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Foreword

It is with great pride and sincere enthusiasm that I welcome you to the 2025 edition of „Dies Doctorandorum“, a distinguished gathering within our Postgraduate Study of Biomedicine and Health at the Faculty of Medicine Osijek, University J. J. Strossmayer Osijek.

This annual event has become a vital academic tradition—an opportunity for our doctoral students to present their research, engage in meaningful scientific exchange, and contribute to the intellectual community that defines our faculty. The abstracts collected in this book reflect the depth and innovation of ongoing research projects in the fields of biomedicine and health sciences. They serve as a testament to the commitment of our young scientists to address complex biomedical challenges through rigorous and ethically grounded research.

The Dies Doctorandorum not only encourages scientific dialogue among students, mentors, and fellow researchers but also fosters an environment of collaboration that transcends disciplinary boundaries. It is through such forums that we strengthen the foundation for scientific excellence, academic growth, and professional development.

I extend my gratitude to all participants, mentors, and organizers whose dedication made this event possible. May this Abstract Book inspire new ideas, fruitful discussions, and continued pursuit of knowledge that improves human health and well-being.

With best regards and encouragement for all your future endeavors,

Prof. Ivica Mihaljević
Dean
Faculty of Medicine Osijek
University J. J. Strossmayer Osijek

Abstracts of annual seminars…..

The list of PhD Candidates, Mentors and Titles of abstracts of annual seminars …..

Abstracts of annual seminars

Abstract Title: Predicting clinical dishonesty among nursing students: the impact of personal and contextual factors

Part of the Dissertation Proposal: This abstract presents a part of the dissertation proposal that investigates the contribution of personal (intrapersonal and interpersonal) and contextual factors to the prediction of clinical dishonesty among nursing students.

PhD candidate: Renata Apatić, MSN, RN, Medical high school Osijek, Croatia

Mentor: Assoc. Prof. Robert Lovrić, Ph.D., Faculty of Dental Medicine and Health Osijek, Osijek Croatia

Co-mentor: Assoc. Prof. Krešimir Šolić, Ph.D., Faculty of Medicine Osijek, Osijek Croatia

Introduction: Academic dishonesty is a global problem in many higher education institutions and is increasing in nursing studies. Studies suggest a severe risk due to the association of nursing students' dishonesty in the classroom with dishonesty in clinical settings when it can directly jeopardize patient safety and healthcare quality. The contributions of various personal and contextual factors (e.g., perception of punishment, peer influence, narcissism, study overload) to academic dishonesty have been studied. However, there is still a gap in understanding the predictors of such behavior.

Aims: This study aimed to identify personal (intrapersonal and interpersonal) and contextual factors predicting students' dishonesty during clinical training.

Materials/Participants and Methods: This two-phase, prospective, predictive study included 398 undergraduate and graduate nursing students from the Faculty of Dental Medicine and Health in Osijek. A non-probabilistic purposive sampling method was used, adhering to the inclusion criteria: (a) the participants were undergraduate or graduate nursing students at the examined institution, and (b) the participants had regularly attended clinical training during the study period.

The validated "Mentor Support Evaluation Questionnaire" was used in the first phase to assess students' evaluations of the quality of mentor support during clinical training. The validated instruments "Optimism/Pessimism Scale" and "Nursing Student Perceptions of Dishonesty Scale" were used in the second phase to examine self-reported dishonesty and its contributing factors. The second phase also investigated the students' knowledge of the university's ethical and disciplinary regulations.

Results: Of 398 participants, 195 (48.9%) reported engaging in clinical dishonesty. Hierarchical regression analysis identified critical predictors of frequent clinical dishonesty: lack of fear of consequences (β = −0.072), positive attitudes toward dishonesty (β= −0.081), higher incidence of academic dishonesty in the classroom (β = 0.221), lack of knowledge of the university's regulations (β = −0.349), and low quality of mentor support (β = −0.430). The final model explained 60.7% of the variance in participants' clinical dishonesty ($p < 0.001$).

Conclusion: The identified predictors indicate that interpersonal factors, i.e., the quality of mentor support, influence students' clinical dishonesty more than intrapersonal factors (e.g., attitudes or knowledge). Contextual factors (healthcare employment and study overload) were unrelated to clinical dishonesty. This finding can help develop strategies to reduce nursing students' dishonesty and improve patient safety.

MeSH/Keywords: dishonesty; clinical dishonesty; clinical settings; dishonest behavior; nursing students

Poster title: The impact of the work environment on job satisfaction and work ability of employees in emergency medicine in Osijek-Baranja and Brod-Posavina county

Part of the Dissertation Proposal: The impact of the work environment on job satisfaction and work ability of employees in emergency medicine

PhD candidate: Nikola Bajan, Institute of Emergency Medicine of the Osijek-Baranja County, Croatia

Mentor: Assoc. Prof. Krešimir Šolić, Faculty of Medicine Osijek, Osijek, Croatia

Co-mentor: Assist. Prof. Marija Raguž Vinković, Faculty of Medicine Osijek, Osijek, Croatia

Introduction: Previous research has revealed and confirmed that a positive work environment has a direct impact on employee satisfaction, which consequently affects productivity and the overall health of employees. Emergency medical personnel, both in the Republic of Croatia and around the world, face various situations in their daily work where they must provide qualified, high-quality, and professional care. Numerous negative factors influence their work. The consequences are manifold and may even lead to employees leaving their jobs and moving to other countries, which can ultimately result in a decline in the quality of patient care. Therefore, it is essential to identify and understand all the negative factors in the work environment that affect the satisfaction and work performance of healthcare professionals.

Aim: To investigate the influence of the work environment on the level job satisfaction and work ability of the emergency medical personnel in institutes of emergency medicine in Osijek-Baranja and Brod-Posavina county.

Materials/ Participants and Methods: This was a cross-sectional study. The participants were employees of the Institutes of emergency medicine in Osijek-Baranja and Brod-Posavina Counties, regardless of their level of education or their specific position within the institution, and all voluntarily agreed to participate in the research. Data collection was conducted from May to July 2024. Approval for conducting this study was obtained from the relevant ethics committees. Two validated questionnaires were used in the study (PES-NWI and WAI). The international questionnaires had previously been validated in the Croatian language and are publicly available.

Results: The study was conducted on 97 participants, of whom 43 (44.3%) were women and 54 (55.7%) were men. The median age of the participants was 32 years, and 74 (76.3%) were employed on a permanent basis. The majority were from Team I, 59 participants (60.8%), while 16 (16.5%)

were employed in dispatch units or medical transport services. Satisfaction with their current work situation and their belief that upcoming improvements in the healthcare system will positively impact their work situation were both rated with a median score of 4 (on a scale from 1 to 5). The median score for the Work Ability Index (WAI) was 40, ranging from 30 to the maximum of 47 (possible range: 7 to 49).

Conclusion: It was observed that certain domains of the work environment have an impact on employee satisfaction and work ability. The results of this study point to the need for further research and analysis of all domains within the work environment in order to improve the efficiency and quality of the entire system, make it more flexible, and at the same time protect employees and preserve their integrity.

MeSH/Keywords: emergency medicine; health worker; job satisfaction; work ability; work environment.

Abstract Title: Antibiotics self-medication practice in the general population as a modern public health challenge

PhD candidate: Almina Bajrektarević Kehić, Sanitary inspector, City of Tuzla, Bosnia and Herzegovina

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Mentor: Assoc. Prof. Ivan Miškulin, Ph.D., Faculty of Medicine Osijek, University of Osijek, Croatia

Co-Mentor: Prof. Maja Miškulin, Ph.D., Faculty of Medicine Osijek, University of Osijek, Croatia

Introduction: The practice of antibiotic self-medication is defined as the use of antibiotics by a patient without prior consultation with a doctor, which includes antibiotics purchased without a prescription, the use of antibiotics remaining from previous therapy, sharing antibiotics, etc. Reasons: cheaper and faster solutions, distance from medical institutions, unavailability of doctors, previous experience in the treatment of diseases, and costs of health services. The practice of self-medication directly affects the spread of antimicrobial resistance. Bosnia and Herzegovina (BiH) does not have a global action plan to prevent antimicrobial resistance, which supports the importance of this research.

Aims: to examine the opinions and knowledge of respondents about antibiotics and the practice of self-medication with antibiotics, to examine the sociodemographic and socioeconomic characteristics of respondents who use antibiotics for the purpose of self-medication, to examine the frequency of self-medication with antibiotics and identify the sources of antibiotics used in this way, to examine the reasons and circumstances why respondents resort to the practice of self-medication with antibiotics, to examine the effectiveness of public health intervention on practices, opinions and knowledge of respondents.

Materials/Participants and Methods: Respondents will be patients recruited randomly at the primary level of health care throughout BiH (Federation of BiH, Republika Srpska and Brčko District) by the doctoral student. The study will include respondents aged 18-69 years. Sample size: 500 respondents will be included in the quantitative part of the study. The qualitative part of the study will include 45 respondents divided into 3 focus groups. The survey will be conducted through a questionnaire.

Results: The results of the quantitative part of the research showed that 94.6% of respondents agreed with the statement that antibiotics slow down the growth and reproduction of bacteria or completely destroy them, and 13.7% of respondents agreed with the statement that antibiotics are used to treat viral infections such as the common cold. 9.2% of respondents believe that antibiotics are the first choice for early treatment of cough or sore throat symptoms. 40.4% of respondents believe that the sale of antibiotics in pharmacies without a doctor's prescription is allowed in BiH, 34,4 % of them have bought antibiotics in pharmacies several times without a doctor's prescription, while 5% of respondents most often buy antibiotics without a doctor's prescription. When asked why they take antibiotics without prior consultation with a doctor, 9.5% of them cited previous experience in antibiotic treatment as the reason, 5.8% cited time savings as the reason. 81% of respondents dispose of antibiotics in regular household waste. The majority of respondents (94%) believe that antimicrobial resistance is a global public health problem, and 17.7% of them do not think that the problem of resistance in BiH is widespread and worrying. 86.3% of respondents believe that health professionals are not doing enough to educate the population about the proper use of antibiotics.

Conclusion: These findings underscore the urgent need for targeted educational initiatives aimed at promoting responsible antibiotic use. The data call for stricter regulatory oversight concerning the sale and distribution of antibiotics, as well as the implementation of proper medication disposal programs. Addressing these challenges is essential in mitigating the risks associated with antimicrobial resistance and safeguarding public health.

MeSH/Keywords: Anti-bacterial agents; Drug resistance, bacterial; Self medication; Health education; Knowledge

Dissertation Proposal Title: "Influence of biochemical values on response to neoadjuvant chemotherapy in breast carcinoma"

PhD candidate: Ivona Barać, M.D. Clinical hospital Center Osijek, Osijek, Croatia

Mentor: Assist. Prof. Josipa Flam, Department of Oncology, Faculty of Medicine Osijek, University of Osijek, Osijek, Croatia

Introduction: Malignant diseases are the second cause of death in the population. Breast cancer is the most common cancer in women and is the leading cause of death for women in the world. The most important division of breast cancer according to molecular type, depending on the expression of hormone receptors, is Luminal A and B, HER2 positive and triple negative. Luminal A subtype of breast cancer is characterized by a low grade, slow growth and the best treatment prognosis with a higher survival rate due to a very good response to hormone therapy. Luminal B subtype has a higher grade and worse prognosis compared to Luminal A subtype. Her2-positive tumors comprise 10-15% of all breast cancers and are characterized by high expression of Her2, without expression of estrogen and progesterone receptors. They have a worse prognosis, but with the development of targeted anti-Her2 therapy, this has been significantly improved. Triple-negative breast tumors have the worst prognosis because they do not express any of the aforementioned receptors and the implementation of neoadjuvant chemotherapy is greatly hampered. Some patients, regardless of the neoadjuvant chemotherapy, do not respond well to it and it is necessary to determine the factors that influence the response to neoadjuvant chemotherapy.

Hypothesis: Different ratios of laboratory values may influence response to neoadjuvant breast cancer treatment

Aims:

1. Determine the frequency of each tumor subtype
2. Examine whether there is a difference in response to neoadjuvant therapy according to tumor subtype
3. Examine whether the examined laboratory value ratios are diagnostic indicators in predicting response to neoadjuvant chemotherapy

Materials/Participants and Methods: The examined group would consist of patients for whom neoadjuvant therapy was indicated, who were treated at the Department of Oncology and then

operated. Patients who developed metastatic disease during neoadjuvant chemotherapy or who were not operated on for any reason after chemotherapy will be excluded form the study.

Research plan: Laboratory values measured before the start of neoadjuvant treatment will be used for research purposes. The response to neoadjuvant therapy will be monitored according to the measured values. Their influence on the response to the given therapy will be determined depending on the subtype of the tumor.

Significance/Expected scientific contribution: The results of the proposed research will contribute to the decision on neoadjuvant treatment of borderline cases and the decision on the intensity of oncological and surgical treatment in patients who, based on laboratory values, are not expected to have an adequate response to neoadjuvant therapy.

MeSH/Keywords: Breast cancer, neoadjuvant chemotherapy, response to treatment (RCB)

Dissertation Proposal Title: Frailty Syndrome and Biopsychosocial Factors in Predicting Successful Aging

PhD Candidate: Marija Barišić, Department of Nursing and Palliative Medicine, Faculty of Dental Medicine and Health Osijek, University of Osijek, Osijek, Croatia

Mentor: Assist. Prof. Ivana Barać, PhD, Department of Nursing and Palliative Medicine, Faculty of Dental Medicine and Health Osijek, University of Osijek, Osijek, Croatia

Introduction: Successful aging is a multidimensional concept involving functionality, psychological well-being, and community engagement. With population aging and growing elderly care needs, identifying key factors supporting successful aging is essential. Frailty syndrome is a clinical risk factor impairing independence, while resilience and ego integrity are psychological resources for adapting to aging. Type of care (institutional vs. community-based) influences aging perception. This study applies a biopsychosocial framework to explore these factors' interrelations and contributions to successful aging.

Hypothesis: Frailty syndrome is negatively linked to successful aging. Resilience and ego integrity mediate this relationship, while type of care moderates its strength.

Aims:

1. Examine associations between frailty, resilience, ego integrity, and successful aging.
2. Compare these factors in institutionalized vs. community-dwelling older adults.
3. Determine predictive value of frailty, resilience, ego integrity, and care type.
4. Explore biopsychosocial mediation and moderation effects.

Participants and Methods: Participants will include individuals aged 65 and over, residing in nursing homes and their own homes. The study will use the following instruments: the Edmonton Frail Scale, the Self-Assessment of Successful Aging Scale, the Brief Resilience Scale (BRS), and the Ego Integrity Scale. Sociodemographic and health-related information will also be collected. The expected sample size is 500 participants.

Research Plan: Data collection. Research implementation. Data analysis. Results dissemination.

Significance/Expected scientific contribution: The results of this research will emphasize the importance of timely identification of functional and psychological risk factors among older adults

within the care system. In the context of the global aging trend, this issue is highly relevant for the planning of high-quality and sustainable care. The study may serve as a foundation for the development and implementation of targeted nursing interventions aimed at preserving independence, functional capacity, and overall well-being in the aging process.

Keywords: Successful aging; Frailty; Psychological resilience; Ego integrity; Nursing

Dissertation Proposal Title: Frailty Syndrome and Biopsychosocial Factors in Predicting Successful Aging

PhD Candidate: Marija Barišić, Department of Nursing and Palliative Medicine, Faculty of Dental Medicine and Health Osijek, University of Osijek, Osijek, Croatia

Mentor: Assist. Prof. Ivana Barać, PhD, Department of Nursing and Palliative Medicine, Faculty of Dental Medicine and Health Osijek, University of Osijek, Osijek, Croatia

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Keywords: Successful aging; Frailty; Psychological resilience; Ego integrity; Nursing

Abstract Title: Distribution of Ki-67 expression as surrogate tumor biology marker among molecular breast cancer subtypes

Part of the Disertation Proposal: Distribution of Ki-67 expression as surrogate tumor biology marker within and among molecular breast cancer subtypes predicts potentially different biological behaviour.

PhD candidate: Ivana Begić, M.D., Nieren- und Dialysezentrum Männedorf, Switzerland; Faculty of Medicine Osijek, University of Osijek, Osijek, Croatia

Mentor: Prof. Branko Dmitrović, M.D., Ph.D., University of Osijek, Faculty of Dental Medicine and Health Osijek and Faculty of Medicine Osijek and Department of Pathology and Forensic Medicine, Clinical Hospital Centre Osijek, Osijek, Croatia

Introduction:

Breast cancer (BC) is globally increasing epidemiological problem still characterized by high mortality rate.

BC is very heterogeneous disease with different gene profiling, histological, molecular, pathophysiological, clinical as well as prognostic subcategories.

Immunohistology methods enable detection of ER, PR, HER2 oncogene expression and expression of Ki-67 proliferative factor.

The determination of hormonal receptor status has a great therapeutic as well as prognostic value.

The St. Gallen Consensus from 2013 (confirmed in 2015) proposed revised BC classification considering these parameters: hormonal receptor expression and Ki-67 value/intensity, distinguishing following BC subtypes:

- Luminal A (ER and/or PR positive, HER2 negative, Ki-67 < 20 %)
- Luminal B1 and B2 (HER2 negative, ER and/or PR positive, Ki-67 ≥ 20 % vs. HER2 positive ER and/or PR positive, any Ki-67)
- HER2 positive– nonluminal (HER2/Erb-B2 overexpression, HER2 positive, ER i PR negative
- Triple negative tumor: ER and PR negative, HER2 negative

The clinicopathological and immunophenotype-based classification of BC and its nomenclature are widely used in standard diagnostic procedures with high impact on therapeutical strategies.

Aims:

The primary aim:

- to examine the relation between Ki-67 expression (as mitotic activity marker) with clinical, pathohistological and immunohistochemical characteristics of BC patients

The secondary aims are:

- to identify differences among BC molecular subtypes and detect distribution of immunophenotype features (hormonal receptors status (ER, PR), HER2 oncogene expression, Ki-67 expression)
- to detect presence und examine differences of Ki-67 expression clusters among molecular BC subtypes
- to detect tumor variants within standard molecular BC subtypes with potentially different biological behaviour, dependent on still less known factors, based on Ki-67 clusters analysis
-

Materials/Participants and Methods:

Participants

2651 consecutive invasive breast cancer patients over 18-years-long period of time (2004 – 2021) were included in this comprehensive retrospective observational cohort study conducted in single-center, at the Clinical Hospital Centre Osijek, Department of Pathology and Forensic Medicine. The average inclusion rate was 147 female patients with newly diagnosed invasive ductal BC per year.

Methods

Evaluation of archived paraffin embedded tumor blocks, routinely processed with hematoxylin-eosin and immunochemical staining for complementary stain/analysis for missing data. All breast cancer specimens were reclassified accordingly to 12th St. Gallen Convention.

Statistical methods

The uniform dataset in Excel was used to study differences in distribution of immunophenotype features, similarities, and differences between molecular BC subtypes and primarily to identify Ki-67 clusters as known for Ki-67 to be a surrogate marker of tumor biology. Among every BC molecular subtype Ki-67 clusters of low (LMA) and high mitotic activity (HMA) were identified using statistical method known as „expectation maximization“(EM) clustering. Cluster detection was automatically performed by statistical program StatSoft, Inc. (2011) STATISTICA using v-fold cross-validation algorithm. Collected database was analysed using program StatSoft, Inc. (2011) STATISTICA (Data Analysis Softwaresystem), version 10, www.statsoft.com.

Preliminary Results:

- The average age of BC patients was 61,3 (12,5) years. The youngest patient was 24 years old and the oldest 95.
- The distribution of immunohistochemical phenotypes differs among age groups. In premenopausal women (under 55 years) the prevalence of triple negative BC was higher.

- The size of most of the tumors under 24 mm. The tumors with HER2 overexpression and triple negative tumors have shown a greater proportion of larger tumors (diameter > 55mm).
- Luminal A tumors had significantly greater proportion of more favorable grade of histological differentiation (grade I).
- HER2-overexpression and TNT patients had larger proportion of unfavorable histological grade of differentiation (Grade III) as well as more often positive axillary lymph nodes.
- Among invasive BC patients 78,5 % were estrogen receptor positive and 74,8% progesterone receptor positive. About 20 % of our patients had HER2-overexpression and 11 % were triple negative BC.
- In low mitotic activity category (LMA, defined as Ki-67 < 25%) were 52% of patients and in high mitotic activity category (HMA, Ki-67 > 65%) 12% of patients.
- Exept immunohistochemical phenotype 1 (IHC1; molecular subtype - luminal A), in all other IHC-phenotypes two clusters of Ki-67 could be identified.
- Accordingly to St. Gallen classification from 2013 (confirmed in 2015, with Ki-67 cut-off 20 %) all luminal A tumors were in LMA category
- Luminal A molecular subtype is an arbitrary unified cluster “amputated” from the luminal B1 first cluster (with lower Ki-67 %).
- Triple negative tumors are significantly more often found in HMA category.
- EM analysis (expectation maximization) detected two Ki-67 clusters in pool of 2651 BC patients: one with lower values (22,6 %) and the second one with Ki-67 average 74,4 %.
- The highest value of proliferative marker Ki-67 (83,4 %) among all BC tumors were found in the second cluster of triple negative tumors (higher Ki-67).

