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EDITORIAL NOTE UVODNA REČ UREDNIKA

Dear Readers,

It is my privilege to introduce the first double issue of Medical Review for 2025. This volume gathers contributions that range from innovative technologies in healthcare to traditional clinical case reports, reflecting the diversity and richness of contemporary medical science.

We open with an editorial by Muhammad Kasim Javaid, who examines the role of artificial intelligence in fracture liaison services [1]. His analysis shows how digital tools may address workforce shortages, support early detection of fragility fractures, and ultimately enhance patient-centered care.

The original studies section provides robust evidence from different fields. Jelena Crnić and colleagues investigate postoperative nausea and vomiting [2], a complication that continues to trouble patients and anesthesiologists alike. Their work identifies motion sickness, opioid therapy, and anti-diabetic medication as leading predictors, underscoring the value of individualized perioperative risk assessment.

Milan Milinkov and co-authors focus on anterior cruciate ligament injuries in athletes [3], demonstrating patterns of lateralization according to sex, sports activity, and injury mechanism. Their results contribute to improved understanding and prevention strategies in sports medicine.

Dragana Stanić and collaborators analyze vascular density in different bone marrow conditions [4]. By comparing normal marrow with acute and chronic myeloid leukemia, they shed light on angiogenesis as a marker of disease activity and progression.

Katarina Šljivić and colleagues explore whether the fear of COVID-19 influenced parental behavior in maintaining children's oral health [5]. Their findings highlight the pandemic's indirect effects on dental care and the importance of sustained preventive education.

Vesna Berović and her team describe characteristics of supracondylar fractures in children, using the

Gartland classification [6]. Their study emphasizes diagnostic accuracy and therapeutic planning in one of the most common pediatric injuries.

Our review article, authored by Nikolina Skočajić and her team, explores artificial sweeteners [7], a subject of ongoing debate among professionals and the public. By examining their safety and health implications, the article provides a balanced overview that can inform dietary counseling and policy-making.

The case reports enrich this issue with practical lessons from unique clinical scenarios. Sonja Lukač Pualić and co-authors describe the radiological features of a giant chromophobe renal cell carcinoma [8], emphasizing the critical role of imaging in diagnosing rare tumors.

Dragan Stajić and colleagues present a remarkable obstetric case of spontaneous vaginal delivery through a posterior cervical tear without cervical dilatation [9], offering valuable insights into rare but possible childbirth complications.

Snežana Deležan and collaborators present a case of Bertolotti syndrome [10], demonstrating the diagnostic value of radiological evaluation in recognizing this uncommon congenital anomaly.

Finally, the In Memoriam section reminds us of our professional and personal bonds, honoring those whose contributions have left a lasting mark on our community.

Together, these articles illustrate the broad spectrum of medicine – spanning technology, surgery, pediatrics, hematology, dentistry, sports medicine, nutrition, radiology, and obstetrics. I encourage you to engage with them thoughtfully, as each contribution offers knowledge that can inspire better practice, stimulate reflection, and strengthen our shared commitment to patient care.

*Sincerely,
Radmila Matijević
Editor-in-Chief*

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EDITORIAL UVODNIK

ROLE OF ARTIFICIAL INTELLIGENCE IN FRACTURE LIAISON SERVICE SETTING

ULOGA VEŠTAČKE INTELIGENCIJE U FORMIRANJU SLUŽBE ZA PREVENCIJU SEKUNDARNIH PRELOMA

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Editorial

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Effective secondary fracture prevention reduces the risk of further fragility fractures, delivering benefits for patients, their families, caregivers, healthcare systems, social care, and society at large [1]. The importance of screening adults aged over 50 who present to healthcare systems with a fragility fracture to diagnose and manage osteoporosis is increasingly recognised as a clinical, political, and societal priority. Secondary fracture prevention also aligns with the UN Decade of Healthy Ageing's objectives to combat ageism, support bone health, and foster age-friendly communities, integrated care, and long-term care systems [2]. The fracture liaison service (FLS) model of care, developed to deliver systematic secondary fracture prevention, has been demonstrated to be both clinically and cost-effective [3]. Organisational and patient-level indicators have been established to guide local implementation and assess FLS delivery for service improvement [4,5]. Evidence-based risk assessment tools and osteoporosis therapies have also been developed, enabling the identification of adults at imminent fracture risk who may benefit from more potent treatments. Healthcare systems are now establishing local FLSs to deliver these expected benefits. However, a significant challenge to universal FLS coverage is the lack of workforce capacity and capability. Globally, there are insufficient numbers of medical staff, nurses, administrators, and other healthcare professionals available to address the needs of the many patients requiring secondary fracture prevention.

Digital solutions, such as artificial intelligence (AI), present a potential solution to this workforce challenge. IBM defines AI as the use of machine learning models to process medical data, offering healthcare professionals critical insights that improve health outcomes and patient experiences. AI models

have already been developed within the field of bone health, with some being integrated into clinical workflows.

While AI models are likely to deliver on their performance expectations, ensuring that these benefits translate into tangible value for patients remains a challenge. This translation depends on the level of AI awareness among healthcare professionals. Despite AI being perceived as a technological innovation, its integration into clinical workflows requires a broad understanding among the clinical workforce. Medical professionals need to comprehend how AI operates, including its underlying assumptions, risks, and mitigation strategies. However, few healthcare professionals are currently trained in AI methodologies, a clear opportunity for the bone community to work together.

AI has the potential to enhance multiple stages of the FLS journey [6]. There is a critical need for FLSs to efficiently identify patients at very high fracture risk. AI can significantly improve the efficiency and effectiveness of identifying high-risk patients by utilising opportunistic vertebral fracture assessment via plain radiography, CT, or MRI scanning, as well as using medical coding data.

Once identified by the FLS, patients require comprehensive assessments involving questionnaires, DXA scans, and laboratory testing. The interaction between the FLS and the patient should be personalised, respecting the patient's health literacy, language preference, and social context. For example, most FLSs do not evaluate adherence to oral therapies for other long-term conditions when recommending osteoporosis treatments. Incorporating these aspects into assessments and treatment recommendations however, increases workforce demands. Current AI solutions can draft patient-clinician con-

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sultations. Future AI systems could interact with patients directly, using chatbots capable of communicating at the patient's language proficiency level and tailoring information to their literacy and education. These assessments could be conducted at a time and place convenient for the patient and caregiver, including weekends and outside traditional working hours.

AI systems could also integrate with patient calendars to schedule bone density scans or laboratory tests at mutually convenient times, ensuring high levels of participation. Algorithms could review the patient's medical history, beliefs, and reimbursement options, allowing flexible and reflective decision-making processes. Unlike current systems that often expect patients to make treatment decisions within the initial consultation, AI could enable consultations to occur over multiple interactions, providing patients with time to digest information and consult with trusted stakeholders.

AI-driven treatment recommendations would align with current regional and national guidelines, ensuring immediate updates to clinical practices and removing local unwarranted variations. AI could present benefits and risks in preferred formats, such as percentages, graphical interfaces, or personalised patient stories based on patient preferences. Initial AI systems would likely produce assessments and recommendations that require clinical confirmation by a human. Over time, AI models, trained on extensive datasets with feedback on outcomes in terms of adherence, re-fracture or unwanted events, could develop decision-making capabilities surpassing local, regional, or national expertise.

Beyond initial consultations, AI has the potential to support ongoing patient care. Current FLS systems often struggle to maintain patient contact at 16 and 52 weeks post-treatment initiation. AI could facilitate continuous engagement, offering tailored reminders for treatment adherence, trusted advice on managing concerns, and rapid responses to side effects. AI also presents opportunities to optimise the performance of FLS systems as a whole. By analysing data from other FLSs, AI could flag early variations with potential future impacts and share successful strategies from comparable services.

However, to maximise AI's benefits, the bone health community needs to upskill in AI processes.

Key knowledge areas include AI training, implementation, monitoring, and post-market surveillance. Operationalising AI in healthcare requires addressing several considerations. These include understanding the parameters used to train AI models, recognising potential limitations and biases, and ensuring appropriate regulatory approvals, such as FDA or CE. Installing AI in a hospital involves a multidisciplinary process, including contractual agreements, IT infrastructure adaptations, and rigorous information governance (IG) assurance. IG processes ensure the safe and secure flow of patient-identifiable and non-identifiable data. Once procurement, IT approval, and IG assurance are secured, shadow testing using recent historical data is crucial. Shadow testing identifies any mismatches between training data and local data, involving patient representatives to ensure risks and benefits are thoroughly evaluated.

To realise value from AI, its insights must translate into changes in the patient journey, supported by appropriate resources. For instance, using AI to identify more vertebral fractures will increase the demand for FLS appointments, DXA scans, laboratory tests, and treatments. Services that fail to account for these downstream costs risk destabilising existing FLS systems.

Current AI models still have limitations, necessitating a human-in-the-loop approach. AI systems require clinical confirmation for identifying vertebral fractures, as radiologists often disagree on mild fractures or anomalies like Schmorl's nodes. Post-marketing surveillance of AI tools is critical to ensure consistent performance. For example, AI models must adapt to variations in imaging techniques, such as low-dose CT scans for lung cancer screening. Other surveillance options include parallel AI models can detect deviations from expected performance and flag areas for improvement.

Osteoporosis management has seen transformative innovations, from advanced therapies to diagnostic tools. AI represents the next phase and could address the mismatch between demand and capacity in bone health care. To realise AI's potential, the bone health community should embrace training in AI, sharing experience and expertise in local AI implementation and monitoring processes, thereby ensuring as many patients as possible benefit from these advancements.

