on its level, thus have public health importance, since vitamin D insufficiency is common and correctable.

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## Association Between Maternal Antibacterial Treatment and Infant Gut Microbiota: Preliminary Data of a Study About Infant Gut Microbiota

Zaharova Margarita<sup>1</sup>, Zelča Egija<sup>1</sup>, Lūse Ērika<sup>1</sup>, Peterleviča Jana<sup>1</sup>, Frīdmanis Dāvids<sup>2</sup>, Gudrā Dita<sup>2</sup>, Rumba-Rozenfelde Ingrīda<sup>1,3</sup>, Daugule Ilva<sup>1,3</sup>

<sup>1</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

<sup>2</sup>Department of Human Genetics and Disease Mechanisms, Institute of Latvian Biomedical Research and Study Centre, Riga, Latvia

<sup>3</sup>Institute of Clinical and Preventive Medicine, University of Latvia, Riga, Latvia

**Background.** The maternal use of antibiotics prenatally or during pregnancy may have adverse effects on the neonatal gut microbiome. It is hypothesized that the effects of antibiotics on the microbiota may also lead to further health problems.

**Aim.** The aim of this study was to analyse the changes of intestinal microbiota in children in respect to prior maternal antibacterial therapy during pregnancy and/or delivery.

**Methods.** A cross-sectional study was performed at primary healthcare centres. The parents of healthy children (aged 1–12 months) filled out a questionnaire (demographic, family and perinatal data, antibacterial therapy) and brought the child's faecal sample. The 16 rRNS gene sequencing was performed to identify the bacterial taxonomic units. The composition of the intestinal microbiota (relative amount and Shannon index (SI)) was compared among infants in respect to type of delivery and information about maternal antibacterial treatment.

Statistical analysis: descriptive statistics, Mann-Whitney test.

**Results.** In total, 73 children were included in the study (58.9% (43/73) girls; the mean age 5.85 months (SD±3.36), range 1–12 months); 57 children were born vaginally and 14 – by C-section.

The study sample included 16 children, whose mothers had received antibacterial therapy during delivery; 10 children – whose mothers had received antibacterial therapy during pregnancy.

The median SI in infants with maternal antibacterial therapy during pregnancy was 5.24 (IQR: 4.17–6.11) compared to 4.51 (IQR: 2.87–5.27) among infants without maternal antibacterial treatment during pregnancy ( $p=0.047$ ).

The median SI did not differ among infants with maternal antibacterial treatment during delivery (4.34; IQR: 3.06–5.24) compared to infants without previous maternal treatment (4.70; IQR: 3.68–5.62),  $p=0.43$ ; and in infants with vaginal delivery (4.43; IQR: 3.21–5.36) compared to C-section (4.92; IQR: 2.68–5.27),  $p=0.61$ .

Relative abundance of *Lachnospirace* family was non-significantly higher in infants with prior maternal antibacterial treatment during pregnancy (27.52; IQR: 3.45–46.42) compared to infants without maternal antibacterial treatment during pregnancy (9.49; IQR: 0.00–35.69);  $p=0.25$ ; as well as in infants with C-section (19.71; IQR: 0.00–41.55) vs vaginal delivery (9.49; IQR: 0.00–33.32);  $p=0.55$ .

**Conclusion.** Relative abundance of *Bifidobacterium* genus did not differ in respect to maternal antibacterial treatment or in respect to the type of delivery.

**Conclusion.** The preliminary data show that maternal antibacterial therapy did not cause huge changes to microbiota and strain diversity of healthy infants, although impact to relative abundance of *Lachnospirace* should be studied further.

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## MENTAL HEALTH

### Self-Destructiveness and Suicidality and Their Impact on Health in Adolescents in Latvia

Zīle Inta<sup>1,2</sup>, Tzivian Lilian<sup>1</sup>

<sup>1</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

<sup>2</sup>I. Zīle-Practice in Psychotherapy, Riga, Latvia

**Background.** Adolescents' health is tightly connected with their inner world of internal objects and interpersonal relationships, influencing both mental and bodily functioning. In the case of high stress, such as extremely important events, adolescents' functioning could decompensate, leading to self-destructiveness.

**Aim.** The aim of the study was to investigate self-destructive and suicidal tendencies in final school year adolescents at the beginning and at the end of the final school year.

**Methods.** A two-stage cross-sectional study was performed in seven schools in Riga, Latvia (three high-rated and four regular secondary schools). Levels of self-destructiveness, suicidality, level of anxiety and somatic complaints were assessed using Achenbach System of Empirically Based Assessment (ASEBA) youth self-reported scale at two time points: at the beginning and at the end of the final school year. According to authors, self-destructiveness and suicidality are prominent in the case of  $\geq 2$  points at the scale of four. Possible range for somatic complaints was from 0 to 13, for anxiety – from 0 to 12. Wilcoxon test was used to investigate differences between both time points. Correlation between self-destruction, suicidality and somatic complaints were checked using Spearman's test. Multiple logistic regression models adjusted for personal covariates were built to investigate the association between self-destructiveness and suicidality, and somatic complaints of last years' Latvian students. Differences of  $p < 0.05$  were considered as statistically significant.

**Results.** Altogether 287 adolescents (the mean age 15.0 (standard deviation 0.3); 49.5% girls) participated in the study. At both time points, 12 students (4.2%) had  $\geq 2$  points in scales of self-destructiveness and suicidality; two of them were from regular and ten from high-rated secondary schools. We observed statistically significant increase in the level of somatic complaints ( $p < 0.01$ ) and in the level of anxiety ( $p = 0.02$ ) at the second time point in adolescents with self-destructiveness  $\geq 2$ . In multiple logistic regression models, girls had a higher possibility of self-destructiveness than boys (odds ratio, OR=5.45; 95% confidence interval, CI=1.17; 25.37).

**Conclusion.** The adolescents' mind and body interaction is complex. During the final school year stress could exacerbate self-destructiveness and suicidality. Furthermore, the level of anxiety and somatic complaints increase, too. Our study demonstrates that adolescent girls in particular need specific screening for self-destructiveness and suicidality during the final school year.

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## Emotion Recognition and Emotion Regulation Skills in Migraine Patients

Lazdiņa Agita<sup>1,2</sup>, Dūdiņa Kristīne<sup>1,2</sup>, Užāns Andis<sup>1</sup>

<sup>1</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

<sup>2</sup>Health Center Vivendi, Riga, Latvia

**Background.** Migraine is related to a generalized hyperexcitability both to sensory and emotional stimuli, involving the cortical-limbic system. This hyperexcitability predisposes migraine patients to more frequent and prolonged negative effects. Previous studies indicate that emotional dysregulation in migraine patients predicts a more severe course of the disease, mental health issues and reduced patient's quality of life. There is a general agreement that psychotherapy improves emotion coping skills that subsequently reduces the frequency and intensity of migraine attacks and improves the quality of life. A better understanding of how to regulate emotion in migraine patients is essential to refine the therapeutic approach and help migraine patients to cope.

**Aim.** To identify differences in emotion recognition and emotion regulation strategies used by a clinical group (patients with migraine) and a control group (adults without diagnosis of migraine).

**Methods.** In total, 242 female participants (the mean age 39 years, SD±9.27) were included in the analysis. 57% (n=139) were previously diagnosed with a migraine. Participants filled in a socio-demographic survey and self-report questionnaire adapted for use in Latvia: Emotion Regulation Skills Questionnaire (ERSQ, Berking & Znoj, 2008). Questionnaires were administered in 2 clinics during routine visits to neurologists and online.

**Results.** Migraine patients experienced anxiety-related emotions (nervous, tense, stressed) more frequently than the control group ( $p<0.01$ ) and experienced positive emotions (ex., courage, interest, happiness, inspiration, pride, excitement, activity) less frequently. Compared to the control group, migraine patients presented less frequent overall use of adaptive emotion regulation skills ( $p=0.002$ ). Lower scores were found in six out of nine scales of ERSQ: clarity ( $p=0.018$ ), understanding ( $p=0.006$ ), acceptance ( $p=0.014$ ), tolerance ( $p=0.003$ ), self-support ( $p=0.01$ ), modification ( $p<0.001$ ).

**Conclusion.** Migraine patients experienced more negative and less positive emotions and showed less adaptive emotion regulation skills. Unpleasant emotions were difficult to tolerate and regulate. Authors suggest emotion regulation skills improving therapies may be addressed to cope better with negative emotions (acceptance, understanding, tolerance and modification) and to address the obstacles for experiencing positive emotions. Prolonged negative effects and pain combined with helplessness are risk factors for developing depression or anxiety disorder – frequent comorbid disorders among migraine patients. Therefore, emotion-focused therapeutic strategies could also lower the risk of these mental disorders. Longitudinal design research is needed to reveal whether improved coping mechanisms influence the course of the migraine, wellbeing, and mental health of the patients.

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## Intrinsic Motivation Assessment of the First Patients Enrolled in DisCoVer Trial – Innovative Major Depressive Disorder Treatment

Konosonoka Liene<sup>1,2</sup>, Rubene Linda<sup>1,2</sup>, Padberg Frank<sup>3</sup>, Bavelier Daphne<sup>4</sup>, Hummel Friedhelm<sup>5</sup>, Bonne Omer<sup>6</sup>, Nahum Mor<sup>7</sup>, Rancans Elmars<sup>1,2</sup>

<sup>1</sup>Department of Psychiatry and Narcology, Riga Stradiņš University, Riga, Latvia

<sup>2</sup>Riga Centre of Psychiatry and Addiction Disorders, Riga, Latvia

<sup>3</sup>Department of Psychiatry and Psychotherapy, University Hospital, Ludwig Maximilian University of Munich, Munich, Germany

<sup>4</sup>Faculty of Psychology and Educational Sciences, University of Geneva, Geneva, Switzerland

<sup>5</sup>Centre for Neuroprosthetics and Brain Mind Institute, Swiss Federal Institute of Technology, Geneva, Switzerland

<sup>6</sup>Department of Psychiatry, Hadassah Medical Center, Faculty of Medicine, The Hebrew University of Jerusalem, Jerusalem, Israel

<sup>7</sup>School of Occupational Therapy, Faculty of Medicine, The Hebrew University of Jerusalem, Jerusalem, Israel

**Background.** Major depressive disorder (MDD) is a highly prevalent and disabling disorder, hence the importance of introducing novel and efficacious treatment approaches. The main goal of the collaborative DiSCoVeR project is to examine the synergistic effects of a novel treatment approach for MDD – a home-administered treatment, combining simultaneous self-administered non-invasive prefrontal transcranial direct current stimulation along with a cognitive control videogame. The effects of this treatment on alleviating depressive symptoms and modulating cognitive control functions in depressed patients will be tested in a multi-site, two-arm, double-blind, sham-controlled, randomized controlled trial conducted at three clinical trial sites (Hadassah, Israel; Riga Stradiņš University, Latvia; Ludwig-Maximilian-University, Germany).

**Aim.** The goal of the current study was to examine patients' intrinsic motivation after completing the first five days of the treatment; and to examine the patients' interest/enjoyment, perceived competence, effort, felt pressure/tension, and perceived choice following the first week of treatment. Intrinsic motivation has been associated with enhanced learning and performance, so it can be used as one of the predictors for patient compliance of the treatment.

**Methods.** We assessed the first 21 patients that were enrolled in the trial from all 3 study sites using the Intrinsic Motivation Inventory (IMI). Patients filled out the IMI following the fifth treatment session, regardless of group assignment. We used the following subscales from the IMI: interest/enjoyment, perceived choice, perceived competence, effort/importance and felt pressure/tension. Each item was scored on a 7-point Likert scale, ranging from 1 ("not at all true") to 7 ("very true"), with the higher scores indicating more of the concept described in the subscale name.

**Results.** Participants rated their overall interest and enjoyment at 4.55 out of 7 (SD±1.25; with probability 95% CI 4.02 to 5.09), the perceived choice score was 5.82 points (SD±1.05; CI 5.37 to 6.27), perceived competence was 4.55 (SD±1.25; CI 4.02 to 5.09), effort and importance subscale score was 5.38 (SD±1.11; CI 4.90 to 5.86) and in the pressure and tension subscale it was 3 points (SD±1.04; CI 2.55 to 3.45).

**Conclusion.** We conclude that overall patients were interested in the interventions and had inherent pleasure while doing the sessions, felt that it was their choice to do them, felt that they performed the task quite effectively, were invested in doing the sessions and the experienced pressure and tension were low. The perceived choice and competence are positive predictors of intrinsic motivation.

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## Criteria for Unauthorised Treatment in Psychiatry

Konstantinova Karīna<sup>1,4</sup>, Olsena Solvita<sup>1,2</sup>, Loseviča Marina<sup>1,3</sup>

<sup>1</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

<sup>2</sup>Latvian Collegium of Sworn Advocates, Riga, Latvia

<sup>3</sup>Riga Centre of Psychiatry and Addiction Medicine, Riga, Latvia

<sup>4</sup>Mental Hospital "Ģintermuiža", Jelgava, Latvia

**Background.** In psychiatric clinical practice, the proportion of patients with incapacity is 45% (Lepping et al., 2015) and some of them do not regain their capacity after treatment. Off-label use and compassionate use of medications (experimental treatment outside of clinical trials for life threatening or life changing diseases) are growing, informal coercion with surreptitious practises in managing persons with serious mental illnesses and dementia appears to be widespread. In this regard, applying shared decision-making and informed choice models is challenging. The abovementioned raises the awareness of safeguarding rights of decisionally incapacitated persons in the mental health treatment process. Surrogate decision-making/proxy consent and prior decision/advance directive are not the game-changers: even close relatives and friends often can poorly predict the type of treatments their loved ones would want and the percentage of the population with living wills remains small. Supported decision-making is not routinely available in medical settings; in emergency situations, the legal representatives might not be readily available for communication. Legal barriers or bias in prescribing unauthorized treatment (off-label use, compassionate use, surreptitious treatment) for patients with limited decisional capacity would preclude them from their right to enjoy the benefits of scientific progress in health care.

**Aim.** To reveal ethical and legal approaches to treatment choices concerning patients with limited capacity in prescribing off-label use, compassionate use of medications and surreptitious treatment.

**Methods.** Scientific papers and national and international legal and ethical regulations have been studied and analysed.

**Results.** The criteria for off-label prescription are: the patient cannot be treated effectively with any on-label medication; the prescription is supported by scientific/medical evidence; the informed consent is obtained (via supported or surrogate decision-making process) or the decision is according to the advanced psychiatric directive. If mental capacity is regained during treatment, the deferred consent has to be obtained. The additional criteria for granting the request for compassionate use are: no known or unacceptable harm was anticipated (nonmaleficence); the patient is stable enough to tolerate the therapy and to realise clinical improvements for a reasonably sustained period. The criteria for surreptitious treatment are: the patient has lost his/her decisional capacity and surreptitious treatment is the only way to minimise sufferings and harm. The decision to prove surreptitious treatment has to be well-supported and documented.

**Conclusion.** The existing legislation concerning off-label use and compassionate use of medications has to be amended; clear criteria of surreptitious treatment have to be implemented.

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## Depression Symptoms and COVID-19-Related Factors in Emergency Room Staff of Psychiatric Hospitals in Latvia During the Pandemic

Počopko Aļona<sup>1,2</sup>, Everte Ieva<sup>1,3</sup>, Brūna Krista<sup>4</sup>, Gaibišele Agnese<sup>1,5</sup>, Dalbiņa Lolita<sup>4,6</sup>, Taube Māris<sup>1,5</sup>

<sup>1</sup>Rīga Stradiņš University, Riga, Latvia

<sup>2</sup>Daugavpils Psychoneurological Hospital, Daugavpils, Latvia

<sup>3</sup>Strenči Psychoneurological Hospital, Strenči, Latvia

<sup>4</sup>Jelgava Hospital "Gintermuiza", Jelgava, Latvia

<sup>5</sup>Rīga Psychiatry and Narcology Centre, Riga, Latvia

<sup>6</sup>Piejuras Hospital, Liepaja, Latvia

**Background.** It is well established that COVID-19 pandemic greatly impacts many aspects of life, including mental health. Healthcare professionals, especially frontline workers are more susceptible to mental disorders [1].

**Aim.** The aim of the current study was to investigate depression symptoms and their severity in emergency room staff of psychiatric hospitals in Latvia and evaluate the connection between impact of COVID-19-pandemic related factors and severity of depressive symptoms.

**Methods.** Permission from the Riga Stradiņš University Research Ethics Committee was obtained. Psychiatry hospital emergency room staff were offered to complete self-report questionnaires, which included demographic data, questions about COVID-19 pandemic impact and its related phenomena, validated screening tool Patients Health Questionnaire-9 (PHQ-9). The survey was conducted from March to May 2021. Data was processed using SPSS v27.0, descriptive statistics.

**Results.** In total, 98 participants from five Latvia psychiatric hospitals were enrolled in this study (the mean age 45.5; SD=11.8), of which 75.5% (N=74) were females. No symptoms of depression were reported by 8.2% (N=8), 43.9% (N=43) showed subclinical depression symptoms, 30.6% (N=30) – mild depression symptoms, 13.3% (N=13) – moderate depression symptoms, 2% (N=2) – moderately severe, and 2% (N=2) – severe depression symptoms. Data showed significant connection between increased depression symptom severity and a positive COVID-19 case in family member or a friend (U=829.5 p=0.013), worry, that COVID-19 could be a threat to participants life, (U=800.5, p=0.006), or life of a family member or a friend (U=523.0, p=0.002). There was a positive correlation between higher workload and severity of depression symptoms (r=0.223, p=0.022), and negative correlation with lack of personal protective equipment (r=-0.312, p=0.002), subjective decline in mental health state in comparison with pre-pandemic (r=-0.241, p=0.017).

**Conclusion.** The results show that 17.3% of respondents reported clinically significant depression symptoms. Depression symptoms were more severe in those with positive COVID-19 cases in family members or a friend, in those who worried that COVID-19 could be a threat to respondent's or a close person's life. Positive correlation between higher workload and severity of depression symptoms, and negative correlation with lack of personal protective equipment and subjective decline in mental health was found. Regarding the high prevalence of depression symptoms among healthcare workers, appropriate support could be planned.

**Acknowledgements.** The authors declare the absence of conflict of interest.

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## Trends in Paediatric Psychiatric Inpatient Characteristics During COVID-19 Pandemic at Children's Clinical University Hospital, Riga, Latvia

Poluņins Ļevs<sup>1,2</sup>, Linde Matīss<sup>1</sup>, Lismane Diāna<sup>1</sup>, Krišjāne Madara<sup>1</sup>, Bezborodovs Nikita<sup>1,2</sup>

<sup>1</sup>Rīga Stradiņš University, Riga, Latvia

<sup>2</sup>Children's Clinical University Hospital, Riga, Latvia

**Background.** The COVID-19 pandemic has caused significant negative changes in the overall daily life of many people. Rise of mental health related problems during COVID 19 pandemic is experienced in many countries. On 12 March 2020, a state of emergency was declared in Latvia for the first time to control the spread of the coronavirus COVID-19. Mental health of the child and adolescent population is particularly at risk because of abrupt changes in their routine, such as restrictions in social contacts, recreational activities, worsening economic states of their families, loss of close ones and overall uncertainty.

**Aim.** The objectives of this study were to identify major trends in psychiatric paediatric inpatient characteristics during the COVID-19 pandemic.

**Methods.** Altogether 1337 inpatient records were analysed, divided in two symmetrical study time periods – pre- and intra-pandemic. The inpatients in the pre-pandemic period (20.07.2018–11.03.2020) were statistically compared to the intra-pandemic period (12.03.2020–01.11.2021). Patient characteristics such as age, sex, place of residence, length of stay, type of admission was compared in these groups, as well as rates of diagnoses related to depression and self-harm.

**Results.** Statistically significant increase in female case proportions (46.1% to 63.1% ( $p<0.001$ )), increase in proportions of patients from rural regions (38.5% to 47.6% ( $p<0.001$ )), increase in urgent administration case proportions (38.9% to 56.9% ( $p<0.001$ )), increase in adolescent age group patient proportions (32.8% to 52.4% ( $p<0.001$ )), increase of length of stay (the mean of 10.86 days (SD 10.19) to the mean of 13.67 days (SD 12.24)), increase in proportions of patients with depression from 12.5% to 22.7% ( $p<0.001$ ), increase in proportions of patients with intentional self-harm by poisoning from 0.9% to 1.9% ( $p<0.05$ ) and intentional self-harm by sharp object from 4.0% to 6.2% ( $p<0.001$ ) were found.

**Conclusion.** Major changes in psychiatric paediatric inpatient characteristics were found during the COVID-19 pandemic, with patients becoming older, being admitted more often in urgent mental states and staying in the psychiatric ward for longer, which may indicate a negative impact on children's quality of lives. These findings can help underline the importance and increasing demand of mental health in Latvia during the COVID-19 pandemic.

**Acknowledgements.** The authors declare the absence of conflict of interest.

## Comparison of Eating Disorders During COVID-19 Pandemic and Pre-Pandemic Period in Clinic for Pediatric Psychiatry of Children's Clinical University Hospital of Latvia

Linde Matīss<sup>1</sup>, Lismane Diāna<sup>1</sup>, Krišjāne Madara<sup>1</sup>, Poluņins Ļevs<sup>1,2</sup>, Bezborodovs Ņikita<sup>1,2</sup>

<sup>1</sup>Rīga Stradiņš University, Riga, Latvia

<sup>2</sup>Clinic for Pediatric Psychiatry, Children's Clinical University Hospital, Riga, Latvia

**Background.** Since the start of COVID-19 pandemic, new challenges arise from its detrimental effects on mental health, including eating disorders, that have seen substantial increase in the number and severity of new and pre-existing cases amongst young people compared to the previous years. Assessment of eating disorder prevalence and risk factors is necessary to identify and seek the best preventive and treatment options.

**Aim.** The aim of the current study was to compare hospitalization dynamics of patients with eating disorders in the Clinic for Pediatric Psychiatry during and before COVID-19 pandemic.

**Methods.** The total of 123 patients with eating disorders were included in a retrospective cross-sectional study, identified with the ICD-10 F50 group of diagnosis (F50.0, F50.1, F50.2, F50.8) from 07.20.2018 to 01.11.2021. Then the patients were divided into two groups (pre-pandemic and pandemic), each representing a 300-day period set by the midpoint of 11.03.2020 when World Health Organization declared the start of COVID-19 pandemic. SPSS 23 was used for statistical analysis, including the Chi-Square test.

**Results.** Comparing the hospitalized patients with eating disorders between both groups, 83 (58%) of them were hospitalized during pandemic ( $p=0.001$ ). The pre-pandemic group of 60 patients included 5 (8.3%) boys and 55 (91.7%) girls with the mean age of 14.47 years ( $SD=1.631$ ,  $p<0.05$ ), the mean hospitalization length of 18.33 days ( $SD=11.444$ ,  $p<0.05$ ), and 49 (81.7%) of these patients were hospitalized emergently ( $p<0.05$ ). The pandemic group of 83 patients included 16 (19.3%) boys and 67 (80.7%) girls with the mean age of 13.55 years ( $SD=3.113$ ,  $p<0.05$ ), the mean hospitalization length of 17.02 days ( $SD=12.308$ ,  $p<0.05$ ) and 56 (67.5%) of which were hospitalized emergently ( $p<0.05$ ). Significantly more cases of 55 (60.4%) patients with anorexia nervosa were prevalent in pandemic group ( $p=0.002$ ) of which 36 (65.5%) were adolescents, 19 (34.5%) pre-pubescent children, in contrast, there was no excess of patients with bulimia nervosa in each group ( $p=0.716$ ).

**Conclusion.** Trends of more hospitalized patients with eating disorders are clearly observed during pandemic ( $p=0.001$ ). Predominance of hospitalized girls is observed, but we observe more hospitalized boys in pandemic than in pre-pandemic group, respectively, 19.3% and 8.3%. Also, the mean age of hospitalized patients has decreased during the pandemic – 13.55 years of age ( $SD=3.113$ ,  $p<0.05$ ) compared with pre-pandemic group patients with 14.47 years of age ( $SD=1.631$ ,  $p<0.05$ ). Also, predominantly 55 (60.4%) patients with anorexia nervosa were hospitalized ( $p=0.002$ ) during the pandemic.

**Acknowledgements.** The authors declare the absence of conflict of interest and funding.

## Anxiety and the Related Factors in Frontline Healthcare Workers at Latvia Psychiatric Hospitals During COVID-19 Pandemic

Gaibišele Agnese<sup>1,2</sup>, Everte Ieva<sup>1,3</sup>, Brūna Krista<sup>4</sup>, Počopko Aļona<sup>1,5</sup>, Dalbiņa Lolita<sup>4</sup>, Taube Māris<sup>1,2</sup>

<sup>1</sup>Rīga Stradiņš University, Riga, Latvia

<sup>2</sup>Rīga Psychiatry and Narcology Centre, Riga, Latvia

<sup>3</sup>Strenči Psychoneurological Hospital, Strenči, Latvia

<sup>4</sup>Hospital "Ģintermuiža", Jelgava, Latvia

<sup>5</sup>Daugavpils Psychoneurological Hospital, Daugavpils, Latvia

**Background.** Several studies have found that the COVID-19 pandemic has had adverse mental health effects in healthcare professionals, especially in intensive care and frontline medical workers. Protracted course of the pandemic along with uncertainty, everyday restrictions, social isolation and financial difficulties have caused a detrimental impact on mental health of the general population. There is limited data on psychological distress of mental healthcare workers who have to handle the increasing burden of mental disorders.

**Aim.** This multi-centre cross-sectional study aimed to screen and assess anxiety and the related factors in frontline healthcare workers at psychiatric hospitals of Latvia.

**Methods.** A questionnaire was designed to incorporate demographic data, COVID-19-related questions, and a validated screening tool for anxiety (Generalised Anxiety Disorder Scale, GAD-7). Healthcare workers at admission wards of five Latvia psychiatric hospitals were eligible for the survey. Data was collected from March to May 2021. Descriptive statistics, nonparametric methods and correlations were applied for data analysis in SPSS 27.

**Results.** From 98 respondents with the mean age 45.5 (SD=11.8) years 75.5% (n=74) were females, the majority had higher education (59.2%, n=58), work experience in psychiatry more than 10 years (56.1%, n=55), one workload (57.1%, n=56). 37.8% (n=37) of questionnaires were completed by nursing assistants, 32.7% (n=32) by nurses and 29.6% (n=29) by doctors. Clinically significant anxiety (GAD-7 cut-off point 10) was found in 12.2% (n=12) respondents. The mean GAD-7 score was 4.7 (SD=4.5). Females scored a higher mean GAD-7 compared to males (5.24 (SD=4.75) and 2.88 (SD=3.03), respectively). There was statistically significant association between anxiety and female gender ( $\chi^2=4.435$ ,  $p=0.035$ ), COVID-19-related death or infection in family ( $\chi^2=4.052$ ,  $p=0.044$  and  $\chi^2=5.650$ ,  $p=0.017$ , respectively), depression symptoms ( $\chi^2=31.701$ ,  $p<0.001$ ), self-reported worsened overall health condition ( $\chi^2=9.454$ ,  $p=0.009$ ). The statistically significant correlation was found between anxiety and younger age ( $r=0.287$ ,  $p=0.004$ ), higher rank position ( $r=0.225$ ,  $p=0.026$ ). The mean GAD-7 score 6.66 (SD=4.75) was the highest amongst doctors, followed by nurses 4.75 (SD=4.21) and nursing assistants 3.03 (SD=3.97). Anxiety was not associated with insufficient personal protective equipment, lack of knowledge about COVID-19, vaccination status, duration of work experience in the field of psychiatry.

**Conclusion.** Clinically significant anxiety was found in 12.2% respondents. This study revealed that females, persons with COVID-19-related death or infection in family, coexisting depression symptoms, self-reported worsened overall health condition, younger age, higher rank position are the healthcare workers groups that could be addressed first regarding anxiety management.

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## INTERNAL MEDICINE

## Role of the Extended-Release Metformin on Host miRNA Composition in the Faeces of Patients with Type 2 Diabetes

Celmiņa Paula Rūta<sup>1</sup>, Silamiķele Laila<sup>1</sup>, Kloviņš Jānis<sup>1</sup>

<sup>1</sup>Latvian Biomedical Research and Study Centre, Riga, Latvia

**Background.** Metformin is the most commonly used medication for treatment of type 2 diabetes mellitus, it is available as an immediate-release formulation and an extended-release formulation, which is designed to release metformin slowly, but with better efficiency than the immediate release metformin, which also has an impact on gastrointestinal tract. Studies have shown that the faecal miRNAs of the host have a direct impact on the gut microbiota.

**Aim.** The aim of the current study was to determine whether an extended-release metformin therapy has a significant effect on the miRNA composition of the host in faecal samples from patients with type 2 diabetes.

**Methods.** The study had a longitudinal design, including two different groups: newly diagnosed patients with type 2 diabetes before starting treatment with an extended-release metformin and the same patients 10 weeks after the treatment. As an additional factor, the gender of the patients was included in the study, thus creating 4 experimental groups – M.B (males before therapy); M.A. (males after 10 weeks of therapy); F.B (females before therapy); F.A (females after 10 weeks of therapy). Altogether 24 patients were enrolled in the study in total, 48 faecal samples were analysed before and after the treatment.

Data were analyzed using CLC Genomics Workbench 20.0.4 and Galaxy Release v21.01. Quality control was performed in Galaxy using tool FastQC (v.0.11.8). Quantify miRNA was used to map the reads against miRBase release v22, pointing out *Homo Sapiens* as prioritized species. Differential abundance testing was performed using edgeR 3.32.1 and limma 3.46.0. Factors which were included in the analysis were sex, metformin therapy status, and time. P-values <0.05 were regarded as statistically significant.

**Results.** When reads were annotated against miRBase, 241 different mature miRNAs with at least one read were identified. Top 20 miRNAs represented 92.1% of the total reads. In all groups, the dominating miRNA was hsa-miR-1246, followed by hsa-miR-192-5p and hsa-miR-21-5p. After multiple comparisons correction using a false discovery rate, no significant differences in miRNA compositions were observed between the studied contrasts.

**Conclusion.** The composition of miRNA in faeces is relatively constant, the dominating miRNA in all groups is hsa-miR-1246. No significant effect of extended-release metformin on miRNA expression was observed.

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## DNA Methylation Profile of *PSMA6*, *PSMB5* and *HIF1A* Gene in Patients with Type 1 Diabetes and Diabetic Retinopathy

Pļaviņa Samanta<sup>1</sup>, Paramonova Natalia<sup>1</sup>, Pahirko Leonora<sup>2</sup>, Siliņš Emīls<sup>2</sup>, Baumane Kristīne<sup>3,4</sup>, Zariņa Līga<sup>3</sup>, Rovīte Vita<sup>5</sup>, Sokolovska Jeļizaveta<sup>4</sup>

<sup>1</sup>Institute of Biology, University of Latvia, Riga, Latvia

<sup>2</sup>Faculty of Physics, Mathematics and Optometry, University of Latvia, Riga, Latvia

<sup>3</sup>Ophthalmology Department, Riga East Clinical University Hospital, Riga, Latvia

<sup>4</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

<sup>5</sup>Latvian Biomedical Research and Study Centre, Riga, Latvia

**Background.** Diabetic retinopathy (DR) is the main reason for vision loss in the developed world. Among different molecular mechanisms of DR, impaired protein degradation and hypoxia-driven processes are of specific interest. DNA methylation of genes of ubiquitin-proteasome system and *HIF1A* have not been described in DR yet.

**Aim.** To study the level of DNA methylation in the promoter regions of *PSMA6*, *PSMB5* and *HIF1A* genes in patients with different severity of DR and type 1 diabetes (T1D).

**Methods.** Bisulfite-free, restriction enzyme-dependent determination of the DNA methylation status in the promoter regions of the genes of interest was performed using real-time PCR procedure, following the instructions given in the manual and using 20 ng DNA for each sample (OneStep qMethyl™ Kit (Zymo research)). DNA methylation extent was calculated using threshold cycle or CT values and the following equation:  $100 \cdot 2^{-(\Delta CT)}$ .

**Results.** DNA methylation was analyzed in 114 patients: 41 with no diabetic retinopathy (NDR), 26 with non-proliferative retinopathy (NPDR), 46 with proliferative retinopathy and/or status post laser photocoagulation (PDR/LPC). The groups differed in age ( $p=0.002$ ), body mass index ( $p<0.001$ ), duration of diabetes ( $p<0.001$ ), smoking ( $p=0.04$ ), HbA1c ( $p=0.09$ ), usage of lipid lowering and antihypertensive medication ( $p<0.05$ ). The highest levels of DNA methylation in the investigated genes were observed in PDR/LPC group. *PSMA6* gene methylation profiles were: NDR 5.5 (3.9–9.2), NPDR 4.2 (3.4–5.4), PDR/LPC 6.1 (4.6–9.9),  $p<0.001$ . *PSMB5* gene methylation profiles were: NDR 2.9 (1.6–3.5), NPDR 1.7 (1.2–2.8), PDR/LPC 3.8 (1.8–5.1),  $p<0.001$ . *HIF1A* gene methylation profiles were: NDR 4.2 (3.4–5.7), NPDR 3.6 (3.1–5.1), PDR/LPC 4.3 (3.7–10.6),  $p=0.03$ . Methylation profile of all investigated genes, correlated positively significantly with diabetes duration (*HIF1A*  $r=0.309$ ,  $p<0.001$ ; *PSMA6*  $r=0.295$ ,  $p=0.002$ ; *PSMB5*  $r=0.282$ ,  $p=0.002$ ) and between each other.

**Conclusion.** DNA methylation of *PSMA6*, *PSMB5* and *HIF1A* genes is higher in advanced stages of DR. The next step will include analysis of the impact of confounding factors of DNA methylation levels.

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## Role of Rheumatoid Factor in Patients with Systemic Sclerosis and Extra-Articular Manifestations

Rubins Pauls<sup>1,2</sup>, Mikena Santa<sup>1</sup>, Bulina Inita<sup>1,2,3</sup>, Zepa Julija<sup>1,2,3</sup>, Andersone Daina<sup>1,2</sup>, Ivanova Kristine<sup>1,2</sup>

<sup>1</sup>Pauls Stradiņš Clinical University Hospital, Riga, Latvia

<sup>2</sup>University of Latvia, Riga, Latvia

<sup>3</sup>Riga Stradiņš University, Riga, Latvia

**Background.** The specificity of several antibodies in patients with systemic sclerosis has been extensively studied, and elevated rheumatoid factor (RF) is known to be more common in patients with joint inflammation. Elevated RF importance in patients with systemic sclerosis and extra-articular involvement has not been extensively studied.

**Aim.** The aim of the study was to determine whether elevated serum RF in patients with systemic sclerosis is associated with extra-articular involvement – pulmonary hypertension, interstitial lung disease, gastrointestinal involvement, skin disease, Raynaud's phenomenon.

**Methods.** Altogether 82 patients were screened. All of them met diagnostic criteria for systemic sclerosis (The ACR/EULAR 2013). Patients' medical data was selected from the hospital database of rheumatology department from 2017 to 2020.

**Results.** Altogether 82 patients were screened, 67 of them females (82%), 15 males (18%). Elevated RF association with any of the affected organ systems was analysed and compared to patients without data on organ system damage. A total of 19 patients (23%) had an elevated RF (range 19–415 IU/ml), 54 (66%) patients were RF negative, and 9 (11%) patients did not have a blood test available for RF, therefore 73 patients were enrolled in the study. Pulmonary arterial hypertension was observed in 23 (32%) patients and RF positive in 10 (43%), interstitial lung disease in 37 (50%) patients and RF positive in 8 (21%), gastrointestinal involvement in 35 (48%) patients and RF positive in 11 (31%), skin lesion in 61 (84%) patients and RF positive in 18 (30%), Raynaud's phenomenon in 63 (86%) patients and RF positive in 18 (29%).

Reliable elevated RF association was observed only for pulmonary hypertension ( $p=0.0420$ ).

**Conclusion.** The data from our study suggests a possible correlation of RF with the development of pulmonary hypertension in patients with systemic sclerosis. In order to evaluate more reliable results of other extra-articular manifestations, it would be necessary to analyse a larger group. In the currently available data in Latvia, 82 patients with systemic sclerosis are known to be consulted in Pauls Stradiņš Clinical University Hospital. Further patient monitoring and research in this direction is needed to evaluate association between RF and extra-articular damage in patients with systemic sclerosis.

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## Prevalence and Causes of Drug Hypersensitivity Reactions Among Inpatients and Outdoor Department Patients at Pauls Stradiņš Clinical University Hospital

Lapiņa Lāsma<sup>1</sup>, Možeitoviča Evelīna<sup>2</sup>, Ciekure Līga<sup>1</sup>, Mauliņš Egīls<sup>1</sup>, Kurjāne Nataļja<sup>1,2</sup>

<sup>1</sup>Pauls Stradiņš Clinical University Hospital, Riga, Latvia

<sup>2</sup>Riga Stradiņš University, Riga, Latvia

**Background.** Drug hypersensitivity is a significant issue worldwide, as it affects provision of medical services – both diagnostic and therapeutic ones. In addition, patients with drug hypersensitivity often develop pharmacophobia and therefore they refuse evidence-based medicine and seek help from the practitioners of alternative medicine. Awareness of these matters affects the decision-making process among health professionals, and it has a major role in patient safety issues and their right to quality medical care. So far, there have been no written reports in Latvia to evaluate drug hypersensitivity reactions. This is the first report in Latvia concerning this problem.

**Aim.** The intent of the current study was to verify the prevalence of drug hypersensitivity cases among inpatients and outpatients in Pauls Stradiņš Clinical University Hospital and to consider the age, gender of these patients, assessing clinical manifestations and most frequent triggers of hypersensitivity reactions.

**Methods.** Retrospective review, based on ICD-10 electronic medical records from Pauls Stradiņš Clinical University Hospital archive from 2015 to 2021. SPSS statistical software was used for analysis of the received data.

**Results.** A total of 73 episodes of hypersensitivity reactions were analysed, of which 36 cases (49.3%) were anaphylaxis, 10 cases (13.7%) were type I, 2 cases (2.7%) – type IV, 2 cases (2.7%) – pseudo allergic and 23 cases (31.5%) – unspecified hypersensitivity reactions. 57 patients (78.1%) were women and 16 (21.9%) were men. The mean age of patients was 51.67±15.7 (22–84) years. The most frequent triggers of drug hypersensitivity reactions were anaesthetics (30.1%), non-steroidal anti-inflammatory drugs (NSAIDs) (27.4%), antibiotics (19.2%), antimigraine drugs (11%) and antiemetics (8.2%). The most prevalent symptoms were urticaria (43.8%), dyspnea (31.5%) and angioedema (30.1%) followed by hypotension (12.3%), loss of consciousness (11%), and bronchospasm (9.6%). One patient died due to anaphylaxis at the age of 68. The trigger that caused the death was not identified.

**Conclusion.** Drug hypersensitivity reactions are rare and have occurred more frequently in women than men. Drug hypersensitivity may affect people of various ages, but the mean age of patients was 51.67 years. The most prevalent causative agents of drug hypersensitivity reactions were anaesthetics, NSAID's and antibiotics. The most frequent clinical manifestations were respiratory and cutaneous symptoms.

**Acknowledgements.** The authors declare the absence of conflict of interest.

## Pigmentation During Pregnancy and Postpartum Period

Rubins Silvestrs<sup>1</sup>, Šaripova Sabīne<sup>1</sup>

<sup>1</sup>*Faculty of Medicine, University of Latvia, Riga, Latvia*

**Background.** Pigmentation is one of the most common changes during pregnancy and the postpartum period, which can affect a woman's self-esteem and quality of life in general. The ongoing hormonal changes such as elevated oestrogen and progesterone levels also cause changes in the skin.

**Aim.** The aim is to establish what pigmentation is the most common in pregnant women and in the postpartum period, how often these pigmentations are found in women in Latvia.

**Methods.** The study includes a survey with 27 questions about most common pigmentations during pregnancy and postpartum, and whether they affect women's quality of life. The survey includes answers from 357 respondents – 116 pregnant women and 240 women in postpartum period.

**Results.** Of the surveyed woman, 19.1% were in the third trimester of pregnancy, 9.3% – in the second, and 4.2% – in the first trimester, whereas 67.4% were in the postpartum period. 37.3% of the surveyed women had experienced the formation of new melanocytic naevi, which often occurs during pregnancy, however, only 22.4% of women reported that they used sunscreen on a daily basis. 55.3% of the surveyed women noted that they had experienced other pigmentations during pregnancy or the postpartum period – 26.4% developed to melasma, 68.6% – linea nigra, and 66.6% – stretch marks. 21.3% of surveyed women say that these pigmentations interfere with daily life – itching or feeling bad.

### **Conclusions.**

1. More than half of women experience pigmentation, which shows that this problem is very common and needs to be discussed more widely.
2. Pigmentation impacts women's quality of life and psyche, especially during pregnancy or the postpartum period, when a woman is even more emotional than usual.

**Acknowledgements.** The present study has received the approval of ethics committee.

## Diagnosis of Abnormally Invasive Placenta by Magnetic Resonance and Correlation with Operative Findings

Lopatina Anna<sup>1</sup>, Miklaseviča Ilze<sup>1</sup>, Liepa Māra<sup>2</sup>

<sup>1</sup>University of Latvia, Riga, Latvia

<sup>2</sup>Pauls Stradiņš Clinical University Hospital, Riga, Latvia

**Background.** Abnormally invasive placenta (AIP) is employed to denote a placenta that does not separate naturally after delivery and cannot be extirpated without causing abnormally high blood loss. AIP may have different degrees of severity, ranging histopathologically from placenta accreta and placenta increta to placenta percreta. Early diagnosis of placental ingrowth is exceptionally important because abnormally invasive placenta affects the clinical outcome, which also impacts the necessities for prenatal hospitalization, prenatal hemoglobin optimization, use of prenatal corticosteroids, use of preoperative cystoscopy, urethral stents, and prophylactic pelvic artery balloon catheters, similarly as invasive radiologist participating during operation to avoid bleeding and hysterectomy. Also, special preparation for surgery is additionally required, which allows manipulations to be performed under the control of ultrasonoscopy. All of this could reduce the number of hysterectomies that may result in life-threatening bleeding further because of infertility later in life.

**Aim.** The current study aimed to elucidate the diagnostic accuracy of prenatal MRI in recognizing the severity of abnormally invasive placenta, defined because of the depth and topography of invasion.

**Methods.** A retrospective cross-sectional study with analysis of records of 88 patients (women) at reproductive age 18–55 y.o. undergoing MRI to Pauls Stradiņš Clinical University hospital Diagnostic Radiology institute. The study used databases (“*Ārsta birojs*”, AIRIS, Datamed, Sectra) to obtain information on the patient’s age, number of pregnancies, previous caesareans, gynecological pathologies, including previous surgical treatments. The results of the performed MRI examination were compared with the outline of the operation and also the histological conclusion.

**Results.** 30 of 88 patients were confirmed with AIP pathology. According to MRI data, the most common type of AIP is placenta accreta 80% (24 patients), according to surgical findings, the same pathology is the most common – 62.5% (20 patients). The lowest type of AIP was reported in both MRI and surgical data; it was placenta percreta at 3.3% (1patient) and 6.3% (2 patients). Based on the collected data, it can be concluded that in a higher number of cases 54.3% (19 patients), the data given the MRI description will also be confirmed surgically.

**Conclusion.** Placenta accreta, placenta increta, and placenta percreta became more frequent, largely due to the increasing rates of a caesarean. MRI increases the accuracy of the workup of high-risk patients and aids in multidisciplinary delivery to improve maternal outcomes. Accuracy and confidence require adherence to examination performance, image interpretation criteria, and awareness of common pitfalls.

## Potential Prognostic Factors for Efficient Treatment of Missed Abortion With Prostaglandin E1 Analogue

Sedleniece Elīna<sup>1,2,3</sup>, Šibalova Anna<sup>1</sup>, Ivanova Laura<sup>1</sup>, Babuškina Antons<sup>3</sup>, Jansone Maira<sup>1,2</sup>

<sup>1</sup>Rīga Stradiņš University, Riga, Latvia

<sup>2</sup>Pauls Stradiņš Clinical University Hospital, Riga, Latvia

<sup>3</sup>Latvian Maritime Medicine Centre, Riga, Latvia

**Background.** Missed abortion (MA) is a nonviable intrauterine pregnancy that has been retained within the uterus without spontaneous abortion. Treatment options of MA include expectant management, medical treatment with Prostaglandin E1 analogue (PGE1) and surgical treatment. Medical treatment is associated with less blood loss and lower risk of infection compared to expectant management, it has shown to reduce the need for surgical treatment and is associated with a high level of patient satisfaction.

**Aim.** To investigate potential prognostic factors of successful therapy using PGE1 in MA.

**Methods.** The prospective study included 61 patients presenting to the Department of Obstetrics and Gynaecology, Pauls Stradiņš Clinical University Hospital from February 2021 to January 2022 with MA.

The study participants were diagnosed with MA using transvaginal ultrasound. Patients who agreed to receive treatment with PGE1, received it according to FIGO 2017 guidelines. The mean maternal age, rate of previous vaginal delivery, Caesarean section, gynaecological manipulations and anembryonic pregnancy, bleeding, pain, use of progesterone, elevated body mass index (BMI),  $\beta$ HCG and CRP level were collected as potential prognostic factors. Treatment efficacy was evaluated using transvaginal ultrasound. Patients were divided in two groups – Group 1 where the treatment was effective and Group 2 where the medical treatment was ineffective and surgical treatment was performed. Clinical and anamnestic factors in both groups were collected and compared. Data analysis was performed using IBM SPSS.

**Results.** The mean age of the participants was 32.9 ( $\pm 6.1$ ) years and the mean gestational age was 68.7 ( $\pm 9.8$ ) days.

Medical treatment was effective in 49.2% ( $n=30$ ) patients, 50.8% ( $n=31$ ) patients required surgical treatment. No significant differences were found in the mean maternal age, rate of previous vaginal delivery, Caesarean section or gynaecological manipulations, current anembryonic pregnancy, bleeding, pain, use of progesterone in current pregnancy, elevated BMI or CRP levels.  $\beta$ HCG levels had a tendency to be higher in Group 2 (53900.6 (95% CI 35239.6–72561.6)) compared to Group 1 (31013.6 (95% CI 200049.5–41977.8)), but the difference was not statistically significant ( $p=0.051$ ).

**Conclusion.** Administration of PGE1 should be offered to all women with a MA who desire medical treatment, as no prognostic factors for medical treatment failure were identified.