Conclusion:

Concerning study design and analysis:

Our preliminary results are comparable to study results conducted in other (post)industrial western countries (percentage of molecular subtypes, distribution over different descriptive categories).

The results of immunohistochemical staining appeared to be in high quality performance range - concordant with literature results.

Concerning clusters:

Beside well known and evaluated differences between BC molecular subtypes, further divergent subgrouping based on Ki-67 clusters among immunohistochemical subtypes (IHC 2-5) was found.

Significantly different distribution in some tumor-nature variables (size, grade, lymph node positivity) between clusters within each conventional molecular subtype was found - addressing the importance of wider view upon BC biology with potentially individualized treatment needs (“out-of-the-box thinking”).

MeSH/Keywords:
breast cancer, immunohistochemistry, molecular breast cancer subtypes, Ki-67 proliferative factor

Acknowledgement:
With deepest gratitude and devotion to our beloved and honoured prof. dr. sc. Sven Kurbel, dr. med.

Dissertation Proposal Title: Lifestyle and Cardio-Renal Risk in Relation to Microcirculatory Changes in the General Population

PhD candidate: Marta Bolješić Dumančić, Faculty of Medicine, University of Osijek, Croatia.

Mentor: Assoc. Prof. Antonio Kokot M.D., Ph.D., Faculty of Medicine, University of Osijek, Osijek, Croatia.

Co-mentor: Acad. Bojan Jelaković M.D., Ph.D., Department of Internal Medicine, UHC Zagreb, University of Zagreb, School of Medicine, Zagreb, Croatia

Introduction: According to data from the Epidemiology of Hypertension in Croatia (EH-UH 1) study the prevalence of arterial hypertension (AH) was 37%, with very poor treatment control - about 20%. In 2010, the American Heart Association (AHA) published new recommendations for the general population to reduce morbidity and mortality from cardiovascular diseases by achieving 7 specific cardiovascular health behaviors and factors (Life's Simple 7). Life's Simple 7 includes factors of smoking, diet, physical activity, body mass index, blood pressure, total cholesterol and fasting glucose. With the new recommendations, the goal of the new research and health projects has been focused more on preserving health and preventing cardiovascular diseases rather than on the disease itself.

Hypothesis: Due to their lifestyle habits, coastal population have a lower overall cardio-renal risk compared to the continental population.

Aims: To compare and analyze differences in lifestyle habits in the continental and coastal population of the Republic of Croatia in order to examine and compare the cardio-renal risk of the continental and coastal population.

Materials/Participants and Methods: Participants will be a randomly selected population of several inhabited islands and several continental cities in the Republic of Croatia. The expected number of respondents is about 2000 people in 4 years.

Exclusion criteria of subjects are age below 18 years, terminal stage of malignant disease, dementia, paresis, amputation or immobilization of one limb, current acute illness and unsigned consent.

The data that will be collected: general health data, dietary habits, data on previous illnesses, blood pressure, first morning urine and 24-hour urine samples, basal metabolism, Body Mass Index, waist circumference, upper arm circumference, visceral fat, total fat and muscle mass. Blood will be sampled.

Research Plan: The study design is a cross-sectional study. The research will be conducted on the population of several inhabited Croatian islands and several continental cities in the Republic of Croatia during 4 years.

Significance/Expected scientific contribution: This research will enable to analyze which risk factors, cardio-renal risk and lifestyle habits in population are most strongly associated with incident hypertension and cardio-renal diseases. This will be important information for planning preventive measures. The data will also be important to the European Society of Hypertension as one of the arguments in negotiations with the European Commission.

MeSH/Keywords: Life Style, Arterial Hypertension, Cardiovascular Risk, Kidney Diseas, Microcirculation

Abstract Title: OncoOrigin: A Machine Learning-Based Tool for Primary Site Prediction in Cancers of Unknown Primary Using Tumor Genomic Data

Part of the Disertation Proposal: Molecular classification of neoplasms using machine learning model and an oncogenetic database with applications in diagnosis and targeted treatment of cancers of unknown primary site

PhD candidate: Petar Brlek, M.D., St. Catherine Specialty Hospital, Zagreb, Croatia. Medical School, Josip Juraj Strossmayer University of Osijek, Osijek, Croatia. Department of Molecular Biology, Faculty of Science, University of Zagreb, Zagreb, Croatia.

Mentor: Prof. Dragan Primorac, M.D., Ph.D., St. Catherine Specialty Hospital, Zagreb, Croatia. Eberly College of Science, The Pennsylvania State University, State College, PA, United States of America. Medical School, University of Split, Split, Croatia. Medical School, Josip Juraj Strossmayer University of Osijek, Osijek, Croatia. The Henry C. Lee College of Criminal Justice and Forensic Sciences, University of New Haven, New Haven, CT, United States of America. REGIOMED KLINIKEN, Coburg, Germany. Medical School, University of Rijeka, Rijeka, Croatia. Faculty of Dental Medicine and Health, Josip Juraj Strossmayer University of Osijek, Osijek, Croatia. Medical School, University of Mostar, Mostar, Bosnia and Herzegovina. National Forensic Sciences University, Gandhinagar, India.

Introduction: Precision oncology increasingly relies on bioinformatics and machine learning to interpret tumor genomic data and support clinical decision-making. Cancers of unknown primary (CUP) are metastatic tumors for which the site of origin remains unidentified despite extensive diagnostics, presenting a major clinical challenge. Computational tools may improve diagnostic accuracy and guide personalized treatment in these complex cases.

Aims: This study aimed to develop and validate OncoOrigin, a machine-learning-based tool for predicting the primary cancer site in CUP patients using metastatic tumor DNA sequencing data. A secondary goal was the development of a user-friendly interface for clinical use.

Materials and Methods: This in silico study used over 20,000 tumor samples from the cBioPortal database (accessed 21 Sept 2024), containing demographic data and mutational profiles across 600+ genes. Data were processed using Python libraries, and four machine learning models were tested: Random Forest, SVM, k-NN, and XGBoost. Performance was evaluated via cross-validation and test set accuracy. Feature importance was analyzed, and the best model was implemented in OncoOrigin with a graphical interface.

Results: XGBoost outperformed other models with a top-2 accuracy of 0.91 and ROC-AUC of 0.97. Several high-impact genetic variants were identified as key predictors. The final OncoOrigin version combines robust performance with practical usability for oncology specialists.

Conclusion: OncoOrigin is a novel diagnostic support tool for CUP cases, integrating advanced machine learning with a clinician-friendly interface. It holds promise for improving diagnostic accuracy and supporting personalized oncology in everyday practice.

MeSH/Keywords: precision medicine, neoplasm metastasis, machine learning, computational biology, genomics

Abstract Title: Association between inflammatory markers and cognitive status in the early perioperative period in patients after bladder tumor surgery

Part of the Disertation Proposal: In patients who undergo transurethral resection of the bladder, there is a postoperative increase in inflammatory markers that are associated with clinical frailty and hand grip test.

PhD candidate: Ana Cicvarić, Clinical Hospital Center Osijek, Department of Anesthesiology, Resuscitation and Intensive Care, Faculty of Medicine Osijek, University of Osijek, Osijek, Croatia

Mentor: Prof. Slavica Kvolik, Clinical Hospital Center Osijek, Department of Anesthesiology, Resuscitation and Intensive Care, Faculty of Medicine Osijek, University of Osijek, Osijek, Croatia

Introduction: Bladder cancer is one of the most common tumors in the world, with a growing prevalence worldwide. This patient population has certain common characteristics, such as smoking or exposure to common risk factors for the development of bladder cancer, such as aniline dyes and solvents. These substances are also associated with the development of neurodegeneration and oxidative stress. In addition to laboratory indicators of organ function, circulating indicators of inflammation will be shown in correlation with the cognitive status of the patient: S100B, NSE, IL4, IL6. A significant proportion of patients are elderly repeatedly exposed to surgery with numerous comorbidities, with a high risk of postoperative complications and the development of cognitive decline, which can complicate the postoperative course and further treatment.

Aims:

1.examine whether the current cognitive status changes after the patient is exposed to surgery and general anesthesia

2.measure changes in inflammatory marker values in the perioperative period

3.examine association between changes in cognitive status and inflammatory markers

4.examine association of inflammatory markers with the MMSE-2, MoCA and hand grip test

Participants and Methods: The prospective study would include adult patients of both sexes (>18 years – 80 years).Blood samples would be analyzed (biomarkers S100B, NSE, IL6, IL4, CKS, HbA1c and standard biochemistry) preoperatively, 2 h and 24 h after surgery. Assessment of the patients' health condition would be done using ASA and CFS scale. Preoperatively, 24h and 48h after surgery hand grip test, MMSE and MoCa tests would be performed.

Results: So far, 16 patients have been included in the study, all of whom are male,average age 69.81. 6 patients have already undergone this type of surgery. Of the total number of patients, more are smokers, more people live in rural areas. Most often patients have cardiovascular diseases. Patients have a decline in cognitive function postoperatively compared to the preoperative period on the MMSE-2, MoCa test with an increasingly weaker hand grip test. It was also noted that preoperatively with lower IL6 values, fibrinogen was higher. If the hand grip test was stronger preoperatively, HbA1c values were lower.

Conclusion: This study will confirm whether perioperative cognitive deficit and clinical frailty are risk factors for the development of laboratory and clinically measurable impairment in patients undergoing transurethral resection of the bladder. If confirmed, this hypothesis will serve as a starting point for research into possible interventions that can reduce the increase in inflammatory markers and new cognitive deficits.

MeSH/Keywords: general anesthesia; cognitive complication, postoperative; urinary bladder neoplasm; perioperative period; frail older adult

Dissertation Proposal Title: Empathy and Professional Identity as a Predictor of the Quality of the Nursing Students–Patient Relationship

PhD candidate: Ivana Debelić, MScN, School of Nursing, Medical School Osijek, Osijek, Croatia.

Mentor: Assist. Prof. Robert Lovrić, Ph.D., MSN, RN, Faculty of Dental Medicine and Health Osijek, University of Osijek, Osijek, Croatia

Introduction: Empathy and professional identity are key elements in nursing education, directly linked to the quality of nurse–patient relationships. These relationships form the foundation of safe, compassionate care and reflect a student's personal and professional development. However, the combined impact of empathy and professional identity on relationship quality is still insufficiently examined, especially among both nursing students and secondary medical school pupils in Croatia. Their development is influenced by education level, clinical experience, and exposure to role models. Understanding these associations can guide improvements in nursing curricula and clinical mentoring.
Hypothesis: The level of professional identity and empathy contributes to the positive perception of medical school students and nursing students about the quality of student–patient relationships.

Aims:
1. Examine students' perceptions of the importance of relationship quality with patients.
2. Assess students' levels of empathy and professional identity
3. Explore the correlation between students' empathy levels and their perception of relationship quality with patients
4. Explore the correlation between students' professional identity and their perception of relationship quality with patients
5. Examine differences in empathy and professional identity based on level of education and clinical experience
6. Assess the individual and combined contributions of empathy, professional identity, and students' general characteristics in predicting perceptions of relationship quality with patients

Materials/Participants and Methods: Research will include one generation of nursing students from the Faculty of Dental Medicine and Health Osijek and one generation of medical school students from Osijek, Slavonski Brod, and Vinkovci. Participants will be assessed through questionnaires: the Croatian version of the CNPI-23 scale, the Jefferson Scale of Empathy – Health Profession Student Version (JSE-HPS), the Professional Identity – Five Factor Scale (PIFFS), along with demographic data. The expected number of participants is 300.

Research plan: Collecting data. Conducting research. Analysis of data and results. Publishing the results.

Significance/Expected Scientific Contribution: This research will provide deeper insight into how empathy and professional identity influence students' perception of patient relationships. It will fill a gap in the literature by jointly analyzing these predictors across student levels which will help educational institutions develop strategies to strengthen these competencies early in training, ultimately improving nurse–patient relationships and care quality.

MeSH/Keywords: empathy; professional identity; nursing students; patient; interaction; caring

Abstract Title: Relationship Between Psychological Factors and Health-Related Quality of Life in Patients with Chronic Low Back Pain

Part of the Disertation Proposal: Biopsychosocial predictors of quality of life in people with chronic low back pain

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Mentor: Assist. Prof. Ivan Radoš, M.D., Ph.D., Clinical Department of Pain Management, University Hospital Centre Osijek, Croatia, Faculty of Medicine Osijek, University of Osijek, Osijek, Croatia

Co-mentor: Prof. Gorka Vuletić, mag.psych., Ph.D., Department of Psychology, Faculty of Humanities and Social Sciences in Osijek, Osijek, Croatia, Andrija Štampar School of Public Health, Faculty of Medicine, University of Zagreb, Zagreb, Croatia

Introduction: Chronic pain (CP) is defined as pain that lasts or recurs for more than three months. It represents a significant public health problem reported by about 20% of adults in the world and is one of the most common reasons people seek medical help. Low back pain (LBP) is described anatomically as reaching from the iliac crest to the 12th rib and has frequently been mentioned as the most common sort of chronic pain. According to the Global Burden of Disease Study from 2017, LBP included 577 million people, including all age groups and genders, and women had a higher prevalence than men. Quality of life (QOL) is a broad concept that includes all aspects of an individual's life, while health-related quality of life (HRQoL) focuses on aspects of quality of life related to an individual's health, including the level of a person's daily functioning and the ability to live a fulfilled life. Numerous studies have confirmed the influence of chronic low back pain (CLBP) on HRQoL in a variety of life domains, including physical and mental health, social relationships and functional abilities. Furthermore, numerous psychological factors, such as kinesiophobia, pain and fear avoidance beliefs, self-efficacy, anxiety, coping mechanisms, sleep quality, locus of control and catastrophizing, were found to be significant QOL determinants in people with CLBP. Despite the existence of numerous studies that have identified individual psychological factors as predictors of impaired HRQoL, a clinical environment that focuses more

on the physical aspect still prevails and this research aims to emphasize the importance of psychological interventions in the treatment of CLBP.

Aims: The aim of this study was to investigate whether pain intensity, pain catastrophizing, depression, anxiety, fear of pain and pain acceptance can predict the physical and psychological dimensions of HRQoL in patients with CLBP.

Participants and Methods: Data were collected from 201 patients with CLBP who came for a medical examination at the outpatient clinic for pain treatment. The inclusion criteria were participants 18 years of age or older with CLBP (≥3 months) with the intensity of 3 or more as assessed by the NRS scale. Sociodemographic dana form collected information about gender, age, residence, education level, working status, marital status and duration of pain. The SF-36 Health Status Questionnaire (SF-36) was used to evaluate health-related quality of life. It consists of eight subscales: physical functioning, bodily pain, role limitations due to physical health, role limitations due to emotional problems, mental health, social functioning, vitality and general health. The Pain Anxiety Symptoms Scale Short Form 20 (PASS-20) was used to evaluate pain-related anxiety. The Pain Catastrophizing Scale (PCS) was used to evaluate catastrophizing associated with the experience of pain. The Hospital Anxiety and Depression Scale (HADS) was used to measure anxiety and depression. The Chronic Pain Acceptance Questionnaire (CPAQ-8) was used to measure chronic pain acceptance. The severity of pain was assessed using the Numeric Pain Rating Scale (NRS).

Results: This study involved 201 patients who met the inclusion criteria, agreed to participate, signed the informed consent form and answered the questionnaires. The mean age was 54.36 +/− 12.072 years (in a range from 27 to 82 years). The majority of the sample were female (78.6%), living in urban areas (65.7%), employed (63.1%), married (68.1%), with secondary education (67.7%) and with CLBP for more than 7 years (51.3%). The data were tested for normality with skewness and kurtosis. Their result proved to be satisfactory for conducting parametric statistics. A summary of the scores of the applied questionnaires is presented in Table 1.

Table 1. Distribution of questionnaire scores.

Variables	Mean +/− SD	Minimum	Maximum
NRS	6.5 +/− 1.722	2	10
SF-PhyH	32.27 +/− 14.590	3.75	78.13
SF-PsyH	44.08 +/− 20.433	0	93.25
PSC	25.06 +/− 11.201	1	52
PASS-20	48.94 +/− 20.822	4	100
CPAQ-8	34.95 +/− 6.347	18	48

HADS-A	8.49 +/− 4.371	0	19
HADS-D	7.36 +/− 3.954	0	18

SF-PhyH—Health Status Questionnaire-Physical Health, SF-PsyH—Health Status Questionnaire-Psychological Health, NRS—Numeric Pain Rating Scale, PSC—Pain Catastrophizing Scale, PASS-20—Pain Anxiety Symptoms Scale Short Form, CPAQ-8—Chronic Pain Acceptance Questionnaire, HADS-A—Hospital Anxiety and Depression Scale (HADS)-Anxiety, HADS-D—Hospital Anxiety and Depression Scale (HADS)-Depression

Table 2 outlines Pearson's correlation coefficients among the measured variables. Significant correlations were found between the SF-PhyH and SF-PsyH dimensions of HRQoL. Moreover, significant correlations were also found between SF-PhyH and age, NRS, PSC, PASS-20, CPAQ-8, HADS-A and HADS-D. Significant correlations were also found between SF-PsyH and NRS, PSC, PASS-20, CPAQ-8, HADS-A and HADS-D.

Table 2. Pearson's correlation coefficients among the measured variables.

	SF-PhyH	**SF-PsyH**	**Age**	**NRS**	**PSC**	**PASS-20**	**CPAQ-8**	**HADS-A**	**HADS-D**
SF-PhyH	1								
SF-PsyH	0.74 *	1							
Age	−0.20 *	−0.11	1						
NRS	−0.53 *	−0.42 *	0.06	1					
PSC	−0.52 *	−0.51 *	0.04	0.38 *	1				
PASS-20	−0.56 *	−0.50 *	−0.01	0.44 *	0.68 *	1			
CPAQ-8	0.32 *	0.31 *	−0.07	−0.08	−0.12	−0.19 *	1		
HADS-A	−0.59 *	−0.70 *	0.12	0.27 *	0.62 *	0.626 *	−0.29 *	1	
HADS-D	−0.61 *	−0.65 *	0.17 *	0.29 *	0.51 *	0.509 *	−0.41 *	0.76 *	1

SF-PhyH—Health Status Questionnaire-Physical Health, SF-PsyH—Health Status Questionnaire-Psychological Health, NRS—Numeric Pain Rating Scale, PSC—Pain Catastrophizing Scale, PASS-20—Pain Anxiety Symptoms Scale Short Form, CPAQ-8—Chronic Pain Acceptance Questionnaire, HADS-A—Hospital Anxiety and Depression Scale (HADS)-Anxiety, HADS-D—Hospital Anxiety and Depression Scale (HADS)-Depression, *—$p < 0.05$

Furthermore, linear regression analysis with a 95% confidence interval was conducted to examine the relationship between SF-PhyH and SF-PsyH as the dependent variables and all the other variables (age, NRS, PASS-20, HADS-A, HADS-D, PCS and CPAQ-8). The regression coefficients of the predictors for the dependent variable SF-PhyH are shown in Table 3. A significant model emerged ($F(7, 201) = 38.951$, $p < 0.05$), explaining 57.6% of the variance in SF-PhyH. Age, NRS, HADS-D, PASS-20 and CPAQ-8 contributed significantly to this model.

Table 3. Summary of linear regression analysis for the dependent variable SF-PhyH.

R^2		**Adjusted R^2**		
0.576		**0.561**		
Predictors	**B**	**β**	**t**	***p*-Value**
(Constant)	66.042		10.941	<0.0001 *
Age	−0.130	−0.107	−2.247	0.024 *

NRS	−2.725	−0.321	−6.196	<0.0001 *
HADS-A	−0.450	−0.135	−1.656	0.099
HADS-D	−0.915	−0.248	−3.274	0.001 *
PASS-20	−0.104	−0.148	−2.119	0.035 *
CPAQ-8	0.250	−0.109	2.146	0.033 *
PSC	−0.084	−0.064	−0.947	0.345

SF-PhyH—Health Status Questionnaire-Physical Health, NRS—Numeric Pain Rating Scale, HADS-A—Hospital Anxiety and Depression Scale (HADS)-Anxiety, HADS-D—Hospital Anxiety and Depression Scale (HADS)-Depression, PASS-20—Pain Anxiety Symptoms Scale Short Form, CPAQ-8—Chronic Pain Acceptance Questionnaire, PSC—Pain Catastrophizing Scale, *—$p < 0.05$.