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ORIGINAL STUDIES ORIGINALNI NAUČNI RADOVI

ASSESSMENT OF POSTOPERATIVE NAUSEA AND VOMITING IN THE EARLY POSTOPERATIVE PERIOD

PROCENA POSTOPERATIVNE MUČNINE I POVRAĆANJA U RANOM POSTOPERATIVNOM PERIODU

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Abstract

Introduction. Postoperative nausea and vomiting remain common complications following general anesthesia and are a significant source of concern for patients prior to surgery. Numerous studies have aimed to identify risk factors that predict the likelihood of postoperative nausea and vomiting. **Material and Methods.** This cross-sectional observational study included 150 adult patients. Data collection occurred 15 to 45 minutes post-surgery, once patients were fully awake and oriented. Pain and nausea were assessed using the Numerical Rating Scale. Relevant data was obtained from patients' medical histories and anesthesia records and documented in the research protocol. **Results.** Postoperative nausea was recorded in 36 patients (24%). The most frequently reported intensity of nausea was 3 on the Numerical Rating Scale. Identified risk factors for postoperative nausea and vomiting included a history of motion sickness, postoperative opioid use, and the use of anti-diabetic medications. A significant correlation was observed between the severity of acute postoperative pain and the presence of nausea, as well as between the Apfel score and the occurrence of postoperative nausea. **Conclusion.** The incidence of postoperative nausea and vomiting in this study was 24%. The most significant predictors of early postoperative nausea and vomiting were a history of motion sickness, use of opioids postoperatively, and anti-diabetic therapy. The occurrence and severity of early postoperative nausea were associated with the intensity of acute postoperative pain.

Key words: Postoperative Nausea and Vomiting; Postoperative Period; Anesthesia, General; Risk Factors

Sažetak

Uvod. Postoperativna mučnina i povraćanje je i dalje česta komplikacija opšte anestezije i značajan uzrok preoperativne zabrinutosti kod pacijenata. Mnoge studije su istraživale faktore rizika koji mogu uticati na pojavu ove komplikacije. **Materijal i metode.** Istraživanje je sprovedeno kao opservaciona studija preseka koja je obuhvatila 150 odraslih bolesnika. Uzimala se kratka anamneza u periodu od 15 do 45 minuta nakon operacije, pod uslovom da su bolesnici bili potpuno budni i svesni. Pomoću Numeričke skale bola i Numeričke skale mučnine ispitivana je jačina bola i jačina mučnine. Uzeti su relevantni podaci iz istorije bolesti i protokola anestezije i evidentirani su u protokol istraživanja. **Rezultati.** Od 150 bolesnika, postoperativna mučnina se javila kod 36 bolesnika (24%). Bolesnici su najčešće ocenjivali jačinu mučnine ocenom tri (3) na numeričkoj skali. Faktori rizika koji su dovedeni u vezu sa pojavom postoperativne mučnine i povraćanja su istorija kinetoza, upotreba opioda postoperativno i upotreba antidijabetesne terapije. Prisutna je korelacija između jačine akutnog postoperativnog bola i postoperativne mučnine, kao i između Apfel skora i postoperativne mučnine. **Zaključak.** Incidencija postoperativne mučnine i povraćanja je 24%. Najznačajniji faktori u predikciji rane postoperativne mučnine i povraćanja su: postojanje kinetoza, postoperativna primena opioda i primena antidijabetesne terapije. Pojava i jačina rane postoperativne mučnine je povezana sa jačinom akutnog postoperativnog bola.

Ključne reči: postoperativna mučnina i povraćanje; postoperativni period; opšta anestezija; faktori rizika

Introduction

Postoperative nausea and vomiting (PONV) is a frequent complication of general anesthesia, affecting approximately 20-30% of patients. It is defined as the occurrence of nausea, retching, or vomiting within the first 24 to 48 hours following surgery [1]. In individuals without identifiable risk factors, the incidence

of PONV is around 10%, whereas in those with three or more risk factors, it can rise to 60-80% [2]. PONV is typically classified as early or delayed, although a universally accepted definition of early PONV is lacking. Some authors define early PONV as occurring within the first 2 hours after surgery [3], while others extend this period to 4 or even 24 hours postoperatively [4,5]. Although often self-limiting, PONV re-

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Abbreviations

PONV – postoperative nausea and vomiting
ASA – American Society of Anesthesiologists

mains one of the leading causes of preoperative anxiety, with many patients reporting greater fear of experiencing nausea and vomiting than postoperative pain itself [6]. While most cases of PONV are mild, it can lead to serious complications such as dehydration, electrolyte imbalance, bleeding, wound dehiscence, aspiration of gastric contents, esophageal rupture, aspiration pneumonia, and arrhythmias. These complications can negatively affect overall morbidity, the surgical outcome, treatment costs, and the length of hospital stay [7–9]. In an effort to reduce the incidence of PONV, numerous studies have investigated its underlying risk factors, leading to the development of predictive tools for the optimal prophylactic use of antiemetics. One of the most widely accepted models is the Apfel score [10], which identifies four independent risk factors: female sex, non-smoking status, history of PONV or motion sickness, and postoperative opioid use. Additional studies have proposed other contributory factors, including intraoperative hypotension [11–13] and acute postoperative pain [14]. Despite extensive research, the pathophysiology of PONV remains incompletely understood, largely due to its complexity and the interplay of multiple risk factors. This study aims to examine the incidence of PONV during the early postoperative period, identify the most relevant risk factors for its prediction, and explore the relationship between acute postoperative pain and early PONV.

Material and Methods

This cross-sectional observational study was conducted at the Clinic of Anesthesia and Intensive Care of the University Clinical Center of Vojvodina to assess postoperative nausea and vomiting (PONV) in the immediate postoperative period. Ethical approval was granted by the Ethics Committee of the University Clinical Center of Vojvodina on December 1, 2023 (Reference No. 00-288). The study included 150 consecutive adult patients scheduled for elective surgical procedures in the fields of abdominal, plastic, maxillofacial, vascular, or neurosurgery. Eligible patients received either general endotracheal anesthesia or a combination of general and regional anesthesia and had provided written informed consent to participate. Following surgery, patients were transferred to the post-anesthesia care unit and assessed between 15 and 45 minutes postoperatively, provided they were fully awake, alert and oriented. A brief medical interview was conducted to evaluate early PONV and acute postoperative pain. Clinical data were extract-

ed from medical histories and anesthesia records and entered into the research protocol. Collected variables included: age, sex, type of surgery, body weight, height, American Society of Anesthesiologists (ASA) physical status classification, smoking status, history of PONV and/or motion sickness, duration of anesthesia, intraoperative use of vasopressors, use of non-opioid analgesics, corticosteroids, antiemetics, and postoperative opioids. The total intraoperative opioid dose, type of anesthesia (general or combined), and anesthetic technique (balanced or total intravenous anesthesia) were also recorded. Body mass index (BMI) was calculated using the standard formula based on weight and height. Comorbidities documented included cardiovascular diseases, thyroid dysfunction, chronic gastritis, obesity, diabetes mellitus, hyperlipidemia, and chronic lung diseases. Due to their low incidence, fatty liver disease, pancreatitis, and Parkinson's disease were excluded from statistical analyses. Regular use of chronic medications was also noted. Preoperative systolic blood pressure and the lowest intraoperative systolic blood pressure were obtained from anesthesia protocols. Intraoperative hypotension was defined as a $\geq 20\%$ decrease in systolic blood pressure from the preoperative baseline lasting at least 5 minutes. The Apfel score was calculated using four criteria: female sex, smoking status, history of PONV or motion sickness, and postoperative opioid use [10]. Pain and nausea intensity were assessed using the Numerical Rating Scale (NRS), a horizontal scale ranging from 0 to 10, where 0 indicated no pain or nausea, and 10 represented the most severe pain or nausea. Data analysis employed descriptive statistics, correlation analyses, and predictive modeling. Descriptive statistical methods included measures of central tendency (mean), measures of variability (standard deviation), and relative numbers (structural indicators). Spearman's rank correlation coefficient (ρ) correlation coefficient was used to assess associations between variables. Binary logistic regression was applied to evaluate predictors of early PONV. Hypotheses were tested at a statistical significance level (α level) of 0.05. Data was processed using standard statistical software packages (IBM SPSS Statistics, version 26).

Results

A total of 150 patients were included in the study, comprising 69 males (46%) and 81 females (54%). The age of participants ranged from 18 to 82 years, with a mean of 54.91 ± 37.98 years. Body mass index (BMI) values ranged from 16.91 to 40.12, with a mean BMI of 27.08 ± 4.51 . According to ASA classification, 18

Table 1. Frequency of nausea severity in all patients

NRS Nausea	Frequency	Percentage
0	114	76.0
1	0	0.0
2	1	0.7
3	11	7.3
4	5	3.3
5	6	4.0
6	0	0.0
7	2	1.3
8	4	2.7
9	4	2.7
10	3	2.0

Legend: NRS – Numerical rating scale

Table 2. Model of binary logistic regression of risk factors as predictors of nausea

Model	df	χ^2	p	McFaden	Negelkerke	Tjur	Cox&Snell
H0	149						
H1	134	36.156	0.002	0.216	0.318	0.242	0.214

Table 3. Posterior classification matrix of participants

Prediction model			
Nausea	NO	YES	Accuracy
NO	107	6	92.92%
YES	22	15	43.24%
Overall accuracy			80.67%

patients (12%) were classified as ASA I, 80 (53.3%) as ASA II, and 52 (34.7%) as ASA III. Among the cohort, 39 individuals (26%) were smokers. Cardiovascular disease was the most common comorbidity, affecting 79 patients (52.7%), followed by diabetes mellitus in 20 patients (13.3%). Chronic medication use was reported by 87 patients (58%). A history of PONV was documented in 11 patients (7.3%), while 35 patients (23.3%) reported a history of motion sickness. Intraoperative hypotension occurred in 53 patients (35.3%). Postoperative opioids were administered to 16 patients (10.7%), and intraoperative antiemetic prophylaxis was used in 93 patients (62%). The mean duration of anesthesia was 87.37 ± 37.98 minutes. The mean intraoperative dose of strong opioids was 195.46 ± 84.41 μ g. Acute postoperative pain was reported by 134 patients (89.3%), with pain intensities most commonly rated as 3 or 5 on the NRS. PONV occurred in 36 patients (24%), with nausea intensity most frequently rates as 3, followed by 5 on the NRS (**Table 1**). Vomiting was observed in one patient (0.67%). The most frequently observed Apfel score was 1 (39.3%), while 21.3% of patients were categorized as high-risk (Apfel score > 2). Of 150 patients, 148 received general anesthesia and 2 (1.33%) received combined gen-

eral and regional anesthesia. Balanced general anesthesia was administered to 146 patients (97.3%), while 4 patients (2.67%) received total intravenous anesthesia. Due to the small sample size in these subgroups, they were excluded from further statistical analysis. Regarding surgical procedures, 82 patients (54.67%) underwent abdominal surgery, 17 patients (11.33%) underwent neurosurgical procedures, 18 (12%) underwent maxillofacial surgeries, 18 (12%) had plastic surgeries, 5 (3.33%) underwent vascular surgery, and 10 patients (6.67%) had endocrine surgery. Laparoscopic techniques were used in 24% of cases. Binary logistic regression indicated that the model incorporating relevant risk factors significantly predicted PONV occurrence ($\chi^2 = 32.188$; $p < 0.01$), with pseudo R^2 values ranging from 0.214 to 0.318 (**Table 2**). The model achieved an overall classification accuracy of 80.67%, with high specificity (92.92%) but relatively low sensitivity (43.24%) (**Table 3**). Among the predictors analyzed, only a history of motion sickness and postoperative opioid use showed statistically significant association with PONV occurrence (**Table 4**). Specifically, a history of motion sickness increased the risk of PONV by 4.2 times, while postoperative opioid use raised the risk by 5.7 times.