There was a tendency of higher beta-HCG level in women with ineffective medical treatment. It would be useful to continue collecting data and enrol more patients in this study to investigate this trend in a larger population.

**Acknowledgments.** The authors declare the absence of conflict of interest.

## Morphological Features of Local Immune Reactions in Placentas in Women Who Had COVID-19 Disease in Early Gestation

Myroshnychenko Mykhailo<sup>1</sup>, Gaponova Ludmila<sup>2</sup>, Kapustnyk Nataliia<sup>3</sup>, Gaponova Elina<sup>1</sup>, Borzenkova Iryna<sup>4</sup>, Pavlova Olena<sup>1</sup>, Myroshnychenko Serhii<sup>5</sup>

<sup>1</sup>Kharkiv National Medical University, Kharkiv, Ukraine

<sup>2</sup>Kharkiv Regional State Administration, Kharkiv, Ukraine

<sup>3</sup>Public Non-profit Organization of the Kharkiv District Council «Regional Clinical Perinatal Centre», Kharkiv, Ukraine

<sup>4</sup>Public Non-profit Organization of the Kharkiv District Council «Regional Clinical Hospital», Kharkiv, Ukraine

<sup>5</sup>Public Non-profit Organization of the Iziium City Council «Central City Hospital of Sandy Mother of God», Iziium, Ukraine

**Background.** Placenta is a potential target organ for the SARS-CoV-2 virus, which leads to the development of COVID-19 disease. The study of the placental damage mechanisms in this category of women is an urgent issue of modern medicine.

**Aim.** To reveal the morphological features of local immune reactions in placentas in women who had COVID-19 disease in early gestation.

**Methods.** The study material consisted of the placentas of women who had a physiological course of pregnancy in group 1 (n=15), and COVID-19 in early gestation (n=44) in group 2. Diagnosis of COVID-19 was carried out according to molecular-genetic examination (polymerase chain reaction). In all groups, childbirth was at 37–40 weeks of gestation. The microscope slides were stained with hematoxylin and eosin. An immunohistochemical study was carried out with monoclonal antibodies to CD3, CD20, CD68. In the field of view of the microscope  $\times 400$ , the absolute number of neutrophilic and eosinophilic leukocytes, CD3-, CD20-, CD68-cells was counted. The obtained digital data were processed, using the program Statistica 10.0. The indicators in groups were compared, using the nonparametric Mann-Whitney U test. Differences were considered significant at  $p < 0.05$ .

**Results.** In group 1, in the decidua, villi, chorionic and amniotic membranes, focally localized CD20-, CD68-, CD3-cells were detected, the absolute numbers of which were respectively ( $0.2 \pm 0.1$ ), ( $28.4 \pm 1.7$ ), ( $30.9 \pm 1.5$ ). In group 2, in comparison with group 1, in the decidua, villi and intervillous space, chorionic and amniotic membranes it was identified expressed focal or diffuse cell infiltration which was characterized by the presence of eosinophilic ( $0.5 \pm 0.2$ ) and neutrophilic ( $15.5 \pm 2.1$ ) leukocytes, and increased ( $p < 0.05$ ) content of CD20-, CD3- and CD68-cells. The absolute numbers of the latter were ( $5.3 \pm 0.5$ ), ( $94.1 \pm 5.5$ ) and ( $117.8 \pm 4.2$ ), respectively.

**Conclusion.** In placentas of women who had COVID-19 in early gestation and gave birth at a gestational age of 37–40 weeks, a change of local immune reactions is determined. The latter is characterized by the appearance of neutrophilic and eosinophilic leukocytes, and an increase in the number of T-lymphocytes, B-lymphocytes and macrophages. The violations of local immune reactions in placentas can cause the development of pregnancy and delivery complications, disorders of the mother, foetus and newborn health.

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## PUBLIC HEALTH AND EPIDEMIOLOGY

### Legal Nature of Agreements in Health Care

Kadile Laura<sup>1</sup>

<sup>1</sup>Faculty of Law, Faculty of Medicine, University of Latvia, Riga, Latvia

**Background.** The patient, as a special right-holder, takes a series of decisions in health care every day by expressing his or her will. Such an expression of will may be done orally, as well as in writing, for example, by signing an agreement for entering a health care institution. When expressing his or her will in health care, every patient must possess a decision-making capacity. On a day-to-day basis, patients must also sign documents which, by their structure and legal nature, can be recognised as legal transactions, in which case the patient has the right to express a will on the content of the transaction, to change and correct it to the extent that the law does not provide otherwise. In such circumstances, the patient should possess legal capacity instead of the decision-making capacity.

**Aim.** The aim of the current study is to ascertain which of the patient's expressions of will are recognised as decision-making in health care and which are expressed as entry into a legal transaction.

**Methods.** The research has been implemented by applying literature review methodology for collecting and analysing data from research in legal sciences; normative legal basis – law and regulations of the Republic of Latvia and other countries, case law and policy documents. In order to compare agreements in health care, comparative empirical research method is being used.

**Results.** As the result of the study, patient's expression of will in a legal transaction is being assessed, including determining decision-making capacity and the meaning of legal capacity to act. The legal nature and force of agreements and other documents in health care institutions is being discussed.

**Conclusion.** This paper firstly distinguishes the Latvian national framework for legal capacity to act and decision-making capacity. Secondly, the role of the expression of intent in a legal transaction and decision-making capacity in health law is being examined. Thirdly, it highlights the importance of the need to establish a common approach for distinguishing agreements in both legal and medical fields to protect the rights of patient as a transaction participant.

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- 1) "Towards a human rights approach for mental health patients with a limited capacity: A legal, ethical and clinical perspective", No. lzp-2020/1-0397;
- 2) "Strengthening of the capacity of doctoral studies at the University of Latvia within the framework of the new doctoral model", No. 8.2.2.0/20/I/006.

## Application of Informed Consent Waiver for Involvement of Persons with Limited Capacity in Clinical Research

Olsena Solvita<sup>1,2</sup>, Loseviča Marina<sup>1,3</sup>

<sup>1</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

<sup>2</sup>Latvian Collegium of Sworn Advocates, Riga, Latvia

<sup>3</sup>Riga Centre of Psychiatry and Addiction Medicine, Riga, Latvia

**Background.** According to data, in psychiatric settings, the average proportion of patients with incapacity is 45% (Lepping et al. 2015). The proportion of patients who are limited in capacity of taking decisions in respect to research should be similar. Legal and ethical norms provide that if a potential research subject has a limited capacity, a legally authorised representative can give informed consent on behalf of a person. However, a person may not have a representative, or there can be a bias when the representative makes the decision. There is a need to perform clinical trials that include all relevant patients with limited capacity. For example, trials for evaluation of the mental capacity of psychiatric patients or studying coercion in psychiatry.

**Aim.** The study aims to reveal ethical and legal approaches suitable for the involvement of patients with limited mental capacity in clinical trials without their explicit consent.

**Methods.** The national and international legal and ethical regulations have been studied. The studies addressing legal and ethical issues in protecting patients with limited capacity in research have been analysed.

**Results.** The research results confirmed that a waiver to the informed consent rule allowing the involvement of subjects who cannot consent in research should be sought. The research protocol proposing the application of a waiver must substantiate that the study: 1) would not be feasible without the particular group; 2) cannot instead be performed with persons capable of providing informed consent; 3) availability of representatives is limited, or there is a bias when representatives are making decisions; 4) has a significant social value and is intended to promote the health of the group represented by the potential subject; 5) poses minimal risk and burden to participants; 6) cannot be delayed; 7) dissent of a person is respected. The proposed waiver must be evaluated by a research ethics committee who should have the authority to grant the exemption.

**Conclusion.** If ethically and legally provided conditions for a waiver of informed consent are met in a research proposal, the research ethics committee can grant exemption from the ordinary consent rule. Article 11 of the Law on the Rights of Patients should be amended, providing that the ethics committee can grant the exemption from the informed consent rule.

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## Adaptive Learning Scale: A Comparison Between Latvian and Foreign Students of the Faculty of Medicine, University of Latvia

Maļceva Danija<sup>1\*</sup>, Brikovska Baiba<sup>2\*</sup>, Rozmane Zanda<sup>1\*</sup>, Knipše Gundega<sup>1</sup>, Krūmiņa Džanna<sup>1</sup>, Tzivian Lilian<sup>1</sup>

<sup>1</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

\*Shared first authorship

**Background.** Psychosocial competence and frustration tolerance are important characteristics of skilled medical professionals. It is reasonable to assume that medical students should have high adaptive possibilities, given the highly competitive process of application, matriculation, and completing medical school. A way to examine adaptive possibilities is the Adaptive Learning Scales (ALS) which examines relationships between learning environment and students' motivation and behaviours. This includes cognitive, affective, and behavioural components, characterized as more or less adaptive. ALS may be useful in predicting academic success in medical students.

**Aim.** The aim of this study was to investigate differences in ALS between medical students from Latvia and foreign students at the Faculty of Medicine.

**Methods.** The cross-sectional study consisted of 112 first year medical students (58% from Latvia). ALS was assessed using 11 Likert scale questions (from 1 "strongly disagree" to 5 "strongly agree"). Descriptive statistics was performed to describe the mean ALS, demographic characteristics, and country of origin of participants. Reliability of scales was checked using  $\alpha$ -Cronbach's test. We investigated relationships between the mean ALS and independent variables using conventional univariate analyses. Multiple logistic regression models were built for the association between mean ALS and demographic factors, for Latvian and foreign students individually. Odds ratio (OR) and 95% confidence intervals (CI) were presented. P values <0.05 were considered statistically significant.

**Results.** The mean age of participants was 21.0 (standard deviation, SD 3.5), most of them (67%) were female. Reliability of ALS was  $\alpha=0.80$  for students from Latvia and  $\alpha=0.71$  for foreign students. Significant univariate relationships were observed between mean ALS and family status for foreign students (Kruskal-Wallis test,  $p=0.03$ ).

In fully adjusted logistic regression model neither age, nor family status, nor country of origin were significantly associated with the mean ALS (OR=1.02 CI 0.85–1.24; OR=1.12 CI 0.76–1.67; OR=1.03 CI 0.87–1.21; and OR=0.61 CI 0.30–1.26 respectively).

**Conclusion.** Students from all countries, all ages, and any gender can be equally successful in medical studies. None of these factors affect students' adaptive learning.

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## Liver Cancer Incidence in Kazakhstan: Component Analysis

Baibusunova Aida<sup>1,2</sup>, Orazbaev Didar<sup>1,2</sup>, Kozhakhmetov Saken<sup>1,2</sup>, Igissinov Nurbek<sup>1,2,3</sup>

<sup>1</sup>Astana Medical University, Nur-Sultan, Kazakhstan

<sup>2</sup>Central Asian Institute for Medical Research, Nur-Sultan, Kazakhstan

<sup>3</sup>Eurasian Institute for Cancer Research Public Association, Bishkek, Kyrgyzstan

**Background.** According to the IARC, about 906 thousand new cases of liver cancer (LC) are registered annually in the world, with the highest incidence in Southeast Asia and West Africa.

**Aim.** The aim of presenting study is to assess the impact of various factors by using a component analysis of the dynamics of LC incidence.

**Methods.** The dynamics of the incidence of LC were studied using a component analysis to evaluate the growth of a number of cases from 2010 to 2019 throughout Kazakhstan. The first 3 components are related to changes in the population number, its age structure, the following components – with the risk of developing a malignancy.

**Results.** 8 335 new cases of LC were registered in the republic. The crude incidence rate of LC was  $5.2 \pm 0.1 / 0000$  (95% CI=5.0–5.4) and in dynamics increased from  $5.22 \pm 0.2 / 0000$  (2010) to  $5.47 \pm 0.2 / 0000$  in 2019 ( $p > 0.05$ ). The overall increase in incidence was  $0.25 / 0000$ , including due to the age structure of the population  $\sum \Delta_A = +0.61 / 0000$ , with the risk of acquiring illness  $\sum \Delta_R = -0.31 / 0000$ , and the combination of these two factors  $\sum \Delta_{AR} = -0.05 / 0000$ . According to the study results, the increase in the number of new LC cases (+160, 18.8%) could be mainly associated with the following components:

1. Population growth  $\Delta P = +114$  (+71.5%).
2. Changes in the age structure  $\Delta A = +99$  (+62.2%).
3. The combined effect of changes in the population and its age structure  $\Delta PA = +13$  (+8.3%).
4. Changes in the risk of acquiring illness  $\Delta R = -51$  (-31.7%).
5. The combined effect of changes in the risk of acquiring illness and changes in the population  $\Delta RP = -7$  (-4.3%).
6. The combined effect of changes in the risk of acquiring illness and changes in the population age structure  $\Delta RA = -9$  (-5.4%).
7. The combined effect of changes in the risk of the population to acquire illness and the population age structure  $\Delta RPA = -1$  (-0.7%).

**Conclusion.** The number of patients with LC in Kazakhstan is increasing. Component analysis indicates that the growth of patients' number mainly is due to population growth and changes in the age structure. The implementation of the results of this study is recommended in management of anticancer activities in the republic.

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## Smoking in Population With Lower Education and Manual Workers – One of the Main Challenges for Public Health in Latvia

Apinis Peteris<sup>3</sup>, Bajare Iveta<sup>1</sup>, Dzerve Vilnis<sup>1</sup>, Jegere Sanda<sup>1,2</sup>, Erglis Andrejs<sup>1,2</sup>

<sup>1</sup>Institute of Cardiology and Regenerative Medicine, University of Latvia, Riga, Latvia

<sup>2</sup>Pauls Stradiņš Clinical University Hospital, Riga, Latvia

<sup>3</sup>Latvian Academy of Sciences, Riga, Latvia

**Background.** Tobacco smoking continues to be one of the leading risk factors for cardiovascular disease (CVD) and cause of premature death globally. The 10-year risk of fatal CVD is approximately doubled in smokers. CVD risk in former smokers is in between that of current and never smokers. According to World Health Organization (WHO) data, professional support and proven cessation medications can more than double a tobacco user's chance of successful quitting.

**Aim.** To analyse the smoking prevalence data obtained from the Population Based Cross-sectional Study of Cardiovascular Risk Factors in Latvia for use in accurate health policymaking and targeted public health campaigns.

**Methods.** 4070 inhabitants of Latvia were enrolled in the study out of the initial statistical sample (6000), formed by random selection from the Housing Register of the Central Statistical Bureau (1 209 756 pers.) representing a cross-section of Latvia's inhabitants (age 25–74). Data on the socio-economic status, prevalence of smoking, diet, physical activity, health self-assessment etc. was obtained using a set of questions approved by WHO in face-to-face interviews. The data were processed using Microsoft Excel and R.

**Results.** The prevalence of current smoking on a regular basis or occasionally was found in 22.8% (n=1096) of the sample (31.5% men; 15.2% women, p<0.001). The overall prevalence of smoking for at least 1 year during lifetime was 45.3%. Education and occupation were significantly related to current smoking in both genders. Individuals with higher (1<sup>st</sup>/2<sup>nd</sup> level) education had a lower current smoking prevalence than regular smokers with primary, secondary or secondary professional education: 17.7% (14.0% men; 24.2% women; p<0.001) and 82.3% (86.0% men; 75.8% women; p<0.001), respectively. Intellectual workers had a lower current smoking prevalence than manual workers: 22.4% (17.6% men; 30.8% women; p<0.001) and 50.0% (57.8% men; 36.6% women; p<0.001), respectively. 50.7% of smokers want to stop smoking (49.9% men, 52.1% women; p<0.001).

**Conclusion.** The people with lower levels of educational attainment and manual workers have a higher risk of regular smoking than the people with higher education and intellectual workers. Significant number of people who want to quit smoking is indicated. There is an urgent need for definite changes in the public health policy. Besides the precisely targeted antismoking campaigns, algorithms how to help smokers to quit smoking are needed.

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## Association Between High Blood Pressure, Low-Density Lipoprotein Cholesterol Level and Compliance With Prescribed Treatment

Maurina Inese<sup>1</sup>, Tzivian Lilian<sup>1</sup>, Dzerve-Taluts Vilnis<sup>2</sup>, Bajare Iveta<sup>2</sup>, Jegere Sanda<sup>1,2,3</sup>, Erglis Andrejs<sup>1,2,3</sup>

<sup>1</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

<sup>2</sup>The Institute of Cardiology and Regenerative Medicine, University of Latvia, Riga, Latvia

<sup>3</sup>Pauls Stradiņš Clinical University Hospital, Riga, Latvia

**Background.** High blood pressure (BP) and cholesterol (in particular, a high level of low-density lipoprotein cholesterol (LDL)) are the major risk factors for cardiovascular disease (CVD). Both risk factors, if undiagnosed and untreated, significantly increase the risk of heart attack and CVD.

**Aim.** The aim of the study was to assess the simultaneous prevalence of high BP and high LDL cholesterol in Latvian population, and to investigate the impact of compliance with prescribed medical treatment on high LDL and BP.

**Methods.** Data of 2200 study participants with measured BP and LDL from the existing population based cross-sectional study was analysed. We evaluated the simultaneous prevalence of high BP (systolic BP $\geq$ 140 or/and diastolic BP $\geq$ 90 mmHg) and high LDL ( $\geq$ 3.00 mmol/l) in the study population. Demographic factors and compliance with prescribed cholesterol-lowering and BP medications were assessed using a self-reporting survey. We investigated relationships of LDL and high BP using conventional univariate analysis. Multiple logistic regression models adjusted for personal covariates were built for the association between LDL/BP and compliance with prescribed treatment.

**Results.** According to research, 32.9% of participants had high BP, 63.0% had high LDL, and 22.5% had high LDL and high BP simultaneously. 68.4% of participants with high BP had also high LDL, and within those who had high LDL 62.8% had also high BP ( $p<0.001$ ). According to data, 86.2% of participants used the prescribed medication regularly for treatment of BP and 72.6% – for treatment of LDL. In a fully adjusted multiple logistic regression model, a non-compliance with prescribed medical treatment significantly increased the probability of high LDL (OR = 5.89; 95% CI 3.25; 10.66,  $p<0.001$ ), while there was no statistically significant association between compliance and high BP.

**Conclusion.** High BP and high LDL simultaneously are common in the Latvian population. Non-compliance with prescribed treatment is a predictor for high LDL. It is highly important to improve patient education, compliance with medical treatment to prevent CVD risks.

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## Evaluation of Patients' Habits, Adherence to Vitamin D Substitution and Frequency of Biochemical Testing in General Practice

Voiskoviča Anna<sup>1</sup>, Ilze Skuja<sup>2</sup>

<sup>1</sup>Rīga Stradiņš University, Riga, Latvia

<sup>2</sup>Department of Family Medicine, Rīga Stradiņš University, Riga, Latvia

**Background.** In recent years, interest in the effects of D vitamin on human health, its positive influence on multiple medical conditions and the immune system has increased.

**Aim.** The aim of this study was to identify patients' habits of using D vitamin oral substitution and the frequency of taking control measurements to determine the status of D vitamin level.

**Methods.** This cross-sectional study was performed using a questionnaire administered to the patients, who take oral D vitamin supplementation via face-to-face interview with 104 respondents aged from 18 to 80 years old from October to December 2021. The serum level of 25-hydroxy vitamin D [25(OH)D] was measured. Data was analysed using IBM SPSS 26.0.

**Results.** A total of 104 patients were included in the final data analysis (female/male: 63/41, the mean age, 44.06±17.4 years). The data analysis has revealed the following main sources that stimulate patients to start taking D vitamin supplementation: family physician (45; 43.3%), other medical specialist (9; 8.7%), both (14; 13.5%). More than half of respondents were taking oral D vitamin supplementation in the morning (70; 67.3%), 37 of whom during or shortly after their breakfast. However, there was no statistically significant correlation in D vitamin level and the time when supplementation was taken ( $p>0.05$ ). The majority of respondents ( $n=54$ ; 51.9%) reported their adherence as moderate, 34 respondents (32.7%) as high and 16 persons (15.4%) as low. There was moderate positive correlation between adherence level and D vitamin level in serum ( $r=0.475$ ;  $p<0.001$ ). Frequency of biochemical testing of D vitamin level in serum was: annually ( $n=42$ ; 40.4%), biennially ( $n=31$ ; 29.8%), semi-annually ( $n=16$ ; 15.4%), triennially ( $n=15$ ; 14.4%). The average serum 25(OH)D level was 33.38±15.25 (range, 9.2–129.7). Vitamin D deficiency ( $<30$  ng/ml) was noted in 46.15% of patients, 51.9% had levels  $>30$  ng/ml, 2 of whom had elevated level of D vitamin  $>80$  ng/ml. Preferred formulation was liquid form for 60.6% of participants, and preferred dosage frequency was weekly for 59.6% of participants.

**Conclusion.** A timely monitoring of D vitamin level is recommended in persons who take oral D vitamin supplementation, especially in the first year of therapy, and it is preferable to take supplements during breakfast in the morning. Adherence to recommendations, including taking control measurements of D vitamin level in serum, given by general practitioner is essential in ensuring safe and effective treatment of vitamin D deficiency.

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## Patient Awareness of Influenza Vaccination in GP Practices During COVID-19 Pandemic Year 2021/2022

Černobajeva Ludmila<sup>1</sup>, Ūdre Marta<sup>1</sup>, Mitule Baiba<sup>2</sup>

<sup>1</sup>Riga Stradiņš University, Riga, Latvia

<sup>2</sup>General Practitioner's Practice of Baiba Mitule, Riga, Latvia

**Background.** Influenza is a highly contagious airborne disease that causes seasonal epidemics, manifests with variable degrees of symptoms and sometimes leads to hospitalization and death. As the flu season approaches, the best prevention is getting an influenza vaccine. State-funded influenza vaccines are offered to certain groups and this has proven to increase the number of people who are vaccinated, especially during the COVID-19 pandemic, which would reduce incidence and morbidity.

**Aim.** To determine patients' awareness and responsiveness to influenza vaccination at general practitioners' practices during the COVID-19 pandemic.

**Methods.** Overall, 336 patients – 215 adults and 121 children's parents – from two GP practices participated in quantitative cross-sectional research which was performed by anonymously filling the questionnaire before an appointment. Statistical data was processed by IBM SPSS and Microsoft Excel.

**Results.** From 215 adults with an average age 46.06 and the median 42 years, 74.88% were women. Out of 121 children 58.68% got vaccinated. A statistically significant association was established between adult age and vaccination status ( $p=0.004$ ) and children age and vaccination status ( $p=0.009$ ). There were 40.47% adult patients with chronic illnesses and a statistically significant association between vaccination status and chronic illnesses was established ( $p=0.003$ ). There was a statistically significant association between this year and previous year vaccination status among adults ( $p<0.001$ ) and children ( $p<0.001$ ). Among adults 75.81% and among children's parents 85.12% know about yearly vaccination and 54.60% of those adults and 63.11% of children got vaccinated this season. There was a statistically significant association between the acknowledgment of yearly vaccination and vaccination status this year among adults ( $p<0.001$ ) and children ( $p=0.022$ ). The most prevalent reason for vaccination was the fear of feeling ill – 74.50% adults and 69.01% children. Primarily, patients received information about vaccination against influenza from their general practitioner (37.20% adults, 57.02% children). Most patients are confident in the efficiency of influenza vaccines (58.60% adults, 65.30% children). There were 12 pregnant women participating in the research, from whom 6 were vaccinated against influenza and 11 – against COVID-19, mostly with Comirnaty vaccine (90.91%).

**Conclusion.** Almost half of the participants got vaccinated against influenza this season and almost all adults – against COVID-19. Patients with chronic illnesses, over 65 years of age and children younger than 2 years of age tended to get vaccinated this season. General practitioners have a big role in acknowledgment and future decisions of their patients, however, information about influenza prevention must be disseminated more often.

## Pregnancy-Related Sickness Absence and the Cost of Lost Productivity in Poland

Genowska Agnieszka<sup>1</sup>, **Strukcinskaite Vaiva**<sup>2</sup>, Strukcinskiene Birute<sup>3</sup>  
<sup>1</sup>Department of Public Health, Medical University of Bialystok, Bialystok, Poland  
<sup>2</sup>Faculty of Health Care, Vilnius University of Applied Sciences, Vilnius, Lithuania  
<sup>3</sup>Faculty of Health Sciences, Klaipeda University, Klaipeda, Lithuania

**Background.** Health problems and complications during pregnancy are the most common cause of sickness absence in the working population in Poland. However, information about the economic burden of pregnancy-related sickness absence in Central and Eastern Europe is limited.

**Aim.** We estimated indirect costs associated with losses in productivity, because of sickness absence due to pregnancy and its changes in Poland.

**Methods.** Data on sick leave durations due to pregnancy, childbirth, and the puerperium (codes O00–O99 in ICD-10) was obtained from the Social Insurance Institution. The costs of lost productivity were estimated based on the measure of gross value added. Joinpoint regression analysis was performed to analyse time trends over the 2010–2019.

**Results.** Estimated losses in productivity due to pregnancy-related absenteeism in 2019 accounted for 0.8% of gross domestic product (GDP), which is 4.26 billion euros; including 3.4 billion euros was for maternal care incurred by conditions predominantly related to pregnancy. The highest overall costs of sickness absence were used for the age groups of 30–39 years (2.25 billion euros) and 20–29 years (1.84 billion euros). In 2010–2019, total cost of lost productivity related to sickness absence due to pregnancy increased by 5.3%/year (95% CI: 4.6, 6.0),  $p < 0.05$ . Faster increase in cost of loss productivity was observed in the age group of 30–39 years – by 7.1%/year (95% CI: 5.9, 8.3),  $p < 0.05$ , and in the age group of 40–49 years by 10.0%/year (95% CI: 8.7, 11.3),  $p < 0.05$ . Among pregnant women in the age group below 30 years, the changes were significant, but their tempo was slower).

**Conclusion.** Pregnancy was a significant economic burden and caused the loss of productivity costs related to sick leave in Poland. Increasing sickness absence due to pregnancy in older mothers indicates the occurrence of medical complications and the need for further interventions. Estimating indirect costs of pregnancy could help health policy makers prioritize the effective treatment of women in reproductive age and prevention measures.

**Acknowledgements.** The authors declare the absence of conflict of interest.

## ANESTHESIOLOGY, REANIMATOLOGY & INTENSIVE CARE

### Changes of Regional Cerebral Oxygen Saturation Using Near Infrared Spectroscopy During Carotid Endarterectomy

Česnokovs Aleksejs<sup>1,2</sup>, Stepanovs Jevgēņijs<sup>2</sup>, Stengrevica Nataļja<sup>2</sup>, Ročāns Rihards Pēteris<sup>2</sup>, Ozoliņa Agnese<sup>2</sup>

<sup>1</sup>University of Latvia, Riga, Latvia

<sup>2</sup>Riga Eastern University Hospital, Riga, Latvia

**Background.** During carotid endarterectomy (CEA), surgery clamp period of one of the carotid arteries can lead to cerebral hypoxia. Cerebral oximetry provides real-time measurements of regional cerebral oxygen saturation (rSO<sub>2</sub>) in non-invasive, continuous manner.

**Aim.** The aim of the study was to explore changes in rSO<sub>2</sub> and to find the main factors affecting rSO<sub>2</sub> values during CEA surgery.

**Methods.** The study includes 33 (16 males) patients undergoing CEA, with average age 69.5 years (CI 95 66.3–76.7). rSO<sub>2</sub> was monitored by INVOS 7100. rSO<sub>2</sub> was fixed at baseline (t<sub>0</sub>), prior to surgical carotid artery clamping (t<sub>1</sub>), while cross-clamping (t<sub>2</sub>) and after re-established blood flow (t<sub>3</sub>). Data was analysed with SPSS v22.0.

**Results.** Results showed that at t<sub>0</sub> median, rSO<sub>2</sub> was 65% on operating side and 64% on non-operating side. At t<sub>1</sub> median rSO<sub>2</sub> was 71% on operation side, and 72% non-operating side. At t<sub>2</sub> median rSO<sub>2</sub> on operation side was 60% and non-operated side 73%. At t<sub>3</sub> median rSO<sub>2</sub> on operation side was 72% and 72% on non-operated side.

We found that rSO<sub>2</sub> at (t<sub>0</sub>) on the non-operative side was higher for males as for females 66.5±5.75 vs 62±8.5; p=0.021.

We found negative correlation between age and the drop of rSO<sub>2</sub> at t<sub>2</sub> on the non-operated side (r=-0.356, p=0.042). Moreover, for age group <73 years, the median rSO<sub>2</sub> difference between t<sub>2</sub>-t<sub>1</sub> was 2 (IQR 5), but for age group ≥73, it was 3 (IQR 7.75) (p=0.012).

In patients with hyperlipidaemia, there was decrease of rSO<sub>2</sub> at (t<sub>3</sub>) by 1.08% (-3.64–1.46). But without hyperlipidaemia, we observed increased of rSO<sub>2</sub> at (t<sub>3</sub>) by 3.1% (-0.43–6.62); p=0.038.

Mean arterial pressure (MAP) negatively correlated with an increase of rSO<sub>2</sub> (t<sub>3</sub>) (r=-0.49, p=0.004). The cut-off value of MAP was 100 mmHg. The median rSO<sub>2</sub> increase is by 14±17 if MAP<100 mmHg and by 5.5±11.75 if MAP≥100 mmHg; p=0.019.

**Conclusion.** Patients during CEA do have decrease in rSO<sub>2</sub>. Values of rSO<sub>2</sub> are mainly affected by sex, age, hyperlipidaemia, and MAP. In patients without hyperlipidaemia, rSO<sub>2</sub> rising after re-established blood flow is better. Older patients, over 73 years of age, have a more significant rSO<sub>2</sub> drop on non-operated side. After re-established blood flow, MAP≥100 mmHg worsens rSO<sub>2</sub> rise. rSO<sub>2</sub> can be useful in intraoperative monitoring during CEA.

**Acknowledgements.** The authors declare the absence of conflict of interest and funding.

## Preanesthetic Vagotonia as a Potential Risk Factor for Sinus Bradycardia and Arterial Hypotension During Induction of General Anaesthesia with Propofol and Fentanyl and After Endotracheal Intubation

Feghiu Iuliana<sup>1</sup>, Tăzlăvan Tatiana<sup>1,2</sup>

<sup>1</sup>Nicolae Testemițanu State University of Medicine and Pharmacy, Chișinău, Republic of Moldova

<sup>2</sup>Institute of Emergent Medicine, Chișinău, Republic of Moldova

**Background.** It is well known that induction of general anaesthesia with propofol is associated with sinus bradycardia and arterial hypotension which can be dangerous in high-risk patients. Prediction of hemodynamic changes during induction and after endotracheal intubation would be beneficial for the elaboration of a management strategy for patients in the preoperative period.

**Aim.** The aim of the study was to explore if preanesthetic heart vagotonia is a predictor of sinus bradycardia and arterial hypotension during induction of general anaesthesia with propofol combined with fentanyl and after endotracheal intubation.

**Methods.** We conducted a prospective, observational study with approval of Ethic Committee of the Nicolae Testemițanu State University of Medicine and Pharmacy. A total of 47 patients scheduled for elective surgery were enrolled in the study. The inclusion criteria were patients aged >18 years old undergoing elective surgeries. The exclusion criteria from the study were cardiac arrhythmia and pregnancy. Autonomic nervous system activity was assessed by the analysis of heart rate variability parameters obtained from Holter ECG recordings. A LF/HF ratio of <1.0 was considered as parasympathetic dominance of the heart. General anaesthesia was induced with propofol 2.5 mg/kg and fentanyl 1.5 mcg/kg. Endotracheal intubation was performed after myorelaxation with atracurium 0.5 mg/kg. Arterial blood pressure and heart rate were measured every minute during induction and after tracheal intubation. Sinus bradycardia was defined as heart rate <60 bpm. Arterial hypotension was defined as SBP < 90 mmHg.

**Results.** Preanesthetic vagotonia was significantly related to sinus bradycardia [RR 7.7 (95% CI 1.9–29.7);  $p < 0.0001$ ] with Se–0.89 (95% CI 0.65–0.99) and Sp–0.72 (95% CI 0.53–0.87) and arterial hypotension [RR 6.2 (95% CI 2.1–18.6);  $p < 0.0001$ ] with Se – 0.83 (95% CI 0.58–0.96) and Sp–0.79 (95% CI 0.60–0.92) during induction of general anaesthesia with propofol and fentanyl. Preanesthetic vagotonia also represented a risk factor for sinus bradycardia associated with arterial hypotension [RR 3.8 (95% CI 1.6–8.9);  $p < 0.007$ ] with Se–0.72 (95% CI 0.47–0.90) and Sp–0.79 (95% CI 0.60–0.92) after endotracheal intubation.

**Conclusion.** Preanesthetic vagotonia is a risk factor for development of sinus bradycardia and arterial hypotension during induction of general anaesthesia with propofol combined with fentanyl and after endotracheal intubation.

**Acknowledgements.** The authors declare the absence of conflict of interest.

## Survey of Choice of General Anaesthetic Agents in Latvia

Birkhans Kaspars<sup>1</sup>, Kazūne Sigita<sup>2,3</sup>

<sup>1</sup>University of Latvia, Riga, Latvia

<sup>2</sup>Rīga Stradiņš University, Riga, Latvia

<sup>3</sup>Hospital of Traumatology and Orthopaedics, Riga, Latvia

**Background.** The environmental and financial impacts of anaesthesia, including those of anaesthetic gases, are increasingly recognised. Strategies to reduce the adverse environmental costs of anaesthesia include choice of agent and fresh gas flows. The current preferences of Latvian anaesthetists are unknown.

**Aim.** Authors aimed to identify the relative usage of, and reasons for, different general anaesthetic agents, the frequency of the use of N<sub>2</sub>O in general anaesthesia and the lowest tolerated maintenance fresh gas flow. We were particularly interested in knowing whether anaesthetists considered environmental and financial factors when making choices about what general anaesthetic agent they used.

**Methods.** Authors surveyed Latvian anaesthetists with the online platform “Survey Monkey”. We calculated proportions and percentages for all quantitative results. For proportions we estimated 95% confidence intervals (CIs).

**Results.** The survey was answered by 88 anaesthetists. Sevoflurane was preferred by 64/88 (77%, 95% confidence interval (CI) 62%–81%), followed by propofol, 6/88 (8%, 95% CI 3%–15%), desflurane 2/88 (3%, 95% CI 0%–9%) and isoflurane 2/88 (3%, 95% CI 0%–9%). Faster induction/awakening times was the most common reason given (48/88 (46%, 95% CI 34%–57%) for sevoflurane and 4/6 (67%, 95% CI 24%–94%) for propofol). Nitrous oxide was used by 41/88 (47%, 95% CI 36%–57%) of respondents in 0–30% of general anaesthetics. Low fresh gas flow rates for sevoflurane were used by 70/88 (80%, 95% CI 69%–87%) Automated end-tidal control was used by 28/88 (32%, 95% CI 22%–42%).

**Conclusion.** A standard general anaesthetic used in Latvia is with sevoflurane, at flows of 1–2 litres/minute and without N<sub>2</sub>O. Most respondents would choose a general anaesthetic agent according to familiarity and faster induction/awakening times, although uncommonly (7%) for environmental reasons.

## Causes of Suboptimal Preoxygenation before Tracheal Intubation in Elective and Emergency Abdominal Surgery

Kalinauskaitė Miglė<sup>1</sup>, Kauzonas Evaldas<sup>2</sup>, Miškinytė Sigutė<sup>1</sup>, **Bubulytė Silvija**<sup>1</sup>, Kontrimavičiūtė Eglė<sup>3</sup>

<sup>1</sup>Faculty of Medicine, Vilnius University, Vilnius, Lithuania

<sup>2</sup>Karolinska University Hospital, Function of Perioperative Medicine & Intensive Care, Stockholm, Sweden

<sup>3</sup>Clinic of Anaesthesiology and Intensive Care, Institute of Clinical Medicine, Faculty of Medicine, Vilnius University, Vilnius, Lithuania

**Background.** Preoxygenation is performed prior to tracheal intubation in order to reduce the risk of arterial desaturation and to prolong the period of safe apnoea. The common methods of preoxygenation are mask ventilation with 100% O<sub>2</sub> for 3–5 minutes or, alternatively, asking the patient to take 8 deep breaths in 1 minute. Preoxygenation may be unsuccessful due to a variety of factors that influence mask ventilation (lack of teeth, presence of facial hair, obesity, snoring, a small mouth) and by additional factors such as the patient's comorbidities and the severity of the patient's condition in emergency surgery.

**Aim.** To evaluate the influence of the most commonly reported risk factors of suboptimal preoxygenation and the effectiveness of preoxygenation in patients undergoing elective and emergency surgery.

**Methods.** A prospective study was conducted at Vilnius University Hospital Santaros Klinikos. Patients undergoing general anaesthesia for elective or emergency abdominal surgery were invited to participate in the study. Preoxygenation was performed using the standard method of mask ventilation with 6 l/min of 100% oxygen for 5 minutes and EtO<sub>2</sub> was documented in 30 second increments. Preoxygenation was considered optimal when EtO<sub>2</sub> values of 90% or more were achieved within 5 minutes.

**Results.** 37 patients were included in the study, of which 18 (48.6%) underwent emergency surgery. 17 patients (46%) did not achieve optimal preoxygenation with EtO<sub>2</sub> ≥ 90%. There were more patients in the elective surgery group that did not achieve EtO<sub>2</sub> ≥ 90% (63% vs 27.7% in the emergency surgery group, Phi = -0.355, p = 0.031). The success of preoxygenation did not depend on age or BMI (p = 0.179; 0.681 respectively), nor on higher Mallampati or ASA scores (p = 0.574; 0.396). The number of factors known to hinder preoxygenation present in our study did not differ significantly between the groups (p = 0.987). No single risk factor was more prevalent in the group of suboptimally preoxygenated patients compared to the optimal preoxygenation group.

**Conclusion.** Almost half of the patients in this study did not achieve optimal preoxygenation and this was more common in elective surgery patients. None of the evaluated risk factors for suboptimal preoxygenation were more prominent in patients who did not receive optimal preoxygenation.

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## Cerebral Oximetry in Patients Undergoing Shoulder Replacement Surgery

Mackevičs Dāvis<sup>1</sup>, Golubovska Iveta<sup>1,2</sup>, Radziņš Mārcis<sup>2</sup>, Vugulis Aigars<sup>2</sup>, Zande Sabīne<sup>1</sup>,  
Miščuks Aleksejs<sup>1,2</sup>

<sup>1</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

<sup>2</sup>Hospital of Traumatology and Orthopaedics, Riga, Latvia

**Background.** Peripheral capillary oxygen saturation (SpO<sub>2</sub>) may not reflect oxygen saturation in the brain, while the mean arterial blood pressure (MAP) does not reflect brain perfusion pressure. Non-invasive measuring of intracranial oxygen saturation with a near-infrared light sensor can provide a more accurate picture of a patient's hemodynamics.

**Aim.** Evaluate oxygen saturation in the brain during shoulder replacement surgery in beach chair position. Determine if there are cerebral desaturation events (CDE) during anaesthesia and surgery, determine in which phase of the operation it is possible.

**Methods.** This prospective, observational study after Ethics Committee approval was conducted at the Hospital of Traumatology and Orthopaedics. A cohort of 24 patients received combined Pl. Brachialis and endotracheal anaesthesia and their cerebral regional oxygen saturation index (rSO<sub>2</sub>) on right and left foreheads, MAP, body mass index (BMI), oxygen reserve index (ORi), oxygen saturation (SpO<sub>2</sub>) were recorded and compared.

Hypotension was defined as the occurrence of any of the following: >30% decline in MAP from the baseline or MAP <66 mmHg.

Cerebral desaturation was defined as a 20% decrease in rSO<sub>2</sub> from baseline or below 55.

Measurement intervals: Before anaesthesia induction, postinduction/presitting were used as baseline, after getting in the sitting position, after cementing and after extubation. Calculations were made using SPSS software (version 14.0.2; SPSS Inc).

**Results.** Hypotension occurred in nine patients, CDE occurred in three patients.

There is a moderately strong correlation between rSO<sub>2</sub> reduction and BMI (Pearson  $r=0.53$ ,  $p$ -value 0.079.)

There is a statistically significant moderately close correlation between MAP after sitting and rSO<sub>2</sub> after sitting (Spearman  $r_s=0.464$ ,  $p=0.030$ ).

There is a statistically significant moderately close correlation between MAP after intubation and rSO<sub>2</sub> ( $r_s=0.459$ ,  $p=0.032$ )

There is a statistically significant moderately close correlation between MAP before intubation and rSO<sub>2</sub> at the end of surgery ( $r_s=0.511$ ,  $p=0.015$ ).

**Conclusion.** One in three patients who experienced hypotension also experienced CDE. rSO<sub>2</sub> fluctuations correlated with MAP. A correlation was observed between BMI and rSO<sub>2</sub> decline, suggesting the use of BMI as a prognostic indicator for a possible decline.

**Acknowledgements.** The authors declare the absence of conflict of interest.

## Comparison Between Obesity and Oxygen Reserve Index in Patients Undergoing Shoulder Replacement Surgery in Beach Chair Position

Mackevičs Dāvis<sup>1</sup>, Golubovska Iveta<sup>1,2</sup>, Radziņš Mārcis<sup>2</sup>, Vugulis Aigars<sup>2</sup>, Zande Sabīne<sup>1</sup>, Miščuks Aleksejs<sup>1,2</sup>

<sup>1</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

<sup>2</sup>Hospital of Traumatology and Orthopaedics, Riga, Latvia

**Background.** Elevated Body mass index (BMI) is associated with difficulty in ventilating the patient and providing adequate oxygenation. Oxygen reserve index (ORi) can be used to provide insight into ventilated patients oxygen reserves.

**Aim.** The goal was to evaluate ORi during shoulder replacement surgery, and assess whether BMI can affect the ORi and at which stage of the operation the risk of ORi reduction is greatest.

**Methods.** This prospective, observational study was conducted at the Hospital of Traumatology and Orthopaedics after approval by Ethics Committee. A cohort of 22 patients received combined Pl. Brachialis and endotracheal anaesthesia, and their ORi were compared with BMI to draw attention to the obese population.

Patients were divided into two BMI groups: group I BMI < 30 and group II BMI > 30.

Measurement intervals: Before anaesthesia induction, postinduction/presitting were used as baseline, after getting in the beach chair position, after cementing and after extubation. Calculations were made using SPSS software (version 14.0.2; SPSS Inc.).

**Results.** In the group I (n=9) the median value was 0.09 (Q1; Q3 = 0 to 0.42).

In the group II (n=13) the median value was 0.34 (Q1; Q3 = 0.05 to 0.49).

There was no statistically significant difference in the distribution of ORi values between groups I and II (Mann-Whitney U test, p=0.357).

There was no statistically significant correlation between BMI and ORi values, so further effects were not tested.

**Conclusion.** The distribution of ORi was the same across categories of BMI groups. In this study, BMI did not affect ORi, but the pilot study will continue to provide statistically significant data.

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## Factors Associated With Functional Outcomes in Status Epilepticus Patients

Kropaitytė Monika<sup>1</sup>, Balčiūnienė Neringa<sup>2</sup>

<sup>1</sup>Lithuanian University of Health Sciences, Kaunas, Lithuania

<sup>2</sup>Kaunas Clinics, Hospital of Lithuanian University of Health Sciences, Kaunas, Lithuania

**Background.** Status epilepticus is one of the most dangerous neurological emergencies that require immediate treatment to prevent further neurological damage due to high mortality (ranging from 7.6 to 39%). Glasgow outcome scale (GOS) is considered a valid, practical and reliable tool to measure functional outcomes of patients with status epilepticus. Determining the factors that may influence those outcomes and recognizing them early may help reduce in-hospital mortality for status epilepticus patients and lead to better outcomes.

**Aim.** The aim of this study was to identify the factors influencing functional outcomes of patients with status epilepticus.

**Methods.** A retrospective chart review of 47 patients with status epilepticus who were admitted to Hospital of Lithuanian University of Health Sciences Kaunas Clinics Neurosurgical intensive care unit (NICU) during 2016–2020 was performed. We analysed age, gender, duration of mechanical ventilation (MV), intensity of treatment, presence of infection, length of stay in NICU and in the hospital, circumstances of the seizure (started in-hospital or not). The functional outcomes were determined using GOS. The scores of 4–5 points were considered a “good outcome” for a patient. Statistical analysis was performed with IBM SPSS Statistics 27. The Chi-square and Fisher’s exact tests were used to determine the relationship between variables. A significance level of 0.05 was chosen for testing the statistical hypotheses.

**Results.** The data of 47 patients were analyzed. The mean age was  $50.74 \pm 17.062$  years (range 20–82), 59.6% (n=28) were males and 40.4% (n=19) were females. Average length of stay was  $18.86 \pm 15.011$  days (range 1–59), average NICU time was  $4.96 \pm 6.769$  days (range 0–35). 87.2 % of seizures were generalized-convulsive. Mortality was 8.511%. 72.3% (n=34) of the patients had good outcomes. Presence of infection was related to worse functional outcomes ( $\chi^2=6.546$ ,  $p=0.011$ ). Shorter hospitalization time in NICU ( $\chi^2=5.009$ ,  $p=0.025$ ) as well as shorter duration of MV ( $p=0.008$ ) were associated with better GOS scores. Relationships between functional outcomes and intensity of treatment, patients’ age, circumstances of the seizure or type of seizure were not statistically significant ( $p>0.05$ ).

**Conclusion.** Factors influencing worse outcomes were presence of infection during hospitalization in NICU, longer duration of mechanical ventilation, as well as longer length of stay in NICU. Other factors did not have a statistically significant relationship with functional outcomes of the patients.

**Acknowledgements.** The authors declare the absence of conflict of interest.

## **Analgesia Nociception Index Effectiveness for Acute Pain Detection in Arthroscopic Shoulder Surgery**

**Zande Sabine**<sup>1</sup>, Golubovska Iveta<sup>1,2</sup>, Miscuks Aleksejs<sup>1,2</sup>, Bogdanovs Arturs<sup>2</sup>, Radzins Marcis<sup>2</sup>, Mackevics Davis<sup>1</sup>

<sup>1</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

<sup>2</sup>Department of Anaesthesiology, Hospital of Traumatology and Orthopaedics, Riga, Latvia

**Background.** Analgesia Nociception Index (ANI) is a new method used to measure acute pain while the patient is unconscious. ANI detection principle is monitoring heart rate variability by using electrocardiography. Technology uses algorithms analysing R-R complexes and breathing rate therefore assesses patient condition and his sympathetic and parasympathetic nervous systems activity. The range of ANI values is from 0 to 100 and the higher the ANI value, the higher the quality of analgesia and thus the patient's comfort level. This innovative technology allows doctors to create an individual technique for dosing analgesic drugs to every patient.