The regression coefficients of the predictors for the dependent variable SF-PsyH are shown in Table 4. A significant model also emerged ($F (7, 200) = 39.049$, $p < 0.05$), explaining 57.7% of the variance in SF-PhyH. The following variables significantly contributed to this model: NRS, HADS-A and HADS-D.

Table 5. Summary of linear regression analysis for the dependent variable SF-PsyH.

R^2		**Adjusted R^2**		
0.577		**0.563**		
Predictors	**B**	**β**	**t**	***p*-Value**
(Constant)	76.964		9.122	<0.0001 *
Age	0.002	0.001	0.030	0.976
NRS	−2.638	−0.222	−4.294	<0.0001 *
HADS-A	−2.134	−0.458	−5.616	<0.0001 *
HADS-D	−0.981	−0.190	−2.509	0.013 *
PASS-20	−0.039	0.040	0.573	0.567
CPAQ-8	0.290	0.090	1.782	0.076
PSC	−0.110	−0.061	−0.890	0.345

SF-PhyH—Health Status Questionnaire-Physical Health, NRS—Numeric Pain Rating Scale, HADS-A—Hospital Anxiety and Depression Scale (HADS)-Anxiety, HADS-D—Hospital Anxiety and Depression Scale (HADS)-Depression, PASS-20—Pain Anxiety Symptoms Scale Short Form, CPAQ-8—Chronic Pain Acceptance Questionnaire, PSC—Pain Catastrophizing Scale, *—$p < 0.05$.

Conclusion: The findings of this study confirm that age, pain intensity, depression, pain-related anxiety and chronic pain acceptance are significant predictors of the physical dimension of HRQoL, while pain intensity, anxiety and depression proved to be significant predictors of the psychological dimension of HRQoL in patients with CLBP.

MeSH/Keywords: chronic low back pain; health-related quality of life; psychological factors

Acknowledgement: This study received funding and support from the Institutional Project (IP11) of the Faculty of Medicine Osijek of the Josip Juraj Strossmayer University of Osijek (MEFOS).

Abstract Title: Analysis of factors related to sleep score: The influence of demographic, occupational, and physiological variables

Part of the Disertation Proposal: The relationship between personality traits and circadian rhytm disorders and attention deficit disoreder in nurses and technicians in shift work

PhD candidate: Željka Dujmić, MSN, General Hospital Dr. Josip Benčević, Slavonski Brod, Croatia

Mentor: Assist. Prof. Štefica Mikšić, Ph.D., MSN, RN, Faculty of Dental Medicine and Health Osijek, University of Osijek, Osijek, Croatia

Co – mentor: Prof. Ivica Mihaljević, Ph.D., MD, Faculty of Medicin Osijek, University of Osijek, Osijek, Croatia

Introduction: Sleep quality is essential for maintaining health and is influenced by various demographic, occupational, and physiological factors. Among nurses, shift work and exposure to stress often disrupt sleep patterns. Understanding these associations is particularly important for protecting the health of the working population

Aims:

1. The correlation of sleep score with demographic variables, working conditions and physiological parameters.

2. Examine the contribution of demographic variables, working conditions and physiological parameters to sleep score.

Materials/Participants and Methods: The preliminary study was conducted at the General Hospital Dr. Josip Benčević Slavonski Brod in 2024. The study included 37 nurses, predominantly female, 30 (83,3%), with 23 (62,2%) working shifts. The median length of work experience was 20 years (interquartile range of 7,5 to 29 years). The research utilized the following questionnaires: a questionnaire with demographic data, sleep monitoring through an application on a smart watch, taking cortisol laboratory tests.

Results: The results showed that the sleep score was moderately negatively associated with the sex of the participants (p = 0,018) and cortisol levels (p < 0,001), and moderately positively associated with light sleep (p = 0,014), deep sleep (p = 0,001), and sleep duration (p = 0,971). Among the variables included in the model (significant in correlations), sleep duration proved to be a significant positive predictor of sleep score (p = 0,007). The variables included in the model significantly explained 61.9% of the variance in sleep score (adjusted R^2 = 0,619; p < 0,001).

Conclusion: It was found that sleep duration was a significant positive predictor of sleep quality score, with the model accounting for 61,9% of the variance.

MeSH/Keywords: Cortisol, Demographic factors, Nurses, Sleep duration, Sleep quality,

Table 1. Correlation of sleep score with demographic variables, work conditions, and physiological parameters

		2.	3.	4.	5.	6.	7.	8.	9.
1.Sleep score	ρ	-0,416	0,127	-0,694	0,098	0,540	0,424	0,671	-0,173
	p	**0,018**	0,480	**<0,001**	0,818	**0,001**	**0,014**	**<0,001**	0,335
2. Gender	r_{RB}		0,181	0,529	0,412	-0,327	-0,120	-0,261	0,321
	p		0,291	**0,001**	0,310	0,068	0,506	0,149	0,056
3. Shift work schedule	ρ			-0,095	0,378	0,248	-0,105	0,244	-0,058
	p			0,586	0,356	0,164	0,555	0,170	0,732
4. Cortizol	ρ				-0,333	-0,428	-0,118	-0,454	0,241
	p				0,420	**0,015**	0,513	**0,009**	0,163
5.Number of daily steps	ρ					-0,119	0,060	0,024	**0,932**
	p					0,779	0,887	0,955	0,001
6. Deep sleep time	ρ						0,078	0,430	-0,159
	p						0,665	**0,013**	0,377
7. Light sleep	ρ							0,461	0,090
	p							**0,007**	0,613
8. Sleep time	ρ								-0,506
	p								**0,003**

9. Years of work experience	ρ	
	p	

Table 2. Results of regression analysis – sleep score as the dependent variable

	β	t	p	adjusted R^2
(Constant)		6,551	<0,001	0,619
Gender	-0,079	-0,588	0,562	
Sleep time	0,474	2,944	**0,007**	
Deep sleep time	0,217	1,595	0,123	
Light sleep time	0,152	1,130	0,269	
Cortizol	-0,192	-1,273	0,215	

Dissertation Proposal Title: The Role of Implantation Endometrial Volume and Perfusion in Predicting Blastocyst Implantation Success

PhD candidate: Stefan Gjoni, Department of Obstetrics and Gynaecology, General Hospital Pula, Pula, Croatia

Mentor: Prof. Siniša Šijanović, Department of Obstetrics and Gynaecology, Clinical Hospital Osijek, Faculty of Medicine Osijek, University of Osijek, Osijek, Croatia

Introduction: Endometrial receptivity, defined as the capacity of the endometrium to support embryo implantation, is a crucial determinant of successful conception, particularly in the context of assisted reproductive technologies (ART). Despite advancements in ART, implantation rates remain suboptimal, highlighting the need for more accurate diagnostic tools. Traditional assessments based on endometrial thickness provide limited information. Emerging methodologies, such as three-dimensional (3D) ultrasound combined with VOCAL (Virtual Organ Computer-aided AnaLysis) software and Doppler ultrasound, enable comprehensive evaluation of endometrial morphology and perfusion. However, successful implantation is a multifactorial process. In addition to morphological parameters, hormonal profiles—particularly serum estradiol (E2),

progesterone (P4), and vitamin D—play a pivotal role in preparing the endometrium for implantation. Estradiol stimulates endometrial proliferation, progesterone induces secretory transformation, and vitamin D has been implicated in modulating immune tolerance and promoting receptivity. Integrating hormonal assessments with advanced imaging techniques offers a promising strategy to more accurately define endometrial readiness and optimize ART outcomes.

Hypothesis: Endometrial volume and perfusion, as measured by 3D ultrasound with VOCAL software and Doppler analysis, in combination with serum levels of estradiol, progesterone, and vitamin D, are associated with blastocyst implantation success in women of reproductive age.

Aims:
- To establish normative values for endometrial volume and vascularity during the implantation window using 3D ultrasound and Doppler analysis.
- To assess correlations between volumetric, perfusion, and hormonal parameters and the likelihood of successful blastocyst implantation.
- To compare these parameters between fertile women and women undergoing ART.
- To evaluate the predictive value of estradiol, progesterone, and vitamin D levels on endometrial morphology and ART outcomes.
- To develop predictive statistical models integrating hormonal and ultrasound parameters to identify patients with the highest likelihood of implantation success.

Materials/Participants and Methods: This prospective cohort study will include 173 women aged 20–45, subdivided into two groups: 109 women undergoing ART and 64 fertile women with a history of successful pregnancies. Inclusion criteria include regular menstrual cycles, no hormonal therapy in the preceding three months, and normal uterine anatomy. Endometrial parameters (thickness, volume, and perfusion) will be measured via transvaginal ultrasound using 3D VOCAL and Doppler modalities. Hormonal analyses (E2, P4, and 25(OH)D) will be performed on day 3 of the cycle and at key points in the ART protocol. The primary outcome will be clinical pregnancy confirmed by ultrasound.

Research plan: The first year will involve participant recruitment, data collection, and ultrasound and hormonal measurements. In the second year, data will be analyzed, followed by manuscript preparation and doctoral thesis writing.

Significance/Expected scientific contribution: This study will provide an integrated diagnostic framework combining morphological and biochemical markers of endometrial receptivity.

Establishing reference values and identifying predictive models will enhance the ability to individualize treatment, improve implantation success, and advance the precision of ART protocols. The findings could contribute to a better understanding of the complex interplay between endometrial environment and systemic hormonal milieu.

MeSH/Keywords:
1.Endometrium
2.Embryo implantation
3.Infertility
4.Reproductive techniques, assisted
5. Ultrasonography

Acknowledgement:
The research is supported by General Hospital Pula and conducted under the mentorship of Prof. Siniša Šijanović

Dissertation Proposal Title: Impact of Neoadjuvant Therapy on Perioperative Complications and Clinical Outcomes in Patients Undergoing Colorectal Cancer Resection

PhD candidate: Josipa Glavaš Tahtler, M.D., University Hospital Centre Osijek, Department of Anesthesiology and Critical Care, Osijek; Faculty of Medicine, University of Osijek, Osijek, Croatia

Mentor: Prof. Slavica Kvolik, M.D., Ph.D., University Hospital Centre Osijek, Department of Anesthesiology and Critical Care, Osijek; Faculty of Medicine, University of Osijek, Osijek, Croatia

Introduction: Colorectal cancer is the third most commonly diagnosed malignancy globally and the second leading cause of cancer-related death. Neoadjuvant therapy, including chemotherapy and radiation, is used to reduce the size of the tumor and improve surgical outcomes. However, it may also cause localized and systemic tissue changes that increase the risk of perioperative complications, such as infections, thromboembolic and cardiovascular events, and poor wound and anastomotic healing.

Hypothesis: Neoadjuvant therapy increases the risk of perioperative complications in patients with colorectal cancer by causing endothelial dysfunction and damaging microvascular structures, which leads to impaired perfusion and healing.

Aims:

1. To assess the impact of neoadjuvant therapy on perioperative complications and early postoperative outcomes.

2. To investigate if there is a connection between microvascular density and postoperative complications, including wound healing disorders.

3. To identify differences in biomarkers between patients with and without complications.

4. To compare clinical outcomes between patients treated with neoadjuvant therapy and those who underwent surgery as the initial treatment.

Materials/Participants and Methods: This is a prospective, single-center study that will involve adult patients (≥18 years) with histologically confirmed colorectal carcinoma scheduled for elective surgery. Patients will be divided into two groups: those receiving neoadjuvant therapy and those undergoing surgery as their initial treatment. Exclusion criteria will include emergency surgery, ongoing corticosteroid therapy, and inability to provide informed consent.

Research plan: Following ethics approval and consent, demographic and clinical data will be collected. Blood samples will be taken preoperatively, 24 hours postoperatively, and before discharge. Tissue samples from the surgical site and tumor will be analyzed for microvascular density and fibrosis. Perioperative data, including use of vasoactive drugs, transfusions, extubation time, and complications, will be gathered. Postoperative outcomes will include ICU and hospital stay duration, mortality, and readmission to the ICU.

Significance/Expected scientific contribution: The results of this study will improve our comprehension of the role neoadjuvant therapy plays in perioperative outcomes, allowing for more effective treatment planning and improved care protocols for patients with colorectal cancer. Additionally, this research may provide valuable information on the pathophysiologic mechanisms of perioperative complications by quantifying microvascular density in patients who have received neoadjuvant therapy.

MeSH/Keywords: Colorectal Neoplasms; Neoadjuvant Therapy; Complications; Wound Healing; Microcirculation

Dissertation proposal title: Correlation between perfusion angiography and clinical outcome following endovascular treatment in patients with critical limb ischemia

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Mentor: Asst. Prof. Tajana Turk, M.D., Ph.D., Diagnostic and interventional radiology clinical department, Osijek University Hospital, Osijek, Croatia

Introduction: Lower extremity ischemia and its consequences are one of the biggest health problems of modern world and its consequences vary from simple skin lesions to severe tissue damage, which requires amputation. One of the most important ways to treat lower extremity ischemia is percutaneous transluminal angioplasty (PTA). Patient's condition may improve immediately after the angioplasty, but it may also remain unchanged, or even worsen, regardless of the primary technical result. This may be the result of inadequate foot perfusion improvement, since its healing primarily depends on the microcirculation status. The use of perfusion angiography allows the quantification of foot perfusion status before and after endovascular treatment and could thus be of use in preoperative assessment of whether the patient is suitable for PTA or not.

Hypothesis: There is a correlation between the foot microcirculation status, measured by perfusion angiography pre- and postoperatively, and condition improvement in patients with critical limb ischemia. Improving the foot perfusion depends not only on the extent of endovascular intervention, but also on the comorbidities and demographic characteristics of the patient.

Aims:

- to determine the parameters of perfusion angiography in patients before and after the endovascular treatment of their crural arteries
- to determine whether there is a correlation between the perfusion angiography parameters and the extent of endovascular intervention
- to determine whether there is an correlation between the perfusion angiography parameters and atherosclerosis factors
- to determine whether there is a correlation between perfusion angiography parameters and the clinical outcome of the treatment (amputation free survival)

Materials/participants and methods: The research will include 200 respondents. Patients with peripheral arterial disease without critical limb ischemia, who underwent endovascular intervention on the supragenicular arteries, would form a control group (100 patients), and subjects with peripheral arterial disease in the stage of critical limb ischemia, who underwent endovascular intervention on infragenicular arteries, would form an experimental group (100 patients).

Research plan: The data which would be gathered on all patients include basic data, comorbidities, habits, symptoms and basic laboratory results. Perfusion angiography of the foot will be performed on any patient undergoing endovascular treatment before and after endovascular intervention so its parameters could be analysed afterwards. Each patient will have a follow-up examination 3 months and 6 months after the intervention to assess the clinical status.

Expected scientific contribution: To corroborate the fact that the preprocedural analysis of multiple parameters, as well as individual and multidisciplinary approach to the patient, bring better quality in the future decisions on the need and cost-effectiveness of treatment of lower extremity ischemia with PTA and, thus, reduce the frequency of unjustifiably indicated and long-term unprofitable interventions.

Keywords: Perfusion angiography, Lower-limb ischemia, Percutaneous Transluminal Angioplasty, Endovascular treatment, Peripheral Arterial Disease

Abstract Title: Molecular Mechanisms Underlying Acute and Chronic Glycaemic Regulation Disruptions During SARS-CoV-2 Infection

Part of the Dissertation Proposal: Preliminary analysis of a subset of collected patient samples, focusing on basic demographic and clinical data

PhD candidate: Barbara Grubišić, M.D.; Clinic of Infectious Diseases, University Hospital Centre Osijek; Faculty of Medicine Osijek, University of Osijek, Osijek, Croatia

Mentor: Prof. Ines Bilić Ćurčić, M.D., Ph.D., Dpt. of Pharmacology Faculty of Medicine Osijek, University of Osijek, Clinical Institute of Internal Medicine, University Hospital Osijek, Croatia

Co-mentor: Assoc. Prof. Marija Santini, M.D., Ph.D, University Hospital for Infectious Diseases, Zagreb, Croatia

Introduction: The COVID-19 pandemic has highlighted a significant connection between SARS-CoV-2 infection and increased risks of severe disease progression and mortality, particularly in individuals with diabetes. This relationship is likely influenced by enhanced immune responses and hyperglycaemia in diabetic patients, predisposing them to pro-inflammatory and procoagulant conditions and impairing immune function through multiple biological mechanisms. Recent findings suggest a complex, bidirectional relationship between COVID-19 and diabetes, indicating that SARS-CoV-2 infection may not only worsen existing metabolic disorders but also trigger new-onset diabetes. The virus interacts with angiotensin-converting enzyme 2 (ACE2) receptors present in key metabolic organs, potentially disrupting glucose metabolism and causing hyperglycaemia, which may initiate novel pathophysiological processes. There has been a noticeable increase in hyperglycaemia cases among COVID-19 patients without previous diabetes history, linked to significant morbidity and mortality. Although inflammation and cytokine activation due to infection likely contribute to insulin resistance and stress-induced hyperglycaemia, the extent of direct viral damage to pancreatic islet cells and consequent insulin production impairment remains unclear. Moreover, COVID-19 has been associated with acute hyperglycaemia in non-diabetic individuals, diabetic ketoacidosis in previously diagnosed diabetic patients, and new diabetes diagnoses following infection. While the precise mechanisms linking COVID-19 and diabetes continue to be investigated, both conditions appear interconnected through stress-induced pathways. Understanding the long-term effects of COVID-19 on glucose metabolism is essential, underscoring the need for ongoing research to determine potential persistent metabolic changes or the development of a distinct, virus-induced diabetes form.

Aims: The primary objectives of this study are to investigate the incidence of disturbances in glycaemic control among patients with acute SARS-CoV-2 infection who had no prior history of diabetes, and to evaluate the potential long-term effects of SARS-CoV-2 infection on glycaemic control after recovery from COVID-19. Additionally, the research aims to explore the role of inflammatory cytokines in the development of insulin resistance both during the acute phase of infection and in the post-infection period. Furthermore, this study seeks to assess how different therapeutic strategies, including the use of corticosteroids and antiviral medications, influence glycaemic control in COVID-19 patients. Lastly, the impact of impaired glycaemic control on the clinical outcomes of COVID-19 infection will be examined.

Materials/participants and Methods: The research will enrol a cohort comprising patients admitted to the Infectious Diseases Clinic who are confirmed to have SARS-CoV-2 infection, categorizing them into those with insulin resistance and newly diagnosed diabetes, and those without diabetes. Each group will consist of a minimum of 64 participants, totalling at least 128 individuals. Upon admission, detailed patient histories will be documented, and serum biomarkers will be examined. The research will systematically assess various parameters such as CBC, CRP, PCT, blood glucose, urea, creatinine, electrolytes, liver enzymes, inflammatory markers, and coagulation factors. Additional assays will include HbA1c, fasting plasma glucose, insulin, C-peptide, HOMA IR, HOMA B, leptin, adiponectin, and the Human Cytokine 17-plex immunoassay. Outcomes related to the disease, including recovery, complications, mortality, and the resolution or diagnosis of diabetes mellitus, will be tracked up to three months post-COVID-19 infection.

Results: Based on the preliminary analysis of a subset of collected samples, data from a cohort of 100 hospitalised adult patients with confirmed SARS-CoV-2 infection and no prior history of diabetes were evaluated, including 55% male and 45% female patients. The mean age was 66.7 years (SD ± 12.1), with an average hospital stay 10.65 days (SD ± 6.4). In the group of patients with glycaemic disturbances, 34% had stress-induced hyperglycaemia, while 16% met the criteria for a diagnosis of new-onset diabetes. The contingency table showed that overall mortality was 24% (24/100), with 9 deaths among 50 normoglycaemic patients (18%), 11 deaths among 34 patients with stress hyperglycaemia (32.4%), and 4 deaths among 16 patients diagnosed with de novo diabetes (25%). Although mortality was higher in patients with glycaemic disturbances, these differences did not achieve statistical significance ($\chi^2 = 2.30$; df = 2; p = 0.3172). Univariable logistic regression showed that increasing glycaemic disturbance was associated with a higher, but statistically non-significant, odds of fatal outcome (OR 1.36; 95% CI 0.74–2.50; p = 0.318). In the multivariable model adjusted for age and sex, only age emerged as an independent predictor of mortality (OR 1.059 per year; 95% CI 1.014–1.105; p = 0.010). After adjustment, stress hyperglycaemia was associated with a non-significant OR of 2.50 (95 % CI 0.85–7.36; p = 0.097) and de novo diabetes with an OR of 1.75 (95 % CI 0.42–7.34; p = 0.443) relative to normoglycaemia, while sex remained non-predictive (p = 0.937). The modest explanatory power of the model underscores the multifactorial nature of COVID-19 outcomes and the need for larger samples to clarify the role of acute glycaemic disturbances.