Table 4. Partial regression coefficients of risk factors and their statistical significance

Risk Factor	Regression coeff	Odd ratio	Wald test	p
Age	-0.117	0.992	0.164	0.686
Female gender	-0.273	1.716	1.344	0.246
BMI	-0.261	0.941	1.294	0.255
ASA status II	0.169	0.972	0.001	0.972
ASA status III	0.540	0.511	0.418	0.518
Chronic diseases	-0.029	0.685	0.204	0.651
Chronic medication	-0.672	1.735	0.507	0.476
History of PONV	-0.379	1.648	0.418	0.518
Motion sickness	0.551	4.205	9.434	0.002*
Anesthesia duration (min)	0.500	0.993	0.865	0.352
Intraoperative hypotension	1.436	1.753	1.219	0.270
Intraoperative use of strong opioids (µg)	0.561	1.002	0.564	0.453
Postoperative use of opioids	1.736	5.673	7.039	0.008*
Use of antiemetics	0.353	1.424	0.469	0.493
Use of corticosteroids	-1.178	0.308	3.618	0.057

Legend: BMI – Body mass index, ASA status - The American Society of Anesthesiologists (ASA) physical status classification system

Table 5. Partial regression coefficients of risk factors and their statistical significance

Risk factor	Regression coeff.	Odd ratio	Wald test	p
Smoking	-0.016	0.788	0.162	0.688
Cardiovascular diseases	-0.971	0.618	0.252	0.616
Thyroid diseases	-0.239	0.524	0.180	0.672
Chronic gastritis	-0.482	2.537×10^{-7}	8.383×10^{-5}	0.993
Obesity	-0.647	0.525	0.296	0.586
Diabetes	-15.187	9.500	2.837	0.092
Hyperlipidemia	-0.644	1.450	0.177	0.674
Lung diseases	2.251	0.258	1.207	0.272
Antihypertensives	0.372	2.131	0.671	0.413
Diuretics	-1,356	0.779	0.111	0.739
Thyroid medication	0.757	5.468	1.039	0.308
Antidiabetics	-0.249	0.008	6.022	0.014*

Table 6. Correlation of pain and Apfel score with Nausea

		NRS Nausea	NRS Pain	Apfel score
NRS Nausea	Correlation coefficient	1.00	0.32**	0.29**
	Significance (p)	-	0.001	0.001
	N	150	150	150
NRS Pain	Correlation coefficient	0.32**	1.00	0.10
	Significance (p)	0.001	-	0.21
	N	150	150	150
Apfel score	Correlation coefficient	0.29**	0.10	1.00
	Significance (p)	0.001	0.21	-
	N	150	150	150

Legend: NRS – Numerical Rating Scale

Among chronic illnesses and long-term medication use, only anti-diabetic medication use was significantly associated with increased PONV risk (Table 5). There is a positive correlation between nausea and pain ($\rho = 0.32$; $p = 0.001$), as well as between nausea and the Apfel score ($\rho = 0.29$; $p = 0.001$) (Table 6).

Discussion

In this study, the incidence of PONV was 24%, which aligns with previously published rates, typically ranging between 20% and 40%. Some studies have reported lower incidences, as low as 9.6% [4],

while others have documented rates exceeding 70% [15,16]. This variation is likely attributable to differences in patient populations, antiemetic prophylaxis strategies, surgical types, and other factors. Over half of the patients in our cohort (54.67%) underwent abdominal surgery, a well-established high-risk category for PONV [17]. Furthermore, 24% of procedures were laparoscopic, which is associated with a heightened risk of PONV due to multiple contributing mechanisms: mechanical effects of pneumoperitoneum (e.g., gastric and intestinal distension), parasympathetic nerve stimulation, and CO₂-induced irritation [18]. In addition, 23.1% of patients were classified as high-risk based on the Apfel score, which likely contributed to the observed PONV incidence. The timing of data collection may have also influenced results. Different studies have collected data at different time intervals after surgery, ranging from 0 to 24 hours [3–5]. In our study, data were collected within the first 15 to 45 minutes after surgery. Previous studies have shown that PONV incidence can vary depending on the postoperative interval evaluated, with some reporting lower rates in the first two hours and higher rates later [19,20], while others found the highest incidence within the first two hours [21]. The majority of patients in our study rated nausea at an intensity of 3, with only 19 patients (12.67%) reporting severe nausea (≥ 5 on the NRS). This relatively low severity may reflect the effectiveness of intraoperative antiemetic prophylaxis administered in 62% of patients. Consistent with the literature [22,23], statistical analysis revealed that motion sickness was associated with a higher incidence of early PONV in our cohort. This risk factor is also incorporated into the Apfel score [10]. Similarly, postoperative opioid use was associated with a higher incidence of early PONV, as demonstrated in several previous studies. For instance, one study found a 6% reduction in PONV with 50% reduction in postoperative opioid dosage [24], while Silva et al. reported a 2.7-fold increase in PONV among opioid users [25]. Our study found an even stronger association, with a 5.7-fold increased risk. Regarding chronic diseases and medication use, our study showed that the use of anti-diabetic medications significantly increased the risk of early PONV. Diabetic patients often experience delayed gastric emptying, often due to autonomic neuropathy or glycemic fluctuations, is a recognized risk factor for PONV [17, 26,27]. Additionally, some of anti-diabetic agents, notably metformin and GLP-1 agonists, are known to cause gastrointestinal side effects such as nausea, vomiting, diarrhea, and bloating [28], with some studies reporting nausea in 11.7% and vomiting in 5.8% of users [29]. The mechanisms are not fully understood,

though gut microbiota alternations and delaying glucose absorption in the intestines, which may lead to increased lactate production in the gut and contribute to gastrointestinal symptoms, are implicated [30]. Similarly, GLP-1 receptor agonists, which slow gastric emptying, have been associated with nausea in up to 51% and vomiting in 19% of patients, due to effects on gastric motility and direct impact on the central nervous system [31,32]. However, our study lacked detailed data regarding diabetes control (e.g., HbA1c), diabetic complications (e.g., neuropathy), or specific anti-diabetic medication types, which represents a limitation. The relationship between anti-diabetic medications and PONV is certainly a very interesting result and could inspire future research on this topic. Previous studies have linked intraoperative hypotension to increased PONV risk [11–13] suggesting that adrenaline release, as a sympathetic response to blood pressure drop, may lead to “triggered emesis” [33]. Other studies found that perioperative hypoperfusion and subsequent gastrointestinal lining ischemia may trigger the release of serotonin – one of the most significant mediators of nausea and vomiting [34], while reduced blood flow to the brainstem may lead to dizziness, nausea, and vomiting [12]. Our study did not demonstrate a statistically significant association between intraoperative hypotension and early PONV. This may be due to variations in how baseline blood pressure is defined. In our study, 35.3% of patients had at least one episode of intraoperative hypotension. However, the systolic blood pressure values we used as baseline were usually recorded before the patient entered the operating room, often during the preoperative visit. Other studies have used blood pressure values measured at the time of anesthesia induction or immediately after induction, which may explain the different results. Our statistical analysis revealed a correlation between the occurrence of PONV and the severity of acute postoperative pain. Some studies have shown a strong correlation between postoperative pain, particularly visceral and pelvic pain, and PONV [14,17]. Trauma and pain increase the concentration of circulating catecholamines, which can trigger nausea, as is often seen in patients with various injuries who experience nausea and intense pain simultaneously. It remains unclear whether PONV is driven by pain itself or by the opioids administered for pain control. Some studies even suggest that postoperative opioid use reduces both pain and nausea [35], while others show that postoperative opioid use is a significant risk factor for PONV. This duality warrants further clarification. Lastly, our statistical analysis showed a connection between PONV and the Apfel score, which is consistent with numerous studies

that have confirmed the Apfel score as a simple and reliable predictor of PONV risk [36–38].

Conclusion

In conclusion, the incidence of postoperative nausea and vomiting in the immediate postoperative period is 24% in patients undergoing elective surgeries

under balanced general anesthesia in abdominal, plastic, maxillofacial, vascular, and neurosurgery programs. The most significant predictors of early postoperative nausea and vomiting in this cohort were a history of motion sickness, postoperative opioid use, and the use of anti-diabetic medications. Furthermore, the intensity of nausea was associated with the severity of acute postoperative pain.

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LATERALIZATION OF ANTERIOR CRUCIATE LIGAMENT INJURIES OF THE KNEE – ANALYSIS BY SEX, SPORTS ACTIVITY, TYPE OF SPORT, AND INJURY MECHANISM

LATERALIZACIJA POVREDA PREDNJEG UKRŠTENOG LIGAMENTA KOLENA – ANALIZA PREMA POLU, SPORTSKOJ AKTIVNOSTI, VRSTI SPORTA I MEHANIZMU POVREĐIVANJA

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Abstract

Introduction. Anterior cruciate ligament injuries represent a major concern among athletes, with recent studies suggesting that sex, sport type, and injury mechanism influence their incidence and characteristics. This study aimed to investigate the lateralization of anterior cruciate ligament injuries and assess associations between the injured side and sex, level of sports activity, sport type, injury mechanism, and playing surface. **Material and Methods.** A retrospective analysis was performed on 1,011 athletes with confirmed anterior cruciate ligament injury. Data were obtained from medical records and included variables as sex, injury side, level of sports activity, type of sport, injury mechanism, and playing surface. Associations were analyzed using chi-square tests. **Results.** A statistically significant association was found between sex and injury side ($p = 0.0066$), with females more frequently sustaining injuries to the left knee and males to the right. Professional athletes had a significantly higher incidence of right-sided injuries compared to recreational athletes ($p = 0.005$). Among sports, rugby and american football showed a predominance of right knee injuries (76.2%), while volleyball exhibited a higher rate of left-sided injuries (71.4%). Contact injuries were more common on the right side (62.7%), whereas non-contact injuries predominantly affected the left side. Injuries occurring on grass surfaces were significantly more frequent on the right side ($p = 0.028$). **Conclusion.** Sex, level of sports activity, type of sport, and playing surface are significantly associated with the lateralization of anterior cruciate ligament injuries. These findings may contribute to improved better understanding of injury risk factors and inform targeted prevention strategies. Further studies incorporating leg dominance are recommended to refine injury risk assessments.