**Aim.** The aim of this pilot study was to determine the usefulness of ANI for pain intensity during shoulder arthroscopic surgery. It was hypothesized that ANI may be useful for better acute pain detection.

**Methods.** The pilot study was conducted in "Hospital of Traumatology and Orthopaedics" after Ethics Committee approval in August 2021. All twelve patients were under general anaesthesia and were divided into two groups – with and without plexus brachialis block. Adequate analgesia during surgery and the postoperative period was provided to all patients. To control group analgesia during surgery was provided with opioids and postoperative period with plexus brachialis block. ANI was monitored all the surgery time – from ET intubation to extubation.

**Results.** ANI was lower in five out of seven fixed periods in the control group "Block after surgery". The median of ANI value at surgeries 30<sup>th</sup> minute were lower (51.5) compared with the group "Block before surgery" (67) – which means analgesia with opioids at this time of period were poorer – and ANI effectively detected that. ANI values at both groups were variable with 95% CI [42.88–85.12]) "Block before surgery" and (95% CI [40.03–73.97]) "Block after surgery" because of variable pain intensity manipulations during surgery.

**Conclusion.** In pilot study, the tendency is observed and it has been concluded that ANI technology at pain detection works effectively and could be a potentially useful tool for measurement of acute pain. Research will continue because a much broader study is needed to obtain statistically significant results.

**Acknowledgments.** The authors declare the absence of conflict of interest.

## Near-Infrared Spectroscopy as a Predictor of Cerebral Deterioration: Case Series of 11 Patients with Aneurysmal Subarachnoid Haemorrhage

Buce-Satoba Ieva<sup>1,2</sup>, Rozkalne Daina<sup>1</sup>, Mamaja Biruta<sup>1,2</sup>, Krūmina Gaida<sup>1,2</sup>, Ozolina Agnese<sup>1,2</sup>

<sup>1</sup>Riga East Clinical University Hospital, Riga, Latvia

<sup>2</sup>Riga Stradiņš University, Riga, Latvia

**Background.** In patients with aneurysmal subarachnoid haemorrhage (aSAH), an early detection of the beginning of cerebral vasospasm (CV) is crucial to prevent ischemic stroke. Near-infrared spectroscopy (NIRS) is a non-invasive, promising, bedside monitoring method of regional cerebral oxygen saturation (rSO<sub>2</sub>) and can help early detection of hypoperfusion of the brain.

**Aim.** The aim of this study was to evaluate the effectiveness of NIRS in detecting early brain deterioration as a sign of CV.

**Methods.** For the first time, NIRS was applied to 11 patients (7 females) with aSAH hospitalised in the Intensive Care Unit of Riga East University Hospital (Riga, Latvia). NIRS was continuously monitored with INVOS 5100 Medtronic (Covidien), started within the first 48 hours after ictus and continued up to 7 days.

**Results.** The mean age of the cohort was 60±9 years. All patients had at least one risk factor (primary arterial hypertension, atherosclerosis, diabetes mellitus, smoking, chronic alcohol intake, obesity), but most or 45.5% had two. The amount of SAH on computer tomography scan was Fisher III for 2 and Fisher IV for 9 patients. The median Glasgow Coma scale was 10 points (5–15).

The mean rSO<sub>2</sub> at baseline (BL) was 72±6% for left, 73±6% for right side. CV occurred in three patients within 7 days, and all patients had a reduction of rSO<sub>2</sub>, while two reached >20% decreases from BL. To one patient with CV experienced brain death with continuous rSO<sub>2</sub> reduction. One patient experienced cerebral stroke without detected reduction of rSO<sub>2</sub>. In another patient NIRS was useful to detect intracerebral hematoma after endovascular embolization, when rSO<sub>2</sub> dropped >20% from BL (left 77 to 55% and right 71 to 53%), and continued to decrease. Mortality was 3/5 vs 3/6 and the median hospitalisation was 8 vs 15 days in patients with changed NIRS vs without.

**Conclusion.** NIRS continuous bedside monitoring helped early detect significant cerebral deterioration in 3 out of 5 aSAH patients. Our first experience shows that NIRS seems to be a promising method for early detection of cerebral deterioration using a clinical course in patients after aSAH.

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## The Effectiveness of Modified Multimodal Analgesia Protocol in Total Knee Replacement

Lebedeva Veronika<sup>1</sup>, Ivančika Andriana<sup>1</sup>, Golubovska Iveta<sup>1,2</sup>, Miscuks Aleksejs<sup>1,2</sup>

<sup>1</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

<sup>2</sup>Hospital of Traumatology and Orthopaedics, Riga, Latvia

**Background.** Knee replacement surgery is one of the most painful orthopaedic surgeries. Postoperative pain management is a complex and challenging process. Multimodal analgesia protocol is the main tool in pain treatment, which consists of opioid and non-opioid analgesics and procedures. Modification and improvement of multimodal analgesia protocol is necessary for optimal pain control. The main goal of pain management is to optimise pain control, using different techniques and to reduce opioid consumption.

**Aim.** The aim of this study was to analyse postoperative pain after knee replacement surgery.

**Methods.** Retrospective cross-section study analyses patient data between January 2018 and December 2021. All patients underwent knee replacement procedures and met inclusion and exclusion criteria. All patients received multimodal perioperative approach and were asked about pain intensity four times a day. Pain level was evaluated by Visual Analogue Scale (VAS) and categorized: 0–3.9 mild pain, 4–6.9 moderate pain, 7–10 severe pain.

**Results.** The study includes 59 patients (12 males and 47 females); 44% of patients used femoral catheters. The opioid consumption was in the range from 8–100 mg (median 20 mg per patient), but 8 patients did not receive any opioids. Pain intensity on POD-1 (postoperative day 1): 25 patients (42.4%) had mild pain, 23 patients (39%) moderate pain, and 11 patients (18.6%) severe pain; on POD-2: 27 patients (45.8%) had mild pain, 22 patients (37.3%) moderate pain and 10 patients (16.9%) severe pain. The average pain intensity of all patients:  $4.2 \pm 2.3$  (on surgery day);  $4.0 \pm 2.2$  (POD-1),  $4.0 \pm 2.3$  (POD-2). Comparison with M. Shokouhi et al (2018) research results:  $4.7 \pm 1.7$  (D0),  $3.6 \pm 1.5$  (D1),  $2.8 \pm 1.4$  (D2).

**Conclusion.** Despite multimodal approach, patients still experience a great deal of pain after knee replacement surgery. Mostly the pain is moderate and severe, this means that pain management needs to be reviewed. Pain intensity is decreased only on the day of surgery.

## Analysis of Factors Affecting COVID-19 Mortality

Ūdre Sintija<sup>1,2</sup>, Aleksejeva Marija<sup>1</sup>, Ročāns Rihards Pēteris<sup>2,3</sup>, Birnbaums Jānis Verners<sup>2,3</sup>, Tsarevskaya Anastasija<sup>3</sup>, Saba Ingrīda<sup>2</sup>, Šuba Oļegs<sup>2</sup>, Ozoliņa Agnese<sup>2,3</sup>

<sup>1</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

<sup>2</sup>Riga East Clinical University Hospital, Riga, Latvia

<sup>3</sup>Riga Stradiņš University, Riga, Latvia

**Background.** Mortality of COVID-19 patients can be affected by many factors, including the patient's age, co-morbidities, hospitalisation day, treatment strategy and others. Nevertheless, the influence of variables associated with local population and hospital guidelines have yet to be determined.

**Aim.** The aim of this study was to analyze factors affecting mortality of COVID-19 intensive care patients.

**Methods.** This retrospective cohort includes 658 COVID-19 Intensive care Unit (ICU) patients, hospitalized in Riga East Clinical University Hospital from January 2020 to November 2021. Data was obtained from the statistical department and manually extracted from electronic data systems according to protocol. Statistical analysis was performed using IBM SPSS 22.0. Differences in data distribution between the groups were evaluated using Mann-Whitney U or Pearson's chi-square tests.

**Results.** Totally, 658 patients were analysed and 390 (59.3%) patients died and 268 (40.7%) survived. In the first wave, n=78 (January–August 2020), in the second wave, n=268 (November 2020–July 2021), in the third wave, n=312 (August–November 2021) patients. The highest mortality (64.7%) was observed in the third wave; p=0.001. Most of died patients presented acute respiratory distress syndrome (68.8%) when compared with survivors, 291 vs 132; p=0.001. Survived patients were younger 58.5±13.2 vs 64.9±13; p=0.001. Pearson's chi-squared test revealed that mortality was affected by coronary heart disease, primary arterial hypertension, and chronic renal disease; 0.013 and 0.001, respectively. Of all the ICU COVID-19 patients, 68% received mechanical lung ventilation. These latter had a higher mortality rate – 72% vs 31%; p<0.001. Tracheostomy was performed in 66 (10%) of cases. Surprisingly, those who had tracheostomy had higher rates of being discharged from ICU 49 vs 19; p=0.039. Remdesivir did not affect mortality (p=0.47). The most often observed complications in those who died were sepsis (87.8%), multiorgan dysfunction (90.6%), acute renal failure (85.9%) and pulmonary artery thromboembolism (75.4%).

**Conclusion.** The highest mortality in COVID-19 ICU patients was observed in the third wave. The mortality was mainly influenced by development of complications (sepsis, PATE, ARF), particularly, in patients with coronary heart disease, primary arterial hypertension, and chronic renal disease. Remdesivir did not affect the mortality significantly. Patients undergoing tracheostomy are much more likely to be successfully discharged from the ICU back to wards.

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## OPHTHALMOLOGY

### Structural and Pathophysiological Changes of the Optic Nerve in Patients With Primary Open-Angle Glaucoma After Traditional Trabeculectomy Surgery

Briede Elīza<sup>1,2</sup>, Baumane Kristīne<sup>1,2</sup>

<sup>1</sup>University of Latvia, Riga, Latvia

<sup>2</sup>Department of Ophthalmology, Riga East Clinical University Hospital, Riga, Latvia

**Background.** Primary open-angle glaucoma is a significant public health issue. One of the main features of glaucoma is the asymptomatic onset of the disease. Therefore, patients often consult with the doctor with substantial functional and structural changes of the optic nerve. It has been found that lower initial macular and peripapillary vascular density is associated with faster progression of the retinal nerve fibre layer defect. Studies have shown that peripapillary retinal microvasculature improves with the decrement of intraocular pressure. However, the exact effect on the deep microvasculature of the optic nerve disc is still unclear.

**Aim.** To evaluate and compare the structural and perfusional changes of the optic nerve in patients with primary open-angle glaucoma after trabeculectomy surgery.

**Methods.** A prospective study was carried out. The study included a total of 21 eyes (21 patients) requiring traditional trabeculectomy due to uncompensated intraocular pressure during the period of this study. On the day before the planned operation and six months after the procedure, all patients underwent examination of best-corrected visual acuity, intraocular pressure, ganglion cell layer thickness, retinal nerve fibre layer thickness, optic nerve disc perfusion, and optic nerve disc flow index.

**Results.** Analysing the results six months after the operation, statistically, significant changes in intraocular pressure, ganglion cell layer thickness, perfusion volume, and flow index were obtained. The changes identified in the retinal nerve fibre layer were not statistically significant. Intraocular pressure decreased from 37.57 mmHg to 12.57 mmHg ( $p < 0.0001$ ), ganglion cell layer thickness increased from 57.19  $\mu\text{m}$  to 60.24  $\mu\text{m}$  ( $p = 0.029$ ), perfusion volume increased from 38.91% to 40.57% ( $p < 0.0001$ ) and the flow index increased from 0.348 to 0.363 ( $p = 0.002$ ). A statistically significant positive weak correlation was found between retinal nerve fibre layer thickness and ganglion cell layer thickness before and after the surgery ( $p = 0.023$ ,  $R^2 = 0.242$ , and  $p = 0.002$ ,  $R^2 = 0.406$ , respectively). A statistically significant positive correlation was found between the ganglion cell layer thickness and the flow index before and after the operation ( $p = 0.018$ ,  $R^2 = 0.261$ , and  $p = 0.035$ ,  $R^2 = 0.214$ , respectively).

**Conclusion.** Trabeculectomy provides effective and sustained reduction of intraocular pressure and improves optic nerve structural and perfusion parameters in primary open-angle glaucoma. The optic disc flow index can be considered equivalent to the ganglion cell layer thickness as an early identifier of glaucomatous damage. Traditional trabeculectomy surgery significantly improves optic nerve disc perfusion at least half a year after the operation.

**Acknowledgements.** The authors declare the absence of conflict of interest.

## Correlation Between Central Macular Thickness and Best Corrected Visual Acuity Outcome After Idiopathic Epiretinal Membrane Surgery

Muhina Olga<sup>1</sup>, Ali Ilgars<sup>1</sup>, Vanags Juris<sup>1,2</sup>, Laganovska Guna<sup>1,2</sup>

<sup>1</sup>Riga Stradiņš University, Riga, Latvia

<sup>2</sup>Ophthalmology Clinic, Pauls Stradiņš Clinical University Hospital, Riga, Latvia

**Background.** The epiretinal membrane (ERM), also known as macular pucker, cellophane maculopathy, preretinal gliosis, is fibrocellular, avascular and most commonly idiopathic condition. This condition is considered to arise from proliferation of retinal glial cells that have migrated through defects in the internal limiting membrane, which in most cases occur during posterior vitreous detachment.

**Aim.** The aim of the research was to analyse whether there is correlation between central macular thickness and visual acuity outcome after *pars plana* vitrectomy (ppV) with ERM peeling.

**Materials and methods.** 32 patients underwent cataract extracapsular phacoemulsification surgery with intraocular lens implantation and 25G ppV with ERM peeling. Best corrected visual acuity (BCVA) was tested before and 1 month after the surgery using ETDRS chart, as well as central macular thickness (CMT) was measured with Heidelberg Spectralis optical coherence tomography (OCT). All patients were divided into three groups depending on preoperative CMT (<500mkm, 501–600mkm, >601mkm). The collected data was assessed using IBM SPSS 26.0 and MS Excel. Spearman's Rho and Kruskal Wallis test was used for the statistics.

**Results.** BCVA improved in each group following *pars plana* vitrectomy, – by 0.338, 0.241, 0.236 lines in the 1<sup>st</sup>, 2<sup>nd</sup> and 3<sup>rd</sup> group, respectively. Central macular thinning was observed in the 2<sup>nd</sup> for 109.2 mkm and the 3<sup>rd</sup> group for 243.1 mkm, but there is a slight increase by 25.7 mkm in the 1<sup>st</sup> group. Comparison of CMT decrease between the groups according to Kruskal Wallis test shows that groups are statistically significantly different ( $p=0.000$ ). Consequently, Spearman's correlation between CMT decreases in groups also is statistically significantly different from zero ( $p=0.000$ ). However, it the same cannot be stated about groups and BCVA outcomes according to Kruskal Wallis test ( $p=0.145$ ) and Spearman's correlation ( $p=0.088$ ). There is negative Spearman's Rho correlation between BCVA outcome and CMT decrease ( $p=0.039$ ).

**Conclusion.** The visual acuity improved in all groups one month following *pars plana* vitrectomy and epiretinal membrane peeling. There is a statistically significant correlation between the best corrected visual acuity outcome and central macular thickness decrease, however, it does not depend on preoperative CMT.

## Best Corrected Visual Acuity Outcome One Month Following *Pars Plana* Vitrectomy in Full-Thickness Macular Hole Cases. Correlation Between Visual Outcome, Macular Hole Height and Residual Subretinal or Intraretinal Fluid

Ali Ilgars<sup>1,2</sup>, Muhina Olga<sup>1</sup>, Vanags Juris<sup>1,2</sup>, Laganovska Guna<sup>1,2</sup>

<sup>1</sup>Riga Stradiņš University, Riga, Latvia

<sup>2</sup>Pauls Stradiņš Clinical University Hospital, Riga, Latvia

**Background.** A macular hole is a retinal break involving the fovea. In most cases, macular hole is an idiopathic condition, which has several risk factors, for instance: age, female gender, myopia, ocular inflammation or trauma. Hole height is a measurement used to calculate macular hole index and can presumably be utilised as an isolated prognostic value to predict visual acuity outcome following a *pars plana* vitrectomy (PPV).

**Aim.** The primary aim of this study was to evaluate if the difference between best corrected visual acuity (BCVA) prior and following PPV is statistically significant. The collateral aim was to ascertain whether hole height and retained subretinal or intraretinal fluid are interdependent with BCVA.

**Methods.** The study has been carried out in retrospective fashion, using no sensitive patient data. 59 anonymous, encrypted, prior the surgery optical coherence tomography (OCT) images have been analysed and the necessary measurements (macular hole height both nasally and temporally) were obtained. OCT images one month following the operation have been reviewed to identify residual subretinal or intraretinal fluid. Statistical analysis was performed using IBM® SPSS® Statistics 27.0.

**Results.** The study involved the data of 57 eyes of 54 patients. The mean hole height was 474.51 (micrometres) with minimum and maximum being 311 and 837, respectively. The mean BCVA prior to the vitrectomy was 0.09 with minimum and maximum being 0.01 and 0.4, respectively. The mean BCVA following the PPV was 0.39 with 0.05 being minimum and 0.9 being maximum values. The difference in BCVA prior to the surgery (group 1) and one month following the surgery (group 2) is statistically significant ( $p < 0.001$ ) (the mean difference between the groups is greater than 0.3). 98% of subjects experienced improvement in visual acuity; 1 subject experienced no changes; no patient had a deterioration in visual acuity. The greatest gain in visual outcome was 0.7. Correlation between the mean hole height and BCVA outcome is not statistically significant ( $p > 0.05$ ). Correlation between residual intraretinal or subretinal fluid and BCVA is not statistically significant ( $p > 0.05$ ).

**Conclusion.** *Pars plana* vitrectomy substantially improved VA in most cases. Hole height and residual subretinal or intraretinal fluid are not interdependent with best corrected visual acuity outcome one month following *pars plana* vitrectomy. Hole height should not be employed as an isolated prognostic value to theorize about the visual acuity outcome of the surgery during a preoperative patient's visit.

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## Effectiveness of Antivascular Endothelial Growth Factor Therapy in Reducing Macular Edema in Various Retinal Pathologies

Kosnarevičs Jurijs<sup>1,2</sup>, Briede Elīza<sup>1,2</sup>, Baumane Kristīne<sup>1,2</sup>

<sup>1</sup>Department of Ophthalmology, Riga East Clinical University Hospital, Riga, Latvia

<sup>2</sup>University of Latvia, Riga, Latvia

**Background.** Age-related macular degeneration (AMD), diabetic macular edema (DME), and retinal vein occlusion (RVO) are diseases with a high risk of visual acuity worsening, and with an untimely diagnosis and appropriate treatment potentially leads to irreversible loss of vision. Although there are several theories to explain the pathogenesis of these diseases, the primary treatment is intravitreal anti-VEGF therapy. The effectiveness of treatment for each of these diseases is different and often hardly predictable. Therefore, it is necessary to investigate the efficacy of anti-VEGF therapy in each of the disease groups, its effect on macular edema, and possible changes in visual acuity and intraocular pressure.

**Aim.** To evaluate the effectiveness of intravitreal anti-VEGF (*Bevacizumab*) therapy in reducing macular edema in various retinal diseases.

**Methods.** This retrospective study included 90 patients with AMD, DME, and RVO. Patients received intravitreal injections of *Bevacizumab* over a three-month period. Changes in best-corrected visual acuity, intraocular pressure, and macular edema thickness using optical coherence tomography (OCT) before and 3 months after intravitreal anti-VEGF (*Bevacizumab*) therapy were documented.

**Results.** The mean age of patients in the AMD group was  $71.4 \pm 13.3$  years, in the DME group  $57.1 \pm 17.1$  years, and in the RVO group  $66.5 \pm 14.4$  years. Statistically significant improvement in visual acuity was found in the DME and RVO groups ( $P_{MV} < 0.05$ ). The mean pre-injection thickness of macular edema was  $379.7 \pm 95.7$   $\mu\text{m}$  in the AMD group,  $421.1 \pm 131.2$   $\mu\text{m}$  in the DME group, and  $508.3 \pm 123.7$   $\mu\text{m}$  in the RVO group. Three months after the start of treatment, the mean thickness of macular edema was  $324.5 \pm 73.8$   $\mu\text{m}$  in the AMD group,  $337.8 \pm 109.3$   $\mu\text{m}$  in the DME group, and  $317 \pm 43.9$   $\mu\text{m}$  in the RVO group. In the AMD group, the average macular thickness decreased by  $55.3 \pm 66.2$   $\mu\text{m}$ . In the DME group – by  $83.3 \pm 91.8$   $\mu\text{m}$ . In the RVO group – by  $190.6 \pm 115.5$   $\mu\text{m}$ .

**Conclusion.** *Bevacizumab* therapy is effective in reducing macular edema in the AMD, DME, and RVO groups. *Bevacizumab* treatment did not show statistically significant results in improving visual acuity in the AMD group. In turn, in DME and RVO groups a significant improvement in visual acuity was shown.

**Acknowledgements.** The authors declare the absence of conflict of interest.

## Vascular Density Changes in Deep Capillary Plexus After Cataract Surgery Among Type 2 Diabetes Mellitus Patients Using Optical Coherence Tomography Angiography

Svjaščenkova Lelde<sup>1,4</sup>, Laganovska Guna<sup>1,2,3</sup>, Tzivian Lilian<sup>4,5</sup>

<sup>1</sup>Pauls Stradiņš Clinical University Hospital, Riga, Latvia

<sup>2</sup>Riga Stradiņš University, Riga, Latvia

<sup>3</sup>Department of Ophthalmology, Riga Stradiņš University, Riga, Latvia

<sup>4</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

<sup>5</sup>Holon Institute of Technology, Holon, Israel

**Background.** The impact of cataract surgery on the central retina, especially among patients with diabetes mellitus type 2 (DMT2), is widely discussed in the literature. Studies reported that vascular density in deep capillary plexus (DCP) is significantly lower in patients with DMT2 compared with those without diabetes followed by an increase in vascular density in those patients 3 months after cataract surgery. The question about vascular changes among patients with and without maculopathy is still open.

**Aim.** The aim of the current study was to evaluate vascular density in DCP at para- and perifoveal areas in patients with and without maculopathy after uncomplicated cataract surgery using optical coherence tomography angiography.

**Methods.** Only patients with DMT2 were included in this prospective longitudinal study. All patients underwent phacoemulsification cataract surgery in Pauls Stradiņš Clinical University Hospital in Latvia. All patients underwent complete routine ophthalmic examinations and additionally optical coherence tomography angiography to evaluate macula (para- and perifoveal density) at baseline, just before the cataract surgery, one, and three months after. Friedman test was used to compare results of those with and without maculopathy separately at different time points. Mann-Whitney test was used to compare results between groups, also at three-time points.  $P < 0.05$  was considered statistically significant.

**Results.** 34 eyes of 34 DMT2 patients were investigated in this study. Of them, 10 (29.4%) had a diabetic macular edema before the surgery and 24 (70.6%) did not have a diabetic macular edema. For patients with macular edema, no significant differences were observed in parafoveal density ( $p=0.87$ ), medians 43.6 (interquartile range 36.3–47.4), 42.4 (40.4–50.7), and 43.7 (39.8–47.5), as well as in perifoveal density ( $p=0.16$ ), medians 34.3 (32.3–39.0), 37.5 (36.4–43.3), and 40.1 (36.6–46.3) for baseline, one-month post-surgery, and three months post-surgery examinations, respectively. For the group without macular edema, no significant differences were observed in parafoveal density ( $p=0.14$ ), medians 48.9 (41.0–51.9), 48.7 (45.6–54.2), and 51.0 (47.7–54.2), however, the difference was observed in perifoveal density ( $p < 0.01$ ), medians 40.0 (34.3–46.4), 42.1 (37.8–48.0), and 44.7 (37.2–49.0) for baseline, one-month post-surgery, and three months post-surgery examinations, respectively.

Significant differences ( $p < 0.01$ ) in the mean parafoveal vascular density were observed when comparing between those with and without maculopathy within each of the time points.

**Conclusion.** Perifoveal vascular density tends to increase three months after cataract surgery in both groups. Vascular density should be evaluated for a longer period to understand how operation changes vascularity.

## Evaluation of Ocular Microvascular Changes in Patients with Type 2 Diabetes Mellitus Using Optical Coherence Tomography Angiography

Agiseva Kristina<sup>2</sup>, Peterfelde Beate<sup>1,2</sup>, Baumane Kristine<sup>1,2</sup>

<sup>1</sup>University of Latvia, Riga, Latvia

<sup>2</sup>Riga East Clinical University Hospital, Riga, Latvia

**Background.** Diabetes mellitus (DM) is a group of metabolic diseases characterized by high blood glucose levels. Worldwide, approximately 463 million adults (9.3% of all adults from 20 to 79 years of age) had diabetes in 2019. Type 2 diabetes mellitus accounts for about 90% of the total number of patients. Diabetic retinopathy is the most common complication of diabetes, disrupting retinal microvascularization, and is a prevalent cause of vision loss worldwide, especially in working-age people. Early diagnosis and treatment are the best way to prevent vision loss in diabetes.

**Aim.** To evaluate and compare the changes in ocular microvascular parameters caused by type 2 diabetes by optical coherence tomography angiography.

**Methods.** The study included 62 patients (62 eyes) who underwent OCTA examination of the retina and optic nerve head. Patients were divided into three groups. The first group had 22 (35.5%) patients as a control group. The second group contained 20 (32.3%) patients with type 2 diabetes without diabetic retinopathy. The third group consisted of 20 (32.3%) patients with type 2 diabetes with nonproliferative diabetic retinopathy (NPDR).

**Results.** In the control group, the median foveal avascular zone (FAZ) area was calculated to be 0.19 mm<sup>2</sup> [0.16–0.23] compared to the group of patients with DM without retinopathy 0.26 mm<sup>2</sup> [0.24–0.29] and DM with NPDR 0.35 mm<sup>2</sup> [0.34–0.42] ( $p < 0.001$ ). The mean FAZ perimeter differed statistically significantly ( $p < 0.001$ ) between the control group (1.96 mm [1.86–2.18]) and DM groups without and with NPDR (2.39 mm [2.25–2.53] and 2.67 mm [2.54–3.01] accordingly). Vascular density differed statistically significant ( $p = 0.011$ ) between control group (11.65 mm [9.18–14.63]) and DM groups without and with NPDR (9.90 mm [7.58–10.60]) and 7.40 mm [6.35–9.98] accordingly). In this study, comparing all three study groups, no statistically significant differences were found when comparing optic nerve head parameters.

**Conclusion.** In this study, we demonstrated an enlargement in the FAZ along with a reduction in the vascular density of the superficial capillary network in the foveal and parafoveal area using optical coherence tomography angiography in patients with nonproliferative diabetic retinopathy. This technique can be used to monitor the disease progression and evaluate the response to treatment. FAZ perimeter and FAZ area can be promoted as a potential biomarker of diabetic retinopathy induced by diabetes mellitus.

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## EEG Signals During the Perception of Physical and Simulated 3D Images

Naderi Mehrdad<sup>1</sup>, Pladere Tatjana<sup>1</sup>, Zabels Roberts<sup>2</sup>, Krumina Gunta<sup>1</sup>

<sup>1</sup>Department of Optometry and Vision Science, Faculty of Physics, Mathematics and Optometry, University of Latvia, Riga, Latvia

<sup>2</sup>LightSpace Technologies, Mārupe, Latvia

**Background.** Innovative displays that show physical three-dimensional (3D) images are on their way to replace conventional devices that only simulate image depth. It is expected that the use of new displays will allow users to visualize high-quality spatial images in many fields, such as surgical and military training, engineering, geospatial analysis, vision research, and entertainment. Nevertheless, the effect of new visualization on the cortical activity remains unknown. Most of the previous research focused on the analysis of electroencephalogram (EEG) signals during the perception of stereoscopic images. However, there is a lack of knowledge on how the cortical activity changes when physical 3D images are viewed.

**Aim.** The study aimed at identifying differences in the power spectral density (PSD) and event-related spectral perturbation (ERSP) for two fundamentally different viewing conditions: stereoscopic visualization and volumetric visualization.

**Methods.** Altogether 20 subjects were enrolled in the study. The visual stimulus contained four constant angular size circles. In each trial, one circle was shown closer to the subject compared to the others. The subject's task was to find the closest circle and submit the answer about its direction by pressing the corresponding key on the computer keyboard. We recorded the electrical activity of the brain and analysed EEG signals.

**Results.** The PSD analysis revealed significantly higher beta-band activity during stereoscopic 3D image viewing than during volumetric 3D image viewing. However, there were no considerable differences in alpha, gamma, and theta bands. Moreover, ERSP results showed different patterns of cortical activity for two visualizations.

**Conclusion.** As the beta band activity is associated with problem-solving and deep thinking, the results suggest that the simulated stereoscopic depth perception requires higher processing load in comparison to the real 3D image perception.

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## NURSING

### The Most Common Factors Motivating Work of Anaesthesia and Intensive Care Nurses

Tkačenko Ilona<sup>1,2</sup>, Mikaliūkštienė Aldona<sup>1,2</sup>

<sup>1</sup>Department of Nursing, Institute of Health Sciences, Faculty of Medicine, Vilnius University, Vilnius, Lithuania

<sup>2</sup>Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania

**Background.** Motivation for work and the process of organizing activities are crucial to ensure not only employee satisfaction, but also to achieve the overall goals and objectives of the organization. Employees in organizations without any motivational system are more likely to experience negative emotions: depression, apathy, burnout syndrome, which can lead to the failure of the entire organization. Therefore, it is important to foster a favorable work environment, maintain friendly relations in the team, promote a positive attitude towards one's work.

**Aim.** The aim of the current study was to assess the most common motivating factors for the work of anaesthesia and intensive care nurses.

**Methods.** The method of questionnaire survey was chosen for the research. The questionnaire consisted of 18 questions and a Spector P. job satisfaction questionnaire. The study involved 166 anaesthesia and intensive care nurses. Statistical analysis was performed using SPSS Statistics 27 computer program.

**Results.** Respondents most often chose the following from the external determinants of motivation: salary (n=106; 63.86%); equal distribution of workload (n=105; 63.25%); provision of rest time (n=95; 57.23%); good working conditions (n=92; 55.42%), clear work tasks and division of labour (n=89; 53.61%), cash bonuses (n=88; 53.01%), safe working conditions (n=85; 51.2%), flexible work schedule (n=55; 39.16%) and the opportunity to earn extra money (n=63; 37.95%). The most common internal factors determining motivation for work were marked by the following: managerial evaluation and praise (n=141; 84.94%); good teamwork (n=97; 58.43%); good relations with colleagues, manager (n=94; 56.63%); work result (n=87; 52.41%); opportunity to discuss problems and mistakes (n=79; 47.59%); responsibility (n=74; 44.58%); career opportunities (n=72; 43.38%); opportunity to participate in decision-making (n=60; 36.14%).

**Conclusion.** Motivation for work is determined by both external and internal factors. Material remuneration for work and proper recognition of the manager, as well as good teamwork and career opportunities are important for nurses.

**Acknowledgments.** The authors declare the absence of conflict of interest.

## Evaluation of Nursing Students' Opinion Regarding Organization of Practical Training in Nursing in Healthcare Institutions

Kersyte Ieva<sup>1,2</sup>, Mikaliūkštienė Aldona<sup>1,2</sup>

<sup>1</sup>Department of Nursing, Institute of Health Sciences, Faculty of Medicine, Vilnius University, Vilnius, Lithuania

<sup>2</sup>Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania

**Background.** For nursing students, practice is an integral part of their studies. The aim is to apply the knowledge acquired during the studies in practice and acquire professional practical skills. It is important that the placement develops the student's independence, is useful and of a high quality. It is crucial that the practical training benefits the nursing student and fulfils the main objectives.

**Aim.** The aim of the current study was to assess the nursing students' opinion about the organisation of the practical training process.

**Methods.** The research was conducted using a 19-question survey prepared in advance by the authors. A total of 163 nursing students took part in the survey. Statistical analysis was performed using SPSS Statistics 22 computer program.

**Results.** Most of students (n=143; 87.7%) affirmed that enough hours were dedicated to practical training, that they had sufficient theoretical knowledge (n=102; 62.6%) and gained all the necessary professional knowledge during the internship (n=115; 70.6%). More than half of the students (n=101; 62.0%) who took part in the survey were supervised by a nurse in the corresponding department. 74.2% (n=121) of the students affirmed that internship supervisors were helpful in solving any issues related to work. The supervisors were attentive (n=115; 70.6%), easy to communicate with (68.7% (n=112), supportive in stressful situations (n=104; 63.8%) and they encouraged to find the right solutions to problems (n=101; 62.0%). On average, the working environment during the internship was given a rating of 8.73 by the students. The internship was useful (n=151; 92.6%), the staff of the department they worked in were competent (n=149; 91.5%), friendly (n=136; 83.4%) and the internship supervisors monitored the implementation of tasks and provided help when needed (n=139; 85.2%). A quarter (n=41; 25.1%) of the students felt under pressure and experienced stress during their internship.

**Conclusion.** The vast majority of students have sufficient theoretical knowledge and are ready for practice.

Most of them are satisfied with their internship, their teachers, and their team, while a quarter of them have experienced tension and stress.

**Acknowledgments.** The authors declare the absence of conflict of interest.

## Effect of Coronavirus Disease on Changes in Body Mass

Gierasimovič Zita<sup>1</sup>, Valiulienė Žaneta<sup>2</sup>

<sup>1</sup>Department of Nursing, Institute of Health Sciences, Faculty of Medicine, Vilnius University, Vilnius, Lithuania

<sup>2</sup>St. Clare's Hospital, Utena, Lithuania

**Background.** The coronavirus disease (COVID-19) restricted the activity of people and had an effect on changes in their body mass. When the body mass index (BMI) exceeds 30, obesity increases the risk of developing cardiovascular diseases, diabetes, high blood pressure, and oncological diseases.

**Aim.** To analyse risk factors that have an effect on changes in weight during the coronavirus disease.

**Methods.** The investigation was conducted in 2021 (for one month). The “Google forms” questionnaire containing questions about changes in body mass, nutritional habits, and physical activity was used. When assessing nutritional and physical activity habits on the basis of the answers, the five-point Likert scale (from ‘strongly disagree’ – 1, to ‘strongly agree’ – 5) was used. A total of 90 respondents, 60% females and 40% males, participated in the survey. The patients were between the ages of 25 and 56 and older. 83.3% of them were city dwellers and 16.7% of the respondents were from rural areas.

**Results.** Changes in body mass. An increase in weight was determined for 72.2% (n=39) of females and 66.7% (n=24) of males, one third of urban research subjects and one fourth of urban research subjects in a group of 56-year-old and older age group. Weight remained unchanged for 60.0% of research subjects from rural areas and for 12.2% of research subjects in a 46–55-year-old age group. When assessing the BMI, Class I obesity was found in 13.3% of research subjects, Class II obesity – in 8.9% and Class III obesity – in 6.7%,  $p < 0.05$ . 17.8% often ate late meals and 16.7% (n=15) consumed fast food. 18.9% of research subjects very often drank sweet aerated drinks, 21.1% of them ate sweets, 10.0% drank strong alcoholic beverages. 8.9% ate vegetables very rarely, 5.6% had breakfast, 11.1% prepared food,  $p < 0.05$ . 32.2% of the research subjects undertook physical activity, 5.6% of them did it online. 22.2% of research subjects devoted 3–4 hours per week to physical activity, 13.3% did not engage in any physical activity, 33.3% often ignored it at all.

**Conclusion.** More than a half the research subjects put on weight during the pandemic, mainly females. One third of the research subjects have Class I–III obesity. Half the research subjects overindulge in sweets, sweet strong drinks, and rarely eat vegetables. One third of the research subjects undertake physical activities, one third of them are often physically passive or engage in the activities involving little movement.

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## Outpatient Wound Care

Gierasimovič Zita<sup>1</sup>, Karpovič Alina<sup>2</sup>

<sup>1</sup>Department of Nursing, Institute of Health Sciences, Faculty of Medicine, Vilnius University, Vilnius, Lithuania

<sup>2</sup>Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania

**Background.** Actions related to the prevention of the infection of postoperative wounds form the basis for the care and nursing of surgical patients.

**Aim.** To analyse post-operative wound care in outpatient departments.

**Methods.** The investigation was conducted at one of Vilnius University hospitals between 2018 and 2019. “The Protocol of Wound Diagnostics, Treatment and Care” containing information about wounds, the condition of surrounding skin, wound pain and infection was used. The research subjects were assessed before the operation (the outpatient stage), continuous wound care in an outpatient department. The patients under investigation were as follows: with festering nidi and in need of surgical treatment. A total of 57 respondents participated in the investigation, 47.4% of females and 52.6% of males. The patients’ age ranged between 16 and 51 years and older.

**Results.** 77.2% (n=44) of patients complained about the pain in the focus of infection, subfebrilitate, skin tension and reddening. One third of the patients had characteristic symptoms of purulent infection. Swelling of tissues was determined in 50.8% of the patients. 31.6% of the patients complained about weakness and feverishness, 26.3% of the patients had edema. 5.2% of them had urination and diarrhoea problems. 52.6% underwent treatment on their own, whereas 7.0% of the research subjects underestimated infection symptoms, 8.8% of them assessed their indisposition based on similar experience of their neighbours and used medicinal products recommended by them. When their health worsened 31.6% of the patients sought help in the outpatient department. Continuous wound care. One third, 31.6% of the research subjects felt pain in the place of the wound. 3.5% of them indicated the problem of discomfort. 28.1% of the patients had skin reddening in the intervention area. Five patients (8.8%) had short breath, skin reddening around the wound, swelling, and wound pain. Bandage was chosen and frequency of dressing was determined after assessing the condition of the wound. The wound of 3.5% of the patients wept, absorptive dressing made of hydrocolloid fibre was used.

**Conclusion.** The reasons for the formation of puss are, as follows: pain in the focus of infection, inflammatory changes in the skin, oedemas. Wound pain, skin reddening, swelling in the place of the incision often persist during the period of continuous care. Actions of the nursing staff are directed towards the assessment of the wound condition and frequency of changing the bandage.

**Acknowledgments.** The authors declare the absence of conflict of interest.

## Poster presentations

### MENTAL HEALTH

#### Quality Indicators in Mental Health Care – Worldwide Experience and Situation in Latvia

Ivaščenko Tarass<sup>1</sup>, Loseviča Marina<sup>2</sup>, Kajandere Anastasija<sup>2</sup>, Lieldidža-Kolbina Jeļizaveta<sup>3</sup>

<sup>1</sup>Riga Stradiņš University, Riga, Latvia

<sup>2</sup>University of Latvia, Riga, Latvia

<sup>3</sup>Day Community Service Centre for Adults “Mēs”, Riga, Latvia

**Background.** Mental health care quality assessment is an essential part of the modern health care system. Therefore, to build evidence-based and human rights based mental health care in Latvia, to assess and improve mental health care, the re-evaluation of available parameters and development of new quality indicators is required, taking into account existing issues and modern trends. There are two main types of indicators that cover different domains and aspects of care: process and outcome indicators.

**Aim.** To determine understanding among professionals and stakeholders regarding the current trends in assessing the quality of mental health care, reveal these current trends and determine the barriers for the practical implication thereof in Latvia.

**Methods.** Scoping literature review to analyse data of current trends, analysis of the available national statistical data from Disease Prevention and Control Centre, online survey among mental health specialists and stakeholders, as well as panel discussion to determine professionals' and stakeholders' opinions and needs regarding quality of mental health care.

**Results.** Based on collected and studied data, 78 mental health care quality indicators were selected: 61 process indicators and 17 outcome indicators. The gap between novel indicators and collecting statistical data was detected.

**Conclusion.** To introduce and monitor the novel indicators, which mental health specialists and stakeholders have found perspective, it is necessary to collect more statistical data, for example, as to what is the average waiting time for outpatient psychiatrist consultation, how fast do patients receive outpatient psychiatric services after hospital discharge etc. Thus, additional resources and funding is required.

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## Indications for Medical Treatment Without Consent – Opinions of Medical Practitioners

Konstantinova Karīna<sup>1,2</sup>

<sup>1</sup>University of Latvia, Riga, Latvia

<sup>2</sup>Mental Hospital “Ģintermuiža”, Jelgava, Latvia

**Background.** Nowadays, the number of involuntary patients is increasing in several countries around the world (Barnett et al., 2018). It is often a challenge for medical practitioners to make a decision about a person’s hospitalization without consent. Some scientists suggest that a pragmatic approach focusing on how a person’s medical decision-making capacity affects the ultimate health decision can help resolve difficult cases (Zhong, Sisti, & Karlawish, 2019). Unfortunately, the capacity of individuals to give informed consent or refusal of treatment is still not assessed in Latvia.

**Aim.** To find out the opinions of healthcare professionals in certain cases included clinical situations with decisionally incapacitated persons; to reveal the relationship between opinions and individual factors of the respondents – age, their speciality, work experience in medicine.

**Methods.** Medical professionals were invited to take part in an anonymous online survey. Respondents were asked to provide personal information (e.g., age, gender, employment location), and they would decide in favour or against an involuntary admission in seven clinical vignettes. The authors’ practical work experience, other studies (Morandi et al., 2020), published court decisions were used in compiling the descriptions of clinical cases.

**Results.** 248 medical professionals completed the online questionnaire. In general, respondents most frequently chose an involuntary admission in case vignettes. Some individual characteristics of respondents were related to opinions in some case vignettes.

**Conclusion.** Latvian medical practitioners can make radically different decisions in identical clinical situations. The need for the following studies of the practice of involuntary treatment to refine its criteria in Latvia was identified.

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## PUBLIC HEALTH AND EPIDEMIOLOGY

### Changes in the Prevalence of Inflammatory Bowel Disease in Lithuania During 2001–2020

Karpavičiūtė Vita<sup>1</sup>, Statkevičienė Karina<sup>1</sup>, Kiudelis Gediminas<sup>2</sup>

<sup>1</sup>Lithuanian University of Health Sciences, Kaunas, Lithuania

<sup>2</sup>Department of Gastroenterology, Lithuanian University of Health Sciences, Kaunas, Lithuania

**Background.** Inflammatory bowel disease (IBD) is a term for two conditions (Crohn's disease and ulcerative colitis) that are characterized by chronic inflammation of the gastrointestinal tract.

**Aim.** To assess changes in the prevalence of IBD in Lithuania during 2001–2020.

**Methods.** Data on the prevalence of Crohn's disease (CD) and ulcerative colitis (UC) (ICD-10 code K50, K51) in Lithuania during 2001–2020 were obtained from the Institute of Hygiene, where the data were systematized from the Mandatory Health Insurance Information System. Changes in prevalence trends in men and women, children and adults during 2001–2020 were assessed using Joinpoint regression analysis.

**Results.** In 2020, the overall prevalence of CD was 33/100,000 and the prevalence of UC was 117/100 000. Gender differences in the prevalence of IBD were not significant. The prevalence of CD among adults in Lithuania has increased 3-fold over 20 years, while the prevalence of UC has increased 4-fold. During 2001–2020, the average annual increase in UC prevalence (8.0%/year,  $p < 0.001$ ) was higher than in CD (6.3%/year,  $p < 0.001$ ). Also, it shows increased UC/CD ratio: in 2001, the ratio was 2.5:1, while in 2020, was observed a higher UC/CD ratio 3.5:1. When comparing changes in the prevalence of IBD, some differences were observed between adults and children. During 2001–2020, the average annual growth rate of CD in children increased not significantly (2.1%/year,  $p > 0.05$ ), while for adults, a significant increase was observed (6.8%/year,  $p < 0.001$ ). Similar trends were noticed in the assessment of the prevalence changes of UC: during 2001–2020, the prevalence of UC in children increased slightly (3.1%/year,  $p > 0.05$ ), while significant growth was observed for adults (7.8%/year,  $p < 0.001$ ). When comparing the children prevalence ratio of CD and UC, it remained almost the same over 20 years, and it was found that CD is more commonly diagnosed in children than UC (CD/UC ratio in 2001 was 1.8:1, while in 2020, it was 1.7:1). In adults, CD/UC ratio was opposite of children, and has changed during 2001–2020: CD/UC ratio in 2001 was 1:2.9, while in 2020, it was 1:3.7.

**Conclusion.** The results show that the prevalence of IBD in adults is steadily increasing, while the number of cases in children has not changed significantly over 20 years. Also, it was observed that Crohn's disease is diagnosed at younger age than ulcerative colitis, which is more commonly diagnosed in older age.

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## Analysis of Gastric Cancer Incidence in Uzbekistan

Djanklich Sayde<sup>1</sup>, Tillyashaykhov Mirzagaleb<sup>1</sup>, Ibragimov Shavkat<sup>1</sup>, Imamov Olimjon<sup>1</sup>,  
Berkinov Alisher<sup>2</sup>, Sabirdjanova Zulfiya<sup>1</sup>

<sup>1</sup>Republican Specialized Scientific-Practical Medical Center of Oncology and Radiology, Tashkent, Uzbekistan

<sup>2</sup>Tashkent City Branch of Republican Specialized Scientific-Practical Medical Center of Oncology and Radiology,  
Tashkent, Uzbekistan

**Background.** According to data of Globocan for 2020, 19.3 million new cancer cases were estimated worldwide (18.1 million excluding nonmelanoma skin cancer), and almost 10.0 million cancer deaths (9.9 million, excluding nonmelanoma skin cancer). Moreover, gastric cancer takes the fifth place in morbidity, including the 10 most common oncological pathologies among both sexes. In the Republic of Uzbekistan, gastric cancer takes the second place among all cancers, thereby remaining one of the most frequent pathology and public health problems both all over the world and in Uzbekistan.

**Aim.** To study morbidity trends in gastric cancer in Uzbekistan.

**Methods.** To analyse the tendency of morbidity of gastric cancer we studied the official state report in Uzbekistan – Information on Malignant Neoplasms.