Conclusion: Preliminary analysis of a subset of the collected data suggests that disturbances in glycaemic control are common among hospitalized COVID-19 patients without a prior history of diabetes and may be associated with increased mortality. Although mortality rates increased stepwise from normoglycaemia to stress hyperglycaemia and de novo diabetes, the lack of statistical significance in these associations likely reflects the limited cohort size and wide confidence intervals. Age emerged as the strongest independent predictor of in-hospital death, reinforcing its primacy in the risk stratification of COVID-19 patients. Nonetheless, the observed two- to three-fold higher odds of mortality in hyperglycaemic patients—albeit statistically non-significant—suggest that acute glucose elevations may exacerbate systemic inflammation and increase the risk of disease complications. Further analysis involving a larger patient cohort and more comprehensive datasets will be essential to obtain more robust and generalizable results, clarify the clinical significance of glycaemic abnormalities.

MeSH/Keywords: COVID-19, SARS-CoV-2, Diabetes mellitus, Hyperglycaemia, COVID-19 induced diabetes

Abstract Title: Diagnostic accuracy of the biological indicator leucine-rich alpha-2-glycoprotein and calprotectin in patients with suspected acute appendicitis: Preliminary Results

Part of the Disertation Proposal: Diagnostic accuracy of the biological indicator leucine-rich alpha-2-glycoprotein and calprotectin in acute appendicitis

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Mentor: Assoc. Prof. Višnja Adam Nesek, Clinical Hospital "Sveti Duh", Faculty of Dental Medicine and Health Osijek, Osijek, Croatia

Co-mentor: Assist. Prof. Zrinka Mihaljević, Institute and Department of Physiology and Immunology, Faculty of Medicine Osijek, Croatia

Introduction: Acute abdominal pain causes up to 10% of emergency visits, with appendicitis being a common surgical indication. Despite improvements, diagnosis remains challenging - negative appendectomy rates reach 40%, while missed cases lead to complications in over 90% of patients. Routine biomarkers like C-reactive protein (CRP) and leukocytes lack specificity, as they increase in many inflammatory states. Newer markers such as leucine-rich alpha-2-glycoprotein (LRG1) and calprotectin, produced locally at the inflammation site, may allow for earlier and more accurate diagnosis.

Aim: To assess the diagnostic accuracy of LRG1 and calprotectin in suspected acute appendicitis. This abstract presents preliminary findings based only on routinely available parameters (CRP, leukocytes, Alvarado score).

Materials / Participants and Methods: A cross-sectional observational study is being conducted in the Emergency Departments of General Hospital Našice and University Hospital “Sveti Duh”. Adults (≥18 years) with clinical suspicion of appendicitis were included. Exclusion criteria were: pregnancy, IBD, malignancy, autoimmune or psychiatric disease, BMI ≥30, or antibiotic use. Participants were divided into two groups: patients with appendicitis confirmed by postoperative histopathology, and controls in whom appendicitis was excluded either histologically or through clinical improvement with 48-hour telephone follow-up after discharge. G*Power analysis determined that at least 125 participants are needed for reliable results. This preliminary analysis includes 20 participants: 10 with appendicitis and 10 controls. Data included CRP, leukocyte count, and Alvarado score. Statistical analysis was performed using appropriate tests based on data distribution, with results presented via box plots.

Results: Among 20 participants (mean age: 37.4 vs. 41.1), CRP and leukocyte values were higher in the appendicitis group (CRP: 39.8 vs. 8.7 mg/L; leukocytes: 11.2 vs. 8.1 $\times 10^9$/L), but with overlapping ranges. Neutrophil percentage and temperature showed minimal differences. Alvarado scores were slightly higher in the appendicitis group (3.9 vs. 3.5), but not clearly discriminatory.

Conclusion: Preliminary results indicate limited diagnostic value of CRP, leukocyte count, and Alvarado score when used alone. These findings support the need to explore more specific biomarkers. Further analysis will include LRG1 and calprotectin.

MeSH/Keywords: Appendicitis, Biomarkers, C-reactive protein, Inflammation, Leukocytes

Dynamics of change in blood coagulation factors protein C and S, factor VII, VIII, IX, X, XI, XIII dependent on liver function before and after liver transplantation

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Mentor: Assist. Prof. Irena Jukić, MD, PhD, Croatian Institute of Transfusion Medicine, Medical Faculty Osijek, Osijek, Croatia

Introduction: Patients suffering from terminal liver failure (complete absence of function) are candidates for liver transplantation (LT). They have reduced or absent ability to produce blood coagulation factors. After LT, it is expected that the transplanted liver will begin functioning in the shortest period of time, including the synthesis of blood cogulation factors. However, this is not the case in all patients after LT.

Hypothesis: Synthesis of blood coagulation factors does not have the same dynamics in all patients after LT. Dynamics of recovery of blood coagulation factors can be an indicator of liver function recovery and a predictor of transplant success or a predictor of graft rejection. By conditioning patients before LT, it is possible to influence the dynamics of recovery and shorten recovery time.

Aims: To examine blood coagulation factors (protein C and S, factors VII, VIII, IX, X, XI, XIII**)** in patients before and after LT. Examine if tested coagulation factors are synthesized more slowly in the absence or delay of recovery of liver function after transplantation. To examine the influence of liver graft quality on the recovery of blood coagulation factors in recipients.

Materials/participants and Methods:

The subjects in this research would be patients, who suffer from terminal liver failure, (regardless to the cause of liver failure), have no absolute contraindication for orthotopic LT from a cadaveric donor and who will undergo the LT procedure at the Merkur University Hospital in Zagreb.

Research plan: Blood coagulation factors (protein C and S, factors VII, VIII, IX, X, XI, XIII) will be monitored at several time points after LT (0 day, 1st day, 3rd day, 7 days, 1 month, 3 months, 6 months). Blood samples will be taken and all obtained results will be analyzed, as well as possible influence of the liver graft quality (macroscopic appearance, pathohistological analysis, status of the liver graft blood vessels, laboratory indicators) on the blood coagulation factors' recovery at the recipient.

Significance/Expected scientific contribution: This research will contribute to better understanding of the delay or absence of blood coagulation factors synthesis in liver transplant patients. This could lead to targeted diagnosis of individual coagulation factors deficiency and, if necessary, application of targeted treatment. Research will show whether blood coagulation factors are a good indicator of liver function recovery, in correlation with other biochemical and clinical parameters, and whether they can be a predictor of liver transplant success.

MeSH/Keywords: liver transplantation, blood coagulation factors, transplants, liver function tests, delayed graft function

Dissertation Proposal Title: Pediatric Inflammatory bowel disease treatment practices and treatment outcomes in Croatia

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Introduction: Inflammatory bowel disease (IBD) in children, an immune-mediated, chronic and relapsing inflammation of the gastrointestinal tract, when diagnosed in children, is usually more extended and severe than in adults. Diagnosing and treating IBD in children is challenging, and harmonization of diagnostic and treatment procedures is necessary to achieve the best treatment outcome. Since 2005. international and national pediatric gastroenterology societies publish guidelines for pediatric IBD management. It is possible that if there is a difference in diagnostic protocols, clinical experience and management strategies, the care for patients my not be optimal.

Whether and to which extent are the guidelines being met, and what are the treatment outcomes if the guidelines are or are not followed are the main interests of this study.

Hypothesis: Adherence to treatment guidelines has positive effect on treatment outcome.

Aims:

1. To evaluate current pediatric IBD treatment practices in Croatia
2. To evaluate adherence to current diagnostic and treatment guidelines
3. To research pediatric IBD treatment outcome after 1 year of treatment
4. To compare adherence to guidelines with treatment outcomes in children with IBD in Croatia

Materials/ Methods: This cohort study would be conducted in all hospitals in Croatia where children with IBD are diagnosed and treated, mainly in tertiary hospital centers with pediatric gastroenterology departments and pediatric endoscopy units. We plan to include all patients diagnosed since 2016. until the end of 2024. (around 450 patients), to review hospital records, diagnostic criteria used, initial treatment, and treatment outcome after 1 year.

Research plan:

1. To contact hospitals with gastroenterology units and selecting patients with diagnosed IBD (ulcerative colitis, Crohn's disease and IBD unclassified)
2. To review relevant patient history, initial workup including laboratory markers, vaccination status, TPMT profile, fecal calprotecin levels, radiology, upper and lower endoscopy findings, pathohistology, and to review inital therapy, therapy after 6 and 12 months
3. Statistical analysis
4. Publication

Significance/Expected scientific contribution: The main interest of this study is to find out whether and to which extent are the guidelines for pediatric IBD management being met in everyday practice, and what is the treatment outcome in correlation with adherence to the guidelines. These informations should detect the areas in need of improvement in disease management, and on the other hand the importance, the use and the adherence to the guidelines in clinical setting. Second contribution would be the data on the one-year treatment outcome in pediatric IBD patients, the first data for this population in Croatia.

We believe that study results will improve care for pediatric IBD patients.

MeSH/Keywords: Inflammatory bowel disease, children, management, outcome, guidelines

Dissertation Proposal Title: Association of insulin-like growth factor 1 level with retinopathy and degree of intracranial hemorrhage in preterm infants

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Introduction: Premature birth disrupts intrauterine homeostasis and exposes infants to environmental stressors, increasing the risk of complications such as retinopathy of prematurity (ROP) and intraventricular hemorrhage (IVH), which significantly contribute to morbidity and long-term neurodevelopmental impairment in preterm infants. Insulin-like growth factor 1 (IGF-1), essential for fetal growth and vascular development, significantly decreases after preterm birth. This drop is associated with impaired retinal and cerebral vascularization.

Hypothesis: Lower IGF-1 levels in umbilical cord blood are associated with a higher risk and greater severity of ROP and IVH in preterm infants.

Aims: The primary aim is to determine the diagnostic value of umbilical cord blood IGF-1 as an early parameter in the development and severity of ROP and IVH in preterm infants.

Participants and Methods: This prospective cohort study will be conducted over one year at the Department of Neonatology, University Hospital Osijek. It will include preterm infants born before 37 weeks of gestation, with birth weight under 2500 g and without visible anomalies. Umbilical cord blood will be collected at birth and stored at –80°C. Clinical data, including outcomes, will be extracted from medical records. ROP will be graded by an ophthalmologist according to international guidelines, and IVH will be diagnosed by cranial ultrasound.

Research plan: Following ethical approval, we will collect samples and clinical data. Statistical analysis will assess associations between IGF-1 levels and the incidence/severity of ROP and IVH.

Significance/Expected scientific contribution: This study will enhance understanding of IGF-1's role in the pathogenesis of ROP and IVH and assess its value as an early biomarker. Findings may inform future screening strategies and early interventions aimed at improving outcomes in preterm infants.

MeSH/Keywords: Insulin-Like Growth Factor 1; Intraventricular Hemorrhage; Premature Infants; Retinopathy of Prematurity; Umbilical Cord Blood

Abstract Title: Barriers in prescribing antidiabetic medications with cardiovascular benefits: practice, experience, and attitudes of GPs in Croatia

Part of the Dissertation Proposal: A practice of prescribing new antidiabetic medications with protective cardiovascular effects in family medicine and possibilities for improvement

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Introduction: Approach to the treatment of type 2 diabetes (T2D) nowadays is currently undergoing a renaissance, due to the novel antidiabetic medications, sodium-glucose co-transporter 2 inhibitors (SGLT2ins), and glucagon-like peptide-1 receptor agonists (GLP-1 RAs). Despite their proven beneficial effects, recent research worldwide points to their insufficient prescription, influenced by various factors, assembled into the common denominator of therapeutic inertia.

Aims: This cross-sectional study aimed to reveal the prescription rates of novel antidiabetics in Croatia and to examine the association of general practitioner's (GP) self-confidence in prescribing them with potential barriers that they encounter in the process of prescribing.

Participants and Methods: This research used a self-designed survey that was delivered to the GP's e-mail addresses in digital format. Exact data on the total number of patients diagnosed with T2D and prescribed new antidiabetic medications were checked by the respondents in their electronic database. Questions about the level of self-confidence in antidiabetic medication prescribing were asked in the form of a Likert scale, and the assessment of the influence of factors on the probability of lower self-confidence was done by bivariate and multivariate logistic regression.

Results: The research was conducted on 168 GPs (66.1% women, 49.4% family medicine (FM) specialists). The total number of individuals with T2D was 23,036, among which the largest proportion was those aged 60 to 80 years. The prescription rates of SGLT2ins and GLP-1 RAs were 21% and 14.4%, respectively. Regarding the self-confidence assessment, 76.2% of GPs stated a high level of self-confidence in prescribing SGLT2ins, and 53.6% of GPs in prescribing GLP-1 RAs. FM specialists showed significantly higher confidence than other respondents. The main factors that were observed as predictors of lower self-confidence in prescribing these medications were related to the unfamiliarity of GPs with the guidelines' recommendations, and the complexity of guidelines. Multivariate regression revealed models that reduced the possibility of high self-confidence, emphasizing factors such as the lack of detailed information about the side effects of these medications and non-clarity of the guidelines, while factor that increased this likelihood considered a greater number of individuals with T2D with already prescribed these medications.

Conclusion: It is of the utmost importance to identify barriers the GPs face when prescribing these medications, as well as to suggest potential strategies to optimize their prescription.

Keywords: Type 2 diabetes, Cardiovascular risk, SGLT2ins, GLP-1 RAs, Prescribing rates, Prescribing barriers, Therapeutic inertia

Dissertation Proposal Title: Possibilities of influencing the psychophysical condition and quality of life of elderly institutionalized persons

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Introduction: There are 869,239 people over the age of 65 living in the Republic of Croatia, and 32,692 in the Vukovar-Srijem County (VSC). There are 1,503 institutionalized elderly people in the VSC, who live within 45 institutions. Croatia is ranked among the oldest nations in Europe, and the number of institutionalized people is continuously growing. It is important to enable all elderly people residents of nursing homes to engage in physical activities adapted to their age and health condition, as well as to participate in various programs of socialization and creative ways of spending free time.

Hypothesis: The psychophysical condition and quality of life of institutionalized elderly persons decline, with better psychophysical condition and higher quality of life experienced by elderly persons living in institutions with better organized programs of physical activities, socialization and creative spending of free time than in institutions where the mentioned programs are very scarce or non-existent.

Aims:

1. To examine the psychophysical state and quality of life of institutionalized persons
2. To investigate the number and type of activities organized in nursing homes
3. To examine the number and proportion of persons who regularly access the offered activities
4. To investigate the trends and changes in the psychophysical state and quality of life of more active and less active users of nursing homes

Materials/Participants and Methods: The participants will be people over 65 years of age who are residents of nursing homes in the VSC. After the participant signs an informed consent to participate in the study, they will answer questions related to demographic and socioeconomic factors and will complete standardized questionnaires for assessment of quality of life, anxiety, depression, physical activity and religiousness.

Research plan: The research will be a prospective cohort study, conducted over a period of one year, with each participant interviewed twice, at the beginning of the study and after six months. The participants will be divided into two groups: an unexposed group of participants residents of nursing homes where the participants do not engage in any physical activity and do not engage in any creative leisure activity per week, and an exposed group of participants who engage in at least one activity per week.

Significance/Expected scientific contribution: The proposed research will determine the psychophysical state and quality of life of institutionalized elderly people, and the possibilities of the influence of different types of activities on increasing or at least maintaining the existing psychophysical state and quality of life of institutionalized people. Public health strategies that will emerge from this research are necessary and justified from the point of view of health economics and public health, where the results of this research will provide a scientific basis for activities aimed at improving the quality of life and psychophysical health of the elderly population residing in nursing homes.

MeSH/Keywords: anxiety, depression, physical activity, institutionalization, quality of life, aged

Dissertation Proposal Title: Modulation of the Gut Microbiome by 13-cis Retinoic Acid and High-Fat Diet in Female Lewis Rats

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Mentor: Assoc. Prof. Anđela Grgić, M.D., Ph.D., Department of Anatomy and Neuroscience, Faculty of Medicine Osijek, University of Osijek, Osijek, Croatia

Introduction: The addition of 13-cis retinoic acid (13 cRA) in individuals on a standard diet has a positive effect on the gut microbiota by stimulating the activation of B lymphocytes and plasma cells, promoting the production of IgA from plasma cells, and strengthening intercellular junctions in the intestines (zonula occludens). A lack of IgA in rat models is associated with more frequent development of colorectal adenomas and dysbiosis. The synergistic effect of 13 cRA and a high-fat diet (HFD) on alterations in the gut microbiome and inflammatory cytokines has not been fully elucidated.

Hypothesis: Administration of 13 cRA for 30 days combined with a high-fat diet over 60 days leads to disruption of gut microbiome homeostasis, reducing the number/proportion of bacterial strains from the genera *Lactobacillus* and *Bifidobacterium*, causing histomorphological changes in the small intestine, and promoting inflammatory processes in the body.

Aims:
To determine the role of 13 cRA and HFD on:
• The absolute number and relative abundance of bacterial strains of the *Lactobacillus* and *Bifidobacterium* genera in the colon
• The absolute number of other bacterial strains and overall changes in the colon microbiome
• Histomorphological changes in the wall of the small intestine (primarily the mucosa and submucosa)

Materials/Participants and Methods: 36 Lewis rats were divided into two groups: those fed a standard diet (STD) and those fed a high-fat diet (HFD), in which saturated fatty acids accounted for 45% of total energy intake. Three additional groups (6 rats each) were included: two groups received 13 cRA (7.5 mg/kg and 15 mg/kg) over a 30-day period, and one control group received sunflower oil. All animals were sacrificed after 60 days.

Research Plan: Following anesthesia, analgesia, and humane euthanasia, 100 mg of colon content will be sampled for probiotic bacteria isolation – specifically for DNA extraction and gut microbiome composition analysis via sequencing.
DNA extraction from colon content samples will be performed using the Maxwell® 16 System (Promega, Madison, USA) and the Maxwell® 16 Tissue DNA Purification Kit (Promega, Madison, USA).
Extracted DNA samples will be sent for further analysis to Molecular Research (MR, Shallowater, TX, USA), an accredited laboratory for Illumina MiSeq sequencing.
Additionally, during animal sacrifice, small intestine samples will be collected for histological analysis. These will be stained with hematoxylin and eosin to assess the degree of steatosis and morphological changes in the mucosa and submucosa, as well as the appearance of the intestinal villi of the small intestine.

Significance/Expected Scientific Contribution: We expect that long-term administration of 13 cRA and a high-fat diet will lead to intestinal dysbiosis and a reduction in the number of *Lactobacillus* and *Bifidobacterium* strains, as well as morphological damage to the small intestine mucosa.
The obtained results could serve as a basis for understanding reduced absorption of certain vitamins and minerals, decreased resistance to infections, increased risk of diabetes development, and increased incidence of colorectal cancer in obese individuals.
The synergistic effect of 13 cRA and HFD on the aforementioned parameters has not been previously studied, which is why we consider this research to be highly valuable and of great interest

MeSH/Keywords: 13-cis retinoic acid; metabolic syndrome; obesity; gut microbiome; histology

Dissertation Proposal Title: Association between echocardiographic parameters of systolic and diastolic myocardial function and serum concentration of growth differentiation factor 15 in patients with sepsis

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Introduction: Sepsis is a systemic and life-threatening condition characterized by a dysregulated immune response to infection, often resulting in multiple organ failure. Septic cardiomyopathy, as a consequence of sepsis, is characterized by reversible myocardial dysfunction, with pathogenesis involving complex mechanisms such as mitochondrial dysfunction, oxidative stress, and inflammatory dysregulation. Although echocardiography is widely available, it has limitations in detecting early and subtle changes in cardiac function. On the other hand, biomarkers such as GDF-15, which reflect mitochondrial dysfunction and cellular stress, are increasingly recognized as promising tools for the early detection of sepsis-associated cardiomyopathy. This study aims to integrate imaging and biochemical diagnostics to improve clinical recognition and understanding of the pathophysiology of myocardial injury in the context of sepsis.

Hypothesis: Serum concentrations of GDF-15 significantly correlate with echocardiographic parameters of systolic and diastolic myocardial dysfunction in patients with sepsis.

Aims:

1. To determine the association between GDF-15 and echocardiographic parameters of systolic and diastolic myocardial function.
2. To investigate the correlation between high-sensitivity troponin I (hs-TnI) and echocardiographic findings.
3. To assess the prognostic value of GDF-15 in relation to treatment outcomes during hospitalization.