Key words: Anterior Cruciate Ligament Injuries; Knee Injuries; Sports; Athletic Injuries; Functional Laterality; Sex Factors; Risk Factors

Introduction

Injuries to the anterior cruciate ligament (ACL) of the knee (*lat. ligamentum cruciatum anterior – LCA*) are among the most frequent sports-related knee injuries, with an increasing incidence observed in both

Sažetak

Uvod. Povrede prednjeg ukrštenog ligamenta predstavljaju značajan problem kod sportista, a sve više istraživanja ukazuje na ulogu polnih razlika, vrste sporta i mehanizma povređivanja u njihovoj učestalosti i karakteristikama. Cilj ovog istraživanja bio je da se ispita lateralizacija povreda prednjeg ukrštenog ligamenta kod sportista, kao i povezanost strane povrede sa polom, sportskom aktivnošću, vrstom sporta, mehanizmom povrede i podlogom. **Materijal i metode.** Sprovedena je retrospektivna analiza 1.011 ispitanika sa povredom prednjeg ukrštenog ligamenta. Podaci su prikupljeni iz medicinske dokumentacije i obuhvatali su pol, stranu povrede, nivo sportske aktivnosti, vrstu sporta, mehanizam povrede i podlogu. Statistička analiza je obuhvatila hi-kvadrat test za ispitivanje značajnosti povezanosti posmatranih faktora. **Rezultati.** Analiza je pokazala statistički značajnu povezanost između pola i strane povrede ($p = 0,0066$), pri čemu su žene češće povređivale levo koleno, a muškarci desno. Profesionalni sportisti su imali značajno veću učestalost povreda desnog kolena u poređenju sa rekreativcima ($p = 0,005$). Ragbi i američki fudbal su pokazali izraženiju asimetriju povreda desnog kolena (76,2%), dok je kod odbojke bila veća učestalost levostranih povreda (71,4%). Kontaktni mehanizmi su bili povezani s povredom desnog kolena (62,7%), dok su nekontaktni mehanizmi češće uzrokovali levostrane povrede. Travnata podloga bila je značajno povezana sa povredama desnog kolena ($p = 0,028$). **Zaključak.** Rezultati ukazuju na značajnu ulogu pola, nivoa sportske aktivnosti, vrste sporta i podloge u lateralizaciji povreda prednjeg ukrštenog ligamenta kod sportista. Ova saznanja mogu doprineti boljem razumevanju faktora rizika i razvoju ciljane prevencije. Potrebna su dalja istraživanja koja uključuju i dominaciju noge radi sveobuhvatnijeg sagledavanja rizika za povrede prednjeg ukrštenog ligamenta.

Ključne reči: povrede prednjeg ukrštenog ligamenta; povrede kolena; sport; sportske povrede; funkcionalna lateralizacija; pol; faktori rizika

professional and recreational athletes [1,2]. Numerous studies have identified a variety of internal and external risk factors, which can be broadly categorized into four main groups: environmental, anatomical, hormonal, and biomechanical [3–7]. ACL rupture risk is multifactorial, and the interplay of these contribut-

ing factors offers a more accurate prediction of injury likelihood [8–10].

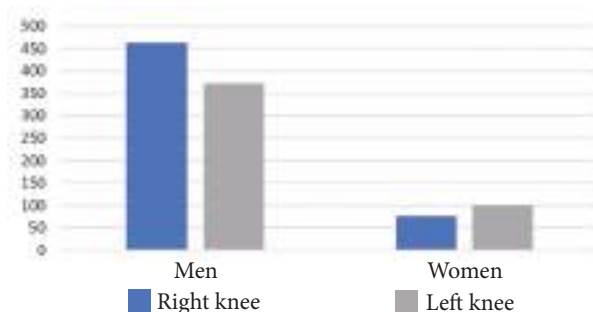
Laterality, or the functional dominance of one side of the body, is a well-established neurological phenomenon reflected in the preferential use of one hand, leg, or eye. Although left-handedness is present in approximately 10% of the population [11], it has been historically misunderstood and stigmatized. Despite this, many notable figures – including Leonardo da Vinci, Nikola Tesla, Marie Curie, Isaac Newton, Ludwig van Beethoven, Jimi Hendrix, and Kurt Cobain – exemplify the diverse capabilities associated with left-side dominance. In political and military history, notable left-handers include Alexander the Great, Napoleon Bonaparte, Winston Churchill, and Barack Obama. Modern sports offer numerous examples of successful left-handed or left-footed athletes such as Rafael Nadal, Lionel Messi, Martina Navratilova, Monica Seles, and Mike Tyson. Their advantage often lies in unusual attack angles, distinct biomechanical patterns, and tactical superiority over predominantly right-handed opponents. These biomechanical and neurological variations may influence movement patterns, balance, and injury risk. Thus, understanding laterality as a broader neurophysiological concept provides foundation for studies exploring differences in sports injury mechanisms. ACL injury lateralization refers to the tendency for injuries to affect one side of the body more frequently [12]. While such injuries are often perceived as random, emerging research suggests a potential association between leg dominance and injury side, influenced by asymmetrical biomechanics, neuromuscular control, and movement strategies [13].

Notably, sex appears to play a critical role: some studies suggest that female athletes more commonly injure the non-dominant, supporting leg [3,14], whereas in male athletes – particularly in sports such as football – injuries tend to occur on the dominant side [15]. These findings highlight the need to explore sex-specific biomechanics and load distribution in ACL injury mechanisms.

The aim of this study was to investigate the lateralization of anterior cruciate ligament injuries and examine its association with sex, level of sports activity, type of sport, injury mechanism, and playing surface.

Material and Methods

The retrospective study was conducted at the Clinic for Orthopedic Surgery and Traumatology, University Clinical Center of Vojvodina. Data were collected from the institutional database of the Clinic, and the study was carried out in accordance with



Graph 1. Distribution of right/left knee injuries by gender

the Declaration of Helsinki [16]. Ethical approval was obtained from the Ethics Committee of the University Clinical Center of Vojvodina.

The study included a total of 1,011 participants of both sexes, aged 18 to 45 years, who underwent anterior cruciate ligament (ACL) reconstruction due to sports-related injuries. Exclusion criteria were previous ACL reconstruction (i.e., re-injury of a reconstructed ligament) and ACL injuries not related to sports activity. Among the participants, 835 were male and 176 were female. Injuries to the right knee were recorded in 539 cases, while 472 cases involved the left knee (**Graph 1**).

The most commonly represented sport was football ($n = 507$), followed by basketball ($n = 153$) and handball ($n = 102$). Other sports were represented in smaller numbers.

Statistical analysis was performed using the chi-square test of independence to assess the association between the side of the injured knee and categorical variables, including sex, level of sports activity, type of sport, playing surface, and injury mechanism. Descriptive statistics are presented as absolute numbers (N) and percentages (%). All analyses were conducted using SPSS software, version 26. A p -value of <0.05 was considered statistically significant.

Results

The majority of participants were male, with a higher frequency of right knee injuries (55.3%). In contrast, female participants more frequently sustained left knee injuries (55.2%). A chi-square test of independence revealed a statistically significant association between sex and the side of ACL injury ($\chi^2 = 7.37$; $p = 0.0066$) (**Table 1**).

A statistically significant association was also observed between the side of the injured knee and the level of sports activity ($\chi^2(2) = 10.5$, $p = 0.005$) (**Table 2**). Professional athletes more often sustained right-sided ACL injuries compared to recreational athletes.

Abbreviations

ACL – anterior cruciate ligament (*LCA – lat. ligamentum cruciatum anterior*)

While non-athletes showed a higher proportion of right-sided injuries (65.4%) than professionals (56.9%), the difference was not statistically significant due to the small sample size of the non-athlete subgroup ($N = 26$). Overall, the chi-square test confirmed that professionals had a significantly higher frequency of right knee injuries than recreational athletes ($p = 0.005$), whereas the influence of non-athletes on this association was negligible.

The distribution of knee injuries varied significantly across different sports (**Table 3**). The greatest side-to-side asymmetry was observed in rugby and american football, where 76.2% of injuries affected the right knee. In contrast, volleyball showed a predominance of left-sided injuries (71.4%). Football and basketball demonstrated a moderate predominance of right knee injuries (56.6% and 55.6% respectively), while handball and combat sports showed a more balanced distribution between sides. The chi-square test confirmed a statistically significant association between the side of injury and the type of sport ($\chi^2(8) = 45.2$, $p < 0.001$).

Although the chi-square test did not show a statistically significant association between injury mechanism and the side of injury ($\chi^2(4) = 8.24$, $p = 0.083$), certain trends were noted (**Table 4**). Contact injuries, particularly collisions, were more frequently associ-

ated with right knee injuries (62.7%), while “other” mechanisms were more commonly linked to left-sided injuries (61.5%). Cutting and landing mechanisms were more evenly distributed. The small number of injuries resulting from falls ($n = 9$) limits the liability of conclusions in this category and underscores the need for further research with larger sample.

A statistically significant association was identified between playing surface and the injured side ($\chi^2(5) = 12.5$, $p = 0.028$) (**Table 5**). The most notable difference occurred on grass surfaces, where right knee injuries predominated (58.4%). In contrast, “other” surfaces showed a higher incidence of left-sided injuries (57.5%). Mat surfaces had a completely balanced injury distribution (50%-50%). These findings suggest that the biomechanical properties of the playing surface may influence the lateralization of ACL injuries.