**Results.** In 2015, there were 1826 newly diagnosed gastric cancer cases in Uzbekistan, but in 2019 there was an increase of new cases – up to 1895. The growth indicator compared to 2015 was 3.6%. In 2015 and 2019, the incidence rate per 100 000 population was 5.8. Moreover, the highest incidence rate per 100 000 population in 2015 was estimated in Tashkent city, Kashkadarya region and Republic of Karakalpakstan with indicators of 10.7; 7.6 and 6.8 per 100 000 population respectively, and the lowest in Navoiy (3.7), Samarkand (3.9) and Namangan (4.2) regions. In comparison with 2019, the highest incidence rate per 100 000 population was in Tashkent city, the Republic of Karakalpakstan and Tashkent region with indicators of 10.1; 8.5 and 7.5, respectively, and the lowest was observed in Sirdarya (3.6), Navoiy (3.8) and Namangan (4.1) regions. Unfortunately, more than 55–60% of these patients in our republic are diagnosed in advanced III–IV stages. According to statistical data, 18–25% of them are patients with stage IV, when palliative chemotherapy or symptomatic therapy can be an essential method of treatment. No more than 38% of them are patients with stage III, where there is still possible to save or prolong the patient's life for several years.

**Conclusion.** In conclusion, it can be shown that gastric cancer tends to increase morbidity in Uzbekistan. Cancer of the gastrointestinal tract is one of the most unfavourable malignant tumours in Uzbekistan, and treatment of these tumours, especially with locally advanced stages, remains an urgent problem.

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## Prevalence of *Candidatus Neohrlichia mikurensis* in Ticks Collected From Migratory Birds in Pape

Birnbauma Alise<sup>1</sup>, Freimane Lauma<sup>2</sup>, Čapligina Valentīna<sup>2</sup>, Seleznova Maija<sup>2</sup>, Sadovska Darja<sup>2</sup>,  
Keišs Oskars<sup>1</sup>, Ranka Renāte<sup>2</sup>

<sup>1</sup>University of Latvia, Riga, Latvia

<sup>2</sup>Latvian Biomedical Research and Study Centre, Riga, Latvia

**Background.** Ticks are vectors of several infectious agents, thus research determining prevalence of pathogens in ticks from different locations is important for evaluating risks to public health. In 2004, a new tick-borne pathogen was discovered – intracellular bacteria *Candidatus Neohrlichia mikurensis* (*Ca. N. mikurensis*) (Kawahara, Rikihisa, Isogai, Takahashi, Misumi, Suto, Shibata, Zhang, Tsuji 2004). The bacteria cause disease mainly in people with weakened immune systems, and due to the low awareness of the new pathogen within the medical community, it is often misdiagnosed.

**Aim.** This study examines whether ticks collected from migrating birds in western Latvia in 2018 are infected with *Ca. N. mikurensis*.

**Methods.** DNA samples from 789 ticks (in nymph and larvae stages) were tested for *Ca. N. mikurensis* using real time polymerase chain reaction (qPCR).

**Results.** The results confirmed the presence of the pathogen in ticks and its prevalence was 4.1%. All the positive samples were obtained from ticks in the nymph stage.

**Conclusion.** The prevalence of *Ca. N. mikurensis* in ticks in Latvia is similar to other countries in Northern Europe. Lack of positive samples from tick larvae, which is also consistent with previous research, suggest that the pathogen is not transmitted from adult ticks to their offspring. The study also highlights the role that birds play in dispersal of ticks and their pathogens. Further studies can expand in several directions, including modelling of tick-borne pathogen dispersal, possible co-infections with other pathogens, and effects on different animal hosts. However, the most important benefit from the results of the study is raising awareness of *Ca. N. mikurensis* as a possible cause of disease in Latvia.

**Acknowledgements.** The study was carried out at Latvian Biomedical Research and Study Centre. The ticks were collected by *Dr. biol.* Oskars Keišs during bird ringing in Pape in the autumn of 2018.

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## Trends in Mortality From Colorectal Cancer in Kazakhstan: Age-Specific Features

Axarin Askhat<sup>1,2,3,4</sup>, Mauyzenova Dana<sup>1,2</sup>, Telmanova Zhansaya<sup>1,2,3</sup>, Kudaibergenova Indira<sup>4,3</sup>,  
Igissinov Nurbek<sup>1,2,3</sup>

<sup>1</sup>Astana Medical University, Nur-Sultan, Kazakhstan

<sup>2</sup>Central Asian Institute for Medical Research, Nur-Sultan, Kazakhstan

<sup>3</sup>Eurasian Institute for Cancer Research Public Association, Bishkek, Kyrgyzstan

<sup>4</sup>Akhunbaev Kyrgyz State Medical Academy, Bishkek, Kyrgyzstan

**Background.** Colorectal cancer (CRC) is the third most commonly diagnosed malignancy and the second leading cause of cancer death in the world (accounting for about 1.9 million new cases and almost 935 173 deaths in 2020), although with some global geographic differences in both incidence and mortality rates, with Asia contributing the highest, 992 755 of incident cases and 498 329 of deaths in the world (IARC).

**Aim.** The aim of the study was to evaluate the age-related changes in mortality from CRC in dynamics.

**Methods.** The study period was 10 years (2009–2018), the data of the Ministry of Health of Kazakhstan on new cases of CRC (ICD – C18–21) in the entire population. The extensive, crude rate (CR) and age-specific mortality rates (ASMR) are determined according to the generally accepted methodology used in sanitary statistics. The annual averages (M, P), mean error (m), Student criterion, 95% confidence interval (95% CI), and average annual upward/downward rates (T%) were calculated.

**Results.** During 10 years (2009–2018) 15 200 people died of CRC, of these 7 505 (49.4%) men and 7 695 (50.6%) women. Extensive proportion of deaths from CRC by age groups (both sexes) of Kazakhstan, characterized by a high proportion of deaths, were identified among people aged 65–69 years (14.9%), 70–74 years (14.7%), 75–79 years (17.2%) and 80–84 years (14.5%). The highest mortality rates per 100 000 in the entire population were found in the age groups 75–79 years –  $114.3 \pm 18.2$  ( $T = -16.4\%$ ;  $R^2 = 0.888$ ), 80–84 years –  $171.1 \pm 13.1$  ( $T = +3.1\%$ ;  $R^2 = 0.159$ ), and 85+ years –  $142.7 \pm 15.9$  ( $T = -10.5\%$ ;  $R^2 = 0.865$ ). An average age of the dead was  $69.8 \pm 0.1$  years (95%CI=69.5–70.0) and in dynamics decreased and average annual rate of decline was  $T = -0.1\%$ . The standardized mortality rate for the country was  $10.2^{0/}_{0000}$  ( $T = -3.6\%$ ;  $R^2 = 0.874$ ). Crude mortality rate was  $8.9 \pm 0.2^{0/}_{0000}$  (95%CI=8.4–9.3). Standardized and crude indicators had differences, in our study we found that the standardized indicator was higher.

**Conclusion.** The results of the study show that despite the fact that there is a decrease in mortality from CRC in Kazakhstan, our republic belongs to the region with high mortality rates. The study of mortality trends from CRC has theoretical and practical significance: monitoring and evaluation of the effectiveness of early detection and treatment of the detected pathology. Health authorities should take into account the results obtained when organizing anti-cancer measures.

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## Changes in Indicators of Colorectal Cancer in Kazakhstan

Telmanova Zhansaya<sup>1,2,3</sup>, Axarin Askhat<sup>1,2,3,4</sup>, Kozhakhmetov Saken<sup>1,2,3</sup>, Kudaibergenova Indira<sup>4,3</sup>,  
Igissinov Nurbek<sup>1,2,3</sup>

<sup>1</sup>Astana Medical University, Nur-Sultan, Kazakhstan

<sup>2</sup>Central Asian Institute for Medical Research, Nur-Sultan, Kazakhstan

<sup>3</sup>Eurasian Institute for Cancer Research Public Association, Bishkek, Kyrgyzstan

<sup>4</sup>Akhunbaev Kyrgyz State Medical Academy, Bishkek, Kyrgyzstan

**Background.** The five-year survival rate for colorectal cancer (CRC) is about 60–95% at the initial stages and sharply decreases to 35% at the stages when metastases are detected. Since the warning symptoms appear at a late date, the neoplasm is most often detected at late stages, which dramatically reduces the chances of using radical treatment.

**Aim.** The aim of the current study was to evaluate the tendencies in CRC incidence in Kazakhstan.

**Methods.** The material of the study was the data of the Ministry of Health (MoH) of the Republic of Kazakhstan, concerning CRC (form 35). The retrospective study employed descriptive and analytical methods of epidemiology.

**Results.** Crude incidence rate of CRC increased from  $15.3 \pm 0.3^0_{0000}$  (2010) to  $17.1 \pm 0.3^0_{0000}$  (2019) ( $t=4.24$ ;  $p=0.000$ ;  $T=+2.0\%$ ).

Table. CRC indicators in Kazakhstan, 2010–2019

Indicators	2010	2013	2016	2019
New cases (%)	2 503 (100%)	2 835 (100%)	3 019 (100%)	3 172 (100%)
Morphological verification (%)	2 206 (88.1%)	2 597 (91.6%)	2 930 (97.1%)	3 054 (96.3%)
I–II stage (%)	1 056 (42.2%)	1 467 (51.7%)	1 802 (59.7%)	2 041 (64.3%)
III–IV stage (%)	1 440 (57.5%)	1 355 (47.8%)	1 212 (40.1%)	1 115 (35.2%)

The rate of morphological verification of CRC increased from 88.1% in 2010 to 96.3% in 2019. In dynamics, the indicators of early diagnosis (I–II stage) increased from 42.2% (2010) to 64.3% in 2019, and the incidence of the population of stage I–II in these years was  $6.5 \pm 0.2^0_{0000}$  and  $11.0 \pm 0.2^0_{0000}$  accordingly ( $t=16.09$ ;  $p=0.000$ ). The incidence of stage III tended to decrease from  $6.2 \pm 0.2^0_{0000}$  (2010) to  $4.0 \pm 0.1^0_{0000}$  in 2019 ( $t=9.21$ ;  $p=0.000$ ), and the incidence of stage IV has decreased and amounted to  $2.6 \pm 0.1^0_{0000}$  and  $2.1 \pm 0.1^0_{0000}$ , respectively ( $t=3.54$ ;  $p=0.000$ ).

**Conclusion.** According to available data, morphological verification has improved over the years. Despite the decrease in the proportion of patients with stage III–IV, their proportion still remains significant. Therefore, it is necessary to take measures to improve early diagnosis, screening and management of patients with this type of neoplasia.

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## On the Incidence of Chronic Diseases of Tonsils and Adenoids in Kazakhstan

Imangaliyev Yermek<sup>1</sup>, **Telmanova Zhansaya**<sup>2,3,4</sup>, Igissinov Nurbek<sup>2,3,4</sup>

<sup>1</sup>City Multidisciplinary Hospital No. 2, Nur-Sultan, Kazakhstan

<sup>2</sup>Astana Medical University, Nur-Sultan, Kazakhstan

<sup>3</sup>Central Asian Institute for Medical Research, Nur-Sultan, Kazakhstan

<sup>4</sup>Eurasian Institute for Cancer Research Public Association, Bishkek, Kyrgyzstan

**Background.** Chronic inflammation of adenoids and tonsils leads to chronic activation of cell-mediated and humoral immune response, which, in turn, leads to hypertrophy of the lymphoid tissue of the tonsils. This hypertrophied tissue is the cause of pronounced clinical symptoms: obstruction of the upper respiratory tract, snoring and sleep apnoea with adenoiditis or angina, dysphagia and bad breath with recurrent tonsillitis.

**Aim.** The aim of the current study was to evaluate the tendencies in chronic diseases of tonsils and adenoids incidence in Kazakhstan.

**Methods.** The material of the study was the data of the Ministry of Health of the Republic of Kazakhstan, concerning chronic diseases of tonsils and adenoids (form 12). The retrospective study employed descriptive and analytical methods of epidemiology.

**Results.** Over the period of study, 651 934 new cases of chronic diseases of tonsils and adenoids were registered, of which 64.6% were children (table).

Table. Chronic diseases of tonsils and adenoids in Kazakhstan, 2009–2018

Age group	Number (%)	P±m, <sup>0</sup> / <sub>0000</sub>	95% CI, <sup>0</sup> / <sub>000</sub>	T, %
Children (under 15)	421 247 (64.6%)	957.3±23.7	910.9-1003.7	-1.8
Adolescent (15–17)	61 687 (9.5%)	847.0±16.6	814.5-879.4	-1.1
Adults (18+)	169 000 (25.9%)	142.6±7.6	127.7-157.6	-5.5
Total	651 934 (100.0%)	383.3±8.1	367.4-399.1	-2.1

The average annual incidence rate was 383.3 cases per 100 000 of the total population. In the dynamics, the indicators tended to decrease from 420.1±1.6 (2009) to 350.3±1.4 in 2018 ( $t=32.83$ ,  $p=0.000$ ), while equalized indicator of the average annual growth rate was  $T=-2.1\%$  ( $R^2=0.7151$ ). In the studied groups the highest rates were found among children – 957.3<sup>0</sup>/<sub>0000</sub> ( $T=-1.8\%$ ,  $R^2=0.4196$ ) and adolescent (847.0<sup>0</sup>/<sub>0000</sub>), while adults (142.6<sup>0</sup>/<sub>0000</sub>) groups have the lowest rates.

**Conclusion.** The analysis of the data showed that despite the high incidence rates, the indicators tend to decrease in dynamics. This decrease is especially pronounced in the adult group. Since more than a half of new cases occur in the child population, the burden on children and their families from both a social/emotional and economic point of view should be taken into account.

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## Analysis of Antioxidative System Markers' Changes Under the Influence of High Physical Load

Pļaviņa Liana<sup>1,2</sup>, Kolesova Oksana<sup>2</sup>

<sup>1</sup>National Defence Academy of Latvia, Riga, Latvia

<sup>2</sup>Riga Stradiņš University, Riga, Latvia

**Background.** The control and management of physical load level during military exercises is an important element of the study process. The high physical load reduces capacity of the inner reserve that manifests as physiological stress with accumulation of oxidative products, which increases risk of trauma and pathological condition. The function of the antioxidative system is essential for improving resistance to oxidative stress.

**Aim.** The aim of the current study was to determine changes of oxidative and antioxidative system elements, as well as to assess possible muscle damage during high intensity physical load.

**Methods.** Participants of study were from 23 to 30 years of age, both genders (male (n=50), female (n=6)). They were tested before physical load and immediately after physical load. We determined the myoglobin concentration level, the antioxidative system activity (catalase activity (CAT), superoxide dismutase activity (SOD), and total antioxidant capacity (TAC) in blood plasma.

**Results.** The high physical load during military exercises did not provoke muscle damage that would be expressed by increasing concentration of myoglobin. We found that concentration of DNA damage marker 8-OHdG diminished, as well as accumulation of H<sub>2</sub>O<sub>2</sub>. The fact pointed out that study group participants adapted to the high level of physical load. Positive finding is the stability of antioxidative system's function. The TAC and SOD markers of the antioxidative system did not decline. The slight diminishing of oxidant level MDA, H<sub>2</sub>O<sub>2</sub> indicated the active functioning of the antioxidative system. The reserves of the antioxidative system increase that are represented by oxidative stress index diminishes.

**Conclusion.** Comparative analysis of physical fitness level and stress parameters showed that participants with higher physical fitness level have lower-level oxidative stress markers. The analysis of antioxidative system marker changes indicated the coordinated body reaction to high physical load effects.

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## Motivation Differences Between 1st Year Latvian and Foreign Medical Students in the Faculty of Medicine, University of Latvia

Baltāne Zane<sup>1\*</sup>, Grunte Laima-Anete<sup>1\*</sup>, Knipše Gundega<sup>1</sup>, Krūmiņa Džanna<sup>1</sup>, Tzivian Lilian<sup>1</sup>

<sup>1</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

\*Shared first authorship

**Background.** Motivation is a major determinant of the quality of learning. Although motivation as a learning behaviour is widely researched in general education, there is limited evidence for research of motivation in medical education. Medical schools aim to select the most motivated students for their programmes since medical education is highly pursued, requiring responsibility, and challenging. Factors affecting motivation of medical students should be investigated in depth to allow the proper selection of the best students.

**Aim.** The aim of the study was to compare motivation between Latvian and foreign 1<sup>st</sup> year medical students of the Medical Faculty, University of Latvia.

**Methods.** Cross-sectional study was performed among 1<sup>st</sup> year medical students (Latvians and foreign students) that completed a self-reporting questionnaire in October 2019. Student's motivation was assessed using Likert scale questionnaire ranged from 1 ("strongly disagree") to 5 "strongly agree"). Reliability of answers was checked using  $\alpha$ -Cronbach's test in each group individually. Nonparametric tests were used for the univariate analysis;  $p$ -value $<0.05$  was considered statistically significant. The mean score of motivation was used as an outcome measure. Multiple logistic regression models were built, and odds ratio (ORs) and 95% confidence intervals (CIs) were presented for the association between the motivation and personal covariates according to the students' group.

**Results.** The study sample included 112 participants, 51% of them were from Latvia. Most of the students were women (69%), single (52%), with very good communication skills (28%), and began studies immediately after school (65%). Reliability of motivation scale was  $\alpha=0.85$  for Latvian students, and  $\alpha=0.780$  for foreign students. Univariate were observed between motivation and age ( $p=0.03$ ), place of birth ( $p<0.01$ ), communication skills ( $p=0.01$ ), and former occupational status ( $p=0.04$ ). A higher proportion of highly motivated students was in the foreigners' group (66%), in comparison with 28% in Latvian group. In multiple logistic regression models, the mean of motivation was associated with the place of birth (OR=1.42, 95% confidence interval, CI 1.59; 10.7). Foreign students were more likely to be highly motivated to study medicine than students from Latvia. Other factors were found non-significant in multivariate analysis.

**Conclusion.** Differences in motivation between Latvian and foreigner medical students should be considered during the study process. Additional factors affecting higher motivation of foreign students should be investigated in order to increase the motivation of Latvian students.

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## Epidemiology of Cervical Cancer in Uzbekistan

Djanklich Sayde<sup>1</sup>, Zakhirova Nargiza<sup>1</sup>, Tillyashaykhov Mirzagaleb<sup>1</sup>, Ibragimov Shavkat<sup>1</sup>, Imamov Olim<sup>1</sup>, Berkinov Alisher<sup>2</sup>, Sabirdjanova Zulfiya<sup>1</sup>

<sup>1</sup>Republican Specialized Scientific-Practical Medical Center of Oncology and Radiology, Tashkent, Uzbekistan

<sup>2</sup>Tashkent city branch of Republican Specialized Scientific-Practical Medical Center of Oncology and Radiology, Tashkent, Uzbekistan

**Background.** Cervical cancer is the third most frequent disease among women in the world, which accounts for more than 9% of the total number of newly diagnosed malignant neoplasms in the female population, with more than 85% newly diagnosed cervical cancer cases referring to developing countries. According to GLOBOCAN 2020, there were more than 604 thousand new cases and more than 341 thousand deaths from cervical cancer all over the world. In the Republic of Uzbekistan, cervical cancer remains the most common cancer type and the leading cause of cancer death.

**Aim.** To study the main statistical indicators of cervical cancer in Uzbekistan.

**Methods.** To analyse the condition of cervical cancer burden, we collected incidence data and TNM stage on cervical cancers from official statistics from Uzbekistan for years 2010–2019.

**Results.** In the structure of the general oncological morbidity over the last 10 years, cervical cancer takes the 3<sup>rd</sup> place, among the female population – the 2<sup>nd</sup> place. Analysis of the number of cervical cancer cases over the 10-year period in Uzbekistan show that 14 499 (6.9%) new cervical cancer cases and 210 881 cases of all malignant neoplasms were registered during this time. Incidence rate tended to increase from 4.3 in 2010 to 5.6 in 2019 per 100 thousand population. For the period 2010–2019, the age category of patients with cervical cancer was distributed as follows: patients under 15 years old were 1 (0.01%), at the age of 15–17 years – 4 (0.03%), at the age of 18–44 years – 3777 (26, 1%), 45–64 years old – 8963 (61.8%), 65 years and older – 1754 (12.1%). In 2010 and 2019, over 41% and 28% cervical cancers in Uzbekistan were registered at stages III–IV, whereas 57.8% and 67.0% cervical cancers were registered at stages I–II respectively. Moreover, 7 662 patients died from cervical cancer over the last 10 years, while the mortality rate was 2.3 in 2010, and 3.0 in 2019 per 100 thousand population.

**Conclusion.** From these facts, one may conclude that cervical cancer morbidity has a tendency to increase in the Republic of Uzbekistan. 45–65 years old women are more likely to develop cervical cancer in the Republic. Over the last 10 years, there has been a decrease of advanced (III–IV) stages of cervical cancer cases. The increase in morbidity is due to implementation of modern diagnostic methods, creation and use of diagnostic and treatment standards.

**Acknowledgements.** The authors declare the absence of conflict of interest.

## The Influence of Warm-Up Procedures on Performance in Vertical Jumps and Sport Exercises

Volkenandt John<sup>1</sup>, Proskurins Jevgenijs<sup>1</sup>

<sup>1</sup>Riga Stradiņš University, Riga, Latvia

**Background.** Most literature and research are aimed towards the effect of pre-activity on professional or elite athletes, whereas papers and scientific material concerning its effect on recreational sportsman and woman are rarely published.

**Aim.** The aim of this study was to investigate the influence of a warm-up or pre-activity on the ability to accelerate in a vertical jump in recreational athletes.

**Methods.** 30 participants, from the Riga Stradiņš University (Riga, Latvia) student body and the Berlin region (Germany) agreed to be part of this investigation. Each participant agreed to give information about their body data (e.g., height, age, weight), current diseases, habits of smoking, and prior infections with SARS-CoV-2. Afterwards, every participant performed three jumps before a warm-up and three jumps after a warm-up. The warm-up consisted of a 5-minute easy run and 7 minutes of specific exercises. For each jump, the acceleration was measured using Pocketlab Voyager. During the warm-up, the heart rate was assessed. Statistical analysis was performed using SPSS.

**Results.** The mean peak acceleration for three jumps was significantly ( $p \leq 0.05$ ) higher after completion of the warm-up ( $1.504 \text{ g} \pm 0.479 \text{ g}$ ) in comparison to the initial performance ( $1.289 \text{ g} \pm 0.339 \text{ g}$ ) with an average increase of 16%. It can be therefore said that a warm-up leads to better availability of vertical jumping force in most people. Gender, weight, and height showed a statistical influence on the outcome, while smoking and prior SARS-CoV-2 infections did not influence the performance. It was also noticed that participants showed different landing styles, which lead to different landing impacts.

**Conclusion.** Warm-up procedures have a positive influence on acceleration and force in recreational athletes and can be recommended independent of a wide variety of factors (e.g., gender, age, BMI).

**Acknowledgements.** The authors declare the absence of conflict of interest.

## Quality of Life Assessment in Aesthetic Dermatology Patients

Bērziņa Anna<sup>1</sup>, Šaripova Sabīne<sup>2</sup>

<sup>1</sup>Clinic of Laserplastics, Riga, Latvia

<sup>2</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

**Background.** One of the main problems affecting the quality of life and the psychological wellbeing of people is the appearance and self-assessment, as well as the views of others thereof. Negative emotions and low self-esteem are often caused by a variety of skin neoplasms, scars, and other skin changes.

**Aim.** The objective is to assess whether human appearance is critical to self-assessment, as well as whether appearance and skin changes affect the quality of human life. Analyse people's motivation to perform aesthetic dermatology procedures to improve their appearance and self-awareness and understand which procedures people perform most frequently.

**Methods.** The study includes a survey with 24 questions on aesthetic dermatology procedures, the importance of the examination, low self-esteem, the impact of aesthetic skin problems on quality of life. The survey includes answers from 899 respondents – 881 women, 18 men.

**Results.** 33.6% of respondents have avoided society due to aesthetic skin problems, while 46.4% have felt ashamed. 43% skin and appearance changes have caused psychological problems, stress and anxiety. 30.9% have restricted their daily activities, while 13% of people have felt negative attitudes towards themselves.

99.1% of respondents believe that a healthy lifestyle affects the quality of the skin. 49.5% of the study participants have performed one of the aesthetic dermatology procedures, and 43.2% of the respondents have performed the procedure to improve their appearance, but only 6.3% have performed it for medical reasons.

82.9% believe that aesthetic skin problems affect people's quality of life, 41.6% have improved their self-confidence due to aesthetic dermatology procedures. 31.6% have applied more cosmetics due to skin problems. A pleasant result of the study is that 50.8% of people plan to perform repeated aesthetic dermatology procedures in the future

### Conclusion.

1. Considering the number of people whose aesthetic dermatological problems have led to stress, psychological problems, affected daily activities and caused shame, it can be concluded that these problems have a significant impact on people's quality of life.
2. People care about their appearance, considering how often they feel depressed when they experience a negative attitude toward themselves with regard to their appearance.
3. Aesthetic dermatology plays an important role in improving people's self-awareness, appearance, and quality of life.

## Coverage of the Article No 18 of the Latvian Law on the Rights of Patients

Martins Osis<sup>1</sup>

<sup>1</sup>*University of Latvia, Faculty of Medicine, Riga, Latvia*

**Background.** The article No 18 of the Latvian Law on the Rights of Patients determines the basics of the protection of rights and lawful interests of patients. It postulates every patient's rights to use all mechanisms for the protection of rights provided for in laws for the protection of the rights or the interests arising therefrom specified in Latvian Law on the Rights of Patients. The article in discussion provides direct indication to the administrative procedure as a legal mechanism to protect patients' rights and interests. Therefore, administrative acts and actual action of an institution could be challenged in the Health Inspectorate of Republic of Latvia and its decisions – in court. There is the opportunity also within a period of two years to apply to this institution in case of necessity. This regulation does not directly cover all legal instruments and does not provide indications for patients to use other opportunities. The existing article is not an example of the principle of good law-making, because patients are not provided with at least a list of legal opportunities to protect their rights and interests. For example, there is even no mention of criminal or civil procedure as a legal instrument for protecting a patient's interests.

**Aim.** The aim of this research is to expand the understanding of the Article No 18 of the Latvian Law on the Rights of Patients and analyse it with a view toward improvement. The author has chosen to analyse the existing regulation and possible modernization of the Latvian Law on the Rights of Patients to ensure a more open and just system, that could be easily used for all patients and persons in need. The existing regulation contains declaration of patients' rights and possible protection instruments, but does not even indicate two of them specifically.

**Methods.** For the interpretation of the Law on the Rights of Patients, the author has used the systemic, grammatical, historical and teleological methods. In addition, the author has analysed recent and historical Latvian court cases and legal literature on this topic from various periods.

**Results.** Research results are: 1) expanded understanding of the Article No 18 of the Latvian Law on the Rights of Patients; 2) opinion that the existing regulation contains declaration, but does not cover the necessary specifics; 3) more precisely defined legislative task to ensure protection of patients' rights; 3) identified proposal to the legislator for improvement of regulation.

**Conclusion.** Article No 18 of the Latvian Law on the Rights of Patients should be supplemented with a new regulation which directly determines that patients, in parallel with the administrative process, can use civil or criminal procedure to ensure their rights and interests.

## INTERNAL MEDICINE

### Evaluation of Vaginal HPV Self-Sampling Test in Clinic of General Practitioner in Riga

Dombrovskā Anastasija<sup>1</sup>, Zodzika Jana<sup>2</sup>, Fjodorova Natalija<sup>3</sup>

<sup>1</sup>Riga Stradiņš University, Latvia

<sup>2</sup>Department of Gynaecology, Riga East Clinical University Hospital, Riga, Latvia

<sup>3</sup>General Practice, Riga 1<sup>st</sup> Hospital, Riga, Latvia

**Background.** Cervical cancer screening population-based programme has been running in Latvia since 2009, but attendance rates are below 35%. It could be one of the reasons for delayed cancer diagnosis and higher mortality. HPV self-testing is an alternative screening method for non-attenders. Women may feel more comfortable taking their own samples, rather than going to see a provider for cervical cancer screening. At present, none of the HPV self-sampling tests is used in Latvia.

**Aim.** The aim of this study was to analyse data on participants' mental and physical feelings during self-sampling of the HPV test and determine which test method women prefer HPV self-test or tests done by gynaecologist.

**Methods.** This was a cross-sectional study of women aged 25–70 who were attending a clinic of the general practitioner in Riga 1<sup>st</sup> Hospital. The women were asked to do vaginal self-sampling, using a cervico-vaginal cotton swab, based on verbal and printed instructions provided by a research group. After taking the sample, the patients filled in a questionnaire that included questions about their feelings during the test and sampling preferences. The study was approved by Ethic Committee of Riga Stradiņš University.

**Results.** 80 patients were included in the study. 41% of all participants would like to do self-sampling, 34% prefer tests taken by gynaecologists, but 33% of women did not know what to choose. Among those women who preferred the test to be done by gynaecologist, 59% did not feel confident that the sample was collected successfully. Experiencing embarrassment during sample taking was reported by 6% of all patients. For 20 % responders, sample taking was uncomfortable.

**Conclusion.**

1. The results show that most participants would prefer HPV self-testing.
2. The main reason among responders for non-preference of self-testing in future – absence of confidence that the sample taking was successful.
3. The study shows that the self-sampling test does not cause any discomfort to most participants.

**Acknowledgements.** The authors thank all the study participants for their contribution and declare the absence of conflict of interest.

## Predictor Factors of Functional Status in Patients with Systemic Sclerosis

Budreviča Olga<sup>1</sup>, Možeitoviča Evelīna<sup>2</sup>, Žukovs Daniils<sup>2</sup>, Ķēniņa Viktorija<sup>2,3</sup>, Kurjāne Nataļja<sup>2,4</sup>,  
Ivanova Kristīne<sup>2,4</sup>

<sup>1</sup>University of Latvia, Riga, Latvia

<sup>2</sup>Riga Stradiņš University, Riga, Latvia

<sup>3</sup>Riga East Clinical University Hospital, Riga, Latvia

<sup>4</sup>Pauls Stradiņš Clinical University Hospital, Riga, Latvia

**Background.** Systemic sclerosis (SS) is an autoimmune connective tissue disease characterized by fibrosis and vasculopathy of the skin and internal organs. SS-caused morbidity has a significant impact on patients' life expectancy and quality of life in all dimensions, including physical and physiological.

**Aim.** The aim of the current study was to assess factors which may have an influence on physical function and disability in SS patients.

**Methods.** The study included 67 SS patients that met the ACR/EULAR 2013 accepted classification criteria. Skin fibrosis assessment was performed by modified Rodnan Skin Score (mRSS). Functioning and disability were assessed using the Health Assessment Questionnaire-Disability Index (HAQ-DI). Anxiety symptoms were also assessed by the Generalized Anxiety Disorder 7-item (GAD7).

**Results.** In our study group (n=67), the mean age was 61.8±12.5 years, with noticeable female predominance: 80.6% (n=54) were females, and 19.4% (n=13) were males. The mean age of onset of disease was 46.3±16.1 years and the mean disease duration was 15.5±10.2 years. There was no significant difference in HAQ-DI between males (1.08±0.89) and females (1.26±1.01), (p=0.13). In our study, we did not find the correlation between patients age and HAQ-DI (r=0.12, p=0.32) and there was weak correlation between HAQ-DI and the duration of disease (r=0.19, p=0.13). We observed that skin thickness (assesses by mRSS) had a weak, but statistically significant correlation with HAQ-DI (r=0.28, p=0.02). HAQ-DI was not influenced by the presence of ANA (p=0.76), however, patients with speckled ANA had higher HAQ-DI scores, but did not reach statistical significance level (p=0.44). In our study we did not find a statistically significant relation between HAQ-DI and limited cutaneous SS, or diffuse cutaneous SS, however in patients without skin involvement, HAQ-DI score was lower. There was a moderately strong and statistically significant correlation between anxiety symptoms (assessed by GAD7) and HAQ-DI (r=0.3, p=0.016).

**Conclusion.** SS patients' function/disability may be influenced by multiple factors, it is worse in cases with increased skin thickness and is affected by the presence of anxiety symptoms. SS patients' function/disability is not influenced by gender, age, duration of disease, presence of ANA and SS type.

**Acknowledgements.** The study was funded by Riga Stradiņš University.

## Dulaglutide and Semaglutide Effect on Weight and Glycemia After Sixteen Months

Treimane Terēze<sup>1</sup>, **Zariņa Rebeka Elīza**<sup>1</sup>, Trapiņa Ilva<sup>1</sup>, Sauša Sintija<sup>1</sup>  
<sup>1</sup>University of Latvia, Riga, Latvia

**Background.** Once weekly injectable GLP-1 receptor agonists (RA) are practical in usage, nevertheless, a doubt remains if efficacy on weight loss and glycemic control continues after a longer period.

**Aim.** To evaluate and compare the effect of dulaglutide and semaglutide in type 2 Diabetes patients after 1.5 years of regular use.

**Methods.** We retrospectively analysed data of 42 patients injecting semaglutide and 44 dulaglutide from the Jaunliepāja Primary Health Care Centre patient database. In total, 51 patients had been receiving medicine over 1.5 years. Changes in weight, body mass index (BMI) and glycated hemoglobin (HbA1c) were determined prior to administration of GLP-1 RA and after sixteen months. For the normality in distribution Shapiro-Wilk and Kolmogorov-Smirnov tests were used, to compare categorical risk factors Chi-squared test or Fisher's exact test was applied, and with Cramer's V test association between two categorical variables was determined. IBM SPSS Statistics version 25.0 software was used.

**Results.** Most of the patients (66.7%) were female. The mean age of patients in both groups was 62 years with  $62.95 \pm 11.89$  in semaglutide and  $62.31 \pm 11.64$  years in dulaglutide groups. In all patients, the mean weight at the start was 116.9 kg ranging from 80 up to 240 kg, in semaglutide group, the mean weight was 116.36 kg, whereas in dulaglutide group 117.31 kg. After 1.5 years of intervention, the mean weight reduction was 6.66 kg ( $P_x = 2.79 \times 10^{-7}$ ) and BMI decreased by  $2.57 \text{ kg/m}^2$  ( $P_x = 1.87 \times 10^{-7}$ ). In semaglutide group, weight decreased by 6.77 kg ( $P_x = 1.31 \times 10^{-4}$ ) but dulaglutide users lost 6.48 kg ( $3.87 \times 10^{-4}$ ). HbA1c levels from a mean of 8.37% dropped to 6.94% ( $P_x = 9.16 \times 10^{-9}$ ).

**Conclusion.** The retrospective analysis confirms that GLP-1 RA treatment is still effective in reducing weight and HbA1c after 1.5 years of intervention.

**Acknowledgements.** Jaunliepāja Primary Health Care Centre.

## Familial Hypercholesterinaemia – a New Challenge for Endocrinologists

Jenbajeva Ksenija<sup>1</sup>, Anufrijeva Alina<sup>1</sup>, Rasa Ingvars<sup>2</sup>

<sup>1</sup>Riga Stradiņš University, Riga, Latvia

<sup>2</sup>Riga East Clinical University Hospital, Riga, Latvia

**Background.** Heterozygote familial hypercholesterolemia (HeFH) is a common genetic disorder resulting in high low-density lipoprotein-cholesterol (LDL-C) levels. It has been established that only 3% of patients among the Latvian population were diagnosed in 2019. The early HeFH diagnosis and treatment can prevent premature cardiovascular complications.

**Aim.** The study aimed to determine the incidence of HeFH in a single-centre endocrinologist's clinical practice in RECUH Outpatient Clinic.

**Methods.** We collected three years of data from medical records with HeFH (E78.01) from January 2019 to December 2021. Based on LDL-C, Apo B, Apolipoprotein index (Apo Index), Lipoprotein (a) (Lp (a)), all patients were divided into two groups: group 1 – definitive FH; group 2 – probable FH.

**Results.** Altogether, there were 3720 patients in the endocrinologist's practice, from which 129 (3.47%) patients were included in the study, 39 (30.2%) males and 90 (69.8%) females. The mean age was  $49.8 \pm 12.3$ SD years. 58 patients (45.0%) were included in group 1 and 71 patients (55.0%) – in group 2. Only 18 patients (14%) received lipid-lowering therapy initially. The laboratory findings in group 1 before the treatment were: LDL-C 4.49 mmol/L ( $\pm 1.29$  SD); Apo B 117.52 mg/dL ( $\pm 25.11$  SD); Apo Index 0.79 ( $\pm 0.20$  SD); Lp (a) 82.76 mg/dL ( $\pm 62.06$  SD). The laboratory findings in group 2 before the treatment were: LDL-C 4.12 mmol/L ( $\pm 0.90$  SD); Apo B 98.22 mg/dL ( $\pm 16.51$  SD); Apo Index 0.64 ( $\pm 0.12$  SD); Lp (a) 17.47 ( $\pm 23.90$  SD). In group 1, 36 (62.1%) patients received statin therapy, 10 (17.2%) – combination therapy with statins and ezetimibe, 6 (10.3%) patients – fibrates, 1 (1.7%) patient – combination therapy with statins and fibrate, whereas 3 (5.2%) patients refused treatment. Meanwhile, in group 2, 50 (70.4%) patients received statin therapy, 10 (14.1%) patients – fibrates, 3 (4.2%) patients – combination therapy with statins and fibrates. In both groups, we found out that LDL-C, Apo B, Apo Index decreased at the end of the study ( $p < 0.001$ ). Nevertheless, Lp (a) in both groups did not decrease at the end of the study ( $p = 0.272$  and  $p = 0.499$ ).

**Conclusion.** Study data suggest that HeFH is much more common than generally thought. The lipid-lowering therapy decreased LDL-C, Apo B, Apo Index.

**Acknowledgements.** The authors declare the absence of conflict of interest.

## Comparison of the Efficacy of Different Forms of Vitamin D3 Supplements

Aleksejeva Marija<sup>1</sup>, Sauša Sintija<sup>1</sup>, Pīrāgs Valdis<sup>1</sup>

<sup>1</sup>University of Latvia, Riga, Latvia

**Background.** Vitamin D deficiency occurs due to improper diet, malabsorption, and lack of sunlight, chronic kidney disease, or medicines that interfere with the body's ability to convert or absorb vitamin D.

**Aim.** The aim of the study was to compare the ability of three commonly used forms of vitamin D3 supplements to increase levels of circulating 25-hydroxyvitamin D3, and to investigate which forms of the vitamin D3 supplements are more effective for patients with altered renal filtration and obesity.

**Methods.** Totally 77 respondents (62% women, 38% men) in outpatient setting with the mean age of 38.3±13.9 years and mean BMI 26.3±4.4 kg/m<sup>2</sup>, and GFR 98.3±17.2 ml/min/1.73 m<sup>2</sup> were recruited in the study and randomly divided into three groups receiving vitamin D3 supplements in forms of oil droplets, spray and capsules. At the beginning of the study, each participant completed a study questionnaire, and the serum vitamin D and creatinine levels were determined. Each participant received 4000 IU of vitamin D preparation for 30 days and then the level of the circulating vitamin D was measured again.

**Results.** The mean increase of vitamin D level ( $\Delta D$ ) was 94.4±102.2%. There was a statistically significant inverse correlation between GFR and  $\Delta D$  0.39 in the spray group ( $p=0.03$ ). There was also an inverse correlation between  $\Delta D$  and BMI in the capsule group -0.49 ( $p=0.01$ ). In patients with higher GFRs, there was a higher increase in vitamin D level in the spray group ( $p=0.03$ ). The increase in vitamin D was statistically significant by 11.7±6.7 ng/ml ( $p=0.004$ ), and inversely related to the initial level of vitamin D in the body ( $\rho=-0.59$  for all respondents). The difference in  $\Delta D$  between the treatment groups was not statistically significant ( $p=0.62$ ).

**Conclusion.** The increase of serum vitamin D level is inversely related to the initial level of circulating vitamin D. Different types of vitamin D3 supplement are effective in increasing the levels of circulating vitamin D; however, the spray form is preferable in patients with higher GFR.

**Acknowledgements.** The study was conducted in Jaunliepāja Primary Health Centre.

## Atopic and Autoimmune Manifestations in Patients with Selective IgA Deficiency in Latvia

Lucane Zane<sup>1</sup>, Prokofjeva Tatjana<sup>2</sup>, Ozola Lota<sup>2,3</sup>, Kurjane Natalja<sup>1,2,3</sup>

<sup>1</sup>Rīga Stradiņš University, Riga, Latvia

<sup>2</sup>Children's Clinical University Hospital, Riga, Latvia

<sup>3</sup>Pauls Stradiņš Clinical University Hospital, Riga, Latvia

**Background.** Selective immunoglobulin A deficiency is the most common hereditary error of immunity, which belongs to group of the predominantly antibody deficiencies. It is characterized by decreased serum level of IgA (<0.07 mg/dL) in the presence of normal levels of other immunoglobulins. Most individuals with IgA deficiency are asymptomatic, however, some patients may present with recurrent infections, atopic and autoimmune manifestations. Some patients develop common variable immunodeficiency over time.

**Aim.** The aim of the study was to assess the frequency of atopic and autoimmune manifestations in Latvia's patients with selective IgA deficiency (SIgAD) and their associations with other serum immunoglobulin levels.

**Methods.** We conducted a retrospective study, reviewing the medical records of patients who were diagnosed with SIgAD in Latvia from January 1994 to December 2021. Diagnosis was based on the diagnostic criteria of the European Society for Immunodeficiencies. Patients' demographic, laboratory (IgA, IgG, IgM, IgE) and clinical data were sourced from patients medical records in Children's Clinical University Hospital (Dr. Prokofjeva's personal data) and Pauls Stradiņš Clinical University Hospital. All data were analysed using IBM SPSS 23.

**Results.** In total, 197 patients with SIgAD were included in the study, 112 (56.7%) of them being male. 183 (92.9%) of these patients were diagnosed before the age of 18. Atopy was presented in 35 (17.8%) of these patients: 23 (11.7%) patients had asthma, 8 (4.1%) – allergic rhinitis, and 9 (4.6%) – atopic dermatitis, one patient had angioedema. Autoimmunity was presented in 51 (25.9%) of these patients, five (2.5%) of patients had more than one autoimmune disease. The frequently reported diagnoses were: type 1 diabetes (16; 8.1%), celiac disease (12; 6.1%), and juvenile idiopathic arthritis (15; 7.6%). Three (1.5 %) patients had both autoimmune and atopic disease. The mean level of IgG was 1405.3 (SD=435.7), the median level of IgM – 113 (IQR=70) and IgE – 36 (IQR=105). No statistically significant difference was found between the presence of atopic or autoimmune disease and immunoglobulin levels in Mann-Whitney U test.

**Conclusion.** Autoimmune diseases were the most common manifestations in Latvia's patients with selective IgA deficiency. No difference in gender was found in SIgAD. Follow-up would be important for an evaluation of severity of clinical symptoms with age.

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## Cutaneous Manifestations Related to COVID-19 in Young South Asian Males

Ahmed Nikhat Kousar<sup>1</sup>, Perera Manodhiya Hansini<sup>1</sup>, Korrapati Naga Harika<sup>1</sup>, Joseph Iris Clement<sup>1</sup>, Kiladze Natalia<sup>1</sup>

<sup>1</sup>Tbilisi State Medical University, Tbilisi, Georgia

**Background.** COVID-19, a disease caused by SARS-CoV-2, which is mostly known to cause upper respiratory tract symptoms, is recently found to present with cutaneous manifestations in a considerable number of patients, especially Caucasians. In a separate study, the role of ACE2 gene has been discovered in the pathogenesis of the COVID-19 infection, and it is seen in several human tissues, including gastrointestinal and skin tissue. According to findings, ACE2 expression was considerably elevated in keratinocytes compared to fibroblasts and melanocytes found in skin tissue. This could be the possible explanation as to why populations of colour or Asian populations have not reported post-COVID cutaneous manifestations as frequently as Caucasians.

**Aim.** The purpose of this study is to analyse the dermatological manifestations of COVID-19 and its variations in South Asian males belonging to the age group 20–29.

**Methods.** After the initial survey obtaining the contact details, interviews of 25 participants were conducted personally, asking them questions about gender, age, the presence of the disease on SARS-CoV-2 in the anamnesis and nature of the course, the presence of nosocomial infection, the use of medications during supervision and the presence of dermatological lesions. Analysis of obtained data was performed to identify the correlation between these factors/incidence of SARS-CoV-2 and different skin manifestations.

**Results.** The results showed that out of our 25 participants 14 developed cutaneous manifestations and the most frequent manifestation was the maculopapular rash (n=8). This is thought to develop because of high viral exanthem or due to possible drug-related interactions through treatment. Others had skin manifestations such as generalized pruritus, petechiae on the feet, vesiculopapular and urticarial rash. Majority of these rashes were generalized. On questioning, none of them reported having any prior allergies or skin lesions.

**Conclusion.** Our research data show that populations of colour are less likely to present with cutaneous manifestations possibly because of the melanocyte content in the skin, and its relation to the ACE receptor. Although less frequent, cutaneous manifestations are detected, along with the respiratory symptoms that arise from infection with COVID-19. Identifying these cutaneous manifestations can be important to diagnosing patients with COVID-19, which may go undetected if it does not present conventionally. Therefore, it is important in preventing the spread of the virus, as well as improving the treatment of and outcomes for patients with the infection.

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## ANESTHESIOLOGY, REANIMATOLOGY & INTENSIVE CARE

### Risk for Sinus Tachycardia and Ectopic Heart Arrhythmias After Endotracheal Intubation Following Induction of General Anaesthesia with Thiopental and Fentanyl

Feghiu Iuliana<sup>1</sup>, Tăzlăvan Tatiana<sup>1,2</sup>, Şandru Serghei<sup>1,2</sup>

<sup>1</sup>Nicolae Testemiţanu State University of Medicine and Pharmacy, Chişinău, Republic of Moldova

<sup>2</sup>Institute of Emergency Medicine, Chişinău, Republic of Moldova

**Background.** Endotracheal intubation under general anaesthesia can be associated with severe rhythm disturbances that cause intraoperative hemodynamic instability and worse postoperative outcomes.

**Aim.** The aim of this study was to assess the risk for cardiac arrhythmias during tracheal intubation after induction of anaesthesia with thiopental and fentanyl and to determine if a relation exists between baseline vegetative tone of the heart and cardiac arrhythmias.

**Methods.** We enrolled in the study 47 patients (aged  $\geq 18$  years) with ASA physical status I or II and normal body mass index scheduled for elective surgical procedures. Exclusion criteria were the presence of cardiac arrhythmia and chronic medications that affect cardiac vegetative tone. Preanesthetic cardiac vegetative tone was assessed by analysis of heart rate variability parameters obtained from Holter ECG recordings. General anaesthesia was induced with thiopental 5.0–6.0 mg/kg and fentanyl 1.5 mcg/kg. Tracheal intubation was performed after administration of atracurium 0.5 mg/kg. Sinus tachycardia was defined as heart rate  $>100$  bpm. Cardiac arrhythmias were detected by ECG Holter monitoring.