Materials/Participants and Methods: A prospective cohort study will include 50 patients diagnosed with sepsis or septic shock, defined by SOFA criteria. Serum concentrations of GDF-15 and hs-TnI will be measured on the second day of hospitalization and again between days 7 and 10. Echocardiographic evaluation will include both standard and advanced parameters of left and right ventricular function. Biochemical analyses will be conducted using the ECLIA method, and statistical analysis will include correlation tests, comparative analyses, and regression models with a significance level of $p<0.05$.

Research plan: The study is designed as a longitudinal analysis of changes in GDF-15 and echocardiographic markers during hospitalization, alongside outcome evaluation. The results are expected to enable integration of biochemical and imaging data, and potentially establish GDF-15 as a clinically relevant biomarker for early detection and prognostic stratification of septic patients.

Scientific significance and expected contribution: The findings of this research may contribute to a better understanding of the role of mitochondrial dysfunction in the development of septic cardiomyopathy. GDF-15 may be positioned as a valuable biomarker for the differentiation and assessment of reversible myocardial dysfunction caused by sepsis. The integration of such biomarkers into routine clinical practice could improve early diagnosis, therapeutic strategies, and outcomes for patients with severe forms of sepsis.

MeSH / Keywords: GDF-15, sepsis, myocardial dysfunction, echocardiography, biomarkers

Dissertation Proposal Title: The Connection Between Inflammatory, Metabolic Factors and Mental Health Challenges in Healthcare Workers

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Introduction: Canadian physician Hans Selye scientifically defined stress for the first time in 1936 as a coordinated physiological response of the organism to harmful stimuli, emphasizing its role in the body's defense mechanisms. Today, in English, the terms 'stress' and 'distress' are used, where 'stress' refers to a state of tension, while 'distress' denotes intense psychological pain, pressure, suffering, and anxiety. While stress can have positive effects, distress is always negative. Stress can significantly impact an individual's work capacity depending on its intensity. Moderate stress can be stimulating, improving productivity and focus. However, insufficient stress levels may lead to a loss of motivation and disinterest in work, while excessive stress can result in overload, burnout syndrome (Burnout Syndrome), or even post-traumatic stress disorder (PTSD). Therefore, educating individuals on stress recognition, prevention, and management is crucial to avoiding negative consequences. The World Health Organization defines burnout as a syndrome characterized by exhaustion, mental detachment from work, a negative attitude towards job tasks, and reduced professional efficacy, arising from chronic occupational stress that is not properly managed. Although not classified as a mental disorder, burnout syndrome is a reason why individuals seek medical assistance and represents a significant issue in the workplace. The key difference between acute work-related stress and burnout lies in their duration—stress occurs in shorter periods, whereas burnout results from prolonged exhaustion of adaptive mechanisms and can be associated with individual or work-related factors. Research indicates that healthcare workers are more susceptible to stress than non-healthcare professionals, which may lead to a higher risk of burnout syndrome and stress-related mental health disorders and physical conditions such as hypertension.

Hypothesis: Biological markers of stress (cortisol levels, blood pressure, heart rate), as well as related metabolic (glucose levels, lipid profile, sex hormones, thyroid hormones) and inflammatory factors (CRP, IL-6, IL-10 levels), are associated with the occurrence of mental disorders, such as anxiety and burnout syndrome, in healthcare workers, particularly those with higher workloads

(longer working hours and tenure) and frequent exposure to stressful situations (working in emergency or intensive care units).

Aims:

To determine which biological stress markers, such as cortisol levels, blood pressure, heart rate, and associated metabolic (glucose levels, lipid profile, sex hormones, thyroid hormones) and inflammatory factors (CRP, IL-6, IL-10 levels), most accurately indicate high stress levels in healthcare workers.

To investigate how these biological stress markers in healthcare personnel correlate with the development of mental disorders such as anxiety and burnout syndrome.

To identify which work conditions and stressors (workload, patient interactions, emotional exhaustion, expossure to stressful situations) most contribute to biological stress markers and their association with mental disorders in healthcare professionals.

Materials/Participants and Methods:

Study Design:

- Cross-sectional study: Data will be collected at a single time point, analyzing the correlation between biological stress markers, stress levels, and mental disorders such as anxiety and burnout syndrome in healthcare workers.
- If the study continues as a longitudinal follow-up, it may take the form of a prospective cohort study, monitoring changes in biological markers and mental health indicators over time or after specific preventive and interventional measures.

Participants:

- Healthcare professionals (physicians, nurses, medical technicians, laboratory personnel, etc.) employed at the Clinical Hospital "Sveti Duh."
- Non-healthcare staff (administrative workers, teachers, technical service personnel, food service staff) as a control group (employed at the Clinical Hospital "Sveti Duh" or included during routine medical examinations at the hospital).

Inclusion Criteria:

- Age ≥18 years
- Employment in the healthcare unit (healthcare personnel) or non-healthcare unit (control group)
- Signed informed consent for participation in the study

Exclusion Criteria:

- Pre-existing diagnosis of severe mental disorders (e.g., bipolar disorder, schizophrenia)
- Acute or chronic illnesses that could significantly influence biological marker levels (e.g., active autoimmune diseases, malignancies)

Sample Size:

- 240 healthcare workers stratified by job type, work environment, and work modality
- 60 non-healthcare workers

Data Collection:

- Socio-demographic data: gender, age, marital status, number of children, education level, occupation, work type, years of service, work modality
- Biological stress markers: Blood pressure, heart rate
- Laboratory parameters: Cortisol, lipid profile (cholesterol, triglycerides), thyroid hormones (TSH, T3, T4), sex hormones (testosterone, estrogen, progesterone), inflammatory markers (C-reactive protein [CRP], interleukin-6 and -10 [IL-6, IL-10])
- Psychological assessments: Validated questionnaires for:
    - Anxiety and depression
    - Burnout syndrome: *Maslach Burnout Inventory (MBI)*
    - Work stress: *Work Conditions and Perceived Stress Questionnaire*

The study tracks socio-demographic data: gender, age, marital status, number of children, education level, occupation, type of workplace, work experience, and work modality;

Biological stress markers: (Data on blood pressure and heart rate frequency);

Laboratory blood parameters: cortisol, lipids (cholesterol, triglycerides), thyroid hormones (TSH, T3, T4), sex hormones (testosterone, estrogen, progesterone), inflammatory markers (C-reactive protein (CRP), interleukin-6 and 10 (IL-6, IL-10));

Psychological assessments – validated questionnaires for:

- Anxiety and depression;
- Burnout syndrome: Maslach Burnout Inventory (MBI);
- Workplace stress: work conditions and perceived stress questionnaire.

The Depression, Anxiety, and Stress Scale (DASS-S) consists of 42 items, divided into three subscales, each containing 14 statements that assess three negative emotional states. Respondents are asked to evaluate each statement based on how frequently they have experienced the described emotions over the past week. Statements related to depression describe low self-esteem, poor mood, feelings of sadness, hopelessness, lack of motivation, and loss of interest. Statements related to

anxiety assess physiological arousal, physical tension, nervousness, and excessive worry. The stress subscale is defined by statements that describe negative affective responses characteristic of both depression and anxiety, such as nervousness, tension, irritability, and difficulty relaxing. Each item in the questionnaire is rated on a four-point Likert scale from 0 to 3, according to symptom frequency over the past week. The total score for each subscale ranges from 0 to 42. Additionally, a composite measure of negative emotional symptoms can be obtained by summing the responses across all items, yielding a total score between 0 and 126. Respondents experiencing psychological difficulties and diagnosed with neurotic disorders tend to score higher on all DASS-S subscales. The DASS is not a diagnostic tool but aids in recognizing symptoms and assessing the need for professional help.

The Maslach Burnout Inventory (MBI) is one of the most commonly used instruments for measuring occupational burnout. Developed by Christina Maslach and Susan Jackson, it assesses the level of professional burnout among various occupational groups, particularly those working in human services.

The MBI consists of three core dimensions:

1. **Emotional exhaustion** – measures feelings of exhaustion, fatigue, and lack of energy due to work. The questions assess subjective experiences of being overwhelmed and the inability to emotionally recover.
2. **Depersonalization** – evaluates the development of a cynical, detached, and impersonal attitude towards colleagues and clients. This dimension indicates reduced empathy and professional commitment.
3. **Reduced personal accomplishment** – reflects a sense of inefficacy, loss of motivation, and negative self-evaluation of professional competence and success.

The Zung Self-Rating Depression Scale (SDS) is used to assess the severity of depressive symptoms in individuals and can be useful in the clinical diagnosis of depressive disorders.

The scale consists of 20 items covering various aspects of depressive symptoms, such as mood, energy, appetite, sleep, and physical disturbances. Each question has four response options, with scores ranging from 1 to 4. The total score is then interpreted in relation to different levels of depression, such as mild, moderate, or severe. The scale is simple to use and is frequently applied in research and clinical settings as a quick tool for assessing depressive states.

The workplace stress questionnaire was designed for the purpose of a doctoral dissertation and includes 27 questions related to socio-demographic data, workplace conditions, work modality, and job satisfaction. It assesses individual stress levels and includes questions addressing various stress factors such as work obligations and family relationships. Participants respond based on their experiences and feelings over the past three months.

Only participants who provide informed consent will be included in the study. Eligibility criteria include a minimum age of 18 years, while individuals with pre-existing diagnoses of severe somatic or mental disorders that could influence the results will be excluded.

Research plan: The study will include a total of 300 participants: 240 healthcare professionals categorized based on job type and work modality, and 60 non-healthcare workers (control group).

Demographic data collected via a Google Forms questionnaire will focus on understanding the personal and professional characteristics of healthcare and non-healthcare workers to better explore the biological mechanisms of stress, inflammatory and metabolic factors, and the development of mental disorders and burnout syndrome. All data will be collected anonymously. Participants will be asked to provide basic information on gender, age, marital status, and number of children. Additional questions will cover education level, occupation, workplace type (hospital, polyclinic, private practice, etc.), work modality (shifts, work experience, and working hours). Other factors related to physical and mental health will also be assessed, including the consumption of nicotine products, alcohol, and the use of medications for regulating blood pressure, thyroid function, and sex hormones.

Categorical data will be presented as absolute and relative frequencies. Numerical data will be described using arithmetic mean and standard deviation for normally distributed variables, and median with interquartile range for non-normally distributed variables. Differences in categorical variables will be tested using the Chi-square test, or Fisher's exact test when necessary. Normality of numerical variable distribution will be assessed using the Shapiro-Wilk test. Differences in normally distributed numerical variables between two independent groups will be tested using the Student's t-test, and the Mann-Whitney U test will be used for non-normally distributed variables. Differences in continuous variables between three or more independent groups will be analyzed using ANOVA (Post-hoc Conover test) or the Kruskal-Wallis test (Post-hoc Conover test), depending on the normality of the data distribution.

Correlation analysis of normally distributed numerical variables will be assessed using Pearson's correlation coefficient (R), while Spearman's correlation coefficient (ρ) will be used for non-normally distributed data. Regression analysis (bivariate and multivariate) will be used to identify factors influencing the occurrence of mental disorders such as anxiety, burnout syndrome, and general stress. ROC (Receiver Operating Characteristic) analysis will be applied to determine the optimal cut-off value, area under the curve (AUC), specificity, and sensitivity of biochemical markers in predicting the likelihood of mental disorders such as anxiety, burnout syndrome, and general stress.

All p-values will be two-tailed, with a significance level set at alpha=0.05. Statistical analyses will be conducted using MedCalc® Statistical Software version 23.0.6 (MedCalc Software Ltd, Ostend, Belgium; https://www.medcalc.org; 2024).

Significance/Expected scientific contribution: The findings of this study could contribute to a better understanding of the biological mechanisms of stress, particularly among healthcare professionals. The research will examine how inflammatory markers (interleukins, TNF-alpha, C-reactive protein) and metabolic indicators (cortisol, glucose, lipids) correlate with stress and the severity of burnout syndrome in healthcare workers. High levels of these biomarkers are expected to be associated with increased stress levels and adverse mental health outcomes. Increased systemic inflammation may be linked to the development of depression and anxiety, while associated metabolic disturbances may indicate long-term physiological consequences of stress.

Additionally, this study could provide deeper insight into how workplace stressors (such as high professional demands, emotional exhaustion, lack of support, and exposure to traumatic situations) activate biological processes leading to mental disorders like depression and anxiety. Understanding these biological stress markers may enable early identification of employees at risk for mental health disorders and facilitate the implementation of preventive and intervention measures tailored to healthcare professionals (e.g., stress reduction programs, improved workplace social support, and education on healthy coping mechanisms). Given the importance of healthcare workers' well-being for the efficiency of the healthcare system, such research may have far-reaching implications for stress reduction policies and mental health preservation within healthcare institutions.

The proposed study will contribute to a better understanding of the complex physiological response to stress and its association with the development of mental disorders in healthcare workers. The study results will enable more precise identification of the most relevant biological stress markers to recognize healthcare professionals at high risk of developing anxiety and burnout syndrome. The collected data may aid in designing targeted preventive approaches and personalized intervention strategies, such as modifications in work organization, optimization of the work environment, stress management techniques, and psychological support programs. These strategies could mitigate the negative effects of stress on the mental and physical health of employees, not only in the healthcare sector but also in other high-stress professions.

MeSH/Keywords: Healthcare Workers, Stress Biomarkers, Burnout Syndrome, Metabolic Disorders, Inflammatory Markers

Dissertation Proposal Title: Association of anti Xa activity of apixaban and rivaroxaban with gastrointestinal bleeding

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Mentor: Assist. Prof. Suzana Mimica, M.D., Ph.D., Clinical Hospital Center Osijek, Faculty of Medicine Osijek, University of Osijek, Osijek, Croatia

Co-mentor: Assist. Prof. Silvija Canecki-Varžić, M.D., Ph.D., Clinical Hospital Center Osijek, Faculty of Medicine Osijek, University of Osijek, Osijek, Croatia

Introduction: New oral anticoagulants are a group of drugs that are increasingly used today in the prevention of thromboembolic events in patients with AF and in the treatment of patients with DVT and PTE. Concerns have been raised regarding their use because they carry a risk of bleeding. Gastrointestinal bleeding is in the spotlight due to its high prevalence and serious economic burden worldwide.

Hypothesis: In patients using rivaroxaban and apixaban and developing drug-induced upper gastrointestinal bleeding (macro- and micro-bleeds), anti-Xa activity is higher and more often above reference values compared to the control group taking the same drugs and not developing micro- and macro-bleeds and pharmacotherapy is more often inadequate compared to the control group.

Aims:

1. Determine anti-Xa activity in patients using rivaroxaban and apixaban who develop medication-induced upper gastrointestinal bleeding (macro and micro bleeding).

2. Determine anti-Xa activity in the control group of patients using rivaroxaban and apixaban who have not developed upper gastrointestinal bleeding (macro and micro bleeding).

3. Assess the adequacy of pharmacotherapy in patients in the primary and control groups.

Materials/Participants and Methods: The study will be conducted on subjects who have been taking rivaroxaban or apixaban, regardless of the reason for the drug. To observe the mean effect in the difference in numerical variables, with a significance level of 0.05 and a power of 0.8, the minimum required sample size is 29 subjects. Subject history and laboratory findings will be collected. A venous blood sample and a urine sample will be collected for relevant hematological and biochemical laboratory parameters. According to the calculation for the sample of two independent groups and for the measurement of continuous variables, with an alpha of 0.05 and a statistical

power of 0.8 and an expected difference between the means of 0.48, the minimum size of each group is 56 subjects (a total of 112 in both groups).

Research plan: Subjects will have one visit during this study at which aforementioned data will be collected.

Significance/Expected scientific contribution: The proposed research will result in new insights into the impact and relationship between rivaroxaban and apixaban plasma concentrations and the development of gastrointestinal bleeding.

MeSH/Keywords: gastrointestinal bleeding, factor Xa inhibitor, rivaroxaban, apixaban

Pharmacogenomic Testing in Croatia: Insights from Clinical use of a 28-gene Pharmacogenomic Panel

Part of the Dissertation Proposal: Potential health and economic benefits of proactive pharmacogenomic testing in the population of the Republic of Croatia

PhD candidate: Vid Matišić, M.D., St. Catherine Specialty Hospital, Zagreb, Croatia

Mentor: Prof. Dragan Primorac, M.D., Ph.D., St. Catherine Specialty Hospital, Zagreb, Croatia and Faculty of Medicine Osijek, University of Osijek, Osijek, Croatia

Introduction: In the field of pharmacogenomics there are currently numerous readily available testing options, making it easily accessible for patients and clinicians to order tests and obtain the results in a short time span, making it clinically feasible to make proper interventions. However, studies have shown that a considerable percentage of medical professionals in Europe did not utilize pharmacogenomic testing, even though the majority of them found it useful for their daily practice. It is prudent to have an understanding of commonly encountered clinical situations, in order for the clinicians to be prepared for what they might encounter should they start ordering pharmacogenetic tests in their practice.

Aim: This study aimed to examine the initial landscape of implementing a panel-based pharmacogenomic test for polymorphisms in 28 genes in the Republic of Croatia, by reporting on the encountered gene drug pairs alongside the patient-reported reasons for performing the test.

Participants and Methods: Retrospective analysis included 319 patients who underwent pharmacogenomic testing by the RightMed panel using a TaqMan quantitative real-time PCR method and CNV analysis to determine the SNPs in the 28 targeted genes. Health records were assessed for the data on pharmacotherapy at the time of testing as well as history stating the reason for pharmacogenomic testing.

Results: 296 patients indicated reasons for testing in their history. Most of the patients (76, [23.8%]) reported multiple reasons for pharmacogenomic testing, while the least number of patients (9 [2.8%]) reported coming to pharmacogenomic testing upon their attending physician's request. 54 patients (16.9%) did pharmacogenomic testing for pre-emptive reasons. 139 (43.6%) patients had significant gene-drug interactions to at least one drug present in therapy. In 84 (26.3%) patients, no interactions were detected between drugs in their therapy. 156 participants had up to 3 drugs in their therapy, 125 had between 4 and 8 drugs in therapy, while 38 patients had 9 or more drugs in their therapy.

Conclusion: The presented results demonstrate a need to enhance the education of clinicians regarding the availability and utility of pharmacogenetic testing in the Republic of Croatia. Even though the limitation of this study inevitably includes its single-centered nature in a private hospital, the proportion of patients who came at their own accord, rather than being referred by their attending physician is striking.

MeSH/Keywords: pharmacogenomics, gene-drug interactions, personalized medicine, clinical-decision making, genetic-testing

Dissertation Proposal Title: Assessment of eye movements as indicators of pathophysiological mechanisms of cognitive impairment in essential tremor

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Mentor: Assoc. Prof. Svetlana Tomić, M.D., Ph.D., UHC Osijek, Croatia

Introduction: Essential tremor (ET), the most common movement disorder, was long considered a benign motor condition, but growing evidence shows it also involves non-motor features such as cognitive impairment. Cerebellar dysfunction and disrupted cerebello-thalamo-prefrontal connectivity are thought to underlie both motor and cognitive deficits in ET. As these circuits influence both cognition and oculomotor control, eye movements may reflect early cognitive changes. Studying oculomotor abnormalities may reveal early neural markers and clarify cerebellar involvement in cognitive decline. While eye-tracking is used in other neurodegenerative disorders, it remains underutilized in ET.

Hypothesis: Patients with essential tremor and cognitive impairment (ET+) will show more pronounced oculomotor abnormalities compared to patients without cognitive impairment (ET-), indicating a key role of cerebellar dysfunction in the development of cognitive impairment in ET.

Aims:

- Compare eye movements in ET patients and healthy controls
- Compare eye movements between ET+ and ET− groups
- Assess associations between oculomotor performance and cognitive status
- Identify potential oculomotor biomarkers of cognitive decline in ET
- Explore the role of cerebello-prefrontal connectivity in ET-related cognitive impairment

Materials/Participants and Methods: Sixty participants: 20 ET+, 20 ET-, and 20 healthy controls, matched by age and sex. Cognitive assessment includes MoCA, FAB, MCST-CA, RAVLT-DR, DSB, BDI-II. Eye movements will be recorded with Tobii eye-tracker and analyzed for saccades, smooth pursuit, and fixation**. Inclusion:** Clinically confirmed essential tremor. **Exclusion:** Neurological, psychiatric, or ophthalmological disorders or diseases, and use of medications that may affect eye movements or cognitive functions.

Research Plan: This cross-sectional study will use group comparisons and correlation analysis, while logistic regression with ROC analysis will assess the predictive value of eye movement parameters as biomarkers.