Discussion

The human body naturally exhibits asymmetry, both morphologically and functionally. Limb dominance – whether of the leg, arm, or eye – results from complex neurological and biomechanical interactions. While biologically determined, dominance is also shaped by cultural and functional factors. Measuring leg preference and understanding laterality hold clinical and sports medicine relevance, particularly in the prevention and rehabilitation of lower extremity injuries [17].

Table 1. Distribution of ACL injuries by gender and side of the injured knee

Side			Sex	
			Female	Male
	Right Knee	N	77	462
	Left Knee	N	99	373

Table 2. Distribution of knee injuries by side and category of sports activity

Side			Sports activity		
			Recreational athlete	Professional athlete	Non-athlete
	Right Knee	N	298	228	17
		%	50.70%	56.90%	65.40%
	Left Knee	N	286	173	9
		%	49.30%	43.10%	34.60%

Table 3. Distribution of knee injuries according to the type of sports activity

			Sports								
			Skiing	Handball	Rugby; American Football	Volleyball	Non-athlete	Basketball	Football	Other	Combat sport
Side	Right	N	15	51	16	10	23	85	287	23	33
	Knee	%	38.50%	50%	76.20%	28.60%	46.90%	55.60%	56.60%	50%	55.90%
	Left	N	24	51	5	25	26	68	220	23	26
	Knee	%	61.50%	50%	23.80%	71.40%	53.10%	44.40%	43.40%	50%	44.10%

Table 4. Distribution of knee injuries according to the injury mechanism

			Mechanism of injury				
			Collision	Fall	Change of direction	Landing	Other
Side	Right Knee	N	133	5	247	148	10
		%	62.70%	55.60%	52%	51.20%	38.50%
	Knee	N	79	4	228	141	16
		%	37.30%	44.40%	48%	48.80%	61.50%

Table 5. Incidence of right and left knee injuries on different surfaces

			Surface					
			Grass	Taraflex	Mat	Parquet	Other	Concrete
Side	Right Knee	N	240	22	24	141	48	68
		%	57.80%	53.70%	50%	52%	42.50%	55.30%
	Left Knee	N	175	19	24	130	65	55
		%	42.20%	46.30%	50%	48%	57.50%	44.70%

In sports, especially football, leg dominance is typically described in terms of a “stronger” or “weaker” leg, with the dominant leg more frequently used for powerful and accurate actions such as kicking. Although bilateral proficiency is advantageous, most athletes exhibit significant functional asymmetry, which can alter movement biomechanics and elevate injury risk. The role of laterality is especially crucial in understanding the mechanism underlying ACL injuries [15,18].

Lower extremity injuries are the most common in many sports, and functional asymmetry and limb dominance have been identified as potential predisposing factors. Wong and Hong [19] emphasized that most football injuries occur through non-contact mechanisms, where body control and stabilization are vital, particularly in athletes with pronounced limb dominance. Extremity dominance has also been shown to play a role in ACL injuries, as uneven biomechanical loading between limbs may lead to increased vulnerability [18].

Additionally, hormonal influences – especially in women – may contribute to injury incidence, raising additional questions about the complex interaction between laterality, sex, and injury risk [20]. Asymmetries are also present in the trunk, where differences in muscle endurance can result in load imbalances that further exacerbate injury risk, particularly in sports requiring repetitive unilateral movements [21].

In our study, we observed a statistically significant association between sex and the side of ACL injury ($p = 0.007$). Left-sided injuries were more frequent among female athletes (55.2%), while male athletes predominantly sustained right-sided injuries (55.3%). These findings align with the hypothesis that neuromuscular differences between sexes and the ten-

dency to rely on the dominant leg in sport-specific tasks [15] contribute to injury lateralization. However, the relatively small asymmetry in our sample, compared to some previous studies [3], underscores the importance of considering sport-specific biomechanics and movement pattern [22].

Professional athletes in our study (56.9%) had a higher proportion of right-sided ACL injuries compared to recreational athletes (50.7%). This difference may reflect the greater loading of the dominant leg in high-performance environments [23], supporting previous findings that suggest increased injury risk among professional athletes due to sport-specific demands [24]. Non-athletes also exhibited a predominance of right-sided injuries, though due to the small sample size ($N = 26$), this finding warrants cautious interpreted.

The relationship between the type of sport and the side of injury indicates that specific movement patterns in certain sports may significantly contribute to injury lateralization [1]. Rugby and American football, which involve frequent directional changes and repetitive loading of the dominant leg, showed a strong predominance of right-side injuries. Grindem et al. [25] reported that the right knee is up to three times more likely to be injured in football and basketball, which aligns with our results (football – 55.6% right knee injuries; basketball – 55.6%). In contrast, volleyball was associated with more left-sided injuries, possibly due to the biomechanics of landing and body rotation. Handball injuries in our sample demonstrated a near-equal distribution, consistent with previous findings by Olsen et al. [26].

In our study, non-contact injury mechanisms were significantly more common, accounting for 79% of all ACL injuries, compared to only 21% caused by contact (collision) events. This finding is consistent

with previous epidemiological research which found that non-contact mechanisms accounted for over 50% of ACL injuries in team sports [27]. These injuries typically occur during activities such as cutting, sudden deceleration, or landing – movements that involve high biomechanical load without external contact. Although our chi-square analysis did not show a statistically significant association between injury mechanism and the side of injury ($p = 0.083$), we observed that contact injuries were more frequently associated with right-sided injuries, while non-contact injuries tended to occur on the left. This asymmetry may reflect neuromuscular and biomechanical differences related to limb dominance and movement strategy. The predominance of non-contact injuries in our cohort underscores the importance of targeted neuromuscular training programs aimed at optimizing lower limb control and reducing asymmetry-related risk.

A statistically significant association was also observed between playing surface and the side of injury, with grass fields linked to a higher frequency of right-sided injuries. This is consistent with Agel et al. [28], who found that grass surfaces increase the likelihood of right-sided ACL injuries by 22%. These findings underscore the potential influence of surface biomechanics on injury lateralization and emphasize the need to consider environmental factors when designing injury prevention strategies and adapting training programs.

The practical implications of our findings are substantial. Recognizing patterns in ACL injury lateralization can inform individualized prevention and rehabilitation programs. Targeted training aimed at enhancing knee stability and control may enhance “prehabilitation” and reduce injury risk. Additionally, these may serve as a foundation for educating coaches and athletes about biomechanical movement patterns that increase injury risk.

However, several limitations should be acknowledged. Small sample sizes in some groups, such as

non-athletes, may affect the stability of statistical estimates. Furthermore, the absence of data on leg dominance precluded deeper analysis of the biomechanical and functional differences contributing to injury lateralization.

For future studies should aim to incorporate larger sample sizes and incorporate data on leg dominance. Comparing results across different sports may also improve understanding of injury risk, and support the development of targeted prevention strategies.

Conclusion

This study demonstrated a statistically significant association between sex and the side of anterior cruciate ligament injury, with male athletes more frequently injuring the right knee (55.3%), and female athletes showing a higher proportion of left-sided injuries (55.2%).

A statistically significant relationship was also observed between the side of injury and the level of sports activity ($p = 0.005$), with professional athletes sustaining right-sided injuries more often than recreational athletes and non-athletes.

The chi-square test confirmed a statistically significant association between the side of injury and the type of sport ($p < 0.001$), with the most pronounced right-sided asymmetry found in rugby and American football.

Non-contact injury mechanisms (79%) were significantly more common than contact injuries (21%). Although contact injuries (collisions) were more common (62.7%), there was no statistically significant association between the mechanism of injury and the side of the injured knee ($p = 0.083$).

Lastly, a significant correlation was found between the playing surface and injury lateralization ($p = 0.028$). Right-sided injuries were more frequent on grass surfaces (58.4%), while mat surfaces exhibited an even distribution (50%-50%).

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COMPARATIVE ANALYSIS OF BLOOD VESSEL DENSITY IN UNCHANGED BONE MARROW, ACUTE AND CHRONIC MYELOID LEUKEMIA

KOMPARATIVNA ANALIZA GUSTINE KRVNIH SUDOVA U NEIZMENJENOJ KOŠTANOJ SRŽI, AKUTNOJ I HRONIČNOJ MIJELOIDNOJ LEUKEMIJI

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Abstract

Introduction. Acute myeloid leukemia and chronic myeloid leukemia are malignant blood cell disorders characterized by increased angiogenesis. This study aimed to evaluate blood vessel density in bone marrow tissue of patients with acute and chronic myeloid leukemia and to determine whether there is a statistically significant difference compared to a control group.

Material and Methods. This retrospective study included 90 bone marrow biopsy samples, categorized into three groups: control, acute myeloid leukemia, and chronic myeloid leukemia. Pathohistological diagnoses were retrieved from the records of the Center for Pathology and Histology of the Clinical Center of Vojvodina. Samples were processed using standard histological and immunohistochemical techniques, examined microscopically, and photographed. Blood vessel density was quantified using ImageJ program, analyzing five microphotographs per sample, with results expressed as percentages. The mean value was calculated for each subject. Data were analyzed statistically and presented numerically, graphically, and in tables.

Results. The mean blood vessel density was 1.85% ($\pm 0.56\%$) in the control group, 3.72 ($\pm 1.67\%$) in the acute myeloid leukemia group, and 5.42% ($\pm 2.28\%$) in the chronic myeloid leukemia group. A statistically significant difference in blood vessel density was observed among the groups. **Conclusion.** The statistically significant difference in blood vessel density between the groups underscores the role of angiogenesis in the pathogenesis of these malignancies and suggests its potential relevance in diagnosis and therapeutic strategies.