**Results.** The study group included 47 patients (24 females and 23 males) aged  $35.4 \pm 11.2$  years. The mean BMI was  $23.9 \pm 4.1$  kg/m<sup>2</sup>. Before surgery most patients (59.6%) had a normal HR. Ectopic heart arrhythmias were detected in 2 patients (4.3%). After endotracheal intubation 33 patients developed sinus tachycardia; 16 of these patients (48.3%) had high baseline sympathetic activity. The maximum HR was 118 bpm. Ectopic heart arrhythmias were present in 19 patients (40.4%). Supraventricular and ventricular extrasystoles were noted in 18 patients; one patient developed ventricular bigeminy that lasted 2 minutes. Statistical analysis revealed a relation between increased sympathetic cardiac tone and risk for ectopic heart arrhythmias: RR – 2.9 (95% CI 1.3–6.35;  $p=0.006$ ) with Se – 0.68 (95% CI 0.46–0.84) and Sp – 0.75 (95% CI 0.56–0.87). No relation has been established between increased sympathetic cardiac tone and sinus tachycardia: RR – 0.99 (95% CI 0.58–1.66,  $p=0.1$ ) with Se – 0.42 (95% CI 0.23–0.63) and Sp – 0.57 (95% CI 0.34–0.78).

**Conclusion.** Endotracheal intubation after induction of general anaesthesia with thiopental and fentanyl is frequently associated with sinus tachycardia and ectopic heart arrhythmias, and enhanced cardiac sympathetic tone is a risk factor for ectopic heart arrhythmias.

**Acknowledgements.** The authors declare the absence of conflict of interest.

## Prognostic Model or Patient Return Visits to Emergency Department Within 30 Days with Hospitalisation

Bilotienė Motiejūnienė Aušra<sup>1</sup>, **Grušnytė Kamilė**<sup>2</sup>, Bilotaitė Laura<sup>2</sup>, Bubulytė Silvija<sup>2</sup>,  
Klimašauskas Andrius<sup>3</sup>, Kontrimavičiūtė Eglė<sup>4</sup>, Jasiūnas Eugenijus<sup>5</sup>

<sup>1</sup>*Institute of Health Sciences, Faculty of Medicine, Vilnius University, Lithuania*

<sup>2</sup>*Faculty of Medicine, Vilnius University, Vilnius, Lithuania*

<sup>3</sup>*Centre of Emergency Medicine, Vilnius University, Lithuania*

<sup>4</sup>*Centre of Anaesthesiology, Intensive Therapy and Pain Management, Vilnius University, Lithuania*

<sup>5</sup>*Centre of Informatics and Development, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania*

**Background.** Return visits (RV) to the ED is an increasingly growing issue. According to various sources, RV with hospitalisation leads to a longer duration of treatment, poorer outcomes and rising treatment costs. Most prognostic tools address rehospitalisation of patients while lacking models for assessing the risk of the ED RV with hospitalisation.

**Aim.** Identification of risk factors and the development of a prognostic tool (Increased Alert Warning program on the Electronic Health Record platform) that identifies high-risk patients on their first visit and predicts the likelihood of RV to the ED and hospitalisation within 30 days.

**Methods.** A retrospective study was conducted in Vilnius University Hospital Santaros Klinikos. From 33470 patients 32215 were involved in the study. Subjects were divided into two groups – who made a single visit to the ED and who made a RV to the ED with hospitalization in 30 days. The development of the prognostic tool was based on the following factors: age, gender, the triage category, consultations, diagnostic tests, the time spent in the ED and the ED final diagnosis group. The development was based on multivariate logistic regression.

**Results.** Single ED visit group had statistically significant differences between the hospitalized patients and the patients receiving outpatient treatment. Meanwhile, the patients who returned to the ED in 30 days with required treatment (inpatient or outpatient) administered, did not show a difference between age, number of consultations provided at the time of the initial visit and time spent at the ED during the initial visit. However, statistically significant dependencies among these patients were found in terms of gender, CEMC, number of laboratory and radiological tests.

The prognostic model is based on a multivariate logistic regression equation. The patient characterizing factors that most accurately impacted the choice of treatment administration were found in patients with a single ED visit.

**Conclusion.** RV to the ED are statistically significantly determined by the number of laboratory tests, time spent during the first visit to the ED and the diagnosis. The predictive Increased Alert Warning tool which measures the likelihood of RV with hospitalisation within 30 days, has achieved excellent efficiency results.

**Acknowledgements.** The authors declare the absence of conflict of interest, and the study received no external funding.

## SURGERY, TRAUMATOLOGY & ORTHOPAEDICS

### Effectiveness of Protease Inhibitor Ulinastatin in Patients with Tendency to Destructive Pancreatitis

Akyshev Olzhas<sup>1</sup>, Rustemova Kulsara<sup>1</sup>, Kozhakhmetov Saken<sup>1</sup>, Chekaev Rinat<sup>1</sup>, Nurtazinova Gaukhar<sup>1</sup>,  
Zalgassbayev Zomart<sup>2</sup>

<sup>1</sup>Astana Medical University, Nur-Sultan, Republic of Kazakhstan

<sup>2</sup>City Multidisciplinary Hospital No. 2, Nur-Sultan, Republic of Kazakhstan

**Background.** Acute pancreatitis is one of the most common, severe, and urgent gastroenterological surgical diseases. In recent years, the use of protease inhibitors has been of great interest as a pathogenetic therapy for acute pancreatitis.

**Aim.** To study the effect of Ulinastatin on the severity of acute destructive pancreatitis.

**Methods.** Examined 50 patients with acute destructive pancreatitis treated in the City Multi-Copro-philic Hospital No. 2, Nur-Sultan. Group 1 or control group (n=50) received standard therapy according to the protocol for the treatment of acute pancreatitis, Group 2 or the main group (n=50) additionally received Ulinastatin at a dose of 100 000 IU intravenously once a day for 3 to 5 days, depending on the severity of the endogenous syndrome. Intoxication, indicators of pancreatic inflammation and mortality were studied.

**Results.** Upon admission, the patients had enzymatic ascites, a sharp increase in pancreatic amylase in the blood and diastase in the urine, neutrophilic leucocytosis with stab shift, and relative lymphocytopenia. LII ranged within 1.5.0–3.0. with Ulinastatin, the frequency of abdominal drainage decreased from 75% to 63%. The levels of pancreatic blood amylase and urine diastase in the Ulinastatin group decreased 1.7 times compared to the control group and returned to normal on the fifth day, while patients in the control group did not reach the norm. The number of leukocytes in the main group decreased 1.7–2.3 times from the initial results on the fifth day while in the control group, it decreased only after nine days. On the fifth day in the main group, the stab shift, LII, and lymphocytopenia decreased. However, these results were not present in the control group. After 3 days, the diagnosis of severe acute pancreatitis was confirmed in 47 people in the main group with mortality of 1 person. On the other hand, the diagnosis of severe acute pancreatitis was confirmed in 48 persons in the control group with mortality of 3 people. The terms of treatment in the main group additionally given with Ulinastatin were  $2.3 \pm 1.3$  k/days less than the control group.

**Conclusion.** Ulinastatin has proven itself a highly effective protease inhibitor in destructive forms of acute pancreatitis

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## Treatment of Patients with Multiple Complicated Fractures of Ribs in Combined Injury

**Chekaev Rinat**<sup>1</sup>, Dzharkeev Kairat<sup>1</sup>, Rustemova Kulsara<sup>1</sup>, Kozhakhmetov Saken<sup>1</sup>, Akyshev Olzhas<sup>1</sup>, Aliev Mazhit<sup>1</sup>

<sup>1</sup>*Astana Medical University, Nur-Sultan, Republic of Kazakhstan*

**Background.** Closed chest trauma occurs in 10–15% of hospitalized patients, in 60% of cases it is complicated by rib fractures and ranks third after limb fractures and traumatic brain injury, posing a threat to the victim's life. Mortality in this case reaches 17–30%, with polytrauma up to 76%.

**Aim.** Analysis and generalization of the experience of providing assistance to victims with multiple, complicated rib fractures.

**Methods.** We treated 374 (100%) patients in the period from 2011 to 2021: the patients with fractures of 2, 3 ribs – 186 (49.7%), with fractures of more than 4 or more ribs – 188 (50.3%), 93 (24.9%) patients had a concomitant injury with fractures of the clavicle, spine, closed head injury, limbs. 170 (45%) patients (control group) underwent conservative treatment, including intercostal blockade (84.7% of cases), taping (18%), the use of corsets, as well as puncture and drainage of the pleural cavities. 204 (55%) patients (main group) underwent surgical interventions – thoracoscopy, video-assisted thoracoscopic surgery (VATS) with intramedullary osteosynthesis, minithoracotomy with suturing of lung and diaphragm ruptures (5.9%).

**Results.** Surgical interventions for multiple, complicated rib fractures were divided into the following groups: 1 – surgery for health reasons; 2 – urgent or delayed operations in the first 2–3 days. Victims with fractures of three or more ribs required inpatient treatment for at least 2 weeks. The duration of rehabilitation with traditional treatment is 4–6 weeks. 373 patients with multiple complicated rib fractures were discharged with recovery, 1 patient died on the first day after admission for reasons not related to rib fractures, the presence of severe concomitant trauma, concomitant diseases. Patients treated with conservative methods of treatment stayed in the hospital for 14 to 22 bed-days. Patients who underwent surgery were hospitalized for an average of 9 to 13 bed-days.

**Conclusion.** VATS treatment of patients with multiple, complicated rib fractures with concomitant injuries has significantly increased the effectiveness of treatment for this category of patients.

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## Modern Approach to Treatment of Abdominal Sepsis

Absatirova Venera<sup>1</sup>, Baibusunova Aida<sup>1</sup>, Rustemova Kulsara<sup>1</sup>, Kozhakhmetov Saken<sup>1</sup>, Saparbayev Samat<sup>2</sup>

<sup>1</sup>Astana Medical University, Nur-Sultan, Kazakhstan

<sup>2</sup>West-Kazakhstan Marat Ospanov Medical University, Aktobe, Kazakhstan

**Background.** The incidence of abdominal sepsis (AS) in developed countries reaches as many as 18 million cases annually, with a steady increase in the number of patients by 5–7%. The rate of mortality is about 30–35%, with the development of multiple organ failure (MOF), this rate rises to 98%.

Thus, the question of studying and carrying out research on effective methods in the search for AS remains relevant. Cell therapy is a new promising method for treating septic conditions in SEI patients with abdominal sepsis. There have been cases of cell mediator disease in patients with MOF and complications of trauma from surgical pathologies.

**Aim.** To study the state of the immune status of patients with AS during traditional therapy.

**Methods.** A retrospective study of 100 patients who were hospitalized from January 2020 to June 2021, in city multidisciplinary hospitals No. 1 and No. 2, Nur-Sultan city.

**Results.** The etiological factors of AS occurrence, haematological parameters, data of bacterial cultures from the wound were studied. The analysis showed the main causes of AS: destructive forms of appendicitis, cholecystitis and pancreatitis. Not the least important factor in the development of AS is occupied by intestinal obstruction.

Analysis of the results of patients' hemograms showed the following: in the pro-inflammatory phase (from 1–3 days) leukocytes, g/l –  $12.95 \pm 1.21$  (16.75–9.68); monocytes, % –  $7.58 \pm 1.88$  (5.37–16.6); neutrophils/monocytes – 6.4 (4.03–6.48); neutrophils, % –  $48.51 \pm 8.73$  (34.79–62.97).

In the transitional phase (5–7 days): leukocytes, g/l –  $10.01 \pm 0.66$  (6.96–11.36); monocytes, % –  $6.83 \pm 0.63$  (4.61–8.14); neutrophils/monocytes – 6.8 (6.66–7.18); neutrophils, % –  $46.42 \pm 6.39$  (30.7–58.42). In the phase of immunoparalysis, there is a sharp decrease in all of the above indicators.

**Conclusion.** A retrospective analysis of the state of hemograms and the immune status of patients with AS with traditional therapy showed the feasibility of including cell mediators in its composition in order to improve the treatment of this category of patients.

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## CARDIOVASCULAR AND REGENERATIVE MEDICINE

### Minimally Invasive Ventricular Septal Defect Closure on a Beating Heart: Experience in Our Center

Adilbekova Akkerbez<sup>1</sup>, Marasulov Shukhrat<sup>1</sup>, Maiorov Rinat<sup>1</sup>, Kozhakhmetov Saken<sup>2</sup>

<sup>1</sup>National Scientific Medical Center, Nur-Sultan, Kazakhstan

<sup>2</sup>Astana Medical University, Nur-Sultan, Kazakhstan

**Background.** Ventricular septal defect (VSD) is one of the most common congenital heart diseases, accounting for about 20% of congenital heart disease. The treatment methods of VSD include repair of VSD under cardiopulmonary bypass (CPB), interventional closure of VSD by percutaneous puncture and minimally invasive operative technique VSD closure on a beating heart (hybrid procedure).

Hybrid procedure in the closure of VSD – this is among the latest developments introduced in cardiac surgery practice. This technique sparing, to minimize surgical trauma, performs without connecting the patient to the CPB, does not require X-ray exposure and wider indications than interventional closure.

**Aim.** To present results of hybrid procedures performed in the treatment of VSD in our center in 2016–2021.

**Methods.** A retrospective study of 360 patients who were hospitalized from January 2016 to December 2021, in the Department of Pediatric Cardiac Surgery in National Scientific Medical Center, Nur-Sultan city. Patients were selected, as follows: the age of patients above 6 months, weight above 4 kg, transthoracic echocardiography (TTE) parameters: VSD size was 3–14 mm. Under constant transoesophageal echocardiography (TEE) control cut length of 2–3 cm in the lower third of the sternum purse-string suture was performed overlay thread «prolene» and puncture of the right ventricle in the epicentre shake defect, delivery and installation of special occluder appropriate size (size of the defect exceeding 1–2 mm) and forms.

**Results.** Successful closure of VSD was performed in 96.1% patients. There were 14 conversions due to underestimating the size and localization of the defects. Residual intraoperative shunt in 5 patients (1.4%), also AV block has been identified in 5 patients (1.4%) after 1 year, in-hospital mortality in 1 patient (0.27%) (cause – arterial hypertension), aortic valvular insufficiency moderate (grade II) in 3 patients (0.83%). In most cases, tricuspid regurgitation after operation was the same as before or less. Duration of surgery ranged from 50 minutes to 2.5 hours, intraoperative blood loss – from 10 to 50 ml, artificial ventilation – from 3 to 5 hours, stay in the ICU – from 3 to 12 hours, cardiotoxic support in 5 patients (1.4%) and blood transfusions in 3 patients (0.83%). Removing drainage on day 1 after the operation, the length of postoperative stay in the hospital – 5 to 7 days.

**Conclusion.** This method has minimal trauma, shortens the duration of hospitalization, rehabilitation, and achieving a good cosmetic effect. It can be used to close the VSD different localizations in infants and older children.

## INFECTIOUS DISEASES AND PULMONOLOGY

### Intrahospital Mortality in Sepsis and Septic Shock Patients in Latvia – Comparison of Outcomes for Explicit and Implicit Case Definitions in Nationwide Administrative Health Data

Pučeta Laura<sup>1,2</sup>, Luguzis Artis<sup>1,3</sup>, Bārzdīņš Juris<sup>1</sup>, Dumpis Uga<sup>1,2</sup>

<sup>1</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

<sup>2</sup>Pauls Stradiņš Clinical University Hospital, Riga, Latvia

<sup>3</sup>Laboratory for Statistical Research and Data Analysis, Faculty of Physics, Mathematics and Optometry, University of Latvia, Riga, Latvia

**Background.** Sepsis as a life-threatening condition requiring hospitalization is a common cause of in-hospital deaths worldwide. Predefined sets of hospital discharge codes are widely used for sepsis surveillance by identification of cases explicitly coded as sepsis or septic shock, as well as cases implicitly attributable to sepsis when concurrently specific codes for infection and organ dysfunction are used.

**Aim.** The aim of the study was to assess intrahospital mortality in comparison to implicit and explicit coding approaches.

**Methods.** In retrospective administrative data study, all hospitalizations with explicit and implicit sepsis ICD-10 discharge codes were identified from 2015 to 2019. For unadjusted analysis, odds ratio (OR) of death was estimated via logistic regression with sepsis group as an independent variable. For adjusted analysis, implicit sepsis hospitalizations were matched to explicit sepsis hospitalizations using 1:1 propensity score matching, where baseline demographic characteristics and comorbidities were used as covariates in propensity score estimation. Adjusted OR was then estimated using matched data and represents the change in odds of death if all implicit sepsis cases would be explicit cases (ATT effect). As a sensitivity analysis, IPTW weighting was employed to compare mortality between groups.

**Results.** From 12 866 sepsis hospitalizations included in the study, 9 449 (73.4%) were in the explicit sepsis cohort, which differed significantly from implicit sepsis group by age (median 34 vs 72,  $p < 0.001$ ), male proportion (19% vs 45%,  $p < 0.001$ ) and comorbidities (median Charlson Comorbidity Index 0 vs 3,  $p < 0.001$ ). Overall unadjusted intrahospital mortality was 20.3% with a substantial difference between the explicit and implicit sepsis cohorts, 16.9% vs 29.7% ( $p < 0.001$ ), OR 2.07, 95% CI [1.89, 2.28]. In the adjusted analysis, comparing 3 417 implicit sepsis cases to 3 417 matched cases, estimated OR was 0.88, 95% CI [0.86, 0.90]. In the sensitivity analysis using IPTW weighting, estimated OR was 1.00, 95% CI [0.98, 1.02].

**Conclusion.** Intrahospital mortality was similar to rates reported from other cohorts in Europe. The crude intrahospital mortality was higher in the implicit code group, however, it was significantly lower than in the explicit sepsis code cohort when matching patients were compared.

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## Prevalence of Methicillin Resistant *Staphylococcus Epidermidis* in Healthy Volunteers and in Hospitalized Patients

Warren Keelan<sup>1</sup>, Zandersone Baiba<sup>1</sup>, Tračevska Tatjana<sup>1</sup>  
<sup>1</sup>Faculty of Medicine, University of Latvia, Riga, Latvia.

**Background.** *Staphylococcus epidermidis* is a coagulase negative staphylococcus (CONS), part of human skin microbiota and an opportunistic pathogen. Resistance to antimicrobials in *S. epidermidis* is of clinical significance, posing a major obstacle in the treatment success, incurring higher medical expenses and a prolonged antibiotic treatment course incurred. We hypothesize an increase in the prevalence of methicillin resistant CONS in the Riga community and hospital setting.

**Aim.** To investigate the tendency in the prevalence of methicillin resistance in *S. epidermidis* in the Riga community and hospital setting.

**Methods.** This study took place over a 13-year period, from 2008 to date, involving 411 participants. The participants were arranged into a control group consisting of healthy volunteers and a hospitalized patient group with suspected CONS infection, comprising 226 and 185 participants, respectively. Nasal swabs were collected from each participant and subjected to *in vitro* microbiological testing. Susceptibility of bacteria to methicillin was detected using the cefoxitin disc diffusion method in accordance with the Clinical and Laboratory Standards Institute 2021 guidelines, version 11.0. The cefoxitin resistance screening breakpoint for *S. epidermidis* was denoted R<25 mm zone of inhibition.

**Results.** This study found that the prevalence of methicillin resistant *S. epidermidis* (MRSE) remained stable among the healthy participant group sampled between the years 2008 to 2021 (see table below). However, among the hospitalized patient participant group, a significant increase in the prevalence of methicillin resistant *S. epidermidis* from 27.0% to 82.0% was detected between sampling years 2008 to 2021.

Table

Year of sampling	Healthy Participant Group		Hospitalized Patient Group	
	MSSE, %	MRSE, %	MSSE, %	MRSE, %
2008–2011	85.0	15.0	73.0	27.0
2019–2021	86.0	14.0	18.0	82.0

**Conclusion.** The current study demonstrates an increasing tendency in the prevalence of methicillin resistance in *S. epidermidis* among Riga hospitalized patients. Our findings support the presupposition that there is increased accumulation of methicillin resistant CONS in the hospital setting, and further research in this area is merited.

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## Forecast Model of Appraisal of Severity of Disease Course in PCR-Positive Pneumonia Cases in Young and Elderly Patients

Nurgaliyeva Bayan<sup>1,2</sup>, Kapustina Victoria<sup>1,2</sup>

<sup>1</sup>Kazakh National Medical University named after S. Asfendiyarov, Almaty, Republic of Kazakhstan

<sup>2</sup>KHAK Medical Center, Almaty, Republic of Kazakhstan

**Background.** According to official statistics, as of 17 of December 2021, there are a total number of 1 065 597 laboratory-confirmed cases of coronavirus infection in Kazakhstan.

**Aim.** This study aims to assess the clinical course of SARS CoV-2-associated pneumonia in young and elderly patients. The correlation between age and the severity of the clinical course of the disease was built into a mathematical model of the severity of the course of a viral disease.

**Methods.** All PCR-positive patients were diagnosed with polysegmental pneumonia-based results of computer tomography. Patients were divided into 2 equal groups: young and elderly. The  $\chi^2$  test was applied to build a multilinear regression analysis of the severity of SAR-S CoV-2-associated pneumonia based on the patient's age, the results of computer tomography and neutrophilic-lymphocyte ratio (NLR).

**Results.** The majority of elderly patients had comorbidities such as arterial hypertension (76%), coronary heart disease (24%), and type 2 diabetes mellitus (20%). No concomitant pathology was revealed in young patients. Analysis of CT results showed that in the elderly group, one third had a greater degree of lung lesion, corresponding to CT 3 and CT 4 (33%). In the group of young patients, CT 2 was more often diagnosed (59%). In 33.3% of elderly patients, the calculation using the  $\chi^2$  criterion made it possible to assess the risk of developing extensive lung lesions. However, in young patients, the risk of developing extensive lung tissue damage was only 7%. Comparative analysis of the two groups revealed that elderly patients are more prone to hypercoagulability than younger patients, they have higher mean values of D-dimer (0.6 mg/dl versus 0.09 mg/dl) and ferritin (400 ng/ml 119 ng/ml). In elderly patients, the average neutrophil-lymphocyte index ratio exceeded the norm (4× in the elderly and 2× in the young), which was found to be a predictor of a more severe course of the disease.

**Conclusion.** The mathematical model made it possible to reveal a different dependence of the severity of the course of the disease. In the group of young people, the clinical course depends on the scale (percentage) of damage to the lung tissue, while in the group of the elderly the clinical course of the disease correlates strongly with age.

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## Prognosis Model of Mortality in PCR-Positive COVID Pneumonia

Bayan Nurgaliyeva<sup>1,2</sup>, Yerden Suraganov<sup>1,2</sup>

<sup>1</sup>Kazakh National Medical University named after S. Asfendiyarov, Almaty, Republic of Kazakhstan

<sup>2</sup>KHAK Medical Center, Almaty, Republic of Kazakhstan

**Background.** Officially as of 14 December 2021, there is a total number of 981 435 SARS-CoV-2 PCR-positive and 83 557 SARS-CoV-2 PCR-negative patients registered with COVID-19 in the Republic of Kazakhstan.

**Aim.** This study aims to assess severity-associated clinical markers for the course of COVID-19 patients and determine the prognosis model of lethal outcome in PCR-positive COVID pneumonia.

**Methods.** A retrospective study was carried out involving 59 patients with PCR-positive COVID-19 pneumonia confirmed by CT with different degrees of lung lesions. A comparative analysis between patients with the lethal outcome (28 patients) and survivors (31 patients) has been implemented to identify clinical markers for the severity of the disease. For the predictive model, a linear regression model was built using the MATLAB program and an online logistic regression calculator.

**Results.** In the group of the deceased, 93% had concomitant diseases, and in the group of survivors, concomitant diseases were detected less frequently (48.4%). Arterial hypertension (82.4%), ischemic heart disease (71.4%), and diabetes mellitus (42.85%) prevailed as a comorbidity in the group of the deceased. In the group of the deceased, more often than in the group of survivors, a higher degree of lung lesion was found by CT3 (50–75% lung lesion) (27.27% vs 20%) and CT4 (over 75% lung lesion) (13.6% versus 10%). In the group of the deceased, mechanical ventilation was performed on 57.14%, in the group of survivors, mechanical ventilation was used in less than a quarter of patients (22.58%). For prognostic assessment, linear regression was built, with the gender and a high degree of lung damage as predictors of lethal outcome used as indicators.

**Conclusion.** In the group of the deceased, a combination of arterial hypertension, ischemic disease, and diabetes mellitus prevailed. According to the regression models, key lethal factors were found to be male gender and a high degree of lung lesion.

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## Mitochondrial DNA Variations and K Haplogroup Frequencies Differ Between TB Patients and Healthy Controls

Freimane Lauma<sup>1</sup>, Igumnova Viktorija<sup>1</sup>, Sadovska Darja<sup>1</sup>, Kivrāne Agnija<sup>1</sup>, Ķimsis Jānis<sup>1</sup>,  
Barkāne Linda<sup>2</sup>, Ranka Renāte<sup>1</sup>

<sup>1</sup>Latvian Biomedical Research and Study Centre, Riga, Latvia

<sup>2</sup>Centre of Tuberculosis and Lung Diseases, Riga East Clinical University Hospital, Riga, Latvia

**Background.** There is an emerging interest in the role of host mitochondria in the innate immune responses during infection with intracellular pathogens such as *Mycobacterium tuberculosis*. Thereby, questions of mitochondrial genome variation impact on the metabolism, innate responses activation and/or possible effect on the predisposition or severity of the disease are of high importance.

**Aim.** The aim of the study was to explore differences in mtDNA mutation distribution patterns in TB patients compared to healthy controls.

**Methods.** Peripheral blood DNA samples of 129 participants were used in this study: 95 TB patients (52 multi-drug resistant (MDR) and 34 drug-susceptible (DS)), and 43 age-matching healthy controls. The study was approved by the Central Medical Ethics Committee of Latvia. Full mitochondrial genome sequencing was carried out using IonTorrent technology. DNA fragment libraries were prepared using Ion Xpress™ Plus Fragment Library Kit and Ion Xpress™ Barcode Adapters Kits (Thermo Fisher Scientific, USA). The data were analysed at usegalaxy.eu web platform. Variants were analysed with FreeBayes tool for haploid genomes. Statistical analysis was performed using XLSTATS and R software, at significance level  $\alpha=0.05$ .

**Results.** The overall mtDNA mutation count per sample or mutation count per gene was similar between groups, although *MT-ND4L* gene variants had greater incidence in the control group; the majority of the variants in this gene were associated with the mitochondrial K haplogroup (K HG). K HG was the only mitochondrial HG which showed statistically significant differences between study groups (MDR-TB patients compared to the controls, Fisher's test,  $p=0.017$ ).

Looking at differences at the level of variations, Pearson's Chi-squared test with simulated p-value showed statistically significant difference between TB patients and controls for several SNPs in the protein coding genes only ( $p=0.0045$ ): m.11299T>C (MT-ND4), m.14167C>T (MT-ND6), m.3480A>G (MT-ND1), m.4715A>G (MT-ND2), m.9055G>A (MT-ATP6), m.9698T>C (MT-CO3). These variants in the TB patient group were less common than predicted. Again, all but one SNP variants (except m.4715A>G) were associated with K HG and were underrepresented in DS-TB patients and absent in MDR-TB group. SNP m.4715A>G was present only in the control group.

**Conclusion.** We indicated six mtDNA variants which were less common in TB patients compared to the healthy controls. Most of the variants were associated with mitochondrial K HG which could indicate the existence of protective effect regarding TB infection. Additional studies in larger cohort are required.

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## Comparing Management of Acute Complicated and Uncomplicated Left-Sided Colonic Diverticulitis

Levensteina Evija<sup>1,2,3</sup>, Ertis Renars<sup>4</sup>, Liepins Maris<sup>1,3</sup>

<sup>1</sup>Riga East Clinical University Hospital, Riga, Latvia

<sup>2</sup>Riga Medical College of the University of Latvia, Riga, Latvia

<sup>3</sup>Riga Stradiņš University, Riga, Latvia

<sup>4</sup>University of Latvia, Riga, Latvia

**Background.** The rapid emergence of resistant bacteria is still a major issue, which requires optimisation of the use of antibiotics. In acute uncomplicated diverticulitis the previous guidelines recommended 7–10-day regimen of broad-spectrum antibiotics, but studies have demonstrated that antibiotics are not necessary in the treatment of uncomplicated left-sided diverticulitis in immunocompetent patients, as it may be a self-limiting condition (2020 WSES guidelines). The role of administration route is uncertain, as orally given (PO) antibiotics may be equally effective to intravenous (IV). Acute colonic diverticulitis is one of the most common clinical conditions by surgeons in the emergency setting.

**Aim.** The aim of the current study was to compare management of complicated and uncomplicated diverticulitis in the current stationary setting and mark a place for improvement.

**Methods.** In 2020 retrospective study was performed in Riga East University Hospital. 42 patients (30 women) were enrolled; 21 patients with uncomplicated and 21 with complicated left-sided diverticulitis. Results for continuous variables are expressed as median (Q1–Q3). Results with values of  $p < 0.05$  were considered as statistically significant.

**Results.** The median age was 57 [53.5; 70.5] years. In the hospital setting, all patients were started on antibacterial therapy within the first day. 16 (76.2%) patients in both groups received IV *Metronidazolum* and *Ceftriaxonum* combination. 2 (9.5%) patients with uncomplicated diverticulitis had PO *Metronidazolum* and *Ciprofloxacinum* as initial treatment. 9 (43%) patients with uncomplicated diverticulitis and 7 (33.3%) with complicated diverticulitis were switched to PO *Metronidazolum* plus *Ciprofloxacinum* after median of 4 [3.00; 4.00] and 4 [3.00; 6.00] days' treatment, respectively ( $p > 0.05$ ). With uncomplicated diverticulitis, inpatient setting antibiotic treatment was median of 6.00 [4.00; 7.00] and with complicated – 7.00 [5.00; 9.00] days ( $p > 0.05$ ), the total treatment 11.0 [9.00; 14.0] and 10.0 [8.00; 14.0] days, respectively ( $p > 0.05$ ).

**Conclusion.** Similar therapeutic treatment tactics are used for complicated and uncomplicated diverticulitis. Antibiotic therapy within the first day of hospitalisation was prescribed in all uncomplicated diverticulitis cases and only to two patients were administered orally. Since studies show that antimicrobial usage increases patient stay in the hospital without lowering the complication rates, it must be seriously considered to apply selective, rather than routine, use of antibiotics in patients with mild acute uncomplicated diverticulitis.

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## Correlation of Potential Biomarkers With COVID-19 Virus Infection Outcome

Zikovs Rems<sup>1,2,3</sup>, Aleksejeva Marija<sup>2,4</sup>, Ūdre Sintija<sup>3,4</sup>, Svareniece Elizabete<sup>3,4</sup>, Ozoliņa Agnese<sup>1,3</sup>, Liguts Viesturs<sup>1,3</sup>, Šuba Oļegs<sup>3</sup>, Saba Ingrīda<sup>3</sup>, Koļesņikova Tatjana<sup>2</sup>

<sup>1</sup>Rīga Stradiņš University, Riga, Latvia

<sup>2</sup>Pauls Stradiņš Clinical University Hospital, Riga, Latvia

<sup>3</sup>Riga Eastern Clinical University Hospital, Riga, Latvia

<sup>4</sup>University of Latvia, Riga, Latvia

**Background.** COVID-19 affects people in different ways. It can cause mild to moderate symptoms, but also lead to severe illness and death. Biomarkers that can be used in clinical practice are known to predict outcome of COVID-19 virus disease.

**Aim.** The aim of this study was to evaluate previously unproven biomarkers as predictors of COVID-19 severity and patient outcome.

**Methods.** We retrospectively analysed data of 100 COVID-19 patients. Such potential biomarkers as IL-6, fibrinogen, D-dimers, leukocytes, C-reactive protein (CRP), lymphocytes, procalcitonin (PCT), ferritin, lactate dehydrogenase (LDH), platelets and lactate plasma level were detected every day for the first 10 days after administration in ICU and compared between survivals and patients who died. Association between plasma levels of biomarkers with patient outcome was analysed. The statistical program IBM SPSS Statistics version 25.0 was used for the analysis,  $p < 0.05$ .

**Results.** A total of 100 (46 females, 54 males) patients were retrospectively included with the mean age  $64.87 \pm 9.89$  years (33–91). Almost half of patients (43) died on average on 14.25 day. It has been observed that D-dimer values were slightly higher in patients who died,  $6.96 \pm 3.85$  vs  $3.85 \pm 1.21$  mg/l compared to survivors,  $p = 0.003$ . The most pronounced effect of risk to die was shown by lactate plasma levels on day 4 and day 10, because we found that it was statistically higher for those who died  $13.6 \pm 5.2$  mmol/l vs  $2.64 \pm 2.32$  mmol/l,  $p = 0.002$  respectively. The mean time spent in hospital was  $24.53 \pm 13.53$  days and it differed between those who survived and those who died (on average 10.24 vs 14.29 days),  $p = 0.0029$ .

**Conclusion.** Increased plasma levels of biomarkers are associated with a higher risk of mortality and, it might be possible that higher lactate plasma levels and D-dimer plasma levels measured on day 4 can be used as a forecast indicator in intensive care COVID-19 patients.

**Acknowledgements.** This study was conducted in Pauls Stradiņš Clinical University Hospital, Riga Eastern Clinical University Hospital.

## NEUROLOGY AND ONCOLOGY

### The Value of Contrast-Enhanced Mammography on Evaluation of Breast Invasive Carcinoma Size Compared With Histopathological Assessment

Sulca Liga<sup>2,4</sup>, Engele Ilze<sup>1,2</sup>, Zablocka Tatjana<sup>1,2,3</sup>, Isajevs Sergejs<sup>1,2,5</sup>

<sup>1</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

<sup>2</sup>Riga East Clinical University Hospital, Riga, Latvia

<sup>3</sup>Pauls Stradiņš Clinical University Hospital, Riga, Latvia

<sup>4</sup>Residency Development Programme, University of Latvia, Riga, Latvia

<sup>5</sup>Institute of Clinical and Preventive Medicine, University of Latvia, Riga, Latvia

**Background.** Breast cancer is the most common cancer in women worldwide. Breast cancer is a heterogeneous disease, and stratification of tumours is paramount to achieve better clinical outcomes. Breast cancer diagnosis and staging is based on mammography, ultrasound, and magnetic resonance imaging (MRI). Breast imaging-reporting and data system (BI-RADS) is a classification system based on imaging data to stratify the breast lesions.

Histopathological evaluation of breast cancer is a gold standard for diagnosis. The stratification of breast cancers based primarily on the tumour size, tumour type and expression of oestrogen receptor (ER), progesterone receptor (PR) and ERBB2 receptor (HER2). It is of particular importance to assess the value of breast imaging data and its correlation with histopathological characteristics, which could guide clinical decisions before the surgical treatment.

**Aim.** The aim of the current study was to assess the value of breast contrast mammography on evaluation of invasive breast carcinoma size compared to standard histopathological evaluation and its association with tumour histopathological characteristics.

**Methods.** Altogether, 82 patients undergoing breast contrast-enhanced mammographic examination with subsequent core needle biopsy in Riga East Clinical University Hospital Latvian Oncology Centre in 2021 were retrospectively enrolled in the study. The breast density according to Breast Imaging Reporting and Data System (BI-RADS) was assessed. The histopathological tumour size was assessed after breast surgical operation by gross evaluation. The tumour type, tumour grade, expression of ER, PR, Her-2/neu and Ki-67 was assessed on core needle biopsies.

Associations between imaging data and clinicopathological findings were analysed using the chi-square test ( $\chi^2$ ). The McNemar test was used to compare the sensitivity and specificity for the assessment of tumour size by contrast-mammography and histopathological examination.

**Results.** The median age of enrolled patients was 62 years (range 31.0–83.0). The median tumour size assessed by contrast mammography was 2.5 cm (0.6–12). The median tumour size evaluated by histopathological examination was 2.1 cm (0.5–6). The study demonstrated the high sensitivity of contrast mammography in evaluation of tumour size compared to histopathological examination ( $p < 0.0001$ ).

The association of tumour size assessed by histopathological examination, and tumour grade and Ki-67 index was revealed (respectively,  $\chi^2 = 0.11$ ;  $p = 0.01$  and  $\chi^2 = 0.07$ ;  $p = 0.03$ ).

However, the association between tumour size assessed by mammography and tumour grade and Ki-67 index by histopathological examination has not been observed.

**Conclusion.** The contrast-enhanced mammography has a high sensitivity and specificity in evaluation on invasive breast cancer size compared to histopathological examination.

## Microcell Functional Activity Differences Based on the TEM

**Simsone Zane**<sup>1</sup>, Freivalds Talivaldis<sup>1</sup>, Harju Līga<sup>1</sup>, Groma Valērija<sup>2</sup>, Buiķis Indulis<sup>1</sup>

<sup>1</sup>*Institute of Cardiology and Regenerative Medicine, University of Latvia, Riga, Latvia*

<sup>2</sup>*Department of Histology (Morphology), Institute of Anatomy and Anthropology, Riga Stradiņš University, Riga, Latvia*

**Background.** Thousands of cancer cases are diagnosed each year, despite the advancements in detection and treatment options. Cancer occurrence and resistance are being studied all around the world. However, there are few studies on cancer cell population after treatment. Great importance is assigned to individual anticancer treatments in the context of antigen blocking therapy. Nonetheless, more research into cancer cell resistance and common patterns in different cancer types is required for effective treatment, as there are known cases of cancer returning and even becoming more malignant during anti-cancer treatment.

**Aim.** The aim of the current study was identified and characterize morphologically microcell functional activity based on the transmission electron microscopy.

**Methods.** Transmission electron microscopy was done in previous pilot experiments inducing microcells by stress factors. The cell line 4/21 was seeded in cell flasks with a density of  $\sim 3 \times 10^5$  cells per well and grown in Eagle medium supplemented (Sigma-Aldrich) with 10% FBS and 1% penicillin/streptomycin in a humidified atmosphere containing 5% CO<sub>2</sub> at 37°C, and treated with Thio-TEPA at a final concentration 20 µg/mL for the 24 h. The incubation medium was removed and 4°C 2.5% glutaraldehyde solution prepared in PBS was added for 15 min. Sequentially the cell monolayer was detached gently using a cell scraper and collected in a test tube, and centrifugated for 10 min at 200 g, and washed twice with PBS at 4°C and postfixed with 2% osmium acid solution prepared in PBS for 10 min. The pellet was dehydrated in 70% ethanol and embedded in Epon (Sigma-Aldrich). Ultrathin sections were contrasted by uranyl acetate and lead citrate, and examined using an electron microscope JEM-100B (TEM).

**Results.** We observe that the microcells are a small cell with cell nucleus, nuclear envelope, cell membranes, cell cytoplasm, and organoids. In the cell cytoplasm are ribosomes, visible as dark spots in the cell cytoplasm. The first type of microcells is characterized by the increased ratio between the cell nucleus and the cytoplasm area. There are ribosomes seen as dark spots in the cell cytoplasm. The heterochromatin known as the inactive part of the cell nucleus in sufficient quantity suggested to partly differentiated cell. The second type of microcells is characterized by the nucleoli and euchromatin, which occupy most of the cell nucleus suggesting to young cell with acquired stem cell properties.

**Conclusion.** New guidelines for predicting therapy could be developed on the basis of microcellular development studies.

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## The Most Common Localizations of Pancreatic Cancer Metastases in Patients of Pauls Stradiņš Oncology Clinic During 2018–2020

Kota Jekaterina<sup>1</sup>, Bloha Milāna<sup>1</sup>, Hasnere Sigita<sup>2</sup>

<sup>1</sup>University of Latvia, Riga, Latvia

<sup>2</sup>Pauls Stradiņš Clinical University Hospital, Riga, Latvia

**Background.** Pancreatic cancer is a deadly disease with high mortality due to difficulties in its early diagnosis and metastases (Bo Ren et al.). Contrary to early pancreatic carcinogenesis, the pathology and molecular features of advanced stage pancreatic cancers are relatively unexplored. As a result, little is known about the mechanisms responsible for uncontrolled local growth and metastatic spread, the very processes ultimately responsible for most pancreatic cancer-related deaths. Metastasis is a characteristic feature of a malignant tumour and the earlier it is detected, the better the prognosis for the patient will be. Pancreatic cancer most often metastasizes to lungs, liver, peritoneum, bones, kidneys. It happens that the primary tumour is very small, and the diagnosis is made precisely by secondary formations – metastases.

**Aim.** The aim of the current study was to find out, in which organ pancreatic cancer metastasizes most often.

**Methods.** Retrospective study was to evaluate the most common localizations of pancreas cancer. The data was taken from Pauls Stradiņš Clinical University Hospital oncological council reports and included data from 2018 to 2020. Collected data were statistically analysed in IBM SPSS Statistics 22.0.

**Results.** The retrospective study included 84 patients. 46.4% (n=39) of analysed patients were men and 53.6% (n=45) were women. Average age of the patient was 69.45, of women – 71.13, of men – 67.28. The retrospective study included caput pancreas cancer in 46.4 (n=39) patients, corpus pancreas cancer in 15.5% (n=15) patients and cauda pancreas cancer in 10.7% (n=9) patients, whereas n=23 patients of study did not have a precise localization of cancer. The most common localization of pancreas cancer metastasis was liver 32.1% (n=27), less often there were metastasis in lungs 6% (n=5) and cavi abdominis 9.5% (n=8). 57 patients did not have pancreas cancer metastasis. Comparing the three metastasis sites (liver, lungs, cavi abdominis), the most common metastasis occurs in the liver. There is a connection between metastasis in the liver and caput pancreas cancer.

**Conclusion.** Pancreatic cancer most often metastasizes in the liver – 32.1%.

## Characteristics of Patients with Brain Tumour During 2018–2020 in Pauls Stradiņš Clinical University Hospital

Vāla Luīze<sup>1</sup>, Mihaļkova Anna<sup>1</sup>, Hasnere Sigita<sup>1,2</sup>

<sup>1</sup>University of Latvia, Riga, Latvia

<sup>2</sup>Pauls Stradiņš Clinical University Hospital, Riga, Latvia

**Background.** In 2018, there were an estimated 162 534 (1.8% out of all cancer types) incidences of brain and CNS tumours in men and 134 317 (1.6% out of all cancer types) in women. The incidence of this type of cancer is increasing, its incidence and mortality rate has been reported to be 3.4 and 2.5 per 100 000 people worldwide. Brain tumours do not typically have obvious symptoms and they can develop at any age, so it is important to prevent people from developing brain cancers, and if the cancer has shown, to start an early and most effective treatment.

**Aim.** The aim of the current study was to characterize patients with brain tumour.

**Methods.** A retrospective study was performed. The data of confirmed brain tumours were obtained from Pauls Stradiņš Clinical University Hospital from 2018 to 2020. Histological type, age, gender, tumour localization, received treatment were analysed.

**Results.** In total, 297 cases of brain tumour were identified within the period from 2018 to 2020 at Pauls Stradiņš Clinical University Hospital. The most common brain tumour type was glioblastoma 40.1% (n=119, p<0.001), the second – diffuse astrocytoma 16.5% (n=49), followed by anaplastic astrocytoma 15.5% (n=46), next – atypical meningioma with 12.1% (n=36), anaplastic oligodendroglioma and ependymoma accordingly with 3.7% (n=11) and 3.4% (n=10), and the rarest brain tumours – Gr2 oligodendroglioma 2.7% (n=8), anaplastic meningioma 2.4% (n=7), gliosarcoma 1.3% (n=4), ganglioglioma; giant cell astrocytoma; Gr1 meningioma with 0.3% (n=1). Patients with confirmed brain tumour was 46.8% (n=139) man and 53.2% (n=158) women (p=0.272), overall, the mean age was 55±15.8. The most common tumour localization was left frontal lobe 17.8% (n=53), but the rarest localizations – the fourth and third ventricle, cerebellum and thalamus – 1% (n=3); 0.7% (n=2); 0.7% (n=2); 0.3% (n=1). 94.6% (n=281) of all patients received surgery and 5.4% biopsy was performed (n=16). From all patients 29% (n=86) received chemotherapy (temozolomide), and 33% (n=99) received radiotherapy.

**Conclusion.** Glioblastoma is the most common brain cancer. Brain tumours most commonly affect the left frontal lobe. No statistically significant difference was found between genders. The mean age was 55±15.8. The most common treatment combination was surgery with consequent radiotherapy plus temozolomide.

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## Treatment Outcomes of Liver Stereotactic Body Radiation Therapy for Colorectal Cancer Liver Metastases

Trofimovica-Krasnorucka Anastasija<sup>1,2</sup>, Maksimova Santa<sup>1,2</sup>, Frolova Julija<sup>1,3</sup>

<sup>1</sup>Department of Radiotherapy, Riga East Clinical University Hospital, Riga, Latvia

<sup>2</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

<sup>3</sup>Faculty of Medicine, Rīga Stradiņš University, Riga, Latvia

**Background.** Colorectal cancer (CRC) is the third most common cancer worldwide and the second most common cause of cancer-related death in 2020. The liver is one of the most typical sites of CRC metastatic spread. The treatment of choice for secondary liver tumours is surgery. Alternative treatment method for such patients is stereotactic body radiation therapy (SBRT). Latest studies have reported that liver SBRT is associated with safety, low toxicity, and high local control rates.

**Aim.** The aim of the study was to evaluate treatment outcomes and survival prognostic factors of liver SBRT in patients with CRC liver metastases.

**Methods.** This retrospective study included 56 CRC patients in whom liver SBRT was conducted at Riga East University Hospital, Oncology Centre of Latvia, between January 2010 and December 2019. One- and two- year local control (LC), progression-free survival rate (PFS) and overall survival (OS) rates were analyzed in these patients. Prognostic factors such as patient age, gender, tumour size and the biologically effective dose (BED 10) were analyzed by Cox analysis. BED 10 was calculated according to the formula  $BED = (\text{prescription dose}) \times [1 + (\text{dose per fraction}/\alpha/\beta)]$ , where the  $\alpha/\beta$  ratio is 10 Gy.

All patients underwent computed tomography (CT) based planning with 4-dimensional CT imaging. Vacuum pillows were used for patient positioning. All patients were treated with volumetric-modulated arc therapy.

**Results.** The study resulted in a total of 56 cases (31 (52.5%) males, 25 (42.4%) females), with median age of 64.9 years (range: 39.0–88.0 years). The median lesion size was 1.4 cm (range: 0.5–4.1 cm). The median follow-up duration was 29.0 months.