Significance/Expected Scientific Contribution: The study may clarify neural mechanisms of cognitive dysfunction in ET and support the use of eye-tracking as a non-invasive tool. Results could aid early detection of cognitive decline and inform differential diagnosis.

MeSH/Keywords: Essential Tremor, Cognitive Impairment, Eye Movements, Cerebellum, Biomarkers

Abstract Title: Alteration of microvascular reactivity in patients with hypertension and chronic kidney disease is related to increased oxidative stress

Part of the Disertation Proposal: The role of miRNAs in the regulation of oxidative stress and microvascular reactivity in chronic kidney disease

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Mentor: Prof. Ines Drenjančević M.D., Ph.D., Department of Physiology and Immunology, Faculty of Medicine Osijek, Osijek, Croatia

Co-mentor: Assoc. prof. Helena Lenasi, Ph.D., Institute of Physiology, Faculty of Medicine, University of Ljubljana, Slovenia

Introduction: The pathogenesis of CKD involves endothelial dysfunction and oxidative stress, but their interplay remains underexplored.

Aims: This pilot study examined alterations in peripheral microvascular reactivity and oxidative/antioxidative status in patients with hypertension and chronic kidney disease (CKD).

Materials/Participants and Methods: A cross-sectional study included 27 age- and sex-matched non-smokers (hypertensive N=10, CKD N=7, controls N=7). Measurements included anthropometry, blood pressure, and biochemical markers. Microvascular function was assessed by laser Doppler flowmetry in response to post-occlusive reactive hyperemia, iontophoresis of acetylcholine, and sodium nitroprusside. Oxidative stress markers (H_2O_2, $ONOO^-$, $O_2\cdot^-$) in PBMCs were assessed via flow cytometry (BD FACSCanto II), and antioxidant enzyme activities (SOD, catalase, GPx) by spectrophotometry. Ethical approval was obtained (#2158-61-46-24-121); participants gave informed consent (ClinicalTrials.gov Identifier: NCT06316284).

Results: CKD patients had higher waist circumference, waist-to-hip ratio, serum urea/urates, and systolic blood pressure than controls, as well as increased urine albumin/protein levels and lower sodium excretion. Acetylcholine-induced vasodilation was reduced in CKD, while SNP responses

and PORH were similar across groups. H_2O_2/$ONOO^-$ levels were elevated in hypertensives vs. controls, while superoxide levels were lower. In CKD, H_2O_2 was increased and superoxide reduced compared to both other groups. SOD activity was reduced in hypertensives but elevated in CKD; catalase and GPx activities were similar across groups. A strong positive correlation between GPx and H_2O_2 levels was found in CKD ($r=0.96$, $p=0.009$).

Conclusion: CKD is associated with impaired endothelial-dependent microvascular function and increased oxidative stress, alongside dysregulated antioxidant responses.

MeSH/Keywords: Antioxidant Response Elements/ Hypertension/ Microcirculation/ Oxidative Stress/ Renal Insufficiency, Chronic

Acknowledgement: Funded by Faculty of Medicine Osijek (IP18-MEFOS-2024 and IP20-MEFOS-2025, PI: I. Drenjančević). Accepted for poster presentation at ESM2025, May 19–22, Szeged, Hungary.

Abstract Title: Effect of consumption of chicken meat enriched with omega-3 polyunsaturated fatty acids on oxidative stress marker levels in young healthy individuals

Part of the Dissertation Proposal: „Effect of consumption of food enriched with omega-3 polyunsaturated fatty acids on vascular function and oxidative stress levels in healthy young subjects"

PhD candidate: Tihana Nađ, M.D., Clinic of Pediatrics, University Hospital Centre Osijek; Department of Pediatrics, Faculty of Medicine Osijek, University of Osijek, Osijek, Croatia.

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Introduction: Functional food not only provides appropriate nutritional benefits but also positively affects one or more targeted functions in the body, enhances health, and reduces the risk of disease. While the mechanisms behind the beneficial effects of n-3 PUFAs on human health are not fully elucidated and are still being intensively researched, their antioxidant and antiinflammatory properties are suggested to be the most important preventive and therapeutic effects. The most notable features of n-3 PUFA's antioxidant and anti-inflammatory activity are competition with arachidonic acid for enzymes involved in the biosynthesis of pro-inflammatory mediators and production pro-resolving lipid mediators. Furthermore, resolvins (Rv) are small molecules formed from n-3 fatty acids that can promote the resolution of inflammation since they decrease pro-inflammatory gene expression and mediators.

Aims: The present study aimed to investigate the effects of n-3 PUFAs enriched chicken meat consumption on the body's oxidative status in young and healthy people, without any disease or inflammatory condition.

Participants and Methods: 39 healthy young participants were included in this double-blind, placebo-controlled, randomized, interventional study. All participants consumed approximately 500 g of quick-roasted chicken meat for 21 days, and were divided in two groups: control group consumed regular chicken meat (breast and thigh muscle, n-3 PUFAs content ~118 mg/day), whereas n-3 PUFAs group ate n-3 PUFA-enriched chicken meat (breast and thigh muscle, n-3

PUFAs content ~1500 mg/day). The participants had two study visits, during which all measurements were taken. Serum biomarkers of oxidative stress were determined using spectrophotometry. Lipid peroxidation products are indicators of the level of created oxidative stress, which are measured using TBARS (thiobarbituric acid reactive substances) method, whereas the ferric-reducing ability of plasma (FRAP) method is considered a serum biomarker of the blood's antioxidant capacity. Further, the serum activities of antioxidant enzymes glutathione peroxidase (GPx) and superoxide dismutase (SOD), and serum concentrations of resolvin E1 (RvE1) and resolvin D1 (RvD) were determined.
The study protocol and procedures met the standards of the latest revision of the Declaration of Helsinki and were approved by the Ethics Committee of the Faculty of Medicine, University of Osijek, Osijek, Croatia (Cl: 602-04/23-08/03; No: 2158-61-46-23-125). This study is part of a clinical research study investigating the effects of functionally enriched chicken eggs on cardiovascular function registered at ClinicalTrials.gov (accessed on 11 September 2023) (NCT04564690).

Results: The serum levels of the lipid peroxidation marker TBARS were not significantly changed with either regular or n-3 PUFA-enriched chicken meat consumption, whereas n-3 PUFA-enriched chicken meat consumption significantly increased the FRAP level, GPx and SOD activities. Furthermore, a three-week dietary protocol of n-3 PUFA-enriched chicken meat consumption significantly increased both RvE1 and RvD1 serum concentrations, whereas regular chicken meat had no significant effect.

Conclusion: Consuming chicken meat enriched with n-3 PUFAs may influence the physiological processes related to oxidative balance in young and healthy individuals. The findings of this study indicate that n-3 PUFAs, when consumed through enriched chicken meat, can serve as effective antioxidants. This can help in preventing or reducing oxidative stress in general health conditions.

MeSH/Keywords: functional food, omega-3 polyunsaturated fatty acid, dietary intake, antioxidant defense.

Acknowledgements: This research was supported by the European Structural and Investment Funds grant for the Croatian National Scientific Center of Excellence for Personalized Health Care, Josip Juraj Strossmayer University of Osijek (Grant Number: KK.01.1.1.01.0010), and by the Faculty of Medicine Osijek Institutional Research Projects IP-05-MEFOS-2023 and IP-08-2025 (PI Ivana Jukić).

Dissertation Proposal Title: The effect of psychotropic drugs on cholesterol metabolism and oxysterol accumulation in the lens and retina of Sprague-Dawley rats

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Mentor: Assoc. Prof. Suzana Matić, M.D., Ph.D.; Department of Ophthalmology, University Hospital Osijek, Osijek, Croatia, Faculty of Medicine, University of Osijek, Osijek, Croatia.

Co-Mentor: Prof. Marija Heffer, M.D., Ph.D.; Faculty of Medicine Osijek, University of Osijek, Osijek, Croatia

Introduction: Smith-Lemli-Opitz syndrome (SLOS), caused by biallelic mutations in 7-dehydrocholesterol reductase (DHCR7), impairs cholesterol biosynthesis, leading to 7-dehydrocholesterol (7-DHC) accumulation. Associated phenotypes include congenital cataracts and retinal degeneration. Several psychotropic drugs inhibit DHCR7, elevating 7-DHC, a highly oxidizable lipid, which promotes oxysterol formation with cytotoxic potential. Oxysterol accumulation is implicated in cataractogenesis and retinal degeneration.

Hypothesis: Aripiprazole and trazodone promote 7-dehydrocholesterol and oxysterol accumulation in ocular tissues, leading to lens opacification and retinal cell damage.

Aims:

1. Compare lens transparency and weight, post 8-week i.p. treatment with: (a) DMSO (control), (b) aripiprazole, (c) trazodone, (d) aripiprazole and trazodone.
2. Quantify cholesterol, 7-DHC, desmosterol, lanosterol, and 8-DHC in lens and retina across all groups.
3. Assess retinal layer thickness via H&E staining across all groups.
4. Quantify photoreceptor, bipolar, and ganglion cell loss; astrocyte and microglial profiles via immunohistochemistry across all groups.
5. Perform lens and retina metabolomic/lipidomic profiling using iMScope TRIO across all groups.

Methods: Forty-eight 12-month-old male Sprague-Dawley rats will be randomized into 4 groups (n=12/group):
a) DMSO; b) aripiprazole (2.5 mg/kg); c) trazodone (10 mg/kg); d) combination Injections: 5x/week for 6 weeks, daily for final 2 weeks.
At endpoint, animals will be euthanized via isoflurane overdose.

- **Right eyes:** Lens transparency (ImageJ analysis of photographs) and mass (ultra-precision balance), lipid profiling of lens and retina (HPLC-MS/MS).
- **Left eyes (6/group):** Fixed for histological (H&E) and immunohistochemical (cell-specific markers) analyses.
- **Left eyes (6/group):** Prepared for iMS-based metabolomic/lipidomic analysis.

Expected Scientific Contribution: This study will clarify how psychotropics disrupt cholesterol metabolism and contribute to cataract and retinal degeneration via oxysterol-mediated cytotoxicity. Data generated will support future translational research and may influence clinical monitoring protocols in psychiatric patients on such medications.

Research plan: This controlled animal experiment will be conducted at the Laboratory for neurobiology, Department of medical biology and genetics, Faculty of medicine Osijek, and the Animal facility of the Faculty of medicine Osijek. Duration of the experiment will be 8 weeks.

MeSH/Keywords:
aripiprazole, trazodone, oxysterols, lens, retina

Dissertation Proposal Title: Association of Endothelium-Dependent Microcirculatory Reactivity with Glycemic Control Assessed by Continuous Glucose Monitoring in Patients with Type 1 Diabetes

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Co-mentor: Assist. Prof. Silvija Canecki-Varžić, M.D., Ph.D., Clinical Hospital Center Osijek, Faculty of Medicine Osijek, University of Osijek, Osijek, Croatia

Introduction: Elevated HbA1c levels and longer duration of diabetes are major risk factors for the development and progression of microvascular complications in patients with type 1 and type 2 diabetes. Patients with type 1 diabetes have a higher risk of developing diabetic retinopathy than those with type 2 diabetes, due to greater glycemic variability and earlier disease onset. Continuous glucose monitoring (CGM) has been proven to improve glycemic control, especially in adolescents and young individuals with type 1 diabetes.

Hypothesis: There is an association between endothelium-dependent vasodilation of the peripheral microcirculation and CGM parameters of glycemic control in type 1 diabetes. Suboptimal CGM parameters, specifically the coefficient of variation, are associated with a greater degree of endothelial dysfunction and oxidative stress.

Aims:

1. To examine the association between endothelium-dependent microvascular reactivity and glycemic control parameters
2. To examine the association between oxidative stress markers and glycemic control parameters
3. To examine the association between endothelium-dependent microvascular reactivity and the control of associated cardiovascular risk factors
4. To examine the association between endothelium-dependent microvascular reactivity and general participant characteristics as well as laboratory markers of metabolic control

Materials/Participants and Methods: The study will be conducted on patients with type 1 diabetes treated with intensified insulin therapy administered via insulin pens or insulin pumps, of both sexes, aged over 18 years. The subject's anamnestic data will be gathered and body composition will be analyzed. A venous blood sample and urine sample will be collected for relevant hematological and biochemical laboratory parameters. All subjects will undergo functional testing for the assessment of endothelial dysfunction.

Research plan: Subjects will have one visit during this study at which aforementioned data will be collected.

Significance/Expected scientific contribution: Previous studies have demonstrated an association between higher glycemic variability with diabetic complications. However, further research is needed to better assess the relationship between CGM-derived metrics and all forms of diabetic complications, particularly in type 1 diabetes. The results of this study could help establish a link between CGM parameters and early functional changes in microvascular endothelial function that precede the development of complications in individuals with type 1 diabetes.

MeSH/Keywords: continuous glucose monitoring; diabetes mellitus, type 1; diabetes complications; endothelial dysfunction; oxidative stress

Dissertation Proposal Title: Psychological and Moral Aspects of Professional Engagement Among Palliative Care Professionals

PhD candidate: Ela Pejić, MSN, Health Center Osijek-Baranja County, Osijek, Croatia

Mentor: Assist. Prof. Štefica Mikšić, Ph.D., MSN, RN, Faculty of Dental Medicine and Health Osijek, University of Osijek, Osijek, Croatia

Introduction: Palliative care includes medical, psychological, social and spiritual support to the patient and family, dealing with ethical dilemmas according to the principles of patient autonomy and dignity. Providing quality palliative care requires a high level of emotional involvement, empathy, interdisciplinary knowledge, communication skills, and professional commitment. Moral distress occurs when a pearson is unable to act in accordance with ethical beliefs due to external factors (institutional, hierarchical, etc.). Prolonged exposure to moral distress can lead to emotional exhaustion, frustration, and burnout. These psychological and moral burdens affect not only the well-being of healthcare providers but also the quality of care delivered to patients. Research suggests that psychological resilience may mitigate the negative effects of distress.

Hypothesis:

1. Higher levels of resilience are associated with lower levels of burnout.
2. There is a significant relationship between moral distress and resilience.
3. Individuals over the age of 50 have lower levels of moral distress compared to younger individuals.

Aims: The main aim is to examine the levels of resilience, moral distress, and professional burnout among palliative care professionals. The study will also explore the relationships between these variables, as well as differences across age groups and professional roles.

Materials/Participants and Methods: A cross-sectional study will be conducted on a sample of professionals working in palliative care: physicians, nurses, psychologists, social workers, occupational therapists, and physiotherapists. The research instrument will include six questionnaires: a sociodemographic questionnaire, **Connor-Davidson Resilience Scale (CD-**

RISC), Oldenburg Burnout Inventory (OLBI), and the **Measure of Moral Distress for Healthcare Professionals (MMD-HP).**

Research plan: The study will be conducted in primary healthcare institutions and hospitals that provide palliative care in the Republic of Croatia. Data collection is planned for the year 2025.

Significance/Expected scientific contribution: This study will provide a deeper understanding of the positive and negative psychological and moral aspects of professional engagement in palliative care. The findings will serve as a basis for proposals for supportive strategies that can improve resilience among palliative care professionals. These strategies can serve as a basis for public health policies and educational programs in healthcare, contributing to improved quality of care for patients and their families, as well as to enhanced working conditions for care providers.

MeSH/Keywords: palliative care, moral distress, resilience, burnout, quality of care

Abstract Title: Carnosine-enriched functional food enhances micro- and macrovascular endothelium-independent vasodilation in competitive athletes

Part of the Disertation Proposal: The influence of the consumption of functional food enriched with carnosine on vascular function, cardiorespiratory endurance and oxidative stress in a population of healthy athletes

PHD candidate: Leon Perić, M.D., Department of Ophthalmology, University Hospital Center Osijek, Osijek, Croatia

Mentor: Assoc. Prof. Ana Stupin, M.D., Department of Physiology and Immunology, Faculty of Medicine Osijek, University of Osijek, Osijek, Croatia

Introduction: Carnosine is a naturally occurring dipeptide composed of β-alanine and histidine, known for its antioxidant, anti-inflammatory, and neuroprotective effects among others. Athletes are especially prone to oxidative stress due to intense physical activity, which may impair vascular function. Previous studies show that acute intense exercise can transiently reduce microvascular reactivity and endothelial function, likely due to oxidative stress and metabolic acidosis. Nutritional strategies targeting these effects are essential for promoting recovery and cardiovascular adaptation. As a dietary antioxidant, carnosine may improve vascular responsiveness and cardiovascular resilience in athletes, but evidence remains limited.

Aims: To evaluate the effect of carnosine-enriched chicken meat consumption on systemic endothelium-dependent and -independent micro- and macrovascular reactivity in healthy competitive male athletes.

Participants and Methods: Thirty-five participants (age 18-45 years) were assigned to Control (n=16) or Carnosine group (n=19) who consumed regular or carnosine enriched chicken meat for 3 weeks. Forearm skin microvascular reactivity in response to vascular occlusion (PORH), acetylcholine (AChID) and sodium nitroprusside (SNPID), brachial artery flow-mediated dilation (FMD) and nitroglycerine-mediated dilation (NTG-MD) were measured. Arterial blood pressure (BP) and biochemical parameters (lipid profile, AST, ALT, GGT) were assessed pre- and post-intervention.

Results: Both micro- and macrovascular endothelium-independent vasodilation were increased, and diastolic and mean arterial BP were decreased in Carnosine group following dietary protocol. Microvascular endothelium-dependent response (PORH) was increased in Carnosine group.

Conclusion: 3-weeks of carnosine supplementation in form of functional food enhances endothelium-dependent and the vascular smooth muscle-dependent vasodilation in both peripheral micro- and microcirculation.

MeSH/Keywords: Carnosine, functional food, endothelium, vascular smooth muscle, microcirculation

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Dissertation Proposal Title: Changes in macrovascular reactivity depending on parameters of glycemic regulation from continuous glucose monitoring system in patients with type 1 diabetes

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Mentor: Assist. Prof. Silvija Canecki-Varžić, M.D., Ph.D., Clinical Hospital Center Osijek, Faculty of Medicine Osijek, University of Osijek, Osijek, Croatia

Co-mentor: Prof. Ines Bilić-Ćurčić, M.D., Ph.D., Clinical Hospital Center Osijek, Faculty of Medicine Osijek, University of Osijek, Osijek, Croatia

Introduction: Endothelial dysfunction represents an early stage of vasculopathy and serves as a prognostic indicator of diabetic complications. In patients with diabetes, endothelial cells are damaged by oxidative stress. Cellular adhesion molecules involved in inflammatory processes-ICAM-1, VCAM-1, as well as adiponectin and endocan are considered potential biomarkers of endothelial dysfunction. The relationship between glycemic variability and the development of complications remains unclear, particularly regarding which period of glycemic variability (time in, above, or below range), in combination with the coefficient of variation, contributes most significantly to the development of complications.

Hypothesis: There is a correlation between functional and structural changes in the conductive blood vessels and glycemic regulation parameters obtained through continuous glucose monitoring (CGM) in patients with type 1 diabetes.

Aims:

1. To investigate the association between macrovessel reactivity and glycemic regulation parameters.

2. To investigate the association between markers of endothelial dysfunction and glycemic regulation parameters.

3. To investigate the association between macrovessel reactivity and the control of associated cardiovascular risk factors, general characteristics and laboratory indicators of metabolic control.

Materials/Participants and Methods: The research will be conducted on subjects with T1D who are treated with intensified insulin therapy administered via insulin pens or pump, and using a CGM system. To observe a medium effect in the difference of numerical variables, with a significance

level of 0.05 and a power of 0.8, the minimum required sample size is 29 subjects. The subjects' anamnestic data will be gathered and body composition will be analyzed. A venous blood sample and urine sample will be collected for relevant hematological and biochemical laboratory parameters. All subjects will undergo functional testing for the assessment of endothelial dysfunction.

Research plan: Subjects will have one visit during this study at which aforementioned data will be collected.

Significance/Expected scientific contribution: The proposed research will result in new knowledge about the impact and association of glycemic variability, using the coefficient of variation from CGM, on the development of macrovascular complications, with a focus on endothelial dysfunction.

MeSH/Keywords: continuous glucose monitoring; diabetes mellitus, type 1; diabetes complications; endothelial dysfunction; oxidative stress

Abstract Title: Role of vestibular rehabilitation in cognitive deficit

Part of the Dissertation Proposal Title: Influence of vestibular rehabilitation on cognitive functions and vestibular recovery in patients with unilateral vestibular impairment

PhD candidate: Matej Rezo, M.D., Department for Otorhinolaryngology and Head and Neck Surgery, University Hospital Center Osijek, Faculty of Medicine, University of Osijek, Osijek, Croatia.