Key words: Blood Vessels; Angiogenesis; Bone Marrow; Leukemia, Myeloid; Biopsy; Morphological and Microscopic Findings

Sažetak

Uvod. Akutna mijeloidna leukemija i hronična mijeloidna leukemija su maligne bolesti krvnih ćelija koje karakteriše pojačana angiogeneza. Cilj ove studije bio je da se odredi gustina krvnih sudova u koštanoj srži kod pacijenata sa akutnom i hroničnom mijeloidnom leukemijom i da se ispita da li postoji statistički značajna razlika u poređenju sa kontrolnom grupom. **Materijal i metode.** Ova retrospektivna studija obuhvatila je 90 uzoraka biopsije koštane srži, podeljenih u tri grupe: kontrolnu grupu, grupu sa akutnom mijeloidnom leukemijom i grupu sa hroničnom mijeloidnom leukemijom. Patohistološke dijagnoze su dobijene iz dokumentacije Centra za patologiju i histologiju Univerzitetskog kliničkog centra Vojvodine. Uzorci su obrađeni standardnim histološkim i dodatnim imunohistohemijskim metodama, pregledani mikroskopski i fotografisani. Gustina krvnih sudova merena je pomoću programa *Image J*, analizom pet mikrofotografija po uzorku, a rezultati su izraženi u procentima. Za svakog ispitanika izračunata je prosečna vrednost. Podaci su statistički obrađeni i prikazani numerički, grafički i u tabelama. **Rezultati.** Prosečna gustina krvnih sudova u kontrolnoj grupi iznosila je 1,85% ($\pm 0,56\%$), u grupi sa akutnom mijeloidnom leukemijom 3,72% ($\pm 1,67\%$), dok je u grupi sa hroničnom mijeloidnom leukemijom iznosila 5,42% ($\pm 2,28\%$). Utvrđena je statistički značajna razlika u gustini krvnih sudova između ispitivanih grupa. **Zaključak.** Utvrđena statistički značajna razlika u gustini krvnih sudova između grupa ukazuje na značaj angiogeneze u patogenezi ovih bolesti i potencijalnu ulogu ovog parametra u dijagnostici i terapiji.

Ključne reči: krvni sudovi; angiogeneza; koštana srž; mijeloidna leukemija; biopsija; morfološki i mikroskopski nalazi

Introduction

Hematopoiesis - the process of generating blood elements in adulthood - takes place in the bone marrow, which is functionally divided into active red marrow and inactive yellow marrow composed primarily of adipocytes [1]. The active bone marrow houses hematopoietic stem cells, nutrient-carrying blood vessels, sinusoidal

capillaries, and supportive tissue cells. Specific sinusoidal capillaries contain adventitial cells that secrete cytokines and factors essential for hematopoiesis [2–4].

All blood elements originate from a common pluripotent stem cell, which differentiates into lymphoid and myeloid lineages [2–4]. Disruptions of this process can lead to malignancies such as acute myeloid leukemia (AML). AML is marked by clonal prolifera-

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Abbreviations

AML	– acute myeloid leukemia
CML	– chronic myeloid leukemia
VEGF	– vascular endothelial growth factor
bFGF	– basic fibroblast growth factor
CONTR	– control group

tion of myeloid cells, accumulation of malignant blasts in the bone marrow, and suppression of normal hematopoiesis [5–8]. This malignant process often leads to bleeding, anemia, and infections in many patients. Diagnosis is based on pathohistological evaluation, with advancements in immunophenotyping (via flow cytometry) and cytogenetics. While the 2016 WHO classification defined AML by $\geq 20\%$ blasts in the bone marrow, the 2022 revision introduced lower thresholds and incorporated new genetic parameters [8,9]. Auer rods may be present in myeloblast cytoplasm, and key cytochemical markers include myeloperoxidase and Sudan Black [10]. The five-year survival rate for AML remains below 30% [8].

Chronic myeloid leukemia (CML), another hematological malignancy, arises from disrupted differentiation of hematopoietic elements due to genetic translocation leading to the formation of the Philadelphia chromosome [11, 12]. CML progresses through three phases: the chronic phase (characterized by leukocytosis $<10\%$ blasts), the accelerated phase (with 10-19% blasts and marked basophilia), and the blast phase (defined by $\geq 20\%$ blasts and extramedullary proliferation), which is the terminal stage indicating clinical progression of CML. The advent of tyrosine kinase inhibitors has dramatically improved outcomes, with a five-year survival rate now exceeding 90% [11].

Angiogenesis - the formation of new blood vessels from existing vasculature - is essential for tissue development and function, providing oxygen and nutrients to cells. However, in malignancies, angiogenesis facilitates tumor growth and dissemination, making it a critical factor in cancer progression. Key mediators of this process include vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (bFGF). While the role of angiogenesis in solid tumors is well-established, its involvement in the onset and progression of leukemias remains underexplored [12–17].

The aim of this study is to assess the percentage of blood vessel density in bone marrow samples from patients with AML and CML, and to determine whether statistically significant differences exist compared to healthy bone marrow.

Material and Methods

This retrospective study was conducted using archival material obtained from the Center for Pathol-

ogy and Histology at the University Clinical Center of Vojvodina, covering the period from January 2020 to December 2022. The study received ethical approval from the Ethics Committee of the University Clinical Center of Vojvodina (No. 00-257). A total of 90 bone marrow biopsy samples were included and categorized into three groups: a control group consisted of subjects with healthy bone marrow (CONTR), a group of patients diagnosed with acute myeloid leukemia (AML), a group of patients with chronic myeloid leukemia (CML), with 30 samples in each group.

Demographic data, including gender and age, were extracted from biopsy records. Based on age, subjects were stratified into three groups: 1) younger than 46 years, 2) 46-65 years, and 3) over 65 years. The age threshold of 46 years was selected according to the study by Aljabban and Alalsaidissa, which identified this as the median age at AML diagnosis [18]. The group older than 65 years was of particular interest due to increased morbidity and reduced survival associated with treatment in this population [19]. Morphological analysis was carried out by the Center for Pathology and Histology in collaboration with the Clinic for Hematology. Bone marrow samples were processed using standardized procedures, including decalcification and full paraffin embedding. Tissue sections were stained with hematoxylin and eosin, Giemsa, and reticulin stains. Immunohistochemical analysis was also performed using CD34 antibody (Product: Monoclonal Mouse Anti-Human CD34 Class II, Clone: QBEnd-10, Catalog No.: M7165, Manufacturer: Dako/Agilent Technologies, Denmark).

Microscopic evaluation was conducted using a ZEISS Axioscope 5 light microscope at magnifications of 50x, 100x, 200x, 400x, and 630x. For each sample, five microphotographs were taken at 200x magnification using a ZEISS AxioCam 105 color camera. Image analysis was performed with ImageJ software to determine the areal density of blood vessels in the bone marrow, expressed as a percentage on each of the five images. The average blood vessel density value for each subject was then calculated.

Statistical analysis was conducted using IBM SPSS Statistics 26. The distribution of variables and the significance of differences in blood vessel density among the three study groups were assessed. Welch's ANOVA was used to evaluate statistical differences between independent parametric samples, followed by the Games-Howell post-hoc test for further analysis. The statistical significance level for these tests was set at $p=0.05$. Results are presented through microphotographs, numerical summaries, graphical displays, and tables.

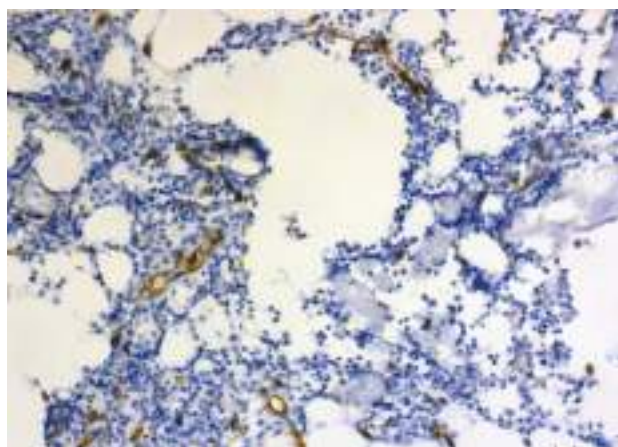


Figure 1. Blood vessels in participants with unchanged bone marrow, CD34, 200x

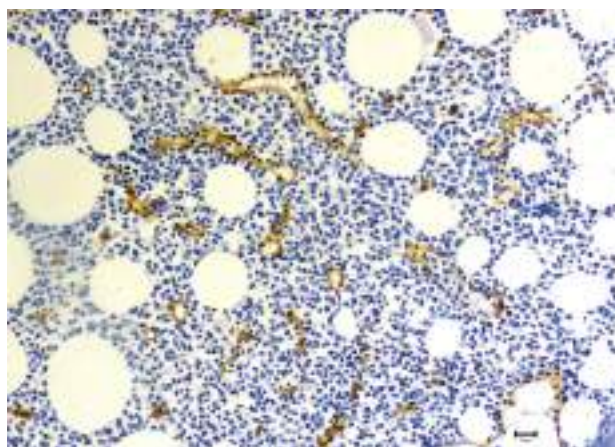


Figure 2. Blood vessels in patients with diagnosed AML, CD34, 200x

Table 1. Age of the participants in the observed groups

Group	Minimum	Maximum	Mean	SD
CONTR	25	75	51	15.18
AML	29	89	58	13.5
CML	32	86	66	14.02

Legend: CONTR – control group; AML – acute myeloid leukemia; CML – chronic myeloid leukemia; SD – standard deviation

Table 2. Distribution of participants by age groups

Observed group	Number and percentage of participants in each age group		
	0-45 years	46-65 years	>65 years
CONTR	11 (36.7%)	11 (36.7%)	8 (26.7%)
AML	5 (16.7%)	14 (46.7%)	11 (36.7%)
CML	4 (13.3%)	8 (26.7%)	18 (60%)

Legend: CONTR – control group; AML – acute myeloid leukemia; CML – chronic myeloid leukemia

Results

In the control group, participants ranged in age from 25 to 75 years, with a mean age of 51 ± 15.18 years. In the AML group, patient ages ranged from 29 to 89 years, with a mean age of 58 ± 13.5 years. Only 5 patients (16.7%) in this group were under 46 years of age. In the CML group, the youngest patient was 32 years old and the oldest was 86, with the mean age of 66 ± 14.02 years. A majority of patients in the CML group (17/30; 57%) were older than 65 years

(Tables 1 and 2). In the control group, 14 participants (46.7%) were female and 16 (53.3%) were male. Among patients with AML, 17 (56.7%) were female and 13 (43.3%) male. In the CML group, there were slightly more male patients (17; 56.7%) compared to females (13; 43.3%). Statistical analysis revealed no significant differences in gender distribution between groups ($p > 0.05$).