The median SBRT dose prescription was 16 Gy in 3 fractions. The median BED10 was 124.8 Gy. The survival results of the study showed that 1-year LC, PFS, and OS were 85.7%, 53.6%, and 100.0%. Two-year LC, PFS, and OS were 55.4%, 32.1%, and 64.3%, respectively.

From all prognostic factors that were analyzed, only BED10 ( $\geq 100$  Gy) showed an association with increased 2-year LC ( $p=0.001$ ) and 2-year PFS rate ( $p=0.002$ ). Patients with larger lesions and elderly patients had a worse 2-year OS rate ( $p=0.04$  and  $p=0.01$ ).

**Conclusion.** Liver SBRT is an effective alternative therapy for CRC patients with liver metastases. The study showed a statistically significant correlation between exceeding 100Gy BED10 and increased 2-year LC and PFS rates.

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## Ketogenic Diet for Epilepsy Treatment – what Predicts Higher Ketosis and Better Seizure Control

Apela Dana<sup>1,2</sup>, Grīnvalde Santa<sup>1,2</sup>, Strautmanis Jurgis<sup>1,2</sup>

<sup>1</sup>Rīga Stradiņš University, Riga, Latvia

<sup>2</sup>Children's Clinical University Hospital, Riga, Latvia

**Background.** Contradictory data about the association between ketone level and the effect on seizure frequency have been published.

**Aim.** The aim of the study was to check whether the way of ketone level assessment, as well as the way of seizure outcome estimation may be the reason for contradictory results.

**Methods.** The data about the age, sex, ketone levels and seizure frequency during the third month of the diet were gathered from medical records. The ketone levels were defined in four ways – the average of all measurements, the average of the morning measurements, the last measurement, the last morning measurement. The seizure outcome was defined in two ways – the absolute number of seizures, percentage decrease in seizure frequency.

**Results.** Overall, 47 patients included – 25 (53%) of them were boys. The median age was 40.9 (IQR 21.7; 91.4) months. The average ketone level was 4.5 (3.0; 5.0) mmol/l, the average morning ketone level 3.6 (2.9; 4.4) mmol/l, the measurement 4.5 (3.2; 5.9) mmol/l, the last morning measurement 3.8 (2.7; 4.6) mmol/l. Seizure count was 58 (9; 141) per month. Seizures had decreased by 73% (50%; 98%). The percentage of seizure decrease correlated significantly only with the average ketone level ( $r=0.54$ ,  $p=0.026$ ), but not with the other ketone values. There was no significant correlation between the absolute number of seizures and any of the ketone level values. There was quite strong ( $r>0.5$ ) and significant ( $p<0.05$ ) correlation between age and each of the ketone variables.

**Conclusion.** The average ketone level per month and the percentage of seizure decrease were found to be the best variables for finding the association between the ketones and efficacy of diet. The youngest children were proved to have the highest ketone levels.

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## Encephalopathy in COVID-19 Patients: Clinical Nature and Association With Biochemical Markers, Disease Severity and Outcome

Khachiashvili Gvantsa<sup>1</sup>, Koniashvili Otari<sup>1,2</sup>, Daraselia Dimitri<sup>1</sup>, Muzashvili Giorgi<sup>1</sup>, Gabunia Luiza<sup>3</sup>, Ghambashidze Ketevan<sup>4</sup>

<sup>1</sup>Tbilisi State Medical University, Tbilisi, Georgia

<sup>2</sup>Department of Neurology, Central University Clinic named after Academic N. Kipshidze, Tbilisi, Georgia

<sup>3</sup>Department of Medical Pharmacology, Tbilisi State Medical University, Tbilisi, Georgia

<sup>4</sup>Department of Pathophysiology, Tbilisi State Medical University, Tbilisi, Georgia

**Background.** Acute SARS-CoV-2 infection is characterized by a great variety of neurologic complications. Of these, encephalopathy is of particular significance due to its potential connection with poor prognosis.

**Aim.** We aimed to assess the frequency of encephalopathy in hospitalized patients during the acute phase of COVID-19, as well as its association with the degree of hypoxic and inflammatory state, the disease severity and outcome.

**Methods.** 4868 cases of acute SARS-CoV-2 infection have been reviewed retrospectively, from which we selected the patients who developed encephalopathy. Clinical and demographic data of these patients have been collected, including the gender, age, oxygen Saturation (SpO<sub>2</sub>), inflammatory markers: C-reactive protein (CRP), Ferritin, Procalcitonin (PCT), IL-6 and temperature. Semi-quantitative analysis for chest CT imaging had been performed to assess the lung injury index (0–24 scale), which was also analysed retrospectively. We investigated the duration of hospitalization (in days) and the disease outcome (mortality).

**Results.** From 4868 Covid-19 cases, 19 (0.39%) were complicated with encephalopathy. Age range of the patients with encephalopathy was 60–89, the mean 75.52 (SD 8.27), 10 (52.63%) of them were female. The lung injury index values ranged from 3 to 24, the mean – 10.55 points (SD 5.59). The mean SpO<sub>2</sub>=88% (SD 3.38). Inflammatory markers: CRP – the mean 49 mg/L (SD 33.05), Ferritin – the mean 569.5 (SD 484.7), PCT – the mean 0.87 (SD 0.65), IL-6 – the mean 23.89 (SD 8.216). Temperature – the mean 36.8 (SD 0.15). The mean duration of hospitalization period was 18.52 days (SD 9.84). In the majority of the patients, encephalopathy manifested with intermittent disorientation, psychomotor agitation, difficulty or inability to execute simple tasks and respond to the questions adequately. In some of the patients, difficulty of speaking and arousal was evident, subsequently leading to deep somnolence. Neither the neurological examination, nor the CT revealed any signs of focal neurologic deficit. Most of the patients required admission to the Intensive Care Unit, 7 patients (36.84 %) died.

**Conclusion.** Encephalopathy is relatively rare (0.39%), but an important complication of acute SARS-CoV-2 infection, since it is associated with the severe disease and poor outcome. Majority of the patients were afebrile/subfebrile but had elevated levels of inflammatory markers, the degree of hypoxemia was generally mild. The episodes of encephalopathy were mostly intermittent and the neurological status became normal after the acute phase of the disease in surviving patients.

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## Characteristic EEG Patterns of Anoxic Brain Injury After Cardiac Arrest and Prognostic Significance of EEG Reactivity

Koniashvili Otar<sup>1,2</sup>, Rukhadze Ia<sup>1</sup>, Muzashvili Giorgi<sup>2</sup>, Khachiashvili Gvantsa<sup>2</sup>, Gabunia Luiza<sup>3</sup>

<sup>1</sup>Department of Neurology, Central University Clinic After Academic N. Kipshidze, Tbilisi, Georgia

<sup>2</sup>Faculty of Medicine, Tbilisi State Medical University, Tbilisi, Georgia

<sup>3</sup>Scientific Research Skills Centre, Tbilisi State Medical University, Tbilisi, Georgia

**Background.** EEG in conditions like cardiac arrest, hypotension, and other disorders that cause an acute decrease in cerebral blood flow reflects attenuation of membrane potential eventually progressing to complete cessation of electric activity. Currently, EEG is considered as an essential utility, providing prognostic value in patients with post-anoxic coma.

**Aim.** Our group aimed to investigate epidemiological characteristics of EEG patterns in patients with anoxic coma and to assess the predictive nature of specific EEG patterns.

**Methods.** We selected 15 patients at Central University Clinic, who had suffered cardiac arrest. Demographic data, survival, and functional outcome were retrospectively assessed. We tried to establish the correlation between the pattern of EEG after anoxic injury and the outcome of selected patients.

**Results.** The mean age of selected patients was 62 years (SD 10), most of the individuals were male (60%). Selected patients suffered from out-of-hospital cardiac arrest. Nine patients showed diffuse Theta waves. In three patients out of nine, EEG recording was dominated by theta activity; however, the remaining patients exhibited mixed alpha-theta activity. Out of these nine patients, two demonstrated reactivity towards stimulation. Three patients showed diffuse delta slowing. Interestingly, two out of these three individuals exhibited variability in EEG patterns upon stimulation. In addition, one patient did not reveal reactivity to stimulation. One patient showed generalized triphasic waves, consisting of medium voltage, three-phased bilateral, and symmetric waveforms with the frequency of 2–2.5 Hz. One patient showed a burst-suppression pattern. Between burst, diffuse and bilateral suppression of EEG activity was noted, ranging from 2 s to 9 s, periodicity of these paroxysms was irregular. Reactivity was absent in this case. In two patients, a low voltage output pattern was evident. None of these patients demonstrated reactivity upon stimulation. In total EEG of four patients out of fifteen exhibited reactivity upon stimulation.

Eventually, care was withdrawn from eight patients, five patients died without regaining consciousness and two patients awoke with significant cognitive deficits.

**Conclusion.** Consequently, it should be emphasized that the most frequent EEG pattern detected in patients with postanoxic coma was either isolated predominance of theta waves or mixed alpha-theta activity, followed by diffuse delta activity. It should be noted that the correlation between the reactivity of EEG has proved to be of predictive value in such patients. It was exemplified by the two surviving patients.

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## Efficacy of Erenumab in Patients with Episodic and Chronic Migraine

Karpavičiūtė Vita<sup>1</sup>, Statkevičienė Karina<sup>1</sup>, Žemgulytė Gintarė<sup>2</sup>

<sup>1</sup>Lithuanian University of Health Sciences, Kaunas, Lithuania

<sup>2</sup>Department of Neurology, Lithuanian University of Health Sciences, Kaunas, Lithuania

**Background.** Migraine is a widespread and disabling disorder, and the treatment options thereof are still inadequate. Previous prophylactic treatments for migraine have been developed to treat diseases other than migraine, and their effectiveness remains limited. Recently, a new class of drugs for migraine prophylaxis in adults, the calcitonin gene-related peptide (CGRP) antagonists has been approved, and there is a growing body of evidence regarding the effectiveness of these drugs.

**Aim.** To evaluate the efficacy and adverse effects of erenumab (CGRP antagonist) in the treatment of patients with episodic and chronic migraine.

**Methods.** A total of 67 patients treated with erenumab for 6 months were enrolled in a retrospective study conducted between 2019 and 2021. Pooled data on patients, disease course (episodic migraine – 0–14 headache days/month, chronic migraine – 15 or more headache days/month in the duration of 3 months or more) and drug side-effects were collected. Efficacy analyses included changes in monthly migraine days (MMD) from baseline at 3 and 6 months. A positive effect was considered to have occurred if the reduction in MMD was greater than 50%. Statistical analysis was performed using SPSS Statistics 25.0 software. The  $\chi^2$  criterion, Fisher's exact test, Wilcoxon test and Spearman correlation were used for data analysis.

**Results.** The mean age ( $\pm$ SD) of the patients was  $42.6 \pm 11.4$  years; 86.6% were women. The duration of migraine median was 18 years (IQR: 7–30.75). The median MMD before erenumab was 15 (IQR: 12–19). The study showed that longer disease duration was positively correlated with higher MMD ( $\rho=0.41$ ;  $p=0.001$ ). Prior to erenumab, 24 patients had received no prophylactic treatment and 43 had received 1 or more drugs. A positive effect of erenumab was achieved in 73.1% of patients at 3 months and in 65.7% of patients at 6 months. There was a statistically significant difference in MMD before treatment and after 3 and 6 months ( $p<0.001$ ). However, the efficacy of erenumab was similar in the episodic and chronic migraine groups. Due to treatment ineffectiveness and side effects, biologic therapy was switched after 3 months in 2 patients and after 6 months – in 8 patients (a total of 14.9%). Two patients experienced side-effects with erenumab (constipation, weight gain and hair loss).

**Conclusion.** The results suggest that erenumab is an effective and safe treatment for episodic and chronic migraine, but further monitoring of its efficacy is needed.

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## PAEDIATRICS

### Impact of COVID-19 Pandemic on Children With Acute Appendicitis

Vansevičienė Idilė<sup>1</sup>, Bučinskaitė Danielė<sup>2</sup>, Malcius Dalius<sup>1</sup>, Lukošūtė-Urbonienė Aušra<sup>1</sup>,  
Beržanskis Mindaugas<sup>1</sup>, Čekanauskas Emilis<sup>1</sup>, Barauskas Vidmantas<sup>1</sup>

<sup>1</sup>Paediatric Surgery Department, Lithuanian University of Health Sciences, Kaunas, Lithuania

<sup>2</sup>Department of Surgery, Lithuanian University of Health Sciences, Kaunas, Lithuania

**Background.** Acute appendicitis (AA) remains one of the most common surgical problems worldwide in the paediatric population, and with more knowledge about the disease and changes in lifestyle, this disease, as any other, has begun to change, especially during the COVID-19 pandemic.

**Aim.** Our aim was to examine if the COVID-19 pandemic led to an increase of time until diagnosis, operation and time spent in emergency room (ER,) and whether it resulted in more cases of complicated appendicitis and complication rates in children.

**Methods.** We conducted a retrospective analysis of patients admitted to the Paediatric Surgery Department with acute appendicitis during a 4-month period of the first COVID-19 pandemic and compared it to the data of previous year– the same 4-month period in 2019.

**Results.** During the pandemic the time patients spent in the ER until arriving at the department increased significantly – 2.85 vs 0.98 hours  $p<0.001$  and the time spent in the department until the operation – 5.31 vs 2.66 hours,  $p=0.03$ . However, the time from the beginning of symptoms until ER, operation time and the length of stay at the hospital, as well as the overall time until operation did not differ, and no increase of complicated appendicitis cases or postoperative complications was found as a direct result to longer time until receiving surgical treatment.

**Conclusion.** The COVID-19-induced quarantine led to an increase of time from the emergency room to the operating room by 4 hours, but it did not result in a higher rate of complicated appendicitis and complication rates, allowing for surgery to be postponed to daytime hours if needed, without risking a more complicated course of disease for the patient.

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## Dynamic Diversity of Gut Microbiota During Infancy: A Pilot Study of Analysis of Infant Microbiota During the First Year of Life

Zelča Egija<sup>1</sup>, Lūse Ērika<sup>1</sup>, Peterleviča Jana<sup>1</sup>, Zariņa Dana<sup>1</sup>, Frīdmanis Dāvids<sup>3</sup>, Gudrā Dita<sup>3</sup>,  
Rumba-Rozenfelde Ingrīda<sup>1</sup>, Daugule Ilva<sup>1,2</sup>

<sup>1</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

<sup>2</sup>Institute of Clinical and Preventive Medicine, University of Latvia, Riga, Latvia

<sup>3</sup>Department of Human Genetics and Disease Mechanisms, Latvian Biomedical Research and Study Centre, Riga, Latvia

**Background.** Gut microbiota is influenced by many factors and linked to different diseases during lifetime. However, the exact changes and stabilization of microbiota in early life has not been examined fully.

**Aim.** The purpose was to prospectively study the composition of gut microbiota and influencing factors thereof in infants in the first year of life.

**Methods.** A prospective study was performed at primary healthcare centres. The parents of children filled out a questionnaire (demographic, perinatal, feeding data, antibacterial therapy) and brought the child's faecal sample – two samples from the same child (one up to the age of six months and one – up to 12 months). The 16 rRNA gene sequencing was performed to identify the bacterial taxonomic units. The composition of the gut microbiota was compared in dynamics: in infants 0–6 months of age (group I) and in infants 6–12 months (group II). Statistics – Wilcoxon, Chi-Square, T-test.

**Results.** In total, 13 children were included in study (69.2% (9/13) girls), the median age in group I was 5.0 months (IQR 3.0–6.0), in group II – 11.0 months (IQR 10.7–11.0). Altogether, 26 faecal samples were analysed. The main genus detected in the study group was *Bifidobacterium*, followed by *Escherichia Shigella*, *Bacteroides* and *Veillonella*. In turn, genera *Lactobacillus*, *Streptococcus*, *Clostridium sensu stricto*, *Prevotella*, *Blautia*, *Ruminococcus* were detected in smaller quantities. The mean Shannon Index in group I was 5.1 (CI 4.3 to 5.9; range 3.2–7.0), in group II – 5.5 (CI 4.8 to 6.1; range 3.7–7.1);  $p=0.2$ . The species *Ruminococcus gnavus* was detected in 30.7% (4/13) of children in group I, but in 53.8% (7/13) – in group II. The relative abundance of *R. gnavus* was more prevalent in the group II compared to the group I (median value 3.0% (IQR 0.0 to 4.5) vs 0.0% (IQR 0.0 to 2.0),  $p=0.03$ ). *R. gnavus* showed positive correlation with the Shannon index ( $r=0.6$ ;  $p=0.02$ ). The relative abundance of *R. gnavus* did not differ significantly in respect to type of delivery, count of family members, gestational week, antibacterial therapy during pregnancy and childbirth.

**Conclusion.** The most abundant gut flora in infants was *Bifidobacterium*, *Escherichia Shigella*, *Bacteroides* and *Veillonella*, showing a tendency for increased strain diversity with age. In the majority of infants, *R. gnavus* was not identified until six months of age, but it tends to increase with age. Factors influencing abundance of the species and the association with health status should be studied in greater detail prospectively.

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## Exploration of Prevalence of Food Intolerance Mediated by Food-Specific IgG Antibodies in Paediatric Asthma in Latvian Population

Bebre-Putka Valda<sup>2</sup>, Paramonova Natalia<sup>1</sup>, Trapiņa Ilva<sup>1</sup>, Pļaviņa Samanta<sup>1</sup>, Ļeonova Elīna<sup>1</sup>, Rumba-Rozenfelde Ingrīda<sup>2</sup>, Sjakste Nikolajs<sup>1,2</sup>

<sup>1</sup>Laboratory of Genomics and Bioinformatics, Institute of Biology, University of Latvia, Riga, Latvia

<sup>2</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

**Background.** Adverse food reactions are generally classified as food allergy and food intolerance. Whereas food allergy is typically mediated by immunoglobulin E (IgE) antibodies, food intolerance is mediated by immunoglobulin G (IgG) class of antibodies. IgG-mediated food intolerance is believed to be caused by increased intestinal permeability and allergy-related symptoms such as rash, hives and asthma. While it is generally accepted that exposure to IgE food allergens can exacerbate asthma symptoms, there is little evidence to study delayed IgG-mediated reactions to food. It was found that there was a decrease in asthma symptoms due to the elimination of products that showed a reaction to the levels of IgG detected in the analysis of serum.

**Aim.** To explore a prevalence of food intolerance mediated by food specific IgG antibodies in a cohort of children with asthma in the Latvian population.

**Methods.** The cohort of examined patients included 40 children diagnosed with bronchial asthma (BA), recruited on the basis of the Riga 1<sup>st</sup> Hospital and clinic and medical institution Gārša Inese – medical practice of paediatrics (Valmiera). Enzyme immunoassay (IgG Food Screen Mediterranean 20 ELISA) for the quantitative measurement of food specific IgG antibodies against 20 allergens was used in human serum (EDTA, Citrate, Heparin). Statistical analysis was performed with SPSS.25 Statistical Package.

**Results.** In the total cohort of studied patients with a diagnosis of BA, 33% of positive cases of food intolerance were the cases for 7 allergens. The most common allergens in BA were wheat (85.00% positive), milk protein and gluten (77.50% positive), and potatoes (70.00% positive). None of the patients in the experimental cohort had a food intolerance to coffee or cocoa, none of them showed a negative intolerance to all 20 allergens. There was no statistically significant difference in the presence/absence of any form of food intolerance between groups of patients, stratified by gender.

**Conclusion.** A pilot study was conducted to determine the spectrum of food intolerance cases mediated by food-specific IgG antibodies in a cohort of BA children. To confirm the hypothesis of the involvement of IgG-mediated food intolerance in the development of bronchial asthma, further clarification of the causal relationship between dietary IgG antibodies and the clinical characteristic of BA is necessary.

**Acknowledgements.** The study was funded by the Taiwan-Latvia-Lithuania cooperation project “Comparative study of vitamin D and its receptor gene polymorphisms in Lithuanian, Latvian, and Taiwanese children and adults with atopic dermatitis and asthma”.

## Respiratory Tract Infections in Children With Tracheostomy

Purviņa Una<sup>1,2</sup>, Aleksejeva Elīna<sup>1,2</sup>

<sup>1</sup>Rīga Stradiņš University, Riga, Latvia

<sup>2</sup>Children's Clinical University Hospital, Riga, Latvia

**Background.** Since the beginning of vaccination, the indications for tracheostomy (TrS) have changed – currently, these are children with chronic, complicated underlying conditions, who are at increased risk for respiratory tract infections due to TrS.

**Aim.** To describe respiratory tract infections for children with TrS – frequency, clinical and laboratory data, microbiological organisms and most common antibiotic sensitivity, and treatment.

**Methods.** This was a descriptive, retrospective study that included medical records of patients with TrS (SSKS-10 diagnosis Z93.0) in Children's Clinical University Hospital in 2010–2019.

**Results.** Study included 30 patients (63.3% were male). The median age at time of TrS was 12 months (range: 1 month to 17 years). The largest patient group was 28 days to 1 year of age – 46.7% (n=14). The most common indication for TrS was upper airway obstruction (50%). Most of the patients (n=28) had more than 1 co-disease. Twenty-one patient (70%) had 79 airway infection episodes (median – 2, range 1–25), of which 57% were in long term respiratory support indication group. Most common symptoms were fever (72.2%), shortness of breath (34.2%), cough (20.3%), thick sputum (15.2%), sputum with streaks of blood (12.7%), lethargy (13.9%). Objective signs – moist crackles (22.8%), increased respiratory rate (15.2%). Normal white blood cell count was present in 39.1% of patients, elevated – 36.2%. C-reactive protein was high in 77.3%. A total of 174 microbiological cultures were performed, in case of infection – 41. The most commonly isolated organisms were *St. aureus* 42.5% of all cultures and 63.4% in case of infection, and *P. aeruginosa* 33.9% and 48.8%. Carbapenem-resistant *P. aeruginosa* was in 6.9% and 9.8%, MRSA – 6.3% and 12.2%. The most frequently used antibiotics were ciprofloxacin 26.2% (sensitivity 77–80%), azithromycin 17%, ceftazidime 13.8% (sensitivity 30–68%), clindamycin 12.3% (sensitivity 76.6%). The best sensitivity for *P. aeruginosa* was found with colistin (94.1%), ciprofloxacin (80%) and piperacillin/tazobactam (79.1%), and for *St. aureus* – 100% vancomycin, linezolid, amikacin. The median duration from TrS to airway infection was 64 days. There was a correlation with count of airway infections and time with TrS (r=0.359; p<0.001).

**Conclusion.** Airway infections were found in 70% of patients, more often for children with long-term ventilation support. The most common organisms were *P. aeruginosa* and *St. aureus* that are consistent with other studies. The most frequently used antibacterial therapy ciprofloxacin had a sensitivity up to 80%. The results of this study provide an insight into pathogens and sensitivity of antibiotics, which should be considered when choosing therapy.

**Acknowledgements.** The authors declare the absence of conflict of interest.

## Differences in Children's and Parents' Perspectives on Children's Mental Health During COVID-19

Milašiūtė Emilija<sup>1</sup>, Leskauskas Darius<sup>1,2</sup>, Bakutyte Martyna<sup>1,2</sup>, Jocys Vilius<sup>1</sup>

<sup>1</sup>Lithuanian University of Health Sciences, Kaunas, Lithuania

<sup>2</sup>Hospital of Lithuanian University of Health Sciences Kauno Klinikos, Kaunas, Lithuania

**Background.** The vast majority of research on COVID-19 impact on the public's mental health is focused on adults. However, studies on the mental well-being of children are published less frequently and to our knowledge, only a few such studies have been conducted in Lithuania. The present study includes both children's and parents' attitudes, and provides a clearer view of children's mental health problems during quarantine.

**Aim.** The purpose of the current study was to assess the impact of the pandemic and quarantine restrictions on the mental health of 11–17-year-old children in the second year of the pandemic and to compare children's and parents' answers regarding children's well-being during COVID-19.

**Methods.** Altogether 389 children and 392 parents/foster-parents from 4 schools agreed to participate in the study. The cross-sectional study used two online questionnaires – one for 11–17-year-old children and another for parents to collect the data within the period from 9 March 2021 to 30 April 2021. Children answered questions about their emotional state, changes in emotions and behaviour during quarantine, and the influence it had on their relationships with parents, siblings, friends. Parents provided information about the ways how quarantine had impacted their children's emotional state, behaviour, relationships, and daily life. The Chi-square criterion was used to determine the differences in the distribution of non-parametric variables between the compared groups. The qualitative variables (children, or parents/foster-parents) and responses in the study sample were categorized and differences were assessed.

**Results.** Children were statistically significantly more likely than parents to report severe loneliness (24.7% vs 8.9%), sadness (37.8% vs 28.6%), fatigue (23.9% vs 13.3%), impaired concentration (45.8% vs 19.9%), increased sleeping time (63.5% vs 39.5%), improved relationships between children and their friends (29.6% vs 17.3%), impaired relationships between children and their siblings (26.9% vs 13.7%), and feeling severely worried about their family members or friends getting infected (24.4% vs 12.5%).

Parents were statistically significantly more likely than children to report children's inability to participate in daily activities (42.1% vs 33.2%), improved relations between children and their parents (34.7% vs 26.6%), and severe children's anxiety to be infected by COVID-19 (12.5% vs 8.7%).

**Conclusion.** As expected, the pandemic had an immense impact on children's mental health, whilst also disturbing their sleep rhythms and daily activities. The study shows discrepancies between children's and parents' understanding about quarantine consequences on children's mental health, as parents tended to underestimate it.

## Congenital Anomalies at Births and Associated Antenatal Care Factors

Zile-Velika Irisa<sup>1,2</sup>, Ebela Inguna<sup>1</sup>, Rumba-Rozenfelde Ingrida<sup>1</sup>

<sup>1</sup>Paediatrics Department, Faculty of Medicine, University of Latvia, Riga, Latvia

<sup>2</sup>The Centre for Disease Prevention and Control of Latvia, Riga, Latvia

**Background.** Congenital anomalies are a worldwide problem, causing perinatal and infant deaths. Prenatal screening for the detection of foetal anomalies is organised by laws and guidelines. Three ultrasound (US) screening examinations during pregnancy are recommended in Latvia. The 1<sup>st</sup> US is performed at the 11<sup>th</sup> to 13<sup>th</sup> week of pregnancy, the 2<sup>nd</sup> is performed at the 20<sup>th</sup> to 21<sup>st</sup>, and the 3<sup>rd</sup> US – for risk group of pregnancies – at the 34<sup>th</sup> to 36<sup>th</sup> weeks.

**Aim.** The aim was to assess congenital anomalies at births and the associated antenatal care factors.

**Methods.** Data source – Health Care Monitoring Datalink (HCMD). We used two data sources: Medical Birth Register and ambulatory care data provided by public and private health care providers about US. All singleton live birth in 2018 (n=18651) were included in the data analysis. Place of residence was categorized in 2 groups: Riga, other biggest cities and rural area (including regional cities). Adjusted OR were calculated. Multiple regression model was adjusted for mother age, living area and antenatal care factors.

**Results.** The mean mothers' age was 30.5 (SD 5.4) and gestational age – 39.3 (SD 1.7). 2.9% (n=536) were registered congenital anomalies at birth. The median number of ultrasounds (US) scans received during pregnancy was 3 (IQR 2). Congenital anomalies at birth have higher and statistically significant odds of the 1<sup>st</sup> trimester genetic screening (OR=1.8; 95% CI 1.3–2.6), invasive diagnostic methods in pregnancy (OR=2.5; 95% CI 1.6–3.9), prenatal detection of congenital anomalies (OR=2.3; 95% CI 1.5–3.4) and preterm deliveries (OR=1.7; 95% CI 1.2–2.4). Slightly higher frequency of congenital anomalies at birth but not statistically significant (p>0.05) were observed for mother with age 35 years and more (OR=1.1; p=0.51), living in urban area (OR=1.2; p=0.12) and US scan in the 3<sup>rd</sup> trimester (OR=1.3).

**Conclusion.** The findings of this study showed a statistically significant association between foetal anomalies and antenatal care factors. Pregnancy outcome as congenital anomalies at birth related with higher maternal screening examinations prenatally. Surveillance systems about pregnancy examinations do not have enough information of US screening results.

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## GASTROENTEROLOGY, NUTRITION, GASTROINTESTINAL ONCOLOGY & MICROBIOTA

### The Use of Shotgun Metagenomic Sequencing for Detection of *H. Pylori* Pre- and Post-Eradication: Bioinformatics Feasibility Assessment

Vangravs Reinis<sup>1</sup>, Čivkulis Kristaps<sup>1</sup>, Leonova Elīna<sup>1</sup>, Daus Edgars<sup>1</sup>, Poļaka Inese<sup>1</sup>, Sjomina Olga<sup>1</sup>,  
Leja Mārcis<sup>1,2</sup>

<sup>1</sup>Institute of Clinical and Preventive Medicine, University of Latvia, Riga, Latvia

<sup>2</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

**Background.** Stool antigen tests are considered to be among the most accurate tests for *Helicobacter pylori* detection. Currently the role of metagenomic sequencing of faecal microbiota is emerging. So far it has not been well demonstrated whether stool shotgun metagenomic sequencing could be applied for *H. pylori* detection.

**Aim.** The main objective of this study was to evaluate stool DNA shotgun metagenomic sequencing and Kraken 2-based sequence classification as a method for detection and quantification of *H. pylori* in the context of different eradication therapies.

**Methods.** Screening of possible *H. pylori* presence in respondents was done with urea breath test and serological analysis. Stool samples were collected from *H. pylori* positive respondents and control in faecal occult blood testing autosampler tubes (Eiken, Japan) and the total DNA was extracted using a commercial kit (FastDNA SPIN kit for soil, MpBio, USA). Shotgun metagenomic sequencing was performed on the DNBSEQ-G400 platform (MGI, China) employing 150 bp paired-end reads and generating at least 20 million reads per sample. Reads were quality trimmed using fastp and classified with Kraken 2, using a database containing all bacterial genomes available in RefSeq (release 180 2020-12-03) and abundances were reestimated to species level with Bracken. We used custom python scripts to look for the presence of *H. pylori*.

**Results.** In total, 216 paired samples were obtained from 108 respondents – the first before and the second 6–12 months after eradication. Among them, 58 underwent eradication and 50 were included in a control group where no treatment was used. We found reads aligning to *H. pylori* in 108 samples, 47 originating from control and 61 from eradication group. The eradication group was further divided into two treatment groups – Triple (amoxicillin and clarithromycin) and Double (high-dose amoxicillin). In the Triple treatment group, we observed *H. pylori* in 17 respondents prior and 9 after eradication, while in the Double treatment group *H. pylori* was present in 19 respondents prior and 16 after treatment. Meanwhile, in the control group both sampling instances showed similar *H. pylori* occurrence at both sampling points – 22 and 25.

**Conclusion.** Kraken 2-based shotgun metagenomics sequence classification method can be used to detect *Helicobacter pylori* species, but in order to reliably estimate their abundances, a deeper sequencing would be required.

**Acknowledgements.** The study was supported by the ERDF (European Regional Development Fund) in Latvia, project No. 1.1.1.1/18/A/184 “Optimisation of *H. pylori* eradication therapy for population-based gastric cancer prevention”.

## Evaluation of Dietary Habits of Jēkabpils Inhabitants: Adherence to Nordic Diet and Association with *Helicobacter Pylori* Infection

Jurkevica Ineta<sup>2</sup>, Daugule Ilva<sup>1,2</sup>, Kojalo Ilona<sup>1,3</sup>, Polaka Inese<sup>1</sup>, Parsutins Sergejs<sup>1</sup>, Leja Marcis<sup>1,2</sup>, Santare Daiga<sup>1,2</sup>

<sup>1</sup>Institute of Clinical and Preventive Medicine of the University of Latvia, Riga, Latvia

<sup>2</sup>Faculty of Medicine, University of Latvia, Riga

<sup>3</sup>Riga Stradiņš University, Riga, Latvia

**Background.** Since the Nordic Diet (ND) has shown beneficial health effects, several dietary recommendations are based on it. Association between ND and presence of *Helicobacter pylori* (*H. pylori*) infection has not been studied yet. Due to the high prevalence of *H. pylori* infection in Latvia, it is possible to analyse the relationship between *H. pylori* infection and dietary habits, including the consumption of some of the food items traditionally belonging to the ND.

**Aim.** The aim of the current study was to evaluate the association of consumption of ND food items with *H. pylori* infection prevalence in a sample of Jēkabpils population.

**Methods.** The study was carried out as a sub-study of the “Multicentric randomized study of *H. pylori* eradication and pepsinogen testing for prevention of gastric cancer mortality (GISTAR study)”. Altogether 560 patients 40 to 64 years old were enrolled in Jēkabpils from October 2019 to November 2020. The questionnaire included an adapted ND score questionnaire. One score point was assigned for each match according to the published references: adherence to ND was evaluated as: low (score 0–3), medium (score 4–5) or high (score 6–10). The frequency (never, several times/week, every day) of consumption of traditional Nordic food items (whole oat, rye, cabbage, root vegetables, Nordic fruits and fermented dairy products) was evaluated. Participants were tested for *H. pylori* IgG antibodies (ELISA Biohit Oyj, Finland, cut off <30.0 EUI). Consumption of traditional Nordic food items was compared in seropositive (*H. pylori*+) and seronegative groups of participants. Characteristics of participants in both groups were compared using Pearson chi-square and Mann Whitney tests. Results were considered as significant with  $p < 0.05$ .

**Results.** Out of the 539 participants (71.2% were females, the mean age was 54 years, SD=6.67), 323 (59.9%) were *H. pylori* positive.

The adherence to ND in the total sample was low – in 34%, medium – in 36.4% and, high – in 15.4% of participants.

The mean adherence to ND in the *H. pylori* seropositive group was significantly lower compared to the *H. pylori* seronegative group: 3.85% vs 4.25%,  $p < 0.05$ .

Overall, frequency of consumption of traditional Nordic food items was not associated with *H. pylori* seropositivity: whole oat ( $p=0.71$ ), rye (0.98), cabbage ( $p=0.54$ ), root vegetables ( $p=0.43$ ), Nordic fruits ( $p=0.71$ ) and fermented dairy products ( $p=0.24$ ).

**Conclusion.** The overall adherence to ND proved to be low. Although adherence to ND was significantly lower in the *H. pylori* seropositive group, no association was identified with consumption of specific traditional Nordic diet food items.

## Addition of *Saccharomyces Boulardii* to Standard Triple Therapy in Eradication of *H. pylori*: Comparison of Adverse Events and Effectiveness

Sjomina Olga<sup>1,2</sup>, Suhorukova Jekaterina<sup>1</sup>, Rūdule Aiga<sup>1</sup>, Vangravs Reinis<sup>1</sup>, Paršutins Sergejs<sup>1</sup>, Poļaka Inese<sup>1</sup>, Daugule Ilva<sup>1,2</sup>, Stonāns Ilmārs<sup>1</sup>, Park Jin Young<sup>3</sup>, Leja Mārcis<sup>1,2</sup>

<sup>1</sup>Institute of Clinical and Preventive Medicine, Riga, Latvia

<sup>2</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

<sup>3</sup>International Agency for Research on Cancer, Lyon, France

**Background.** A wide spectrum of adverse events by *H. pylori* eradication may lead to therapy discontinuations and decrease of eradication rates. *Saccharomyces boulardii* addition to standard clarithromycin-based *H. pylori* eradication regimen is associated with lower harm related to a less frequent induction of gut resistome and a better profile of adverse events.

**Aim.** To compare the effectiveness and frequency of adverse events related to standard clarithromycin-based *H. pylori* eradication regimen after adding *Saccharomyces boulardii*.

**Methods.** Clinical trial participants were healthy individuals aged 40–64. Eradication subgroup underwent urea breath test; positive patients were randomly allocated into four eradication subgroups – standard triple therapy (Amoxicillin 1000 mg ×2, Clarithromycin 500 mg ×2 and Esomeprazole 40 mg ×2) with or without addition of 500 mg *Saccharomyces boulardii*, each group received medication 10 or 14 days. Patients were called in 21–28 days; adverse events and patients' compliance were registered.

**Results.** Data from 265 patients was acquired. Overall, adverse events were reported by 43.4% of respondents. The addition of *Saccharomyces boulardii* showed general tendency to lower frequency of adverse events (52.5% vs 41.0% without and with probiotic respectively, OR 1.6), in particular nausea (15.4 % vs 8.4%, OR 2.0) and significantly in diarrhoea in 14-day regimen (25.2% vs 13.3%, OR 2.7, p=0.02). The effectiveness of the therapy regimens in groups with and without probiotics did not show significant difference.

**Conclusion.** Lower frequency of adverse events by the same effectiveness increases chance of positive outcome. The ongoing research on the effect on the microbiome and resistome induction in subgroups will complement the results.

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## Correlation Between the Host Gut-Related miRNAs and Gut Microbiome Composition in Patients Undergoing Colonoscopy Procedure

Celmiņa Paula Rūta<sup>1</sup>, Silamiķele Laila<sup>1</sup>, Zukule Nanija Lība<sup>1</sup>, Vilkoite Ilona<sup>2,3,4</sup>, Silamiķelis Ivars<sup>1</sup>, Kloviņš Jānis<sup>1</sup>

<sup>1</sup>Latvian Biomedical Research and Study Centre, Riga, Latvia

<sup>2</sup>Department of Doctoral Studies, Riga Stradiņš University, Riga, Latvia

<sup>3</sup>Department of Gastroenterology and Gastrointestinal Endoscopy, Health Centre 4, Riga, Latvia

<sup>4</sup>Digestive Diseases Centre “Gastro”, Riga, Latvia

**Background.** The human gastrointestinal tract contains a diverse microbiome that has a fundamental role in the health condition of their host. Microbiome disruption affects the immune function, metabolism, and is involved in several diseases. Studies have shown that miRNAs of the host have a direct impact on gut microbiome, thus potentially providing a promising strategy to modify the microbiome in a targeted manner.

**Aim.** The aim of the current study is to determine whether there is a correlation between faecal, gut luminal, intestinal biopsy miRNAs and the gut microbiome composition in a sample of patients undergoing colonoscopy procedure.

**Methods.** To pursue the study, we have collected biological material from 96 patients and currently are performing shotgun metagenomic sequencing and miRNA sequencing to determine the microbiome and miRNA composition, respectively.

For microbiome composition analysis, sequencing libraries were prepared using microbial DNA and MGIEasy Universal DNA Library Prep Set, MGI Tech. Metagenomic sequencing was performed on DNB-SEQ-G400. Taxonomic classification was performed with mOTUs2.

MiRNA composition analysis was performed by miRNA sequencing on Illumina MiSeq using total RNA and Qiaseq miRNA Library Kit, Qiagen. MiRNA data were analyzed using CLC Genomics Workbench 20.0.4. Quantify miRNA was used to map the reads against miRBase release v22, pointing out *Homo Sapiens* as prioritized species.

Correlation analysis of metagenome and miRNA datasets was performed using sparse partial least squares regression as implemented in R package mixomics 6.15.45.

**Results.** Initial correlation analysis between these datasets has shown that the abundances of certain miRNA and microbiome representatives correspond to each other. Set of miRNAs, including hsa-miR-141-3p, positively correlated with members of *Clostridia* and *Actinobacteria*, but negatively correlated with members of *Bacteroidia*. Another set of miRNAs with hsa-miR-29c-3p as a representative displayed a correlation to the above-mentioned taxonomic groups in the opposite direction.

**Conclusion.** Different sets of miRNAs identified in gut-related samples correlate with members of the gut microbiome in opposite directions.

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## Evaluation of Intestinal Ultrasonography Protocol in Patients with Inflammatory Bowel Diseases: Experience of One Centre

Suhorukova Jekaterina<sup>1</sup>, Mokricka Viktorija<sup>1</sup>, Pukitis Aldis<sup>1</sup>

<sup>1</sup>Centre of Gastroenterology, Hepatology and Nutrition, Pauls Stradiņš Clinical University Hospital, Riga, Latvia

**Background.** Inflammatory bowel diseases (IBD) Crohn's disease (CD) and ulcerative colitis (UC) are chronic, relapsing inflammatory disorders of gastrointestinal tract, which impair the quality of life. Inflammatory lesions can involve colonic segments in UC, and both small and large intestinal segments in CD. A treat to target strategy with close monitoring of intestinal inflammation is strongly recommended in IBD care. Intestinal ultrasound (IUS) is a non-invasive imaging technique without ionizing radiation, which has gained popularity for the monitoring of IBD. IUS can be performed by gastroenterologists and is an acceptable alternative to endoscopy.

**Aim.** The aim of the current study was to evaluate IUS protocol in the diagnostics and differential diagnostics of IBD in the tertiary healthcare centre.

**Methods.** 42 patients, 18 men and 24 women (mean age 31 years) were enrolled in the study; 33 with known or relapsing IBD (6 patients with UC, 24 – with CD, 3 – with terminal ileitis) and 9 patients with suspected IBD. IUS was performed using Diagnostic Ultrasound System Arietta S70 (Hitachi, Japan) and thickness of intestinal wall, Limberg scale, the hypertrophy of mesenteric adipose tissue and lymphadenopathy were evaluated.

**Results.** The majority of patients were presented with lesions in the terminal ileum (21 patients – 78%), 5 in colon (16%) and 1 patient with ileocolonic lesions. 10 patients had active disease, relapse was detected in 17 patients. Increased wall thickness ( $\geq 3$  mm) was detected in 19 patients (RI 95% 0.41), loss of stratification of the bowel wall was detected in 24 patients (RI 95% 0.47); mesenteric enlargement was detected in 6 patients (RI 95% 0.18) and enlarged lymph nodes were in 9 patients (RI 95% 0.25). IBD complications as abscesses, bowel strictures and fistulae were not detected.

**Conclusion.** The IUS protocol is an effective diagnostic method both for in-patient and out-patient care. IUS is a non-invasive, easy repeatable alternative to endoscopy or magnetic resonance enterography, and is well tolerated by patients. The intestinal ultrasound protocol can help to evaluate disease activity (early intestinal changes) and extension in the colon in UC patients, although with less well-established data than for CD.

## Initial Results of Electronic Nose for Colorectal Cancer Specific Breath Detection

Mezmale Linda<sup>1,2,3</sup>, Polaka Inese<sup>1</sup>, Anarkulova Linda<sup>1,4,5</sup>, Lescinska Anna Marija<sup>1,2,3</sup>, Pcolkins Andrejs<sup>1,2,3</sup>, Mizaikoff Boris<sup>6</sup>, Mitrovics Jan<sup>7</sup>, Shani Gidi<sup>8</sup>, Haick Hossam<sup>8</sup>, Leja Marcis<sup>1,2,3,9</sup>

<sup>1</sup>Institute of Clinical and Preventive Medicine, University of Latvia, Riga, Latvia

<sup>2</sup>Riga East Clinical University Hospital, Riga, Latvia

<sup>3</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

<sup>4</sup>Liepaja Regional Hospital, Liepaja, Latvia

<sup>5</sup>Faculty of Residency, Riga Stradiņš University, Riga, Latvia

<sup>6</sup>Institute of Analytical and Bioanalytical Chemistry, University of Ulm, Ulm, Germany

<sup>7</sup>JLM Innovation GmbH, Tuebingen, Germany

<sup>8</sup>Technion – Israel Institute of Technology, Haifa, Israel

<sup>9</sup>Digestive Diseases Centre GASTRO, Riga, Latvia

**Background.** Health experts worldwide recommend colorectal cancer (CRC) screening. The screening modalities for CRC do exist and are recommended for routine clinical applications in most of the developed countries, nevertheless, there clearly still remains a space for improvement. Analysis of exhaled air using sensors is a novel and unique approach for cancer detection that could solve the limitations of CRC screening tests. However, a number of issues have to be solved before these tests can reach practice.

**Aim.** The aim of the study was to evaluate the applicability of electronic nose to discriminate between breaths of CRC patients' and healthy individuals' breaths.

**Methods.** Altogether 14 patients were enrolled in the study: 6 patients with CRC (histologically confirmed CRC) and 8 healthy individuals (histologically without CRC). Their breath was measured with a modular multi-sensor VOC analyser developed for other applications within the H2020 project VOGAS. The device included 48 repeated gold nanoparticle sensors (GNP) for improved robustness (6 sets of 8 different sensors), 11 analogue metal oxide sensors (MOX), 12 digital MOX sensors and infrared detection unit. The sensor responses were analysed using the mean signal at the end of the measurement after the sensor readings were stabilized.

**Results.** All replicates of one of the GNP sensors showed significantly different responses to healthy and cancer patient breaths (all  $p < 0.05$ ), and half of two other GNP sensor replicates showed a statistically significant difference between responses to cancer *vs.* healthy breaths ( $p < 0.05$ ). Also, two of the MOX showed a statistically significant difference in responses ( $p < 0.05$ ).

**Conclusion.** The results demonstrate that the proposed approach is feasible for detection of CRC. The study should be continued to build and evaluate more specific detection models.

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## ***Clostridium Difficile* and Cytomegalovirus Infections in Immunocompromised Patients**

**Karpavičiūtė Vita**<sup>1</sup>, Kiudelis Gediminas<sup>2</sup>

<sup>1</sup>Lithuanian University of Health Sciences, Kaunas, Lithuania

<sup>2</sup>Lithuanian University of Health Sciences, Department of Gastroenterology, Kaunas, Lithuania

**Background.** In recent years, inflammatory bowel disease has been recognized as a strong risk factor for cytomegalovirus (CMV) and *Clostridium difficile* infection (CDI). Co-infection between CMV and CDI has been increasingly reported, but its frequency remains unclear.

**Aim.** To describe the prevalence of CDI, CMV and co-infections in ulcerative colitis (UC) patients hospitalized for severe flare-ups requiring intravenous steroid administration.

**Methods.** 127 UC patients with severe flare-ups were retrospectively identified. CDI was diagnosed on the basis of clinical symptoms and positive enzyme immunoassay-based stool test results for *Clostridium difficile* toxin A. CMV infection was diagnosed by quantitative PCR of CMV DNA in plasma and/or histological analysis of colonic biopsies. Statistical analysis was performed using SPSS statistics 25.0. Mann-Whitney U test, the  $\chi^2$  criterion and Fisher's exact test were used for data analysis.