Mentor: Assoc. Prof. Tihana Mendeš, M.D., Ph.D., Department for Otorhinolaryngology and Head and Neck Surgery, University Hospital Center Osijek, Faculty of Medicine, University of Osijek, Osijek, Croatia.

Introduction: In clinical practice, often is found that patients with unilateral vestibular impairment have poor cognitive functions, most commonly short term and work memory, language barriers and time and space orientation. The exact mechanism behind said claim is not fully understood. One suggested explanation is low and weak transmission of vestibular information towards hypocampus. Furthermore, the most favorable option for treatment for these patients is vestibular rehabilitation, specialized set of exercises designed to gain and maintain central compensation. Besides vestibular rehabilitation, exercises designed for enhancing cognitive functions can also help in inhibiting primitive reflexes that can reappear later in life in patients with vestibular impairment and other neurological conditions.

Aims:

1. Compare subjective scope of vestibular sense recovery based on results of DHI and SF-36 questionnaire before and after therapy.

2. Compare differences in cognitive functions among patients with and without unilateral vestibular impairment using MoCA questionnaire before therapy.

3. Compare cognitive functions before and after therapy among patients with unilateral vestibular impairment based on results of Montreal Cognitive Assessment score (MoCA).

4. Compare objective scope of vestibular sense recovery based on result of covert and overt saccades before and after therapy.

5. Compare subjective scope of cognitive functions recovery based on carried out cognitive exercises and MoCA test results.

Materials/Participants and Methods: The study will include 64 patients divided into three groups. All patients must be diagnosed with unilateral vestibular impairment. Difference between first and second group will be result of MoCA test and third group will be control group. Subjective progress will be measured by DHI and SF-36 questionnaires in both groups while cognitive functions will be measured in all patients by Montreal Cognitive Assessment (MoCA). Primitive reflexes will be tested in first group before and after therapy among patients with vestibular and cognitive impairment.

Results: So far we collected data from ten different patients diagnosed with unilateral vestibular impairment who also referred to us on regular checkup 12 weeks after suggested treatment. Initial MoCA score in these patients was ranged from 17-24 thus confirming cognitive dysfunction. Eight patients out of ten had improvement in MoCA after treatment with average score of 27 with slight difference among group who perform cognitive exercises along vestibular rehabilitation contrary to those who only perform exercises from vestibular rehabilitation program. All patients also had improvement in both DHI and SF-36 questionnaire after treatment. However, none of these patients had positive primitive reflexes on clinical exam prior to treatment.

Conclusion: Specially designed exercises for improving cognitive functions have positive impact on vestibular recovery when they are performed simultaneously with standard vestibular rehabilitation. However, we have yet to investigate whether these exercises also can or can’t supress primitive neurologic reflexes among targeted group of patients with cognitive impairment.

MeSH/Keywords: cognitive functions, instability, rehabilitation, vestibular dysfunction, dizziness

The response of healthcare workers in the Republic of Croatia to the National Colorectal Cancer Screening Program

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Introduction: According to the Cancer Registry of the Republic of Croatia, 3,863 new cases of colorectal cancer (CRC) were diagnosed in 2022. In terms of cancer-related mortality, CRC was the second leading cause of death from malignant neoplasms in 2023, with 1,996 deaths recorded marking the lowest figure in the past six years. The National Program for Early Detection of Colorectal Cancer (CRC Screening Program) was launched in 2007. The program invites individuals aged 50–74 to undergo a guaiac fecal occult blood test, followed by a colonoscopy for those with positive results. However, consistent support from healthcare professionals may be lacking, potentially influencing public participation. The National Registry of Healthcare Workers (NRHW) maintains data on individuals employed in the healthcare system, while the CRC Screening Program Registry a web-based application tracks the screening process. Regional differences in participation have been observed, with northern counties demonstrating higher response rates.

Hypotheses: Healthcare workers with higher levels of education are more likely to respond to the CRC screening program. Healthcare workers in northern counties of Croatia exhibit higher response rates to CRC screening compared to those in other counties.

Aims: The aim of this study is to examine the response of healthcare workers to the colorectal cancer (CRC) screening program, with a focus on differences based on the level and type of professional education. Additionally, the study seeks to compare the response rates of healthcare workers from northern and southern regions of Croatia. It also aims to analyze variations in response according to age (grouped in five-year intervals), gender, and place of work.

Materials/Participants and Methods: This is a cross-sectional study. Data will be obtained by merging anonymized records from the CRC Screening Program Registry and the NRHW. Variables will include professional education level, type of healthcare worker, age, gender, county, and workplace. The NRHW contains data on 56,155 individuals. For this study, the sample will be limited to those born between 1944 and 1972. Respondents are defined as individuals who responded to the screening invitation letter. Nominal variables will be analyzed using proportions across groups. Logistic regression will assess factors associated with screening response. Both univariate analyses and multivariate logistic regression models will identify independent predictors of response. Chi-square tests (χ^2) will be used for group comparisons, with Fisher's exact test applied when necessary.

Research Plan: Data merging will be performed using a common anonymized identifier, without access to personal information. The final dataset will replace personal identification numbers (OIBs) with anonymized codes. Results will be analyzed and compared by NUTS2 regions.

Significance/Expected Scientific Contribution: This study aims to contribute to understanding healthcare workers' participation in CRC screening programs. The findings are expected to be uniquely relevant to Croatia, as responses to such programs are influenced by a complex interplay of cultural, behavioral, educational, and systemic factors. Moreover, the methodology merging data from two national registries represents a novel approach not previously documented in available scientific literature.

MeSH/Keywords: colorectal cancer screening, CRC screening registry, response to CRC screening, registry of healthcare workers, education level

Dissertation Proposal Title: Molecular factors in the development of morbid obesity and their correlation with cardiovascular, metabolic and tumor status

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Mentor: Prof. Dragan Primorac, M.D., Ph.D.,St. Catherine Specialty Hospital, Zagreb; School of Medicine, Josip Juraj Strossmayer University of Osijek, Osijek, Croatia; Medical School, University of Rijeka, Rijeka, Croatia; Medical School, University of Split, Split, Croatia; Faculty of Dental Medicine and Health, Josip Juraj Strossmayer University of Osijek, Osijek, Croatia; Department of Biochemistry & Molecular Biology, The Pennsylvania State University, State College, PA, USA; University of New Haven, Henry C. Lee College of Criminal Justice and Forensic Sciences, West Haven, CT, USA; Medical School REGIOMED, Coburg, Germany

Co-Mentor: Prof. Martina Smolić, M.D., Ph. D., Faculty of Dental Medicine and Health Osijek, University of Osijek, Osijek, Croatia

Introduction: Obesity is multifactorial disease with genetic and environmental factors. Pathophysiologically, obesity is chronic inflammation state which results in many metabolic disorders (diabetes mellitus, hyperlipidemia), but also hypertension, cardiovascular diseases and tumors.

Hypothesis: There is a genetic predisposition that leads to morbid obesity (BMI >40 kg/m2). Since obesity is an inflammatory process, it can be quantified by analysing total N-glycans in plasma as a predictor of inflammation. Also, since obesity is a cardio-metabolic disease, there is a connection between obesity genes and genes for cardiac and metabolic diseases, and possibly also with genes for tumors. Weight loss leads to a decrease in inflammation and an improvement in metabolic parameters.

Aims: The goals of this research are to determine the molecular basis of morbid obesity through whole-genome analysis and the correlation of genes responsible for obesity with genes associated with the development of cardiovascular, metabolic and tumor diseases. Also, the impact of weight loss on inflammatory processes and certain metabolic disorders will be investigated.

Materials/Participants and Methods: This study is designed in two phases. Firstly, case control study with aim to determine molecular basis of morbid obesity and potential correlation with genes linked to cardiovascular, metabolic and tumor disease. Twenty participants, both gender, aged between 20-55 years with morbid obesity will be enrolled in the study. Control group will be subjects with normal BMI. To the both group genome testing on 1130 genes will be done. Second phase is prospective interventional study in which only group with morbid obesity will be included and aim is to observe impact of loosing weight on inflammatory condition and specific metabolic disorders. Initially clinical assessment and plasma N-glycom Ig analysis will be done.

Participants will be then given consultation regarding nutritional plan and exercise during next 6 months and their progress will be monitored. Another clinical assessments will take place after 3, 6 and 12 months.

Research plan: Study will be conducted at St. Catherine Specialty Hospital, Zagreb.

Significance/Expected scientific contribution: This research will provide data on the possible causes of morbid obesity and the correlation with genetically determined cardiovascular, metabolic and tumor status, thus contributing to timely prevention and personalized treatment.

MeSH/Keywords: cardiovascular disease; glycosylation; metabolic disease; morbid obesity; neoplasms; whole genome sequencing

Dissertation Proposal Title: The Correlation between HLA Class I Alleles and KIR Receptors in Women with Idiopathic Infertility

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Co-mentor: Assist. Prof. Mirjana Suver Stević, Osijek University Hospital Center, Clinical Institute for Transfusion Medicine, Department of Laboratory Diagnostics and Clinical Transfusion Medicine, Laboratory of Molecular and HLA Diagnostics, Osijek, Croatia

Introduction: Infertility affects between 8 to 12% of couples worldwide. In 15% of cases, no clear infertility cause is found, which is an idiopathic infertility diagnosis. Immune system issues are one of the potential causes of infertility. Since KIR receptors, located on the surface of NK cells, have a significant role in the defense of the immune system, contemporary research has emphasized their role in recurrent miscarriages and implantation failure. Moreover, the research focuses on the interaction between KIR receptors on uterine NK cells and HLA class I molecules, with the dominant role of HLA-C that is located on the embryo cell surface and is important for embryo implantation. The discovery of correlations between KIR and HLA-C has provided valuable information about the complexity of maternal-fetal immunological interactions that may determine the pregnancy success. A great diversity of maternal KIR and fetal HLA-C ligands is associated with KIR/HLA-C combinations on the trophoblast which suggests that some combinations may be more favorable for embryo implantation and pregnancy maintenance. The potential similarity and high degree of HLA class I genotype matching between partners, especially at the -A and -B loci, as well as the presence of alleles that have a major role in the development of various autoimmune diseases, could be the cause of unsuccessful pregnancy.

Hypothesis: There is a potential correlation between HLA class I locus genotype, KIR haplotype, and idiopathic infertility.

Aims:

To explore the correlation between idiopathic infertility and a high degree of concordance in HLA-A and -B between partners

To explore the homozygote KIR A and B haplotype distribution difference among the patients

To analyze the distribution of certain HLA class I alleles in patient study groups who are at increased risk of autoimmune diseases

Materials/Participants and Methods: The data sample will include 100 female patients, 50 with an idiopathic infertility diagnosis and 50 who had accomplished a successful pregnancy.

Peripheral blood samples of all patients will be collected and its genomic DNA will be isolated using the QIAamp® DNA Mini Kit. Isolated DNA samples will be spectrophotometrically determined for concentration and purity, after which they will be stored at -20 °C.

Patients included in the study will undergo molecular typing of HLA class I (HLA-A, -B and -C) and KIR receptors by hybridization of biotin-labeled amplification products to specific oligonucleotide probes (SSO) attached to the surface of the microspheres. Thus, commercial kits from the manufacturer Werfen will be used for all loci and analyzed on the Luminex 200 device through the computer program xPonent.

Research Plan: An observational case/control study will be conducted at the Department of Human Reproduction and the Laboratory for Molecular and HLA Diagnostics at the University Hospital Center for a period of two years.

Expected Scientific Contribution: The research of polymorphic KIR genes, their HLA-C ligands, and the HLA-A and -B loci alleles are justified in the idiopathic pregnancy response context and could represent the future for predicting a successful pregnancy.

Keywords: assisted reproductive technic, HLA class I, infertility, KIR receptors, pregnancy

Dissertation Proposal Title: The infuence of health literacy to the patient satisfaction after radiologic examination

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Mentor: Prof. Maja Miškulin, M.D., Ph.D., Faculty of Medicine Osijek, University of Osijek, Osijek, Croatia

Introduction: Health literacy is a multidimensional concept conventionally defined as the degree to which individuals have the capacity to attain, understand, and use health information as a basis for making correct health decisions and following treatment-related advice. Healthcare professionals are expected to provide more information and a better quality of service to patients. In recent years, there has been a growth in organizations dedicated to analyzing the development and dissemination of healthcare information. Some studies have shown that most patients who come for a particular examination do not know well why they are there. Shared decision-making in patient care is a sensitive, ethical and legal concept that requires well-developed communication skills on both sides. The partnership between patient and physician enables the healthcare system to develop an efficient method for delivering the highest quality healthcare. That is why it is important to work as intensively as possible on informing patients.

Hypothesis: Health literacy affect patient satisfaction after radiologic examination

Aims: to determine whether there is a connection between health literacy and patient satisfaction with the provided radiological examination; to investigate whether there is a difference in satisfaction with radiological examinations between patients who are coming for the first time and those who have come for the same examinations multiple times

Materials/Participants and Methods: Participants will be patients referred for radiological examinations. Participants will be assessed throught questionnaires. The expected number of participants is 300.

Research plan: Collecting data. Conducting research. Analysis of data and results. Publishing the results. Participants in this study will be voluntary and recruited from the University hospital „Sveti Duh” Zagreb, Department of radiology.

Significance/Expected scientific contribution: The results will raise awareness of the need to improve patients' health literacy. At the hospital level, they will contribute to additional education of radiological technologists and physicians.

MeSH/Keywords: health literacy; access to care; unmet medical need; radiology, patient satisfaction

Dissertation Proposal Title: Systemic endothelium-dependent vasodilation and endothelial activation in prehypertension.

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Co-Mentor: Prof. Ines Drenjančević, Faculty of Medicine Osijek, University of Osijek, Osijek, Croatia

Introduction: Prehypertension (PreHT), defined as high-normal blood pressure (130–139/85–89 mmHg), is associated to an elevated risk of cardiovascular disease (CVD). Studies suggest that effective PreHT control could prevent over 10% of CVD cases. Proposed mechanisms underlying this risk include endothelial dysfunction, oxidative stress, sympathovagal imbalance, inflammation, and renin-angiotensin system activation. Endothelial injury and oxidative imbalance has been suggessted as pivotal to this process, yet controlled clinical studies directly assessing vascular function and oxidative stress in PreHT are limited.

Hypothesis: PreHT induces systemic endothelial dysfunction and activation in both micro- and macrocirculation, reduces the regenerative potential of endothelial progenitor cells (EPCs), and is associated with elevated oxidative stress.

Aims: This study aims to assess endothelial function, activation, and regenerative capacity in PreHT individuals compared to those with optimal or high-normal blood pressure (BP). It also aims to explore the contribution of oxidative stress to observed endothelial alterations.

Participants and Methods: This cross-sectional study will include 90 adults (both sexes), divided into three groups: normotensive (≤129/84 mmHg), prehypertensive (130–139/85–89 mmHg), and newly diagnosed stage 1 hypertensive (140–150/90–100 mmHg), based on 24-hour ambulatory BP monitoring. Two study visits are planned: the first for BP monitor placement, and the second for venous blood sampling and cardiovascular measurements. Endothelium-dependent and -

independent dilation of microcirculation (forearm skin) will be assessed via laser Doppler flowmetry, and of macrocirculation (brachial artery) via ultrasound. Arterial stiffness will be assessed using impedance cardiography. EPCs will be detected via flow cytometry. Biomarkers of endothelial activation, and oxidative stress will be measured using spectrophotometry and ELISA.

Research plan: The study will include 90 participants (30 per group) over 48 months.

Significance/Expected scientific contribution: This research will enhance understanding of PreHT pathophysiology and support early interventions - lifestyle changes and targeted therapies - to preserve endothelial health and prevent CVD progression in prehypertensive individuals.

MeSH/Keywords: Prehypertension; Endothelium; Oxidative stress; Endothelial progenitor cells; Arterial stifness

Dissertation proposal Title: The Effect of continuous Femoral Nerve block on Oxidative Stress and Quadriceps Strength in Patients Undergoing Knee Arthroplasty: A Randomized Controlled Trial

PhD candidate: Ninoslava Vonić, M.D., Clinical Hospital Center Osijek, Osijek, Croatia

Mentor: Assist. Prof. Ivan Radoš, M.D.,Ph.D., Clinical Hospital Center Osijek, Faculty of Medicine Osijek, University of Osijek, Osijek, Croatia

Introduction: Knee arthroplasty is often accompanied by considerable pain, particularly in the early postoperative period. The operative procedure involve the application of a tourniquet to the thigh, which leads to ischemia of the limb below the site of application, thereby causing oxidative stress and ischemia-reperfusion injury via release of inflammatory cytokines and reactive oxygen species. This study aims to investigate whether the use of a femoral nerve catheter with continuous low-concentration ropivacaine infusion affects systemic oxidative stress markers and postoperative quadriceps strength.

Hypothesis: Hypothesis is that patients with continuous femoral nerve block after knee arthroplasty with tourniquet use, are expected to have lesser degree of oxidative stress and inflammatory response.

Aims:

1) To determine the influence of continuous femoral nerve block on developement of oxidative stress and inflamatory response in patients with knee arthroplasty
2) To evaluate influence of continuous femoral nerve block on quadriceps muscle weaknes and function
3) To evaluate how continuous femoral nerve block affects pain (measured by VAS pain scores)
4) To measure aditional analgesic required in both groups

Materials/participants and methods: This study is designed as randomised controled trial. It will include patients who undergo knee arthroplasty with the use of torniquet.

Inclusion criteria: patients ASA status I-III

Exclusion criteria: patients who take imunosupressive and imunomodulative medications .

Patients will randomly be divided into two groups. Both groups will have spinal anesthesia. Patients in the first group will also have femoral nerve block and cathether will be inserted alongside femoral nerve. They will receive continuous local anesthetic ropivacaine 0.2%, 2ml/h until 72h postoperative. After 72 h cathether will be removed. The control group will not receive femoral nerve block nor cathether.

We will measure product of oxidative stres (SOD,MDA) and inflamation (CRP, IL6) by venous blood sampling. There will be four measurements (T0- before the start of ansthesia procedure, T1- 1hour after release of torniquet, T2- 24 hours after end of the operation and T3-72 hours after the procedure).

We will measure quadriceps muscle weakness and function by TUG(timed up and go test) and MMT (manual muscle testing) .

VAS (visal analog scale) score for pain will be assesed every 4 hours up to 72 h. We will measure analgesic requirements and need for aditional analgetic drugs.

Postoperative complications will also be recorded. Before hospital discarge patients will take QoR-15C test.

Research plan:

1. Screening of patients for inclusion/exclusion criteria
2. Laboratory analysis of venous blood sampling
3. Statistical analysis
4. Publication of the result

Expected scientific contribution: To determine whether continuous femoral nerve analgesia using low concentrations of ropivacaine can modulate systemic oxidative stress while preserving quadriceps function following knee arthroplasty with tourniquet use.3

Keywords: knee arthroplasty, pain, continuous femoral nerve block, oxidative stress

Dissertation Proposal Title: Application of gold nanoparticles for more efficient treatment of Parkinsons disease with levodopa

PhD candidate: Filip Vrban, M.D.; UHC Sisters of Charity, Zagreb, Croatia

Mentor: Prof. Krešimir Rotim, M.D., Ph.D.; University of Applied Health Scienties, Zagreb, Croatia.

Associate Mentor: Prof. Ivana Vinković Vrček, Ph.D.; Institute for Medical Research and Occupational Medicine, Institute of Toxicology, Zagreb, Croatia

Introduction: Parkinson's disease is a chronic, progressive neurodegenerative disorder that primarily affects movement control. The gold standard treatment for Parkinson's disease remains dopamine replacement therapy (DRT), which has its own negative effects. The blood brain barrier (BBB) is the one that needs to be overcome by new pharmacological formulations because it represents the most resistant barrier between the brain and the bloodstream, which makes it extremely difficult to deliver pharmacologically active substances to the targeted areas in the brain. Application of gold nanoparticles (AuNPs) as levodopa delivery system is the main backbone of this doctoral research. Antioxidant and anti-inflammatory properties, immunomodulatory activities, low toxicity, biocompatibility, BBB penetration ability, high bioavailability and biodegradability are the main characteristics of AuNPs making them suitable for use in drug delivery. This doctoral research aims to examine the efficacy and safety of AuNPs as an innovative nanoformulation of levodopa to improve efficacy and reduce side effects in the treatment of Parkinson's disease.

Hypothesis: Gold nanoparticles (AuNPs) are safe for use as levodopa carriers, reduce oxidative damage in tissues caused by long-term levodopa administration, and improve the effectiveness of levodopa administration in the treatment of Parkinson's disease.