Blood vessel density in unchanged bone marrow samples ranged from 0.87% to 2.84% per analyzed field, with an average density of $1.85 \pm 0.56\%$ (Figure 1). In

Table 3. Results of the Games-Howell Post-Hoc Test with the dependent variable “blood vessel density”

(I) Group	(J) Group	Mean difference (I-J)	Standard error	p	95% Confidence Interval	
					Lower bound	Upper bound
Control group	AML	-1.87*	.321	.000	-2.66	-2.66
	CML	-3.578*	.428	.000	-4.62	-2.52
Group with AML	CONTR	1.87*	.32	.000	2.66	2.66
	CML	-1.7*	.52	.023	-2.94	-.45
Group with CML	CONTR	3.57*	.43	.000	2.52	4.62
	AML	1.7*	.52	.023	-.45	2.94

Legend: CONTR – control group; AML – acute myeloid leukemia; CML – chronic myeloid leukemia; p – significance

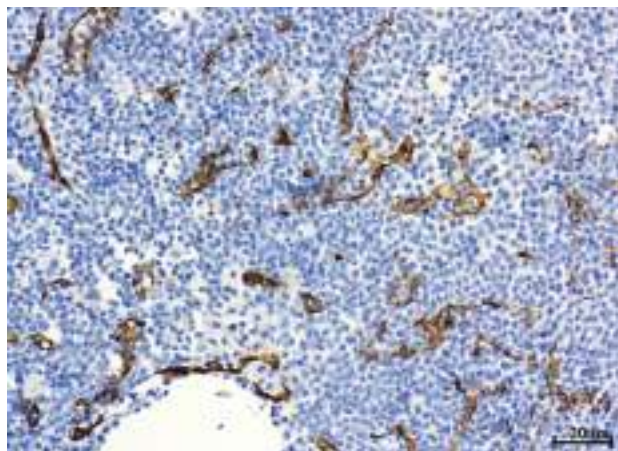


Figure 3. Blood vessels in patients with diagnosed CML, CD34, 200x

patients with AML, vessel density ranged from 1.33% to 7.1%, with a mean of $3.72 \pm 1.67\%$ (**Figure 2**), indicating increases number of blood vessels in this condition.

The CML group exhibited the highest vascular density, ranging from 2.83% to 13.19%, with a mean of $5.42 \pm 2.28\%$ (**Figure 3**). In 29 out of 30 CML cases (97%), the blood vessel density exceeded the highest value recorded in the control group.

Statistical analysis using Welch's ANOVA for independent samples within each predefined group demonstrated a statistically significant difference in blood vessel density among the three groups ($F_{2,44.364} = 47.724$, $p < 0.05$). Post-hoc analysis using the Games-Howell test confirmed statistically significant differences in blood vessel density between all pairwise group comparisons: control vs. AML, control vs. CML, and AML vs. CML (**Table 3**).

Discussion

In malignant hematologic neoplasms such as acute myeloid leukemia (AML) and chronic myeloid leukemia (CML), angiogenesis is markedly accelerated and intensified. This process is essential for tumor growth and progression, with its extent often correlating with the malignancy grade and potential dissemination. Our study analyzed this parameter and compared the results with previously published findings.

The average age of patients with AML in our study was 58 ± 13.5 years, aligning with previous literature that consistently reports a predominance of AML cases in individuals over 50 years of age [17,20–22]. In the CML group, the mean age was 66 ± 14.02 years, which slightly differs from other studies. For instance, Lopez-Hidalgo et al. reported the mean age of 49 years, while Hehlmann et al. documented an age range of 44 to 53 years [12,15,23].

The gender distribution in our study was relatively balanced. In the control group, 47% were female. In the AML group, 57% of the samples were from females, whereas in the CML group, 57% were from males. These findings are consistent with other studies that report no significant gender predominance in AML or CML, even in larger cohorts [12,15,17,20,21,23,24].

Angiogenesis is well-documented as a key factor in the progression of solid tumors, facilitated by growth factors such as VEGF and bFGF. These molecules stimulate rapid formation of new blood vessels, supporting tumor survival and expansion. In solid tumors, an increased number of blood vessels is detected upon biopsy analysis, which puts emphasis on this process, and underscores the potential importance of analyzing this parameter in hematologic malignancies as well [13–17].

Our study demonstrated a statistically significant increase in bone marrow blood vessel density in patients with AML and CML compared to healthy controls. The average blood vessel density per field was $1.85 \pm 0.56\%$ in healthy individuals, $3.72 \pm 1.67\%$ in AML patients, and $5.42 \pm 2.28\%$ in CML patients. These findings are in line with those reported by Agauayo et al., who found blood vessel densities of 2.8% in healthy controls, 4.3% in AML, and 6.2% in CML patients [14]. Hussong et al. similarly observed twofold increase in bone marrow blood vessels in AML patients compared to controls [13]. Korkolopoulou et al., reported a threefold increase in CML [15], and Lundberg et al. observed twofold increase [25]. These and other studies confirm the heightened angiogenesis in these malignant neoplasms, which supports our findings [16,17,20,21].

Importantly, our results revealed a statistically significant difference in bone marrow blood vessel density not only between leukemia patients and healthy controls, but also between the AML and CML groups.

Conclusion

Analysis of 90 bone marrow biopsies demonstrated that patients with acute myeloid leukemia were most frequently aged between 46 and 65 years, while those with chronic myeloid leukemia were predominantly over 65. Gender distribution was relatively balanced across all groups. Statistical analysis revealed a significantly increased bone marrow blood vessel density in both acute myeloid leukemia and chronic myeloid leukemia patients compared to the control group, with a significant difference in blood vessel density between acute myeloid leukemia and chronic myeloid leukemia patients.

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DID THE FEAR OF COVID-19 INFLUENCE PARENTS' BEHAVIOR IN MAINTAINING CHILDREN'S ORAL HEALTH?

DA LI JE STRAH OD KOVIDA 19 UTICAO NA PONAŠANJE RODITELJA U ODRŽAVANJU ORALNOG ZDRAVLJA DECE?

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Abstract

Introduction. Parental fear of SARS-CoV-2 infection may have negatively affected children's oral health by reducing the frequency of dental visits. The study aimed to evaluate the influence of parental fear on children's attendance at dental check-ups during the COVID-19 pandemic. **Material and Methods.** This cross-sectional study was conducted using a specially designed questionnaire consisting of nine items, including a Likert scale. The first section collected socio-demographic data, while the second focused on parental fear and the maintenance of children's oral hygiene during the pandemic. The study included 187 parents of children and adolescents aged 3 to 17 years who were patients at the dental department of the Health Center in Brus, Serbia. Data were analyzed using Microsoft Excel and SPSS software version 18.0. **Results.** The highest average agreement score on the Likert scale (3.48 ± 1.525) reflected a moderate level of fear, while the greatest disagreement (2.57 ± 1.636) was with the statement indicating an absence of fear. Regarding dental visits, 75.4% of parents reported they would bring their child for both regular and urgent check-ups, whereas 24.6% would only attend urgent appointments. However, fear intensity did not significantly influence this behavior ($p > 0.05$). Although a correlation was observed between moderate fear levels and the choice of dental facility and visit type, it was not statistically significant ($p > 0.05$). **Conclusion.** The study suggests that a moderate level of parental fear of SARS-CoV-2 infection did not significantly impact the frequency of children's regular dental visits during the pandemic.

Key words: COVID-19; SARS-CoV-2; Dental Health; Dentistry; Child; Parents; Fear

Introduction

The COVID-19 pandemic posed a major challenge to healthcare systems worldwide, including the field of dentistry [1]. Healthcare resources were redirected to address the crisis, resulting in delays or limitations in treatment, particularly for non-emergency services. Furthermore, stringent sanitary protocols, social distancing, and lockdown measures were implement-

Sažetak

Uvod. Strah roditelja od zaraze virusom SARS-CoV-2 je mogao nepovoljno uticati na oralno zdravlje dece. Cilj istraživanja bio je proceniti uticaj straha roditelja od infekcije SARS-CoV-2 virusom na odlazak dece na stomatološki pregled. **Materijal i metode.** Studija je dizajnirana kao studija preseka uz upotrebu originalno konstruisanog upitnika koji se sastojao od devet pitanja i Likertove skale. Prvi deo upitnika je obuhvatao socio-demografske karakteristike ispitanika, a drugi deo upitnika se odnosio na strah roditelja i održavanje oralne nege dece tokom pandemije. Istraživanje je obuhvatilo 187 ispitanika, roditelja dece i tinejdžera, uzrasta od tri do 17 godina, koji su bili pacijenti stomatološkog odeljenja Doma zdravlja Brus, Srbija. Statistička analiza urađena je korišćenjem Excel programa iz Microsoft Office programskog paketa i SPSS programa u verziji 18.0. **Rezultati.** Najveći prosečni skor slaganja odgovora po Likertovoj skali ($3,48 \pm 1,525$) bio je sa umerenim stepenom straha, a najveće neslaganje ($2,57 \pm 1,636$) bilo je sa tvrdnjom da nema straha. U pitanju koje se odnosilo na redovne posete deteta stomatologu, 75,4% ispitanika bi odvelo dete i na redovnu kontrolu, kao i na hitnu intervenciju, a 24,6% ispitanika samo na hitnu intervenciju, ali to nije bilo značajno uslovljeno jačinom straha ($p > 0,05$). U ispitivanoj korelaciji intenziteta straha, odgovora „bio/la sam uplašen/a, ali ne previše“ i odgovora o odabiru ustanove i realizaciji redovne kontrole ili hitne stomatološke intervencije, nađena je korelacija, ali nedovoljno statistički značajna ($p > 0,05$). **Zaključak.** Dokazan umereni strah roditelja od infekcije virusom SARS-CoV-2 u stomatološkoj ordinaciji, u našem istraživanju, nije doveo do promena u redovnim odlascima dece na stomatološki pregled.

Ključne reči: COVID-19; SARS-CoV-2; oralna nega; stomatologija; dete; roditelj; strah

ed in most countries to curb the spread of the virus, leading to widespread health, economic, and social consequences [2]. In addition to physical health concerns, the pandemic significantly impacted mental health across all age groups, with heightened levels of fear and anxiety being especially prominent [3]. Studies indicate that the prevalence of clinical anxiety among adults nearly doubled during the pandemic [4]. Given the widespread prevalence of dental

Abbreviations

SARS-CoV-2 – Severe Acute Respiratory Syndrome Coronavirus 2

anxiety even before the pandemic, fear associated with COVID-19 may have further influenced individuals' decisions regarding dental visits [5].