**Results.** Of the 127 patients, 28 (22%) were infected with CMV and 21 (16.5%) with CDI. The median number of CMV DNA copies per millilitre was 321.5 (IQR: 56.3–2360) in patients diagnosed with CMV infection. In this group, 24 patients underwent biopsy with histological analysis and cytomegalovirus inclusions were found in exactly half of the samples. There were no significant differences in the number of CMV copies per millilitre of plasma between patients with or without histological findings (U=64, p=0.644). However, the timing of biopsies differed between patients depending on the date of ganciclovir administration, which may explain the results. The prevalence of CDI and CMV co-infection was 4.7% (n=6). The overall colectomy rate was 8.7% (n=11) and the prevalence of colectomy was not significantly different in the 4 groups: CMV infection, CDI, co-infection, or undetected infection group ( $\chi^2=2.13$ , Fisher's p=0.501). However, we observed that patients with co-infection were more likely to be repeatedly hospitalized for severe UC flare-ups (U=103.5, p<0.001, flare-ups median 3 (IQR: 1.75–5) vs median 1 (IQR: 1–1) overall in all other groups). Also, in the co-infection group, the response to biological therapy was poor: 2 non-responders (1 underwent colectomy), 3 patients had no response to at least 2 biologics.

**Conclusion.** The results suggest that more severe cases of ulcerative colitis are often accompanied by CMV infection (22%), CDI (16.5%) or co-infection (4.7%). Meanwhile, this co-infection is associated with a poorer response to drug therapy.

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## Effectiveness of Neoadjuvant Chemotherapy in Gastric Cancer Patients at Pauls Stradiņš Clinical University Hospital in Years 2017–2020

Bloha Milāna<sup>1</sup>, Anarkulova Linda<sup>1</sup>, Hasnere Sigita<sup>1,2</sup>, Kota Jekaterina<sup>1</sup>

<sup>1</sup>University of Latvia, Riga, Latvia

<sup>2</sup>Pauls Stradiņš Clinical University Hospital, Riga, Latvia

**Background.** Gastric cancer is the fifth most frequently diagnosed cancer worldwide and takes the third place of cancer deaths. The high-grade gastric cancer treatment only with surgery typically has a worse prognosis than its combination with preoperative or neoadjuvant chemotherapy (NAC), whose aim is to improve overall survival by reducing the stage of the tumour, improving pathological responses and to diminish the risk of local and distant relapses.

**Aim.** To summarize the effectiveness of neoadjuvant chemotherapy in gastric cancer patients at Pauls Stradiņš Clinical University Hospital Oncology Clinic within years 2017–2020.

**Method.** The retrospective study included 57 patients with histologically diagnosed gastric cancer who then received neoadjuvant chemotherapy. All data were taken from Pauls Stradiņš Clinical University Hospital oncological patients council reports from 2017 to 2020. Statistical analysis of data was performed in IBM SPSS Statistics 22.

**Results.** 50.1% (n=29) of analysed patients completed NAC and underwent surgery, which has been a total gastrectomy in 62.9 % patients, but in 37.1% – subtotal gastric resection. Only these 29 patients were included in further analyses, because others do not correspond to the research topic. 31.1% (n=9) were women, 68.9% (n=20) – men. The mean age of included patients was 62.2±10.23 (min=36, max=76) years. Women were on average 1.1 year older than men. 31% (n=9) of included patients were younger than 50 years. The most common chemotherapy regimen was FLOT (fluorouracil, leucovorin, oxaliplatin, docetaxel) in 26 (89.7%), 2 (6.9%) patients received combination of fluorouracil and cisplatin, but only 1 (3.4%) person – FLO (fluorouracil, leucovorin, oxaliplatin) regiment. In 15 (51.7%), pathomorphological evaluation was assessed, and all of them achieved pathologic response. FLOT was used in 14 (93.3%) patients of these group, while one patient – with fluorouracil and cisplatin. 9 (64.3%) of patients, who received FLOT chemotherapy had poor pathologic response, but complete pathologic response (pCR) was observed in 5 (35.7%) patients. This one patient, who received fluorouracil and cisplatin also showed complete pathological response.

**Conclusion.** The majority (2/3) of analysed patients had poor pathologic response after receiving FLOT chemotherapy regimens. However, 5 (40%) patients had complete pathological response and it is a relatively good result.

## Outcomes of the Colon Cancer Prevention and Early Diagnosis Program at the Hospital of Lithuanian University of Health Sciences Kaunas Clinics Family Medicine Clinic

Minelgaitė Rūta<sup>1</sup>, Čekanauskaitė Paulina<sup>1</sup>, Minelgienė Rūta<sup>2</sup>, Jonikaitė Laura<sup>2</sup>, Mačiukaitienė Jomantė<sup>2</sup>

<sup>1</sup>Faculty of Medicine, Lithuanian University of Health Sciences, Kaunas, Lithuania

<sup>2</sup>Department of Family Medicine, Hospital of Lithuanian University of Health Sciences Kaunas Clinics, Kaunas, Lithuania

**Background.** The problem is of outstanding importance, since colorectal cancer is one of the leading causes of cancer-related mortality worldwide. In most cases, colon cancer is diagnosed incidentally in the patients who seek medical attention for various reasons or when the typical symptoms of colon cancer appear. To detect colon cancer as early as possible in most countries every 2 years, an early cancer diagnosis program is being suggested for patients aged 50 to 74 years by family physicians. It includes performing and evaluating immunochemical secret blood test (iFOBT) in faeces. This detailed examination allows to confirm or deny the diagnosis of colon cancer and establish it at an early stage.

**Aim.** The aim of the current study was to evaluate outcomes of the colon cancer prevention and early diagnosis program at the Hospital of Lithuanian University of Health Sciences Kaunas Clinics Family Medicine Clinic.

**Methods.** The study was conducted at LSMUL Family Medicine Clinic. Data were collected from personal health histories to evaluate the results of patients undergoing a colonoscopy under the prophylactic program. Patients' age ranged in from 50 to 74 inclusive. We studied 1015 patients' charts. Patients, who had positive iFOBT results, underwent colonoscopy. Statistical analysis of the data was performed using the software package SPSS 22.0 and Microsoft Office Excel 2010.

**Results.** Overall, 1015 charts were examined. The hidden blood in the stool test was found to be positive for 112 subjects: 48 (43%) men and 64 (57%) women,  $p=0.66$ . The study found that iFOBT results were positive in patients with the mean age of 62.79 years,  $SD=6.14$ . The test did not show gender dependency,  $p=0.66$ , however, the tendencies show the higher incidence of positive iFOBT results in women 57% than in men 43%. Furthermore, 14.4% patients with positive iFOBT result declined further testing. Other tendencies demonstrate that after colonoscopy most common diagnoses were colon polyp 22.9%,  $p=0.17$  and hemorrhoidal nodes 20.8%,  $p=0.55$ .

**Conclusion.** The tendencies demonstrate the higher incidence of positive iFOBT results in women than in men. The most frequent pathology among colonoscopy findings are colon polyps, which are also more common in men compared to women. The vast majority of patients seek further examination after getting a positive result of iFOBT.

**Acknowledgements.** The authors declare the absence of conflict of interest.

## OPHTHALMOLOGY

### Effect of Mydriasis on Intraocular Lens Calculations

**Kozlovska Ingrida**<sup>1</sup>, Baumanė Kristīne<sup>1,2</sup>

<sup>1</sup>Riga East Clinical University Hospital, Riga, Latvia

<sup>2</sup>University of Latvia, Riga, Latvia

**Background.** When preparing patients for cataract surgery, eye biometry to calculate the power of IOL and mydriasis is being performed. Therefore, it is essential to clarify whether mydriasis can impact biometric measurements.

**Aim.** To evaluate the effect of mydriasis on biometric measurements of the eye and calculation of intraocular lens strength.

**Methods.** An optical biometer (TOMEY OA2000, Japan) was used to obtain the biometric measurements of the eye before and after drug-induced mydriasis. The Okulix program was used to assess the strength of the IOL to achieve target refraction.

**Results.** This prospective study included 151 patients (213 eyes). IOL calculations were analyzed for the Alcon SN60AT spherical lens. Before and after mydriasis in 83%, the difference of the IOL calculation was within  $\pm 0.5$  D, but 95% was within  $\pm 1.0$  D. For short-sighted eyes, in 73%, the difference of the calculation was within  $\pm 0.5$  D, in 91% was within  $\pm 1.0$  D, but for long-sighted eyes, 90% was within  $\pm 0.5$  D, and 100% was within  $\pm 1.0$  D.

**Conclusion.** Using an optical biometer with the Okulix program, mydriasis has no significant effect on calculating the IOL's strength.

**Acknowledgments.** The authors declare the absence of conflict of interest.

## Trends in Prevalence of Myopia in Lithuania

Statkevičienė Karina<sup>1</sup>, Karpavičiūtė Vita<sup>1</sup>, Simonavičiūtė Dovilė<sup>2</sup>

<sup>1</sup>Lithuanian University of Health Sciences, Kaunas, Lithuania

<sup>2</sup>Department of Ophthalmology, Lithuanian University of Health Sciences, Kaunas, Lithuania

**Background.** Myopia (nearsightedness) is one of the refractive errors, when the image is focused in front of the retina instead of on the retina. It occurs if the eyeball is too long or the cornea and/or lens is too curved. Myopia is usually diagnosed before the age of 20 (in most cases, at 6–14 years of age) and it is associated with genetic and environmental risk factors.

**Aim.** To assess changes in the prevalence of myopia in Lithuania during 2001–2020.

**Methods.** Data on the prevalence of myopia (ICD-10 code H52.1) in Lithuania during 2001–2020 were obtained from the Institute of Hygiene. The prevalence of myopia in children and adults was calculated per 100 000 population. Changes in the prevalence in adults and children as well as girls and boys during 2001–2020 were assessed using Joinpoint regression analysis.

**Results.** In 2020, the overall prevalence of myopia was 2838/100 000 population. The prevalence was significantly higher in children (7123/100,000 population) than in adults (1908/100 000 population) (Fig. 1). During 2001–2020 the average annual increase in myopia was higher among children (7.1%/year,  $p < 0.001$ ) than adults (2.4%/year,  $p = 0.043$ ). The prevalence of myopia in Lithuania has increased about twofold over 20 years. During 2001–2005, the prevalence of myopia among children increased by 20.8%/year ( $p < 0.001$ ). Between 2005 and 2018, disease growth rates slowed down but remained positive 5.9%/year ( $p < 0.001$ ). A sudden decrease was observed in the prevalence of myopia in adults (about 26%) and in children (about 16%) during 2020. When comparing the incidence of myopia in children, differences were observed between sexes. During 2001–2020, the average annual change in myopia was slightly higher among boys (8.2%/year) than girls (6.7%/year) ( $p < 0.001$ ). In 2020, the ratio of myopia between girls and boys was similar 1.3:1 ( $p > 0.05$ ).

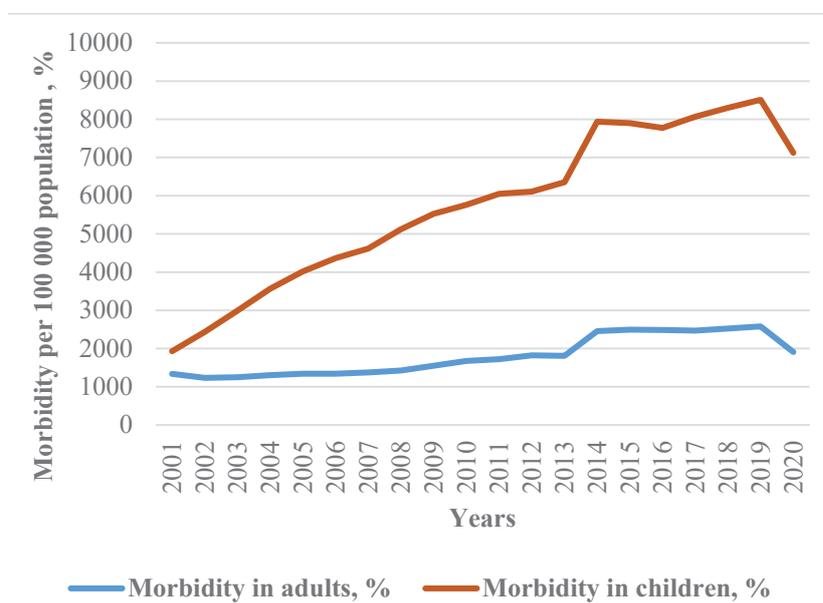


Fig. 1. Morbidity between adults and children per 100 000 population

**Conclusion.** The results show that the prevalence of myopia is on an upward trend. In recent years, a decrease in cases has been observed. This could be related to COVID-19 pandemic lockdown, when many healthcare facilities were closed and during that period myopia cases were not identified and registered.

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## Confocal Biomicroscopic Findings in Corneal Subbasal Nerve Plexus in Case of Different Stages of Primary Open-Angle Glaucoma

Agiševa Kristīna<sup>2</sup>, Leščenko Svetlana<sup>2</sup>, Briede Elīza<sup>1,2</sup>, Baumane Kristīne<sup>1,2</sup>

<sup>1</sup>University of Latvia, Riga, Latvia

<sup>2</sup>Department of Ophthalmology, Riga East Clinical University Hospital, Riga, Latvia

**Background.** Glaucoma is an optic neuropathy characterized by structural damage and functional impairment of the optic nerve. The most important task to preserve good visual acuity is to diagnose glaucomatous damage early and start adequate therapy, if necessary. The mainstay is topical medical therapy, which eventually affects corneal structures.

**Aim.** The current study aimed to evaluate corneal parameters in primary open-angle glaucoma patients and control subjects using a confocal biomicroscope.

**Methods.** The prospective study included 34 patients with primary open-angle glaucoma. The control group consisted of 21 patients without glaucoma. Patients with primary open-angle glaucoma (POAG) were divided into four visual field test classification groups. A complete ophthalmic assessment was performed for all the patients who participated. Corneal structures were analyzed using Heidelberg HRT III in vivo confocal biomicroscope. The following parameters were assessed: length of nerve fibres, corneal nerve fibre density, the density of corneal nerve fibres branches, the structure of endothelium, and endothelial cell count.

**Results.** Overall, 23 (68%) women and 11 (32%) men with POAG were included in the study. All patients in the POAG groups received daily medical glaucoma treatment. The average POAG disease length was  $1.9 \pm 0.36$  years,  $3.77 \pm 0.68$  years,  $4.78 \pm 1.14$  years, and  $5.61 \pm 1.02$  years in group I, II, III and IV group respectively. The mean corneal nerve fibre density in control group patients was  $28.1 \pm 2.3$  fibres/mm<sup>2</sup>, and in POAG patients, it was  $20.3 \pm 3.2$  fibres/mm<sup>2</sup>,  $18.3 \pm 2.4$  fibres/mm<sup>2</sup>,  $17.1 \pm 1.9$  fibres/mm<sup>2</sup> and  $14.2 \pm 3.1$  fibres/mm<sup>2</sup> in the POAG group I, II, III and IV accordingly with statistically significant difference between groups ( $p < 0.001$ ). The mean corneal nerve fibre length differed statistically significantly ( $p < 0.001$ ) between the control group ( $30.7 \pm 2.5$  mm/mm<sup>2</sup>) and the POAG groups I, II, III, and IV ( $26.1 \pm 1.4$  mm/mm<sup>2</sup>,  $24.3 \pm 1.2$  mm/mm<sup>2</sup>,  $22.3 \pm 1.5$  mm/mm<sup>2</sup> and  $16.7 \pm 1.5$  mm/mm<sup>2</sup> accordingly). The mean number of endothelial cells differed between the control group ( $2549 \pm 211$  cells/mm<sup>2</sup>), POAG groups I ( $2403 \pm 318$  cells/mm<sup>2</sup>) ( $p = 0.041$ ), and IV ( $1905 \pm 295$  cells/mm<sup>2</sup>) ( $p = 0.005$ ).

**Conclusion.** In the case of POAG, corneal structures are being affected using topical medical therapy in timely manner. These data should be considered in long-standing medical glaucoma treatment and planning potential intraocular surgeries.

**Acknowledgments.** The authors declare the absence of conflict of interest.

## Ocular Trauma Score Predicted Visual Outcome and Comparison to Final Visual Outcome

Nīmane Dārta<sup>1,2</sup>, Grava Laura<sup>1,2</sup>, Baumane Kristīne<sup>1,2</sup>

<sup>1</sup>Riga East Clinical University Hospital, Riga, Latvia

<sup>2</sup>University of Latvia, Riga, Latvia

**Background.** Open globe injury (OGI) is one of the most destructive forms of ocular trauma, which represents a visually and economically devastating cause of vision loss. OGI is defined as a full-thickness injury to the eyewall. Blunt trauma may cause globe rupture, whereas sharp trauma may be associated with penetrating or perforating injuries with or without an intraocular foreign body (IOFB).

**Aim.** The aim of the study is to determine the visual outcomes in adult patients with open globe injuries and compare results with predicted visual outcomes according to the Ocular trauma score (OTS).

**Methods.** A retrospective study of all patients with open globe injuries presenting to Riga East Clinical University hospital from 1st April 2020 to 1st August 2021 was performed. We performed calculation of the OTS which includes six factors that have the highest prognostic significance: initial visual acuity, as well as five anatomical factors (globe rupture, endophthalmitis, perforating injury, retinal detachment, and relative afferent pupillary defect (RAPD)). A scoring system has been developed whereby each of these six factors is assigned a point value whose sum helps to predict a patient's visual acuity after recovery. The obtained data were analysed by using the statistical software IBM SPSS Statistics 25.0. Analysis of actual final visual acuity (VA) compared to predicted final VA based on OTS group was done using Z test for proportion.

**Results.** Between April 2020 and August 2021, a total of 18 patients presented with OGI. The majority of the patients (77.8%) were male and mean age was  $43.89 \pm 19.04$  years. At the emergency department, 50% had visual acuity hand motions or worse. Four eyes (22.3%) had globe rupture, but 14 eyes (77.7%) had suffered a perforating injury. The total of six eyes (33.3%) had a retained intraocular foreign body. Six months after the treatment, 61.12 % of all patients had the best-corrected visual acuity – better than 20/40. 64% of patients had a final VA with no statistically significant difference compared to the predicted outcome ( $p > 0.05$ ).

**Conclusion.** OTS can be used for estimating final visual acuity even for a short follow up period of 6 months. In this study, the OTS predicted visual acuity outcome was consistent with the actual in 64% of cases. The most significant variables in the predictive analysis are initial visual acuity. It provides a better means for patient counselling and aids in clinical decision making. Prospective studies with larger sample sizes are required for further research.

## Is Vision Screening Important for School-Age Children?

Slabcova Jeļena<sup>1</sup>, Švede Aiga<sup>1</sup>, Kassaliete Evita<sup>1</sup>, Krūmiņa Gunta<sup>1</sup>  
<sup>1</sup>Faculty of Physics, Mathematics and Optometry, University of Latvia, Riga, Latvia

**Background.** In recent years, the literature has increasingly raised the issue of the shortcomings of the vision care system in school-age children. In many European countries, also in Latvia, school-age children do not have regular eye examinations and only go to a vision care specialist if the child begins to complain about their vision. However, children under 12-13 do not understand their vision problems and do not complain about their vision. The problem is of outstanding importance since the visual load of modern schoolchildren is associated not only with reading and writing but also with the use of a wide range of digital devices at close distances both in the educational process and for leisure. This high near visual effort is associated with high prevalence of myopia in school-age children. Additionally, it is noted that at present the number of school-age children with near vision impairment reaches 39%. After all, the uncorrected refractive errors and near vision problems can negatively affect children's academic performance and their behaviour.

**Aim.** The purpose of the study was to develop a vision screening protocol for school-age children. We have focused on the developed vision screening model that will be able to select children with vision problems at near.

**Methods.** Firstly, the manual vision screening protocol that also includes a range of near vision tests was developed in our department. 11033 school-age children were examined by this method in an epidemiological study. Secondly, a computerised vision screening protocol was developed based on the manual vision screening protocol. This method requires minimal staff involvement and was tested on 242 school-children.

**Results.** Using the manual vision screening protocol (test sensitivity 87%, specificity 77%), it was found that 22% of Latvian children had reduced visual acuity at a distance, and 30.9% had near vision problems. The sensitivity of the computer vision test method is 82%, and the specificity is 71%. At this time the visual function assessment and vision training device is developed in our department. This device includes a sequential set of tests and is implemented with a lens-filter device connected to a computer and controlled by a computer program.

**Conclusion.** Regular eye examinations are important for school-age children. The computerised vision screening method is fast, provides reliable results, and requires minimal staff involvement.

**Acknowledgements.** The study is based on project No. KC-PI-2020/10 "Development of vision screening and training device".

## Corneal Biomechanical Parameters for Keratoconus Patients

Jansone-Langina Zane<sup>1,2</sup>, Miķelsone Rita<sup>1</sup>, Gertnere Jana<sup>2</sup>, Trukša Renārs<sup>1</sup>, Solomatins Igors<sup>2,3</sup>

<sup>1</sup>Optometry and Vision Science Department, Faculty of Physics, Mathematics and Optometry, University of Latvia, Riga, Latvia

<sup>2</sup>Dr. Solomatin Eye Rehabilitation and Vision Correction Centre, Riga, Latvia

<sup>3</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

**Background.** Keratoconus is an eye disorder that results in progressive thinning of the cornea. In the cases of severe keratoconus, measurements of corneal biomechanical parameters can be modified due to eye lid tension. That is why it is advised to measure all the parameters 3 times to ensure the changes of the corneal parameters.

**Aim.** The aim of this study was to determine differences in corneal biomechanical parameters in keratoconus patients depending on the stage of keratoconus.

**Methods.** Our research altogether included keratoconus patients (256 eyes) and control group patients (122 eyes). Corneal thickness (Oculus Pentacam) was measured, and their corneal biomechanical response (Oculus Corvis) was evaluated. We analysed the Corvis biomechanical index (CBI), tomographic biomechanical index (TBI), and corneal elevation deviation index (BAD D). The results were compared between the control group and the different stages of the keratoconus patients and were analysed with ANOVA (two factor) and linear regression.

**Results.** As the keratoconus progresses, corneal thickness ( $R=-0.97$ ) and elasticity decreases ( $R=0.94$ ) while elevation height ( $R=0.77$ ) and the deviation of the corneal elevation from the normative values increases ( $R=0.98$ ).

**Conclusion.** Statistically significant differences of CBI, TBI, BAD D indices were seen in stages 0 and 1 of keratoconus.

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## BASIC MEDICAL SCIENCE

### Effects of Catechin on the Electroporation of Pancreatic Cancer Cells

Szlasa Wojciech<sup>1</sup>, Michel Olga<sup>2</sup>

<sup>1</sup>Faculty of Medicine, Wrocław Medical University, Wrocław, Poland

<sup>2</sup>Department of Molecular and Cellular Biology, Faculty of Pharmacy, Wrocław Medical University, Wrocław, Poland

**Background.** Electroporation is the phenomenon of increased cell permeability occurring under the influence of an external electric field. In oncology it is often used to increase the delivery of chemotherapeutics, therefore it is called electrochemotherapy. Catechin is a polyphenolic compound known for its anti-cancer properties. Aside from the interactions with various proteins, it may also be involved in the regulation of transmembrane transport, hence, it has a potential to enhance the effects of cell membrane permeabilization during electrochemotherapy and electroporation.

**Aim.** The aim of the current study was to evaluate the potential of catechin in the modulation of the cell membrane permeabilization in the pancreatic cancer model and to unravel the molecular mechanism of catechin interaction with the cell membrane.

**Methods.** Molecular dynamics simulations were performed to evaluate the differences in membrane permeabilization following the addition of catechin to the membrane system. Further, we analysed the interactions of catechin with the cell membrane on the molecular level and validated the results with the uptake of fluorescent iodide with flow cytometry method. Afterwards, we examined the effects of catechin preincubation on the cytotoxic effects of electrochemotherapy with cisplatin and calcium ions.

**Results.** We showed that catechin exerts the standalone cytotoxicity against EPP85-181P, EPP85-181RDB and EPP85-181RNOV cell lines in 100  $\mu$ M concentration. Combined with electroporation, catechin localizes in the membrane-water interphase in the neighbouring of the forming pore. We demonstrated that catechin does not affect the electroporation threshold. However, preincubation with catechin enhanced the cytotoxic effect of electrochemotherapy with cisplatin and calcium ions under very specific conditions.

**Conclusion.** Catechin may be applied to enhance the cytotoxic effect of calcium and cisplatin aided electroporation. However, despite catechin interaction with the membrane, the positive effect of electrochemotherapy does not rely on the increased permeabilization of the cell membrane.

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## Liver Mitochondria Functionality Changes After Acute Mesenteric Ischemia

Bahire Ksenija Lūcija<sup>1</sup>, Makrečka-Kūka Marina<sup>2</sup>, Volrāts Olafs<sup>1</sup>, Jansone Baiba<sup>1</sup>

<sup>1</sup>Department of Pharmacology, Faculty of Medicine, University of Latvia, Riga, Latvia

<sup>2</sup>Latvian Institute of Organic Synthesis, Riga, Latvia

**Background.** Acute mesenteric ischemia (MI) is a life-threatening condition that requires emergency treatment. Rapid diagnosis is considered as a key factor in avoiding the damage as partial or complete intestinal necrosis, extensive bowel resections, and short bowel syndrome (Bryski *et al.*, 2020). That requires research for new biomarkers in different organs and as the liver is particularly vulnerable to intestinal ischemia, abnormal liver mitochondrial functioning may predict further damage. Mitochondria, as the main energy source in hepatocytes, play a major role in extensive oxidative metabolism and normal function of the liver.

**Aim.** To investigate an acute mesenteric ischemia effect on the liver mitochondria in a rat experimental model.

**Methods.** Intestinal ischemia model was performed by the occlusion of the superior mesenteric artery and vein in male rats 250–330 g weight (17–18 weeks old (n=5–7) per group). Rats underwent artery and vein occlusion accordingly 30, 60, 120 minutes and Sham group underwent laparotomy without ischemia. Mitochondrial respiration and reactive oxygen species (ROS) production in the form of hydrogen peroxide were analysed in isolated liver mitochondria with high-resolution fluoroimetry.

**Results.** Lower mitochondrial respiration was seen in Complex I supported mitochondrial oxygen consumption at oxidative phosphorylation-dependent state in the 30-minute and 120-minute ischemia groups, compared to Sham group. The longest ischemia time resulted in the most significant impairment of Complex I&II-linked maximal oxygen consumption (ET state), compared to Sham group. Higher ROS production was observed in the 60-minute ischemia group when compared to the 120-minute group at Complex II supported ET state.

**Conclusions.** Liver mitochondria assessment has shown a partial impairment of mitochondrial functionality. Mitochondrial dysfunction may also play a significant role in the pathophysiology of acute mesenteric ischemia.

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## Development of Human Dermal Vasculature and Epidermis Morphogenesis

Markovs Jurijs<sup>1</sup>, Knipše Gundega<sup>1</sup>, **Galuzā Agate**<sup>1</sup>, Krūmiņa Džanna<sup>1</sup>, Krūmiņa Beata<sup>1</sup>  
<sup>1</sup>Department of Anatomy and Histology, Faculty of Medicine, University of Latvia, Riga, Latvia

**Background.** The skin develops by the juxtaposition of ectoderm and mesoderm. A layer of cells, of unknown function, called the periderm, transiently overlays the ectoderm during embryonic development.

**Aim.** In this study we attempt to find associations that are related to the chronology of epidermis development, maturity changes in the dermal blood vessels and dynamic changes in the periderm morphology.

**Methods.** We examined 6 embryos and 10 fetuses at the age of 6 to 24 developmental weeks and placental tissue from the embryological collection of the Department of Anatomy and Histology. Samples of an archival collection of skin of the finger and lateral surface of the trunk of the embryo/fetus, were stained with haematoxylin–eosin, PAS stain and immunostained with antibodies against smooth muscle actin (SMA).

**Results.** Capillary-like vessels are morphologically identifiable in presumptive dermis of a 6-week embryo by light microscopy. They are organized in first a single plane, and then two planes parallel to the epidermis. At the same time the epidermis forms a second layer that lies outer and originates simple squamous epithelium called periderm. At 14 weeks gestation, stratification of the epidermal layer is apparent along with budding of the basal layer as the primordial hair follicle develops. Concurrently the cells of the periderm and intermediate layer exhibit large amounts of glycogen and periderm cells project superficial blebs, but by week 16 their surface becomes dimpled. Once the stratification is completed, the periderm is shed, and the epidermis has fully differentiated. By the end of the 16th week, the major vascular organization of the foetal dermis was established, and dermal arterioles and venules could be distinguished. Postcapillary (pericytic) venules became the predominant type of vessels in the upper part of the dermis.

**Conclusion.** Results showed that differentiation of periderm cells has been occurring in tandem with epidermal differentiation. The formation of new blood vessels is a crucial step in the development of any new tissue during embryogenesis as without sufficient perfusion the tissue will be unable to grow beyond the size where nutrition and oxygenation can be managed by diffusion alone. At the beginning of the second trimester, when the dermal blood vessels are still not fully differentiated, the periderm, absorbing the carbohydrates from amniotic fluid and creating the glycogen may serve as additional source of energy substrates for developing non-vascular epidermis and its derivatives.

## Genetic Inactivation of Sigma-1 Receptor Induces White Adipocyte Hypertrophy and Changes in Lipid and Energy Metabolism in Mice

Miteniece Anna<sup>1,2</sup>, Stelfa Gundega<sup>1,3</sup>, Svalbe Baiba<sup>1</sup>, Vavers Edijs<sup>1,4</sup>, Makrecka-Kuka Marina<sup>1</sup>, Dambrova Maija<sup>1,4</sup>, Zvejniece Liga<sup>1</sup>

<sup>1</sup>Latvian Institute of Organic Synthesis, Riga, Latvia

<sup>2</sup>Imperial College London, London, United Kingdom

<sup>3</sup>Latvia University of Life Sciences and Technologies, Jelgava, Latvia

<sup>4</sup>Riga Stradiņš University, Riga, Latvia

**Background.** The Sigma-1 Receptor (S1R) has emerged as an important player in a multitude of cellular processes, ranging from synaptic transmission to Endoplasmic Reticulum stress response. Sigma-1 receptor (S1R) is also known to participate in intracellular lipid synthesis and transport. Moreover, recent studies have shown that genetic inactivation of S1R impairs adipogenic differentiation *in vitro*, but the role of S1R in white adipose tissue (WAT) function remains unclear.

**Aim.** The aim of this study was to investigate changes in WAT morphology, plasma metabolites and biochemical parameters in S1R knockout (S1R<sup>-/-</sup>) mice.

**Methods.** The body weight and visceral fat mass of male S1R<sup>-/-</sup> and wild-type (WT) mice were recorded every 4 weeks until 25 weeks of age. WAT sections were stained with hematoxylin & eosin, and the average adipocyte size was determined with AdipoCount software. Metabolomic and biochemical analyses of plasma were performed to assess lipid metabolism markers. Oxygraph-2k was used to evaluate WAT mitochondrial functionality.

**Results.** While S1R<sup>-/-</sup> mice had increased visceral fat mass (764±53 mg) compared to WT (429±96 mg), no differences in body weight were observed. The average adipocyte size was 64% larger in S1R<sup>-/-</sup> mice than in WT mice. Metabolomic analysis revealed that S1R<sup>-/-</sup> mice had significantly decreased plasma concentrations of short-chain acylcarnitines, ceramides, sphingomyelins, and phosphatidylcholines. Fasting plasma leptin levels were increased in S1R<sup>-/-</sup> mice (1.8±0.3 ng/ml) compared to WT mice (0.4±0.1 ng/ml). No differences in plasma concentrations of insulin, glucose, triglycerides, or free fatty acids were found between groups. A 5-fold increase in the mitochondrial fatty acid oxidation rate and a 43% elevation in electron transfer (ET) coupling capacity were detected in S1R<sup>-/-</sup> WAT, while the function of other ET system components remained comparable to the control group.

**Conclusion.** Here, we show that genetic inactivation of S1R induces visceral adiposity and changes in lipid and energy metabolism without affecting total body weight or insulin and glucose homeostasis. Our findings provide evidence for a role of S1R in WAT function in mice. Further studies are needed to elucidate the molecular mechanisms underlying these observations.

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## Validation of Antibodies for the Complement System in a Schizophrenia Mouse Model Using a Western Blot Method

Rožkalne Rebeka<sup>1</sup>, Jaako Külli<sup>1,2</sup>, Jansone Baiba<sup>1</sup>

<sup>1</sup>Department of Pharmacology, Faculty of Medicine, University of Latvia, Riga, Latvia

<sup>2</sup>Department of Pharmacology, Institute of Biomedicine and Translational Medicine, University of Tartu, Tartu, Estonia

**Background.** The complement system is a set of immune proteins involved in first-line defense against pathogens and the removal of damaged cells<sup>1</sup>. In addition, increasing evidence indicates that components of the complement system are important regulators in neurobiological processes in developmental neurogenesis, neuronal migration, remodelling and organization of synaptic contacts, and response to prenatal or early postnatal brain insults. It could be expected that in an early postnatal period the activity of the complement system activity is lower as compared to the levels detectable in animal models of adult brain injury. Therefore, finding suitable tools for evaluating the roles of the complement system in the early postnatal period is crucial. In the current study, we aimed to test and validate antibodies for the complement system for further evaluation of its roles in mouse models of schizophrenia in the early postnatal period.

**Methods.** In this study, C1q and C3 were selected as major contributors in the complement system and following antibodies were selected for validation. Rabbit anti-C1q (Invitrogen MA1-40311) and Rabbit anti-C1qA (bCam: ab155052) were tested for C1q protein level and Anti-C3 Rabbit mAb (Abcam ab200999) for the C3 protein level in the brain tissues at early postnatal period. Total protein concentration was determined using the Bradford reagent and proteins of interest were detected by Western blot analysis and different experimental conditions (lysis buffer, reducing agent, etc.) were tested. The blots were digitally captured using LI-COR Odyssey<sup>®</sup> Imaging Systems (Lincoln, Nebraska USA).

**Results.** Signal intensity for C1q protein level was lower in C1q mouse brain as compared to adult mouse brain. Among tested antibodies, for C1q the specific signal intensity was detected by using C1q antibody (Invitrogen MA1-40311) and the specific signal was detected at size 70 kDa. For C3 rabbit Anti-C3 antibodies provided specific signals when adequate protein levels were used. Specific 187 kDa band for complement C3, 115 kDa- alpha chain, 68 kDa band- alpha chain fragment iC3b, and 43 kDa band- alpha chain fragment 2 were detected.

**Conclusion.** The findings emphasize the importance of careful antibody characterization to study the complement pathways in brain tissue which is necessary for the elucidation and further studies of the roles of the complement system in schizophrenia knockout mouse models.

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## Morphofunctional Characteristics of Hematopoietic Progenitor Cells of Human Bone Marrow in a Humanized *In Vivo* Model

Pakharenko Marharyta<sup>1</sup>, Bilko Denis<sup>1</sup>, Lahodniuk Ihor<sup>1</sup>

<sup>1</sup>National University of Kyiv-Mohyla Academy, Kyiv, Ukraine

**Background.** Over the decades of hematopoietic research, the best way to assess the viability of hematopoietic stem cells has been to move them to an endogenous microenvironment with subsequent growth. It is impossible to perform such a detection operation in the human body, so the solution to this problem can be an implantable humanized model “human–mouse”, using a gel diffusion chamber, which creates conditions closest to real.

**Aim.** The aim of our study was to determine the characteristics of the cultivation of hematopoietic progenitor cells of human bone marrow extracted from different parts of the bone, under conditions of cultivation in diffusion chambers *in vivo*.

**Methods.** Bone marrow samples from 37 patients without oncohematological diseases obtained from diagnostic sternal puncture, trepan biopsy of the iliac crest, and rib fragments were examined. Cell suspensions were centrifuged to obtain a mononuclear fraction, washed in PBS and cultured for 12 days in gel diffusion chambers placed in the abdominal cavity of recipient animals (CBA mice). The obtained cell aggregates were analysed under an inverted microscope with subsequent study of the morphological composition of the colonies.

**Results.** It was found that the colony-forming ability of human bone marrow progenitor cells taken from different parts of bone tissue is comparable. Thus, the efficiency of colony formation for the sternal puncture was  $35.4 \pm 2.2$  per  $1 \times 10^5$  of explanted cells, for the bone marrow from the fragment of the rib  $39.4 \pm 3.6$  per  $1 \times 10^5$  of explanted cells.

**Conclusion.** The results of the study indicate that the results of the evaluation of the functional activity of stem cells extracted from different areas of bone tissue are comparable and equally suitable for transplantation. The obtained data deepen the understanding of the peculiarities of growth and functioning of stem cells and progenitor cells in the human body *in vivo* and can be used for further studies of normal hematopoiesis and malignancies.

**Acknowledgments.** The authors declare the absence of conflict of interest.

## Histological Evaluation of Jejunal Wall Changes *in Vivo* Model After Ligation of Mesenteric Artery and Vein

Volrats Olafs<sup>1</sup>, Jansone Baiba<sup>1</sup>, Bancevica Lilija<sup>3</sup>, Melderis Ivars<sup>2</sup>, Makrecka-Kuka Marina<sup>4</sup>, Poppela Elga<sup>1</sup>

<sup>1</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

<sup>2</sup>Children's Clinical University Hospital, Riga, Latvia

<sup>3</sup>Rīga Stradiņš University, Riga, Latvia

<sup>4</sup>Latvian Institute of Organic Synthesis, Riga, Latvia

**Background.** Acute mesenteric ischemia (AMI) can occur due to emergent occlusion of superior mesenteric artery. Early diagnosis of AMI is crucial. To improve early diagnosis and treatment results we need to search for new blood plasma biomarkers, therefore it is important to evaluate the right time of microscopic bowel wall changes after ischemia ranging from reversible mucosal injury to transmural necrosis of intestine.

**Aim.** To determine precise time of initial histological changes in intestinal villi to necrosis onset of the bowel wall after ligation of superior mesenteric artery and vein on rats.

**Methods.** *Wistar Hannover* male rats (n=20) were subjected to the occlusion of superior mesenteric artery and vein by ligation of blood vessels under Isoflurane anaesthesia and Buprenorphine 0.08 µg/kg s.c. Animals were divided into three groups (n=6–7): 30 minutes ischemia as group 1; 60 min ischemia as group 2 and sham operated as group 3. Biopsy samples of rat jejunal wall were obtained and fixed for 48 hours in a 10% buffered formalin, stained with hematoxylin and eosin. Mucosal injury was determined under light microscope using Chiu classification.

**Results.** Changes along the jejunal wall were uneven in 1<sup>st</sup> and 2<sup>nd</sup> group rats, we examined three different intestinal fragments, where least, moderate and significant bowel ischemia was noticed. In group 1 (n=7) jejunal wall mucosa injury ranged from development of subepithelial (Gruenhagen's) spaces near the apex of villus, congestion in the capillaries to breaking into pieces of lamina propria with haemorrhage and ulceration. Inflammation ranged from locally in lamina propria to diffuse subendothelial collections; hyperaemia and haemorrhage – from dilated capillaries in lamina propria to subendothelial haemorrhage.

Group 2 (n=6) jejunal wall mucosa injury ranged from intensive separation of epithelium to breaking into pieces of lamina propria with haemorrhage and ulceration. Inflammation ranged from diffuse inflammation in lamina propria to massive collections; hyperaemia and haemorrhage – from local haemorrhage in lamina propria to massive haemorrhage.

Group 3 (n=7): intestinal mucosa was normal without any signs of inflammation, hyperaemia and haemorrhage.

**Conclusion.** Thirty minutes of intestinal ischemia caused an irreversible ischemic change in the intestinal villi, and those were even more pronounced after 60 min of intestinal ischemia indicating that changes of intestinal villi appear even earlier.

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## Effect of Selenium Supplementation on Selenium Concentrations and Lipid Peroxidation in Mice Liver and Blood

Ruzgaitė Aušrinė<sup>1</sup>, Sadauskienė Ilona<sup>2,3</sup>, Liekis Arūnas<sup>3</sup>, Baranauskienė Dalė<sup>3</sup>, Šimakauskienė Vaida<sup>3</sup>, Naginienė Rima<sup>3</sup>

<sup>1</sup>Lithuanian University of Health Sciences, Kaunas, Lithuania

<sup>2</sup>Department of Biochemistry, Medical Academy, Lithuanian University of Health Sciences, Kaunas, Lithuania

<sup>3</sup>Neuroscience Institute, Lithuanian University of Health Sciences, Kaunas, Lithuania

**Background.** Selenium (Se) is a trace element with a wide spectrum of biological action. The liver is known to hold the highest concentrations of selenium and is responsible for regulating whole-body selenium levels by synthesizing selenoproteins. These proteins contribute to selenium-dependent reactions in the body: redox signalling, protein folding, cytoskeletal assembly. However, higher-than-recommended doses of selenium may act as prooxidant by generating reactive oxygen species (ROS), which disturb cellular redox balance. Significant changes in body selenium concentration could lead to various diseases.

**Aim.** The aim of the current study was to evaluate effect of selenium supplementation on selenium concentrations and lipid peroxidation marker malondialdehyde (MDA) levels in mice liver and blood.

**Methods.** Experiments were performed on 4–6-week-old BALB/c mice. Animals were divided into three groups: control group, 0.2 Se group (0.2 mg of Se/kg body weight) and 0.4 Se group (0.4 mg of Se/kg body weight). Control mice were given tap water, whereas Se treated mice received Na<sub>2</sub>SeO<sub>3</sub> in tap water for 8 weeks. Se concentrations were determined by inductively coupled plasma mass spectrometry (using NexION 300 D). Lipid peroxides were estimated by measuring thiobarbituric acid reactive substances and were expressed as malondialdehyde (MDA), a marker of lipid peroxidation. License of the State Food and Veterinary Service for working with laboratory animals No. G2-80.

**Results.** The exposure to 0.2 Se dose caused a 3.1-fold increase of Se concentration in mice blood in comparison with Se concentration value (271.23 µg/L, p<0.05) of control. Administration of 0.4 Se dose also increased blood Se concentration (936.17 µg/L, p<0.05). Treatment of mice with 0.2 and 0.4 selenium doses increased Se concentration in mice liver by 215% (1.946 µg/g, p<0.05) and by 240% (2.108 µg/g, p<0.05) respectively. It was shown that MDA concentration in mice blood decreased by 41% (p<0.05) and increased in mice liver by 193 % (p<0.05) after treatment with 0.2 Se dose. Meanwhile, the exposure to 0.4 Se dose caused a decrease of MDA concentration in the blood by 27% (p<0.05) but increased MDA concentration in the liver by 257% (p<0.05).

**Conclusion.** Both Se doses increased Se concentration in mice blood and liver, as well as MDA levels in liver, but decreased MDA concentration in the blood.

## Role of Copper and Iron Storage Diseases Associated Genetic Variants in Coxarthrosis Development and Their Influence on the Disease Features

**Budreviča Olga**<sup>1</sup>, Džeriņš Andris<sup>2,3</sup>, Isakovs Aleksejs<sup>2,4</sup>, Studers Pēteris<sup>2,3</sup>, Gailīte Linda<sup>2,4</sup>

<sup>1</sup>Residency Development Programme, University of Latvia, Riga, Latvia

<sup>2</sup>Department of Traumatology and Orthopaedics, Rīga Stradiņš University, Riga, Latvia

<sup>3</sup>The Traumatology and Orthopaedics Hospital, Riga, Latvia

<sup>4</sup>Scientific Laboratory of Molecular Genetics, Riga Stradiņš University, Riga, Latvia

**Background.** Hereditary hemochromatosis (HH) and Wilson's disease (WD) are autosomal recessive disorders of metal (iron and copper, respectively) overload usually caused by pathogenic variants in HFE and ATP7B genes. Joint pain and arthritis, including secondary osteoarthritis, is a well-known manifestation of HH and WD related to iron and copper deposition.

**Aim.** To investigate the role of HFE and ATP7B common pathogenic variants in the development of hip joint osteoarthritis (coxarthrosis) and influence on the disease characteristics.

**Methods.** The study included 108 coxarthrosis patients who were genotyped for HFE variants C282Y, H63D, S65C, and ATP7B variants H1069Q by using PCR-RFLP and Bi-PASA-PCR. The patients with severe coxarthrosis scheduled for joint replacement surgery were recruited at the Traumatology and Orthopaedics Hospital. Coxarthrosis severity was evaluated using an AAOS score.

**Results.** In our study group (n=108), the mean age of patients was 66±8 years. 51 of them were females (mean age 66±8.3 years), and 40 were males (mean age 60.1±8.5 years) (p=0.62). The mean BMI of patients was 31±7 kg/m<sup>2</sup>. None of the individuals had the ATP7B variant, so it was not further analysed. The C282Y variant was present in a heterozygous state in 5/108 cases (4.63%), and there was no statistically significant difference between the age of patients in males (68.3±5.9 years) and females (68±1.4 years) (p=0.94). 22/108 cases (20.37%) were heterozygous for H63D, and there was no statistically significant difference between the age of patients in males (63.6±9.1 years) and females (60.9±9.3 years) (p=0.5). 5/108 (4.63%) cases were heterozygous for S65C, while one patient was compound heterozygous for C282Y and H63D, and two – homozygous for H63D. The age of onset of pain in the hip joint between cases with at least one HFE variant vs wild types was not significantly different (59.4±9 vs 62.2±9 years, p=0.17).

The coxarthrosis severity measured by the AAOS score was also not significantly different between cases with at least one HFE variant vs. wild types (35±7 vs 33.7±6, p=0.1).

**Conclusion.** HH and WD are not common causes of coxarthrosis, and there were no confirmed cases in our study group. Heterozygous HFE variants are not associated with increased risk of coxarthrosis, age of the joint pain onset, and AAOS score. Further studies with larger groups of patients are necessary to evaluate the role of ATP7B and HFE homozygous and compound heterozygous variants in coxarthrosis development.

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## RNA Composition of Exosomes from Urine of Bladder Cancer Patients

Fortūna Ksenija<sup>1</sup>

<sup>1</sup>Institute of Oncology, Riga Stradiņš University, Riga, Latvia

**Background.** Bladder cancer (BC) is the most common malignant tumour associated with the urinary system in the world. Its incidence and mortality rates in Latvia for the last 30 years have increased. Expensiveness, invasiveness, and insufficiently high sensitivity of modern BC diagnosing methods are creating a necessity for a new diagnosing and monitoring method. The identification of specific biomarkers of exosome cargo, including identification of long non-coding RNAs (lncRNA), is considered as a potential solution to this problem.

**Aim.** The aim of the current study was to identify differences in the composition of exosomal lncRNAs between bladder cancer patients and people without oncological diseases.

**Methods.** The study has obtained the permission of the RSU Research Ethics Committee. Altogether 16 patients were enrolled in the study – ten low-grade patients and six case control group participants. lncRNAs isolated from urine exosomes were analysed with Qiagen polymerase chain reaction arrays, which were meant for the identification of lncRNAs, and the recognition of the signal pathways involved. The statistical processing of the results was carried out using the GeneGlobe Data Analysis Center system from the Qiagen website. The p-value significance threshold was set to 0.05.