Aims: The main goal of this doctoral dissertation is to examine the application of AuNP as a levodopa carrier in an animal model of Parkinson's disease.

Materials/Participants and Methods: Animal rodent model was used, i.e. Wistar Han rat strain, 12 weeks old with equal sex distribution. Rats were divided in 2 groups, healthy rats and Parkinson disease rat model. Different dosage of levodopa and/or AuNp-levodopa will be administered to the

PD group of rats. After the application of nanoparticles, behavioral tests, biochemical and hematological tests, as well as oxidative stress analysis will be performed on PD and healthy rats.

Research plan: Investigation was carried out using an in vivo hemiparkinsonian rat model of PD. This model was performed by injection of 6-hydroxydopamine into the right hemisphere of the rat brain according to the stereotaxic atlas. Behavioral assays including the rotarod test, gait analysis and neurological severity score were used to evaluate the changes in motor activity in rats before and after surgery as well as the efficacy of the treatment.

Significance/Expected scientific contribution: The research results will demonstrate the potential of nanoAu as an innovative nanoformulation with the aim of reducing drug doses, reducing side effects, increasing sustainability and neuroprotective effects.

MeSH/Keywords: Parkinsons disease, Gold nanoparticles, Levodopa

Dissertation proposal tittle: The influence of Hoffa's adipose tissue on the development of knee osteoarthritis

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Mentor: Assoc. Prof. Anđela Grgić , M.D. , Ph.D., Faculty of Medicine Osijek, University of Osijek, Osijek, Croatia

Co-Mentor: Assist. Prof. Vjekoslav Wertherimer, M.D., Ph.D.

Introduction: Osteoarthritis of the knee is a chronic disorder that causes damage to cartilage and surrounding tissue, and is characterized by pain, stiffness and loss of function. It is a disorder that also has it's inflammatory component. Hoffa's adipose tissue in the knee has an endocrine function that influences the inflammatory response and thus the degree of osteoarthritis development. The data collected from the analysis of Hoffa's adipose tissue will be used to gain new knowledge about its influence on the development of osteoarthritis.

Hypothesis: The hypothesis of the proposed research is that by sampling Hoffa's adipose tissue from osteoarthritic knees and analyzing it along with serum analysis, we can gain new insights into the influence of Hoffa's adipose tissue on the degree of development of knee osteoarthritis.

Aims: Aim of proposed research is to examine the influence of pro- and anti-inflammatory cytokines secreted from Hoffa's adipose tissue on the degree of development of knee osteoarthritis with respect to sociodemographic indicators.

Materials and methods: Proposed research will use serum and Hoffa's fatt samples from patients of both sexes operated on at the Department of Orthopaedics of the Osijek Clinical Hospital Center who underwent knee alloarthroplasty and arthroscopy with osteoarthritis development grades from 1 to 4, considering sociodemographic indicators.

Research plan: After preparing the documentation and obtaining approval from the ethics committees, we plan to collect samples of Hoffa fat pad in the first year. The following time is planned for sample analysis. The time after that is reserved for statistical processing , writing and publishing a scientific paper and writing of the doctoral thesis.

Significance/contribution: We hope that after a completion of proposed research we will gain a clearer insight into how and to what extent the endocrine Hoffa adipose tissue influences the development of knee osteoarthritis.

Mesh/ Keywords: Endocrine function , Hoffa fat pad, Knee osteoarthritis

Abstract title: The influence of intervertebral disc colonization with low-virulence bacteria on degenerative disc changes, clinical status and postoperative recovery

Part of the Disertation Proposal: Microbiological processing of sampled disc and paraspinal tissue to verify colonization of disc tissue by anaerobic bacteria.

PHD candidate: Milutin Vukadinović, M.D., Clinical Hospital Center Osijek, Faculty of Medicine Osijek, University of Osijek, Osijek, Croatia

Mentor: Prof. Domagoj Drenjančević, M.D., Ph.D., Clinical Hospital Centar Osijek Faculty of Medicine Osijek, University of Osijek, Osijek, Croatia

Introduction: Research indicates that C.acnes is the most commonly isolated bacterium in the intervertebral disc. It was assumed that bacteria together with biomechanical processes have an impact in the spinal degenerative.

Aims: To determine the occurrence of bacteria in degeneratively altered discs that cause radicular and/or myelopathic symptomatology as well as the correlation with radiological changes in the spine with the clinical picture of patients in the examined sample, pathohistological description of the disc sample with reference to the patient's clinical status for a maximum of 6 months after surgery.

Participants and Methods: The observed sample will include all adult, immunocompetent patients with a clinical presentation of radiculopathy and/or myelopathy caused by degenerative disc disease of the spine with MRI scans of the appropriate part of the spine operated in the period from 2024 to 2026. As a type of surgery, microdiscectomy will be performed as an elective procedure. Paraspinal tissue which serves as a control sample and disc tissue will be sampled at each operation. Samples will be delivered in saline followed by inoculation in the biocabinet using the usual aseptic technique. Each sample will be inoculated on nutrient substrates under aerobic and anaerobic conditions. Cultures isolated from non-nutrient media will be identified by MALDITOF-MS. The aim of the pathohistological analysis is to determine, after adequate preparation of the disc tissue, whether there is a subclinical, acute or chronic infection

Results: Within a year, 76 disc and paraspinal tissue samples were sampled in 75 patients. The positive group consists of 7 samples (4 C.acnes, 2 S.epidermidis and 1 S.haemolyticus). There were 18 contaminations (11 C.acnes) in the negative group.

Conclusion: None of the patients developed postoperative wound infection or spondylodiscitis. The results support the colonization of the disk with mostly C.acnes.

MeSH/Keywords: Disc herniation, lumbar spine, colonisation, radiculopathy, anaerobic bacteria

Dissertation Proposal Title: The role of dysnatremia and hormonal imbalance in the pathophysiology and prognosis of COVID-19

PhD candidate: Mihaela Zlosa, M.D.; Clinic of Infectious Diseases, University Hospital Centre Osijek, Osijek, Croati

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Introduction: The COVID-19 pandemic caused by the SARS-CoV-2 virus has posed a global health challenge, including endocrine disorders and electrolyte imbalances, such as dysnatremia and thyroid dysfunction, which are associated with poor disease outcomes. Hyponatremia is present in 20-30% of COVID-19 patients and is linked to higher mortality, while hypernatremia can lead to a mortality rate of up to 60% in severe cases. Additionally, low T3, low vitamin D, and elevated cortisol levels are frequently observed in patients with severe disease, contributing to increased susceptibility to infection and poorer outcomes.

Hypothesis: Dysnatremia and hormonal imbalances, including thyroid dysfunction, cortisol elevation, and vitamin D deficiency, significantly influence the pathophysiology and prognosis of COVID-19, with alterations in these biomarkers correlating with disease severity, adverse clinical outcomes, and higher mortality rates in hospitalized patients.

Aims: This study aims to explore the prevalence of thyroid disorders and dysnatremia in patients with acute SARS-CoV-2 infection without prior thyroid conditions. It will assess the predictive value of thyroid hormone and sodium levels for COVID-19 outcomes in hospitalized patients, as well as the relationship between dysnatremia and thyroid disturbances. Additionally, the study will assess cortisol, growth hormone, and IGF-1 as biomarkers for severe COVID-19 and explore the connection between low vitamin D levels and adverse clinical outcomes.

Materials/Participants and Methods: The study will include hospitalized patients over the age of 18 with a confirmed SARS-CoV-2 infection at the Clinic of Infectious Diseases, University Hospital Centre Osijek. Patients who fulfill the previously defined inclusion criteria and provide written informed consent will be enrolled in the study.

Research plan: This prospective cohort study will be conducted over a period of approximately 2 years. The study will focus on monitoring changes in biomarkers (sodium, thyroid hormones, cortisol, vitamin D, growth hormone, IGF-1), length of stay, disease outcomes, anamnesis, comorbidities, and clinical status. It will also include laboratory findings such as complete and differential blood counts, C-reactive protein, procalcitonin, coagulation tests (PV, INR, fibrinogen levels, d-dimer), BUN, electrolytes, liver profile, lactate dehydrogenase, IL-6, ferritin.

Expected scientific contribution: The study will provide a comprehensive insight into the interplay between electrolyte imbalances and endocrine disturbances during SARS-CoV-2 infection, focusing on their impact on disease outcomes. By identifying key biomarkers - such as sodium, thyroid hormones, cortisol, growth hormone, IGF-1, and vitamin D - it aims to uncover predictors of disease progression. The results will serve as a foundation for future research into the link between viral infections and endocrine/electrolyte disturbances.

MeSH/Keywords: dysnatremia, endocrine disorders, COVID-19, thyroid dysfunction, biomarkers

Abstract Title: Antimicrobial and antibiofilm properties of melittin and surfactin

Part of the Dissertation Proposal: "*In vitro* evaluation of antimicrobial and antibiofilm properties of melittin, nisin and surfactin "

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Introduction: Biofilms are complex communities of microorganisms that adhere to various surfaces and produce a protective matrix of polysaccharides, proteins, and DNA. One of the major challenges of biofilm infections is their increased resistance to antibiotics and they also pose a serious threat to public health. Therefore, there is an urgent need for novel strategies to prevent and treat biofilm infections, such as antimicrobial peptides.

Aims: To evaluate minimum inhibitory concentrations and antibiofilm effects of melittin and surfactin on thirteen different ATCC strains of bacteria and yeasts.

Materials and Methods: The minimum inhibitory concentration (MIC) of melittin and surfactin was determined by the two-fold serial dilution method in Mueller Hinton broth and microtiter plates with 96 wells. Stock solutions of melittin and surfactin were prepared, two-fold serial dilution was made in microtiter plates, and bacterial inoculum was added. The microtiter plates were incubated overnight and after incubation the MIC was observed. MIC represents the lowest concentration of the tested substance that inhibited the visible growth of bacteria.
The effect of melittin and surfactin on biofilm formation was tested using the co-incubation method. Two-fold serial dilutions of the tested substance were prepared again, and bacterial inoculum was added. After overnight incubation, the rest of the procedure was carried out by modifying the method described by Stepanović et al. The plates were washed with phosphate buffer saline (PBS), then 0.2% crystal violet was added, and after 15 minutes they were washed again with PBS.

Solubilization was performed with 96% ethanol. The absorption of the solution was measured with a spectrophotometer at 550 nm.

Results: MIC of melittin was 4 – 8 µg/ml for Gram-positive strains and 16 – 128 µg/ml for Gram-negative strains, except for *P. aeruginosa* (>128 µg/ml). MIC of *C. albicans* was 16 µg/ml. Biofilm reduction was observed for most of the strains. On the other hand, MIC of surfactin was above tested concentration of 1024 µg/ml. Surfactin had different effects on biofilm, causing both production and reduction depending on concentration or even type of bacteria.

Conclusion: This study shows that melittin has stronger antimicrobial and antibiofilm properties than surfactin. Antimicrobial spectrum of melittin was oriented against Gram-positive and Gram-negative bacteria, as well as *C. albicans*. Antibiofilm spectrum of both molecules covered most of isolates, although surfactin showed biofilm induction at certain concentrations. Further investigation of the combination of these molecules could provide information about their potential synergistic effects.

MeSH / Keywords: antimicrobial peptides, biofilms, melittin, microbial sensitivity tests, surfactin

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The list of PhD Candidates, Mentors and Titles of abstracts of annual seminars

PhD candidate	Mentor	Title of abstract
Renata Apatić, MSN, RN	Assoc. Prof. Robert Lovrić, Ph.D.	Predicting clinical dishonesty among nursing students: the impact of personal and contextual factors
Nikola Bajan	Assoc. Prof. Krešimir Šolić	The impact of the work environment on job satisfaction and work ability of employees in emergency medicine in Osijek-Baranja and Brod-Posavina county
Almina Bajrektarević Kehić, Sanitary inspector	Assoc. Prof. Ivan Miškulin, Ph.D.	Antibiotics self-medication practice in the general population as a modern public health challenge
Ivona Barać, M.D.	Assist. Prof. Josipa Flam	Influence of biochemical values on response to neoadjuvant chemotherapy in breast carcinoma
Marija Barišić	Assist. Prof. Ivana Barać, Ph.D.	Frailty Syndrome and Biopsychosocial Factors in Predicting Successful Aging
Ivana Begić, M.D.	Prof. Branko Dmitrović, M.D., Ph.D.	Distribution of Ki-67 expression as surrogate tumor biology marker among molecular breast cancer subtypes
Marta Bolješić Dumančić	Assoc. Prof. Antonio Kokot M.D., Ph.D.	Lifestyle and Cardio-Renal Risk in Relation to Microcirculatory Changes in the General Population
Petar Brlek, M.D.	Prof. Dragan Primorac, M.D.	A Machine Learning-Based Tool for Primary Site Prediction in Cancers of Unknown Primary Using Tumor Genomic Data
Ana Cicvarić	Prof. Slavica Kvolik, M.D., Ph.D.	Association between inflammatory markers and cognitive status in the early perioperative period in patients after bladder tumor surgery
Ivana Debelić, MScN	Assist. Prof. Robert Lovrić, Ph.D., MSN, RN	Empathy and Professional Identity as a Predictor of the Quality of the Nursing Students–Patient Relationship
Iva Dimitrijević, mag.psych.	Assist. Prof. Ivan Radoš, M.D., Ph.D.	Relationship Between Psychological Factors and Health-Related Quality of Life in Patients with Chronic Low Back Pain
Željka Dujmić, MSN	Assist. Prof. Štefica Mikšić, Ph.D., MSN, RN	Analysis of factors related to sleep score: The influence of demographic, occupational, and physiological variables

Stefan Gjoni	Prof. Siniša Šijanović	The Role of Implantation Endometrial Volume and Perfusion in Predicting Blastocyst Implantation Success
Josipa Glavaš Tahtler, M.D.	Prof. Slavica Kvolik, M.D., Ph.D.	Impact of Neoadjuvant Therapy on Perioperative Complications and Clinical Outcomes in Patients Undergoing Colorectal Cancer Resection
Mateo Grigić, M.D.	Asst. Prof. Tajana Turk, M.D., Ph.D.	Correlation between perfusion angiography and clinical outcome following endovascular treatment in patients with critical limb ischemia
Barbara Grubišić, M.D.	Prof. Ines Bilić Ćurčić, M.D., Ph.D.	Molecular Mechanisms Underlying Acute and Chronic Glycaemic Regulation Disruptions During SARS-CoV-2 Infection
Lea Gvozdanović	Assoc. Prof. Višnja Adam Nesek	Diagnostic accuracy of the biological indicator leucine-rich alpha-2-glycoprotein and calprotectin in patients with suspected acute appendicitis: Preliminary Results
Damir Jemendžić, M.D.	Assist. Prof. Irena Jukić, M.D., Ph.D.	Dynamics of change in blood coagulation factors protein C and S, factor VII, VIII, IX, X, XI, XIII dependent on liver function before and after liver transplantation
Vlatka Konjik, M.D.	Assist. Prof. Iva Hojsak, M.D., Ph.D.	Pediatric Inflammatory bowel disease treatment practices and treatment outcomes in Croatia
Ema Kuna	Prof. Silvija Pušeljić, Ph.D.	Association of insulin-like growth factor 1 level with retinopathy and degree of intracranial hemorrhage in preterm infants
Tomislav Kurevija, M.D.	Assist. Prof. Silvija Canecki-Varžić, M.D., PhD.	Barriers in prescribing antidiabetic medications with cardiovascular benefits: practice, experience, and attitudes of GPs in Croatia
Vedrana Lanc Čurdinjaković, M.D.	Assist. Prof. Jelena Kovačević, Ph.D.	Possibilities of influencing the psychophysical condition and quality of life of elderly institutionalized persons
Marko Lovrić, M.D.	Assoc. Prof. Anđela Grgić, M.D., Ph.D.	Modulation of the Gut Microbiome by 13-cis Retinoic Acid and High-Fat Diet in Female Lewis Rats
Ivana Lukić, M.D.	Assist. Prof. Lana Maričić, M.D., Ph.D.	Association between echocardiographic parameters of systolic and diastolic myocardial function and serum concentration of growth differentiation factor 15 in patients with sepsis
Tanja Lupieri mag.med.techn.	Prof., Dunja Degmečić, M.D, Ph.D.	The Connection Between Inflammatory, Metabolic Factors and Mental Health Challenges in Healthcare Workers

Domagoj Majetić, M.D.	Assist. Prof. Suzana Mimica, M.D., Ph.D.	Association of anti Xa activity of apixaban and rivaroxaban with gastrointestinal bleeding
Vid Matišić, M.D.	Prof. Dragan Primorac, M.D., Ph.D.	Potential health and economic benefits of proactive pharmacogenomic testing in the population of the Republic of Croatia
Sara Matoša, M.D.	Assoc. Prof. Svetlana Tomić, M.D., Ph.D.	Assessment of eye movements as indicators of pathophysiological mechanisms of cognitive impairment in essential tremor
Justina Mihaljević, M.D.	Prof. Ines Drenjančević M.D., Ph.D.	Alteration of microvascular reactivity in patients with hypertension and chronic kidney disease is related to increased oxidative stress
Tihana Nađ, M.D.	Assoc. Prof. Ivana Jukić, M.D., Ph.D.	Effect of consumption of chicken meat enriched with omega-3 polyunsaturated fatty acids on oxidative stress marker levels in young healthy individuals
Vedran Nemet, M.D.	Assoc. Prof. Suzana Matić, M.D., Ph.D.	The effect of psychotropic drugs on cholesterol metabolism and oxysterol accumulation in the lens and retina of Sprague-Dawley rats
Klara Ormanac, M.D.	Prof. Ines Bilić-Ćurčić, M.D., Ph.D.	Association of Endothelium-Dependent Microcirculatory Reactivity with Glycemic Control Assessed by Continuous Glucose Monitoring in Patients with Type 1 Diabetes
Ela Pejić, MSN	Assist. Prof. Štefica Mikšić, Ph.D., MSN, RN	Psychological and Moral Aspects of Professional Engagement Among Palliative Care Professionals
Leon Perić, M.D.	Assoc. Prof. Ana Stupin, M.D.	Carnosine-enriched functional food enhances micro- and macrovascular endothelium-independent vasodilation in competitive athletes
Matea Petrinović, M.D.	Assist. Prof. Silvija Canecki-Varžić, M.D., Ph.D.	Changes in macrovascular reactivity depending on parameters of glycemic regulation from continuous glucose monitoring system in patients with type 1 diabetes
Matej Rezo, M.D.	Assoc. Prof. Tihana Mendeš, M.D., Ph.D.	Role of vestibular rehabilitation in cognitive deficit
Marinka Šimunović Gašpar, mag.med.techn.	Prof. Nataša Antoljak M.D., Ph.D.	The response of healthcare workers in the Republic of Croatia to the National Colorectal Cancer Screening Program

Irena Šnajdar, M.D.	Prof. Dragan Primorac, M.D., Ph.D.	Molecular factors in the development of morbid obesity and their correlation with cardiovascular, metabolic and tumor status
Andrea Teodosić, M.D.	Prof. Siniša Šijanović, M.D. Ph.D.	The Correlation between HLA Class I Alleles and KIR Receptors in Women with Idiopathic Infertility
Sanja Trtica	Prof. Maja Miškulin, M.D., Ph.D.	The infuence of health literacy to the patient satisfaction after radiologic examination
Ivo Vincetić	Assist. Prof. Marko Stupin	Systemic endothelium-dependent vasodilation and endothelial activation in prehypertension
Ninoslava Vonić, M.D.	Assist. Prof. Ivan Radoš, M.D.,Ph.D.	The Effect of continuous Femoral Nerve block on Oxidative Stress and Quadriceps Strength in Patients Undergoing Knee Arthroplasty: A Randomized Controlled Trial
Filip Vrban, M.D.	Prof. Krešimir Rotim, M.D., Ph.D.	Application of gold nanoparticles for more efficient treatment of Parkinsons disease with levodopa
Milutin Vukadinović, M.D.	Prof. Domagoj Drenjančević, M.D., Ph.D.	The influence of intervertebral disc colonization with low-virulence bacteria on degenerative disc changes, clinical status and postoperative recovery
Marko Zelenić , M.D.	Assoc. Prof. Anđela Grgić , M.D. , Ph.D.	The influence of Hoffa's adipose tissue on the development of knee osteoarthritis
Mihaela Zlosa, M.D.	Assist. Prof. Tomislav Kizivat, M.D., Ph.D.	The role of dysnatremia and hormonal imbalance in the pathophysiology and prognosis of COVID-19
Marko Živkov, M.D.	Assist. Prof. Maja Bogdan, M.D., Ph.D.	Antimicrobial and antibiofilm properties of melittin and surfactin