**Results.** Comparing the lncRNAs expression represented in both groups, downregulation of 102 lncRNAs was observed in the cancer group, which is statistically significant. Differently expressed lncRNAs mainly belong to the following groups: cancer-associated lncRNAs, antisense transcripts, host genes, long intergenic protein non-coding RNAs. Among those downregulated, following lncRNAs were associated with cancer: CCAT1, CCAT2, GACAT1, HULC, LUCAT1, MALAT1, PCAT1, PTCSC1, PTCSC3, TUSC7, PCGEM1, UCA1, HEIH, BCAR4, BLACAT1, CAHM, CRNDE, DLEU2, H19, PCA3, PRNCR1, PVT1, RMST. Three lncRNAs (LINC00853, TINCR, HAND2-AS1) were not statistically significant up-regulated in the cancer group.

**Conclusion.** There is a difference in the composition of exosomal lncRNAs between bladder cancer patients and people without oncological diseases. In total, 119 lncRNAs in exosomes of BC patients and 113 lncRNAs in exosomes of control group participants were identified.

## Assessment of Mesenchymal Progenitor Cells of Mice Bone Marrow Under Ionizing Radiation Influence in Cell Culture *in Vitro*

Russu Iryna<sup>1</sup>, Bilko Nadiia<sup>1</sup>

<sup>1</sup>National University of Kyiv-Mohyla Academy, Kyiv, Ukraine

**Background.** Mesenchymal cells at present are widely investigated, particularly because of their usage in the therapy of many diseases. It is known that bone marrow is the source of mesenchymal, as well as hematopoietic cells. In case of impact by stress factors, such as chemotherapeutic agents or ionizing radiation, the earliest reaction is usually observed in bone marrow. Previously it was generally assumed that mesenchymal cells are rather radioresistant, but there is data showing presence of radiosensitive sub-populations among them.

**Aim.** The aim of the current study was the assessment of functional activity of mesenchymal progenitor cells of mice bone marrow under ionizing radiation influence in cell culture *in vitro*.

**Methods.** Investigation was performed using 30 Balb/C mice divided into three groups. The first group was acutely irradiated in the sublethal dose of 5.95 Gy. The second group was irradiated chronically during 18 months in the general dose of 1.5 Gy. The third group was the control.

To assess functional activity of mesenchymal progenitors we used cultural methods. Bone marrow was cultivated *in vitro* during 10 days with further counting of fibroblast colony-forming units (CFU). We have also studied the ability of obtained feeder layers to support hematopoiesis in cell culture *in vitro*. Bone marrow hematopoietic cells of intact mice were placed in gel diffusion chambers providing the permeation of nutrients and growth factors from medium and feeder layers. Cultivation was performed during 11 days with further evaluation of CFU number.

**Results.** The authors have revealed the decrease in colony-forming efficiency of mesenchymal progenitor cells in both irradiated groups compared to control. In particular, the number of CFU in the first group was  $1.9 \pm 0.6$ , in the second –  $6.1 \pm 0.8$ , and in control –  $11.1 \pm 1.8$  CFU per  $1 \times 10^6$  explanted cells. Besides, irradiated mesenchymal cells have shown the alteration in their ability to support hematopoiesis. Hematopoietic progenitors expressed reduced colony-forming efficiency on the irradiated feeder layers compared to control. These indices were  $8.6 \pm 1.3$  in the first group,  $17.4 \pm 1.6$  in the second, and  $26.6 \pm 1.2$  CFU per  $1 \times 10^5$  explanted cells in control group.

**Conclusion.** The performed investigations yielded conclusion that mesenchymal progenitors of mice bone marrow possess a rather high radiosensitivity, which is revealed both in case of single acute and long-term chronic irradiation. This should be taken into account when assessing the consequences of ionizing radiation action on the functioning of bone marrow and the state of the hematopoietic system in general.

**Acknowledgements.** The authors declare the absence of conflict of interest.

## The Influence of Long-Term Supplementation with Aluminium or Selenium Ions on Antioxidant Enzymes Activities in Mouse Organs

Sadauskiene Ilona<sup>1,2</sup>, Liekis Arunas<sup>1</sup>, Staneviciene Inga<sup>2</sup>, Naginiene Rima<sup>1</sup>

<sup>1</sup>Neuroscience Institute, Lithuanian University of Health Sciences, Kaunas, Lithuania

<sup>2</sup>Department of Biochemistry, Medical Academy, Lithuanian University of Health Sciences, Kaunas, Lithuania

**Background.** In our previous studies, we evaluated the effect of acute exposure of Al ions on oxidative stress and the capacity of the antioxidant system in mouse organs by using the Al intoxication model that involved the injection of AlCl<sub>3</sub> solution into the abdominal cavity of the mouse. However, the obtained results encouraged us to select a different route of administration of Al: the oral administration. This is a natural route of entry of Al into the body. In addition, such administration does not cause inflammation at the site of the injection. Several studies performed with experimental animals have demonstrated changes in the cognitive functions and morphological peculiarities of the CNS following the consumption of water with elevated concentrations of Al. Even through the absorption of Al through the gastrointestinal system is very poor, a long-term negative effect of Al cannot be ruled out completely, even if the concentrations of Al that enter the body with potable water are lower.

**Aim.** The aim of this study was investigated the effects of Al or Se ions on the “primary” antioxidant defense system enzymes in mice brain and liver after 8-week exposure of drinking water supplemented with AlCl<sub>3</sub> (50 or 100 mg Al/L) or Na<sub>2</sub>SeO<sub>3</sub> (0.2 or 0.4 mg Se/L).

**Methods.** The experiments done on BALB/c laboratory mice. The antioxidant enzymes activities in mice brain and liver homogenates determined spectrophotometrically. Results expressed as the mean ± SEM.

**Results.** Results shown that higher dose of Se increased the activities of superoxide dismutase and catalase in both mouse organs. Exposure to lower dose of Se resulted in an increase of catalase activity in mouse brain but did not show any statistically significant changes of superoxide dismutase activity in both organs. Meanwhile, the administration of both doses of Al caused no changes in activities of these enzymes in mouse brain and liver. The greatest sensitivity to the effect of Al or Se was exhibited by glutathione reductase. Exposure to both doses of Al or Se resulted in statistically significant increase of glutathione reductase activity in both brain and liver.

**Conclusion.** It was concluded that long-term exposure of Se ions caused statistically significant increase of superoxide dismutase, catalase, and glutathione reductase activities in mouse brain and/or liver, however, these changes were dependent on the used dose. The exposure to both Al doses caused statistically significant increase only activity of glutathione reductase in both organs.

## Selenium Influences Homeostasis of Trace Elements in Mice Brain and Blood

Stanevičienė Inga<sup>1</sup>, Sadauskienė Ilona<sup>1,2</sup>, Liekis Arūnas<sup>2</sup>, Baranauskienė Dalė<sup>2</sup>, Šimakauskienė Vaida<sup>2</sup>, Naginienė Rima<sup>2</sup>

<sup>1</sup>Department of Biochemistry, Medical Academy, Lithuanian University of Health Sciences, Kaunas, Lithuania

<sup>2</sup>Neuroscience Institute, Lithuanian University of Health Sciences, Kaunas, Lithuania

**Background.** The most important trace elements selenium (Se), iron (Fe), zinc (Zn) and copper (Cu) play a significant physiological role in brain development and function. These elements, which are involved in metabolic and redox processes in CNS, may affect cognitive functions. It is therefore important to maintain adequate levels of these elements in the brain. However, the data contained in literature on physiological concentrations of trace elements in humans and experimental animals' brains are quite conflicting. There is even less data on how an excess of Se affects the balance of other elements. Therefore, the purpose of this study was to elucidate the changes in levels of Fe, Cu, Zn related to Se administration.

**Aim.** Experiments were done on 4–6-week-old BALB/c mice. Control mice were given tap water, whereas Se-treated mice – Na<sub>2</sub>SeO<sub>3</sub> (0.4 mg Se/kg body weight) in tap water for 8 weeks.

**Methods.** Trace element concentrations were determined by inductively coupled plasma mass spectrometry (using NexION 300 D) in the Toxicology Laboratory of Neuroscience Institute. License of the State Food and Veterinary Service for working with laboratory animals No. G2–80.

**Results.** It was shown that after 8-week oral consumption of Na<sub>2</sub>SeO<sub>3</sub> solution, Se concentration in mice blood increased 3.5-fold (from 271.23 to 936.17 μg/L, p<0.05), meanwhile, in brain it increased 2.5-fold (p<0.05) in comparison with Se concentration value (0.061 μg/g) of control. The exposure to Na<sub>2</sub>SeO<sub>3</sub> caused a statistically significant increase in Cu level both in the mice blood and brain as compared to control. An increase in Cu concentration in mice blood and brain was found by 22% (1.52 μg/L) and 17% (4.36 μg/g) respectively. In contrast, administration of Na<sub>2</sub>SeO<sub>3</sub> decreased Fe concentration in mice blood by 13% (786.46 mg/L, p<0.05), while Fe concentration in the brain increased by 20% (from 27.27 to 32.73 μg/g, p<0.05) as compared to control. The exposure to Na<sub>2</sub>SeO<sub>3</sub> caused no changes in Zn concentration either in mice blood or brain.

**Conclusion.** It was determined that Se affects levels of trace elements in mice brain and blood. The exposure to Na<sub>2</sub>SeO<sub>3</sub> for 8 weeks increased Se concentration in mice blood resulting in higher accumulation of Se in the brain, which respectively increased Cu and Fe levels without influencing the level of Zn. Meanwhile, the raised Se level in the blood is related to increased Cu, but decreased Fe concentrations.

## Effect of Bio-Elements on Maintenance of Sodium and Potassium Ion Homeostasis in Model of Isolated Porcine Kidneys Stored in Modified Preserving Solution for Organ Transplantation

Ostróżka-Cieślak Aneta<sup>1</sup>, Dolińska Barbara<sup>1,2</sup>, Ryszka Florian<sup>2</sup>

<sup>1</sup>Department of Pharmaceutical Technology, Faculty of Pharmaceutical Sciences in Sosnowiec, Medical University of Silesia, Katowice, Poland

<sup>2</sup>“Biocheffa” Pharmaceutical Research and Production Plant, Sosnowiec, Poland

**Background.** The success of a transplant depends to a large extent on the quality of the organ taken from the donor, as well as its effective storage and storage time. Our team is conducting research into the optimal formulation and manufacturing technology for organ transplantation fluid. Bio-elements added to the preservation solution formulation can potentially increase the safety and efficacy of the transplant during perfusion and preservation of the organ.

**Aim.** The aim of our study was to analyse the effect of selenium, zinc and manganese, as a component of the preservative fluid, on the maintenance of K<sup>+</sup> and Na<sup>+</sup> ion homeostasis in an isolated porcine kidney model.

**Methods.** The study was conducted in the isolated porcine kidney model Polish “Large White”. The experiment was conducted with the approval of the II Local Ethics Committee Krakow; No. 1046/2013. Optimization of fluid composition was based on Biolasol (FZNP “Biocheffa”, Poland) / reference fluids. Modified / tested fluids: Biolasol+Se<sup>4+</sup> (1 µg/l), Biolasol+Zn<sup>2+</sup> (1 µg/l), Biolasol+Mn<sup>2+</sup> (1 µg/l). The kidneys were washed, then stored using the static method for 48 h under hypothermia (4°C). In the collected perfusate samples the concentrations of Na<sup>+</sup> and K<sup>+</sup> were determined by spectrophotometric methods (Kit Pointe Scientific, INC, USA).

**Results.** Analysis of Biolasol+Se<sup>4+</sup> fluid perfusates confirmed hyponatraemia ([Na<sup>+</sup>]: 48h30'/80±10 mEq/l; p<0.05) and hyperkalaemia ([K<sup>+</sup>]: 48h30'/19.0±2.3 mEq/l; p<0.05). The addition of Zn<sup>2+</sup> ions caused hypernatremia ([Na<sup>+</sup>]: 48h30'/218±10 mEq/l; p<0.01) and an increase in [K<sup>+</sup>] (48h30'/18±1 mEq/l; p=ns). The presence of manganese in the Biolas fluid formulation affected the occurrence of hyperkalaemia ([K<sup>+</sup>]: 48h30'/24±2 mEq/l; p<0.05), while maintaining normal [Na<sup>+</sup>] (48h30'/145±10 mEq/L; p<0.05).

**Conclusion.** The bio-elements analysed as components of Biolasol fluid do not favourably influence the maintenance of sodium and potassium ion homeostasis during renal ischaemia. Manganese may show the activity as a calcium channel blocker.

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## PHARMACY

### A Focus on a Beam Walking Test to Study Motor Impairments in a Mouse Model of Stroke

Brinuma Undine<sup>1</sup>, Dzirkale Zane<sup>1</sup>, Jelisejevs Ilja<sup>1</sup>, Upite Jolanta<sup>1</sup>, Jansone Baiba<sup>1</sup>

<sup>1</sup>Department of Pharmacology, Faculty of Medicine, University of Latvia, Riga, Latvia

**Background.** Many patients suffer from motor impairments after stroke that typically affect the control of movement on one side of the body. Functional assessment tests used in stroke preclinical models are an excellent tool to study the level of balance impairments and reduced muscle tone. It is crucial to apply standardized tests that are highly replicable, sensitive and specific for animal species. To date, there has been no general agreement on the test conditions that would be most applicable. Therefore, choosing appropriate behavioural tests and conditions is crucial in assessing preclinical stroke studies and later connecting the findings in rodents to clinical trials.

**Aim.** To examine the dysfunction of the mice's hind limbs by using a beam walking test after the experimental ischemic stroke induction in mice.

**Methods.** There were three experimental groups of C57BL/6NHsd male mice (12 weeks old; n=9–10 per group): stroke – an endovascular filament-induced middle cerebral artery occlusion (fMCAo) in the left hemisphere for 60 minutes and followed by reperfusion; sham – the filament was inserted and immediately withdrawn from the blood vessel; naïve – animals did not receive any surgery. Motor function of the mice's right and left limb was assessed using a beam walking task. It was performed using two different widths of wooden beams: 6 mm and 12 mm wide. The length of the beams was 100 cm. Two testing trials were performed at 3 and 7 days post-stroke. The number of hind-limb slips on the right side that occur in the process was recorded.

**Results.** The obtained results indicated significantly higher numbers of right (contralateral side to fMCAo injury) hind limb drops for stroke group mice compared to both naïve and sham group animals tested on 6 mm wide beam on both day 3 and 7 after induction of fMCAo. Besides, stroke group animals had statistically higher numbers for right hind limb drops compared to the left side on both tested days. Test results on a 12 mm wide beam did not show any statistical difference either on day 3 or day 7 among the experimental groups.

**Conclusion.** A beam walking test with an appropriate beam width can be used to assess stroke-induced neurological disturbances in motor coordination and balance in mice in the early post-stroke period.

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## Assessment of Motor Function in Ischemic Stroke Mice Model Using Rotarod and Kondziela's Inverted Screen Tests

Islamgarajeva Evita<sup>1</sup>, Jelisejevs Ilja<sup>2</sup>, Upīte Jolanta<sup>2</sup>, Rožkalne Rebeka<sup>2</sup>, Piļipenko Vladimirs<sup>2</sup>, Jansone Baiba<sup>2</sup>

<sup>1</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

<sup>2</sup>Department of Pharmacology, Faculty of Medicine, University of Latvia, Riga, Latvia

**Background.** Cerebral cortex is a brain region that is one of the most affected areas in stroke patients. Aberrations in the functioning of the motor cortex can lead to impaired patient mobility, thus limiting their daily activities and lowering the overall quality of life<sup>1</sup>. Hence, it is substantial to investigate the functional interactions between brain regions that contribute to motor disability after stroke in mice. To assess motor activity and muscle strength, we performed two behavioural tests – rotarod and Kondziela's inverted screen tests.

**Aim.** To investigate the muscle strength of all four limbs and motor activity of healthy, sham-operated and ischemic stroke model mice at distinct timepoints during a two-month period using Kondziela's inverted screen and rotarod tests.

**Methods.** Middle cerebral artery occlusion (MCAo) was performed experimentally in 12-week-old C57BL/6 male mice. Mice were divided into 3 groups: naïve, sham and stroke (n=9–10/group). Motor coordination was determined by rotarod and muscle strength by Kondziela's inverted screen test. The time in seconds until the mice fell off the grid was assessed on day 3, 10, 15, 30 and 60 after MCAo using the Kondziela's inverted screen test, with maximum test duration time of 120 seconds. Rotarod test was done on day 5, 26 and 30 after MCAo. Starting speed was 4 rpm with acceleration rate 40 rpm and test duration time of 300 seconds. End times were noted when the mice fell off from the rotarod apparatus.

**Results.** Hanging time of our four paws was significantly lower in the MCAo group compared to naïve and sham controls in the Kondziela's inverted screen test only on day 3 after MCAo surgery. No significant differences in this parameter were observed among the experimental groups at later times following MCAo. Walking time was not significantly changed in the rotarod test among the experimental groups in all tested periods.

**Conclusion.** The data obtained in young mice following MCAo surgery have shown no influence of MCAo on motor performance starting from day 5 until day 30 after MCAo injury. Muscle strength was affected only during the first 3 days of MCAo injury. Further studies in older MCAo mice could provide additional perspective on the importance of age and the specificity of behavioural tests in stroke studies.

**Acknowledgements.** The study was supported by UL funding for “Biomedicine and pharmacy” and ERA-NET project “Multi-scale investigation of synaptic dysfunction after stroke (MISST)” No. ES RTD/2018/29.

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## Polyphenols as Protease Inhibitors: Focus on Angiotensin Converting Enzymes 1 and 2, Plasma Kallikrein and Neutrophil Elastase Activity *in Vitro*

Namniece Jana<sup>1</sup>, Rembergs Reinis<sup>1</sup>, Jēkabsons Kaspars<sup>1</sup>, Birzniece Zane<sup>1</sup>, Kaļķe Kitija<sup>1</sup>,  
Vavutkina Kristīne Laura<sup>1</sup>, Muceniece Ruta<sup>1</sup>  
<sup>1</sup>University of Latvia, Rīga, Latvia

**Background.** Nowadays, the inhibitory effects of polyphenols on various proteases have gained new relevance. Protease inhibitors can serve as promising prophylactics to prevent the manifestation and progression of COVID-19 by blocking the virus entry in the cells via angiotensin-converting enzyme 2 (ACE2) and transmembrane protease serine 2 (TMPRSS2) and inhibiting viral 3-chymotrypsin-like cysteine protease (3Cl), neutrophil elastase (NE) and plasma kallikrein (PK) to prevent replication and acute respiratory distress syndrome. Up to now, protease inhibiting properties of the many polyphenols are evaluated using *in silico* approach. However, experimental proofs for such activities have been demonstrated less frequently.

**Aim.** The aim of the current study was to explore the effects of rutin, quercetin, phloretin, cyanidin-3O-glucoside on ACE1, ACE2 and PK activities, as well as to assay the influence of polyphenol-rich *Vaccinium* spp. berry pomace extracts on ACE1, ACE2 and NE activity *in vitro*.

**Methods.** Inhibition of ACE1, ACE2 and PK activities by test and reference substances was assessed according to the corresponding kits' manufacturer BioVision, Inc. (Milpitas, California, USA) instructions. Inhibition of elastase by the test samples was assayed using N-succyl-(Ala)<sup>3</sup>-nitroanilide (SANA) as the substrate and monitoring the release of *p*-nitroanilide. In ACE1 and ACE2 assays fluorescence was measured at 320/420 nm, in PK and NE assays absorbance was measured at 405 nm using a Tecan Infinite 200 PRO plate reader and i-control software.

**Results.** Polyphenols and berry pomace extracts inhibited all the proteases tested here. However, phloretin, rutin, quercetin, cyanidin-3O-glucoside and extracts of bilberry and lingonberry inhibited ACE2 activity more than that of ACE1. Specific enzyme inhibitors used as reference substances exerted very selective activity, namely, captopril for ACE1, MLN4760 for ACE2, BCX7353 for PK. Phloretin was the strongest ACE2 inhibitor (inhibition 79%) among here tested substances whereas lingonberry extract – NE inhibitor (inhibition 88%).

**Conclusion.** Polyphenols are known for their antiviral activity and pleiotropic effects. Targeting host cell proteases might be a potential treatment strategy to limit the spread of SARS-CoV-2. Proteases inhibiting properties of the plant products may add new knowledge to the ongoing search for the new drugs against SARS-CoV-2 and provide a perspective on the possibility to use polyphenols in the development of natural approaches against virus entry in the cells.

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## Analysis of Antibiotic Use in Paediatric Hospital in Latvia

Sviestina Inese<sup>1,2</sup>

<sup>1</sup>Faculty of Medicine, University of Latvia, Riga, Latvia

<sup>2</sup>Children's Clinical University Hospital, Riga, Latvia

**Background.** Inappropriate use of antibiotics increases both microbial resistance and hospital costs. There is still a need to change prescribing practice for children through improved antimicrobial stewardship and identification of the factors, which have the greatest influence on antimicrobial prescribing.

**Aim.** The aim of the current study was to compare antibiotic use in 2021 and 2012 in order to analyse both prescription tendencies and the impact of antimicrobial stewardship programme.

**Methods.** Point prevalence surveys were undertaken during November 2021 and 2012 using validated and standardized methodology of project “Antibiotic Resistance and Prescribing in European Children”.

**Results.** Antibiotics were prescribed to 41 (29.3%) patients in 2021 and 128 (37.0%) in 2012. A treatment for surgical disease was the most common indication for antibiotic use in 2021, whereas respiratory tract infections as an indication prevailed in 2012. The most common age group of patients receiving antimicrobials was children above 12 years of age (14; 34.1%) in 2021 and children 1–5 years of age (36; 28.1%) in 2012.

The most commonly used antibiotic classes for the treatment and prophylaxis of paediatric patients were the 2<sup>nd</sup> generation cephalosporins – 9 (17.3%) prescriptions in 2021 and the 3<sup>rd</sup> generation cephalosporins – 38 (27.0%) prescriptions in 2012. The most often prescribed antibiotic for paediatric patients was cefuroxime – 9 (17.3%) prescriptions in 2021 and ceftriaxone – 24 (17.0%) prescriptions in 2012. Ceftriaxone was used in none out of 10 prescriptions for surgical prophylaxis in 2021 and in 4 (30.8%) prescriptions in 2012.

Antibiotics were most predominantly used parenterally: 46 (88.5%) prescriptions in 2021 and 111 (78.7%) prescriptions in 2012. Antibiotics were prescribed empirically to paediatric patients in 48 (92.3%) cases in 2021 and 117 (83%) cases in 2012.

There was only 1 neonatal patient in 2021 and 19 in 2012.

**Conclusion.** Although the point prevalence survey has limitations, e.g., no data on local resistance patterns informing antibiotic choice or how long antibiotics were used, it is a useful method to identify areas of improvement. This study shows some improvements in antibiotic prescriptions, e.g., ceftriaxone was no longer the most often prescribed antibiotic both for treatment and surgical prophylaxis. At the same time, the point prevalence survey identified problem areas for improvement, e.g., predominant use of parenteral antibiotics. Further studies are still required to determine the appropriateness of the choice of antibiotics.

**Acknowledgements.** This study was supported by UL fundamental research grant “Research of biomarkers and natural substances for acute and chronic diseases’ diagnostics and personalized treatment”.

## Anti-Inflammatory, Free Radical Scavenging, and Reducing Activities of *Malus × domestica* Borkh. Apples Extracts

Butkevičiūtė Aurita<sup>1</sup>, Petrikaitė Vilma<sup>2,3</sup>, Liaudanskas Mindaugas<sup>1</sup>, Janulis Valdimaras<sup>1</sup>

<sup>1</sup>Department of Pharmacognosy, Lithuanian University of Health Sciences, Kaunas, Lithuania

<sup>2</sup>Laboratory of Drug Targets Histopathology, Institute of Cardiology, Lithuanian University of Health Sciences, Kaunas, Lithuania

<sup>3</sup>Institute of Physiology and Pharmacology, Lithuanian University of Health Sciences, Kaunas, Lithuania

**Background.** Cancer initiation and development are closely related to oxidative stress and chronic inflammation. It has been established that many elements of a vegetarian diet, especially fruits and vegetables can prevent the development of cancer. Apples are one of the most consumed fruits worldwide. In nutrition, apples are a relevant source of phenolic and triterpenic compounds, which possess anti-inflammatory and antioxidant activities, neutralizing harmful reactive free radicals that trigger structural damage to the body's macromolecules, which, in turn, is directly related to the progression of various diseases including inflammatory diseases and cancer.

**Aim.** The aim of this study was to evaluate apple extracts antioxidant, and anti-inflammatory activities *in vitro*.

**Methods.** This study included the five apple cultivars 'Auksis', 'Kosteles', 'Ligol', 'Paprastasis antaninis', and 'Rubin'. Free radical scavenging, and reducing activities were estimated, using spectrophotometrical DPPH, ABTS, FRAP, and CUPRAC assays, respectively. Results of antioxidant activity assays were expressed as micromolar of Trolox ( $\mu\text{M TE/g DW}$ ). Anti-inflammatory activity was determined evaluating hyaluronidase (HYAL) inhibition. The absorbances of the test solutions were measured at multiscan plate reader. HYAL inhibition was calculated:  $\text{HYAL inhibition (\%)} = 100 \times (1 - [\text{Absorption of sample} / \text{Absorption of control}])$ .

**Results.** The radical scavenging activity assessed by DPPH and ABTS assays ranged between 19.37 to 328.32  $\mu\text{M TE/g}$ , and 67.07 to 805.52  $\mu\text{M TE/g}$ , respectively. The reducing activity estimated by CUPRAC and FRAP assays ranged between 3.24 to 70.81  $\mu\text{M TE/g}$ , and 229.83 to 3191.09  $\mu\text{M TE/g}$ , respectively. The strongest antiradical and reducing effects were determined of apple extracts of 'Paprastasis antaninis' cultivar. Apple extracts inhibited hyaluronidase from 26.38 to 35.05 %. The strongest inhibition activity of hyaluronidase was evaluated in the apple extracts of 'Kosteles' cultivar. A moderate positive correlation ( $r_{\text{DPPH}}=0.397$ ,  $r_{\text{ABTS}}=0.422$ ,  $r_{\text{FRAP}}=0.420$ , and  $r_{\text{CUPRAC}}=0.449$ ) between the antioxidant and hyaluronidase inhibition activities of apple extracts was found.

**Conclusion.** Understanding the mechanisms of apple extracts and their biological active compounds as hyaluronidase inhibitors and antioxidants may be a useful tool for future study *in vivo*, or development of new, innovative food supplements that could be used for prevention of chronic diseases.

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## Bioactive Constituents in *Vaccinium vitis-idaea* L. Leaves: Geographical Variation Throughout Lithuania and Associations With External Factors

Vilkickyte Gabriele<sup>1</sup>, Raudone Lina<sup>1,2</sup>

<sup>1</sup>Laboratory of Biopharmaceutical Research, Institute of Pharmaceutical Technologies, Lithuanian University of Health Sciences, Kaunas, Lithuania

<sup>2</sup>Department of Pharmacognosy, Lithuanian University of Health Sciences, Kaunas, Lithuania

**Background.** *Vaccinium vitis-idaea* L. (lingonberry) leaves exhibit a broad spectrum of biological activities and constitute a promising source of bioactive components, therefore they are of great interest in the pharmaceutical industry. Selection in plant breeding, determination of perspective wild clones with optimal growing conditions, leading to standardized extracts are the key factors for achieving phytochemical quality, which meets consumers' needs.

**Aim.** Our research aimed at investigating the effects of geographical conditions, as well as environmental, edaphic, and external factors on accumulation of phenolics and triterpenoids in wild-growing lingonberry leaves.

**Methods.** Lingonberry leaves were collected at the end of September 2019 from different regions and 28 natural habitats of Lithuania and were immediately air-dried, extracted afterward, and analyzed using validated HPLC-PDA techniques. The quantitative analysis data were further analyzed by principal component analysis (PCA). Soil samples in the plant root zones were taken in each collecting location and were subjected to macronutrients analysis. Climatic data, geographical (altitude, longitude, and latitude), and soil quality parameters were correlated using Pearson's correlation test ( $\alpha=0.05$ ) with the phytochemical composition of lingonberry samples.

**Results.** A total of 43 bioactive compounds, belonging to groups of phenolics and triterpenoids, were identified and quantified in lingonberry samples. Multivariate data analysis clustered the investigated samples into distinct groups, which differed by their geographical origin and chemophenetic markers. Chemophenetic differences among lingonberry leaves were found most likely due to variations in the climatic and geographical conditions of their collecting localities. Correlation analyses revealed significant negative correlations between contents of particular constituents and sunshine duration, temperature, and precipitation, and positive correlation with air humidity, longitudes, and altitudes of collecting locations and macronutrients in soil, suggesting that harsh weather conditions are favorable for most identified compounds.

**Conclusion.** Our study provided further evidence for high contents and a wide diversity of bioactive components of lingonberry leaves, thus contributing to medicinal value data. Macronutrient status, soil quality, light, temperature, and humidity regimes may be employed to manipulate the phenolic and triterpenoid content in lingonberry leaves, eligible for the production of phytopharmaceuticals.

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## Phylogenotypic Flavonols' Profiles and Antioxidant Activity Variation in Fruit Samples of the American Cranberry (*Vaccinium Macrocarpon* Aiton)

Urbštaitė Rima<sup>1</sup>, Janulis Valdimaras<sup>1</sup>

<sup>1</sup>Department of Pharmacognosy, Lithuanian University of Health Sciences, Kaunas, Lithuania

**Background.** Phenolic compounds in the fruit of American cranberry determine the antioxidant, anti-inflammatory, anticancer, and antibacterial effects. Fruit of cranberry are used in the production of food supplements, which highlights the importance of qualitative and quantitative analysis of phenolic compounds in cranberry fruit raw material. The use of cranberry fruit raw material with the determined composition of phenolic compounds may help to produce high-quality food products and food supplements.

**Aim.** The aim of the current study was to determine the qualitative and quantitative composition of flavonols in samples of eight cultivars and genetic clones of cranberries by ultra-high performance liquid chromatography method and to evaluate the antioxidant activity *in vitro* of the cranberry extracts.

**Methods.** The object of the study was cranberry fruit of cultivars 'Black Veil', 'Franklin', 'Hollister Red', 'Mathews', 'Vilcox' and genetic clones 'Bain-11', 'BL-6', 'Bain-10'. The samples of lyophilized cranberries extracted with 70% (v/v) ethanol in the ultrasonic bath for 15 min at room temperature. Analysis of flavonols was performed by ultra-high performance liquid chromatography method. The antioxidant activity was evaluated by spectrophotometric methods using the FRAP assay and the ABTS<sup>+</sup> scavenging assay.

**Results.** During the study, the following compounds were identified and quantified myricetin-3-galactoside, quercetin-3-galactoside, quercetin-3-glucoside, quercetin-3- $\alpha$ -L-arabinopyranoside, quercetin-3- $\alpha$ -L-arabinofuranoside, quercetin-3-rhamnoside, myricetin, and quercetin. The results of the study suggest that quercetin-3-galactoside and myricetin-3-galactoside predominated in the studied fruit samples. The highest sum of the flavonols was determined in fruit samples of the 'Vilcox' cultivar  $3.37 \pm 0.06$  mg/g DW. The strongest antiradical activity *in vitro* evaluated by the ABTS assay was observed in American cranberry fruit extracts of the 'Hollister red' cultivar  $608.76 \pm 11.36$   $\mu$ mol TE/g DW. When applying the FRAP assay, the strongest reducing activity *in vitro* was found in American cranberry sample extracts of the 'Franklin' cultivar  $496.66 \pm 8.64$   $\mu$ mol TE/g DW. The correlation between the total amount of flavonols and antioxidant activity was not determined.

**Conclusion.** Chromatogram profiles of the studied American cranberry samples were identical but differed in the area sizes of the analyte peaks. This study provides new knowledge about the phytochemical composition of the fruit of different cranberry cultivars and genetic clones and the possibility of using quercetin-3-galactoside and myricetin-3-galactoside as analytical quality markers in *Vaccinium macrocarpon* raw materials and extracts.

**Acknowledgements.** The authors declare the absence of conflict of interest.

## Evaluation of Properties of Chewable Gel Tablets With Nutmeg Essential Oil

Matulytė Inga<sup>1,2</sup>, Bernatoniene Jurga<sup>1,2</sup>

<sup>1</sup>Department of Drug Technology and Social Pharmacy, Lithuanian University of Health Sciences, Kaunas, Lithuania

<sup>2</sup>Institute of Pharmaceutical Technologies, Lithuanian University of Health Sciences, Kaunas, Lithuania

**Background.** Chewable gel tablets have a gel base and are similar to gummies. Gel-based tablets are usually prepared by using silicones or metal forms. These tablets contain water, a vast amount of sugar, and active ingredients (usually vitamins and extracts) in their composition. Active substances such as essential oils and microcapsules are a new field in gel-based tablets.

**Aim.** The aim of this study was to create chewable gel tablets with nutmeg essential oil and its microcapsules and evaluate their physical properties.

**Methods.** Nutmeg essential oil was prepared by hydrodistillation. Microcapsules with essential oil were prepared by lyophilization (emulsion composition for microcapsules: 25% nutmeg essential oil, 15% excipients, 60% water). Chewable gel tablets (three series: control (9% gelatine, 18% water, 68.5% thyme syrup, 2.5% thyme extract, 2% citric acid solution), with nutmeg essential oil (0.469%) and with microcapsules (3.75%)) were prepared by using silicone forms, and firmness, hardness, springiness, and stickiness were evaluated by texture analyser TA.XT.plus. Measuring was repeated 3 times and an average with a standard deviation is presented. Also, mass variation of gel tablets after day, week, and month were measured (n=10).

**Results.** Chewable gel tablets' masses after one day were  $3.32\pm 0.14$ ,  $3.55\pm 0.09$ , and  $3.64\pm 0.05$  g (control, tablets with essential oil and with microcapsules, respectively). After a month, the mass changed about  $22.41\pm 6.17\%$ ,  $p<0.05$ . Firmness and hardness after one day were  $700.58\pm 12.66$ – $1407.70\pm 51.07$  g and  $501.44\pm 18.24$ – $1104.62\pm 101.79$  g (the least hard tablets were from the control group, the most – with microcapsules). After a month, the results were opposite and tablets with essential oil and its microcapsules had better parameters. The smallest changes in elasticity (about 42%) were observed in tablets with microcapsules, also, they had the lowest stickiness, results were compared after one month.

**Conclusion.** Freshly prepared control gel tablets have the best properties of texture, described by firmness and hardness parameters. However, after one-month, nutmeg essential oil and its microcapsules protected gel-based tablets from strong hardening, and the quality of these two samples' was better.

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## The Influence of Vinylpyrrolidone-Vinyl Acetate Copolymer in Extraction on Isoflavones Aglycones Yield from *Trifolium Pratense* L. Flowers

Kazlauskaitė Jurga Andrėja<sup>1,2</sup>, Bernatoniene Jurga<sup>1,2</sup>

<sup>1</sup>Department of Drug Technology and Social Pharmacy, Lithuanian University of Health Sciences, Kaunas, Lithuania

<sup>2</sup>Institute of Pharmaceutical Technologies, Medical Academy, Lithuanian University of Health Sciences, Kaunas, Lithuania

**Background.** Red clover and its supplements have been the subject of much interest for the reduction of menopausal symptoms and conditions related to aging because of their high concentrations of phytoestrogens, specifically – isoflavones, which are thought to be especially healthful. These compounds are usually not fully recovered in the extracts, but the use of excipients can improve extraction.

**Aim.** The aim of the current study was to use excipient vinylpyrrolidone-vinyl acetate copolymer on *Trifolium pratense* L. extracts to increase the yield of isoflavones aglycones.

**Methods.** Ultrasound assisted extraction (frequency 38 kHz) was performed using 1.0 g of dried and milled flower heads and 30 mL of water. Temperature during extraction – 40°C. Ultrasound power 250 W and extraction time 10 min. Thermal hydrolysis was performed after sonication placing extract in a heating mantle under a reflux condenser for one hour. Excipient vinylpyrrolidone-vinyl acetate copolymer was added to the extraction media before ultrasound processing, its quantity in the samples was from 1 to 5% (v/w). The excipient amount was based on solvent quantity. Control sample was prepared using the same conditions without excipient. Extraction samples for identification and quantification of aglycones genistein and daidzein were investigated using HPLC.

**Results.** Using excipient vinylpyrrolidone-vinyl acetate copolymer in the extraction media the yield of isoflavones significantly increased compared to the control samples without excipients. Using 1% of excipient in the extraction the yield of isoflavones were 135.13±6.75 and 186.30±9.31 µg/g (genistein and daidzein respectively). The control sample that was extracted using the same conditions without excipient only yielded in 67.06±3.35 µg/g daidzein and genistein was not detected. It was also estimated that increasing the amount of vinylpyrrolidone-vinyl acetate copolymer in the extract increased the yield of genistein 2.5-fold.

**Conclusion.** The results of the present study showed that vinylpyrrolidone-vinyl acetate copolymer can increase solubility of isoflavones in the aqueous extraction media. Increasing the amount of excipient in extraction further than 5% will not further increase isoflavones aglycones yield.

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## Effect of Broccoli (*Brassica Oleracea* Var. *L. Italica*) Sprout Extract on the Leak State Respiration Rate of Rat Heart and Liver Mitochondria

Kuršvietienė Lolita<sup>1</sup>, Svaldenytė Laurita<sup>1</sup>, Bernatoniienė Jurga<sup>2,3</sup>, Kopustinskiienė Dalia Marija<sup>3</sup>

<sup>1</sup>Department of Biochemistry, Faculty of Medicine, Medical Academy, Lithuanian University of Health Sciences, Kaunas, Lithuania

<sup>2</sup>Department of Drug Technology and Social Pharmacy, Faculty of Pharmacy, Medical Academy, Lithuanian University of Health Sciences, Kaunas, Lithuania

<sup>3</sup>Institute of Pharmaceutical Technologies, Faculty of Pharmacy, Medical Academy, Lithuanian University of Health Sciences, Kaunas, Lithuania

**Background.** Broccoli (*Brassica oleracea* var. *L. italica*) sprout extract is rich in various biologically active compounds such as vitamin C,  $\beta$ -carotene, phenolic compounds and glucosinolates. Phenolic compounds, especially flavonoids in the extract composition, have a variety of biological effects, including antioxidant and anti-cancer activity. Mitochondria are known not only as energy producing organelles of cells in different tissues. They are also involved into antioxidant and anti-cancer mechanisms taking place in living cells. However, there is no data regarding the effect of biologically active compounds of broccoli sprout extract on mitochondrial function.

**Aim.** In this work, we evaluated the effect of broccoli sprout extract on the leak state respiration rate of rat heart and liver mitochondria.

**Methods.** Mitochondria from *Wistar* rat heart and liver were isolated by differential centrifugation. Protein quantity was determined by the Biuret method. The mitochondrial respiration (oxygen consumption) rates were measured using the high resolution respirometry system Oxygraph-2k. Data were presented as mean  $\pm$  SEM. A value of  $p < 0.05$  was taken as the level of significance.

**Results.** Pyruvate + malate was used as respiratory substrates for rat heart mitochondria, glutamate + malate – for liver mitochondria. Authors found that ethanolic broccoli sprout extract does not affect the leak state respiration rate of rat heart and liver mitochondria in the concentration range 0.05–0.2 mg/ml. However, ethanolic broccoli sprout extract significantly increased the leak state respiration rate of rat heart mitochondria within concentrations 0.5–3 mg/ml; the most pronounced uncoupling effect 87.3% was obtained, when final concentration of extract was 1 mg/ml. Though, ethanolic broccoli sprout extract has no uncoupling effect in rat liver mitochondria. Therefore, ethanolic broccoli sprout extract has a tissue-specific effect on the leak state respiration rate within concentrations 0.5–3 mg/ml. Moreover, there is growing evidence that a mild uncoupling is a very important mechanism of cardioprotection.

**Conclusion.** Ethanolic broccoli sprout extract significantly increases the leak state respiration rate of heart mitochondria respiring on pyruvate + malate in the concentration range 0.25–3 mg/ml; i.e., it has uncoupling effect. Ethanolic broccoli sprout extract has no effect on the leak state respiration rate in liver mitochondria respiring on glutamate + malate within this concentration range.

## Identification of Flavanones in *Citrus Xparadisi*. L Fresh Fruit Parts Using Different Extraction Methods

Stabrauskienė Jolita<sup>1,2</sup>, Bernatoniene Jurga<sup>1,2</sup>, Marksa Mindaugas<sup>3</sup>

<sup>1</sup>Department of Drug Technology and Social Pharmacy, Lithuanian University of Health Sciences, Kaunas, Lithuania

<sup>2</sup>Institute of Pharmaceutical Technologies, Lithuanian University of Health Sciences, Kaunas, Lithuania

<sup>3</sup>Department of Analytical and Toxicological Chemistry, Lithuanian University of Health Sciences, Kaunas, Lithuania

**Background.** Grapefruit (*Citrus xparadisi*. L). is an essential member of the Citrus fruits, which have been recently studied for their health benefits. The most predominant flavanones naringin and his aglycone naringenin, which have high biological activity, antioxidants, anti-inflammatory, metabolic diseases, anti-virus, neuroprotective, and antitumor effects. They can be found in different concentrations depending on the part of the fruit.

**Aim.** This work aims to compare the yield of flavanones naringin and naringenin from grapefruit parts using different extraction methods.

**Methods.** The grapefruit was obtained at the local market. Fruit parts were separated into *flavedo*, *albedo*, and *segmental* parts, then fragmented and frozen in a freezer (18°C) until extracted. Flavanones were extracted using different methods: Ultrasound-Assisted Extraction Bath (UAE), Ultrasound-Assisted Extraction using an ultrasonic homogenizer (UAE\*), and Heat Reflux Extraction (HRE). The samples were centrifuged for 10 minutes at 4000 rpm. The extracts were filtered through PVDF syringe filters (pore size of 0.22 µm) before HPLC analysis.

The operating conditions of each extraction method are given in the table below.

Table. Operating conditions of the different extraction methods

Extract. methods	Solvent	Ratio	Processing time	Temperature C°	Raw material
HRE	Ethanol (v/v) 70%	1:10	60 min	100°C	<i>Flavedo</i> <i>Albedo</i> <i>Segmental</i>
UAE	Ethanol (v/v) 50% and 70%	1:10	20, 30 min	50°C 70°C	<i>Flavedo</i> <i>Albedo</i> <i>Segmental</i>
UAE*	Ethanol (v/v) 70%	1:10	1, 3, 5 min	33.5±40°C	<i>Flavedo</i> <i>Albedo</i> <i>Segmental</i>

**Results.** After applying different extraction methods, it was detected that using UAE with optimal conditions (processing time of 30 min, ethanol 50% (v/v), t°-50°C), obtained the highest extraction of naringin in a sample from the *albedo* part 17.45±0.87 mg/g. The high yield of naringenin was detected using the HR method from the *segmental* part 35.85±1.79 µg/g. We did not find naringenin in the *flavedo* using different methods. The comparing different methods, HR extraction increases naringenin by two times more from the *albedo* (UAE naringenin 4.63±0.23 µg/g; HR naringenin 12.6±0.63 µg/5), and shows better results from the *segmental* part (UAE naringenin – not found; HR naringenin 35.80±1.79 µg/g; UAE\* naringenin 7.40±0.37 µg/g).

**Conclusion.** The yield of naringin from grapefruits was significantly higher in the *albedo* part using UAE 17.45±0.87 mg/g compared with HR 14.17±0.8 mg/g and UAE\* 6.67±0.33 mg/g; a higher yield of naringenin was found using HR from the *segmental* part 35.80±1.79 µg/g.

## The Morphofunctional State of Cerebral Hemispheres Neuropil in Rats with Scopolamine-Induced Dementia of Alzheimer's Type After Intravenous Injections of Mesenchymal Stem Cells

Lukyanova Yevgeniya<sup>1</sup>, Pavlova Olena<sup>1</sup>, Gubina-Vakulyck Galina<sup>1</sup>

<sup>1</sup>Kharkiv National Medical University, Kharkiv, Ukraine

**Background.** The scientific world shows a special interest in stem cell therapy, especially in mesenchymal stem cells (MSC), which seems to be a promising, effective, safe therapeutic strategy for Alzheimer's disease. The question of assessment of the impact of MSC on the brain white matter neuropil after its intravenous administration using simple morphological methods remains relevant.

**Aim.** The aim of the current study was the assessment of cerebral hemispheres neuropil's morphofunctional state in rats with scopolamine-induced dementia of Alzheimer's type after mesenchymal stem cells intravenous injections.

**Methods.** The experiment was performed on 48 male WAG rats with 14- and 28-days scopolamine-induced models of Alzheimer's type dementia. Half of the animals received a single intravenous injection of MSC in a dose of 500 000 cells for each rat at the appropriate time after scopolamine injections (Scop, 1 mg/kg). Control animals (gr. C) received 0.1 ml isotonic saline. Cognitive functions were evaluated using the Extrapolation Escape Task (EET) and Passive Avoidance Test (PAT). The animals were sacrificed on the 14<sup>th</sup> day after all injections. The content of acetylcholine (ACh) in brain homogenates was determined by the spectrophotometric method. The brain slices were stained with Congo-red, bromophenol blue (BPB), according to Einarson's method and studied using Zeiss Axiostar plus binocular microscope and software GIMP.

**Results.** In "PAT" the conditioned reflex was not formed in most rats of gr. Scop-28 whereas in "EET" rats of gr. Scop-14, Scop-28 failed this test. It was accompanied by a decrease in the ACh level. In gr. Scop-14, Scop-28 the neuropil had more homogeneous focal structure with multiple congophilic clusters which were resistant to hypoxia, and neuropil optical density was sharply reduced compared with gr. C. The MSC injections improved the values of neuropil optical density and the ACh level in the brain homogenates but did not have resorption effect on amyloid areas. Moreover, in the brain slices stained with BPB, the areas of neuropil with reduced optical density were observed. The cognitive functions of rats of gr. Scop-14-MSC, Scop-28-MSC were improved.

**Conclusion.** The intravenous injection of mesenchymal stem cells led to amelioration of cognitive and cholinergic system functions, morphofunctional state of cerebral hemispheres neuropil in rats with scopolamine-induced dementia of Alzheimer's type.

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