The elevated risk of SARS-CoV-2 transmission in dental settings is largely attributed to aerosol generation during routine procedures [6]. As a result, dental care during the pandemic shifted its focus on emergency interventions, while preventive and routine care was often postponed, potentially leading to deterioration of oral health [7]. In this context, parental fear of infection may have discouraged them from taking their children to dental appointments, thereby jeopardizing children's oral health [8]. Moreover, the expression of fear by parents in the presence of their children can negatively affect children's attitudes towards dental care and treatment compliance [9].

During the COVID-19 pandemic, a notable decline in children's dental visits was observed, likely

influenced by increased parental fear. Therefore, the aim of this study was to assess the impact of the intensity of parental fear of SARS-CoV-2 infection on the frequency of children's dental visits.

Material and Methods

This cross-sectional study was conducted using a specially designed questionnaire (**Attachment 1**), developed based on a review of similar studies in the literature [9–11]. The research took place at the Dental Department of the Health Center Brus, Serbia, from August to December 2021. Prior to participation, written informed consent was obtained from the Health Center's administration, from parents or legal guardians, and – where appropriate – from the children themselves, after being informed about the study's aims. The study received ethical approval from the Ethics Committee of the Health Center Brus, Serbia (approval number: 257, dated July 9, 2021), and was

Attachment 1. Questionnaire

Questions	Answers																								
Gender?	a) male b) female																								
How old are you?																									
Place of residence																									
4. Level of education?	a) primary, b) secondary c) college or university																								
How old is your child?																									
Have you or anyone in your family tested positive for SARS-CoV-2?	a) yes b) no																								
	a) I was very scared b) I was scared, but not that much c) I wasn't scared																								
How would you rate your level of fear during the pandemic regarding the possibility of virus infection in the dental clinic?	<table border="1"> <thead> <tr> <th></th><th>1. Absolutely disagree</th><th>2. Disagree</th><th>3. Can't decide</th><th>4. Agree</th><th>5. Absolutely agree</th></tr> </thead> <tbody> <tr> <td>a) I was very scared</td><td></td><td></td><td></td><td></td><td></td></tr> <tr> <td>b) I was scared, but not that much</td><td></td><td></td><td></td><td></td><td></td></tr> <tr> <td>c) I wasn't scared</td><td></td><td></td><td></td><td></td><td></td></tr> </tbody> </table>		1. Absolutely disagree	2. Disagree	3. Can't decide	4. Agree	5. Absolutely agree	a) I was very scared						b) I was scared, but not that much						c) I wasn't scared					
	1. Absolutely disagree	2. Disagree	3. Can't decide	4. Agree	5. Absolutely agree																				
a) I was very scared																									
b) I was scared, but not that much																									
c) I wasn't scared																									
Would you take your child for a regular dental check-up or only for emergency treatment during the pandemic?	a) yes, I would take them for a regular check-up, as well as for an emergency intervention b) no, I wouldn't take them for a regular check-up, but only for an emergency intervention																								
If your child needs dental treatment during the pandemic, where would you take them?	a) to a state institution b) to a private dental clinic																								

conducted in accordance with the principles of the Declaration of Helsinki regarding children's rights.

The study sample included 187 participants - parents or guardians of children and adolescents aged 3 to 17 years - who were patients at the Health Center's dental department. Participation was voluntary and required informed consent. The questionnaire required approximately 10 minutes to complete, and participants either wrote or circled their responses. Each participant was assigned a specific number in order to protect their identity. The first section of the questionnaire comprised 5 questions related to socio-demographic characteristics, including gender, age, place of residence, level of parental education, and the child's age (**Attachment 1**). The sixth question asked whether the respondent or any family members had previously been infected with the SARS-CoV-2. Question seven (Q7) assessed the level of parental fear of SARS-CoV-2 infection during dental visits, for both themselves and their children. This question utilized a Likert scale [12], a widely accepted method for quantifying attitudes. Respondents indicate the extent of their agreement with the provided statements using a 5-point scale: 1 – strongly disagree, 2 – disagree, 3 – neither agree nor disagree, 4 – agree, 5 – strongly agree. A neutral response category was included to ensure balanced measurement.

The eighth question asked whether parents took their children for regular dental check-ups during the pandemic, or only sought treatment in urgent cases. The final question addressed parents' choice of health-care institution - whether they preferred state or private dental clinics during the pandemic (**Attachment 1**).

Descriptive statistics were used to summarize the data, including arithmetic mean, standard deviation (SD), absolute frequency (N), and index of structure (%). Analytical methods were applied to test the statistical significance of differences between variables. The Pearson chi-square test was used for categorical data comparisons, while Student's t-test was employed

to compare mean values between two independent groups. Non-parametric correlation analysis (Spearman's rank correlation coefficient) was used to assess associations between ordinal or non-normally distributed variables. Statistical analysis was performed using Microsoft Excell and SPSS version 18.0. The results are presented in both tabular and graphical formats, with statistical significance set at $p < 0.05$.

Results

In the analyzed sample of parents ($n=187$), slightly less than half were men - 90 (48.13%) - while women comprised 97 (51.87%). The average age of male respondents was 44.7 ± 7.4 years, and the average age of female respondents was 40.4 ± 7.4 years. The age difference was statistically significant ($p < 0.001$) (**Table 1**).

Regarding the place of residence, a smaller proportion of participants lived in urban areas (10.2% of men and 16.6% of women), while a larger proportion lived in rural areas (38% of men and 35.2% of women). With respect to education level, 5.9% of men and 5.3% of women had completed primary education, 34.8% of men and 31% of women had completed secondary education, and 7.5% of men and 15.5% of women had obtained higher education. The differences in distribution by place of residence and education level were not statistically significant by gender ($p > 0.05$). The children of the respondents had a mean age of 10.1 ± 3.41 , with girls averaging 10.45 ± 3.5 and boys averaging 9.67 ± 3.2 years (**Table 1**).

Table 2 presents the distribution of responses to question 7 abc (Q7), which addressed the level of fear of SARS-CoV-2 infection, as well as differences in distribution by gender, education, place of residence, and history of SARS-CoV-2 infection.

There was no statistically significant gender-based difference in the level of fear regarding SARS-CoV-2 infection in the dental office ($p > 0.05$). Approximately one-quarter of respondents (22.4% of men and

Table 1. Socio-demographic structure of participants

Participants	Male	Female	Total	test
N (%)	90 (48.13%)	97 (51.87%)	187 (100%)	
Parents' age	44.69 ± 7.389	40.37 ± 7.366	42.45 ± 7.669	$< 0.001^{**}$
Child's age	9.67 ± 3.243	10.45 ± 3.530	10.07 ± 3.409	$> 0.05^{**}$
Residence city	19 (10.2%)	31 (16.6%)	50 (26.7%)	
Village	71 (38%)	66 (35.2%)	137 (73.3%)	$> 0.05^*$
Education primary	11 (5.9%)	10 (5.3%)	21 (11.2%)	
Secondary	65 (34.8%)	58 (31%)	123 (65.8%)	
College or university	14 (7.5%)	29 (15.5%)	43 (23%)	$> 0.05^*$

******Student's t-test; *****Pearson chi-square test

Table 2. Level of fear in relation to gender, education, residence, and previous SARS-CoV-2 infection

Q7	a	%	b	%	c	%	Total	%	χ^2 test
By gender									
m	22	24.4%	42	46.7%	26	28.9%	90	100%	>0.05
f	22	22.7%	56	57.7%	19	19.6%	97	100%	
By education									
Primary	6	28.6%	6	28.6%	9	42.9%	21	100%	<0.05
Secondary	32	26%	63	51.2%	28	22.8%	123	100%	
College or University	6	14%	29	67.4%	8	18.6%	43	100%	
By residence									
City	10	20%	24	48.0%	16	32%	50	100%	>0.05
Village	34	24.8%	74	54.0%	29	21.2%	137	100%	
By SARS-Cov-2 infection									
Yes	32	47.1%	31	45.6%	5	7.4%	68	100%	<0.0001
No	12	10.1%	67	56.3%	40	33.6%	119	100%	
Total	44	23.5%	98	52.4%	45	24.1%	187	100%	

Legend: Q7: a) I was very scared; b) I was scared, but not that much; c) I was not scared

22.7% of women) reported being very scared, while nearly half (46.7% of men and 57.7% of women) reported a moderate level of fear. A smaller portion (28.9% of men and 19.6% of women) reported having no fear at all (**Table 2**).

Differences in the level of fear by education level showed statistical significance ($p < 0.05$). Among parents with primary education, 28.6% reported being very scared, 28.6% moderately scared, and 42.9% not scared at all - a statistically significant difference compared to those with secondary and higher education ($p < 0.05$). Among parents with secondary education, 26% reported being very scared, 51.2% moderately scared, and 22.8% not

scared at all. For respondents with higher education, 14% were very scared, 67.4% were moderately scared, and 18.6% reported no fear of SARS-CoV-2 infection (**Table 2**).

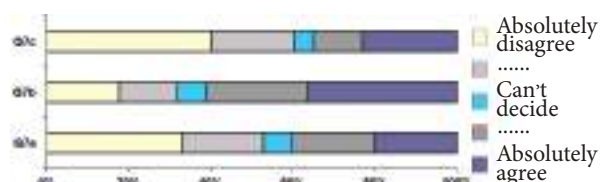
No statistically significant differences were observed in fear levels based on place of residence ($p > 0.05$). In urban areas, 20% of respondents reported being very scared, 48% moderately scared, and 32% not scared at all. In rural areas, 24.8% were very scared, 54.0% moderately scared, and 21.2% had no fear (**Table 2**).

Regarding SARS-CoV-2 infection history, 47.1% of parents who reported confirmed infection in their families stated they were very scared, 45.6% were mod-

Table 3. Parental attitude towards the type of intervention and choice of dental institution during the pandemic in relation to the level of fear

			Level of fear Q7			Total	χ^2 test
			a	b	c		
Type of intervention Q8	A	N	28	79	34	141	>0.05
		%	15.0%	42.2%	18.2%	75.4%	
	B	N	16	19	11	46	
		%	8.6%	10.2%	5.9%	24.6%	
Choice of institution Q9	A	N	20	60	26	106	>0.05
		%	10.7%	32.1%	13.9%	56.7%	
	B	N	24	38	19	81	
		%	12.8%	20.3%	10.2%	43.3%	
Total	N		44	98	45	187	>0.05
	%		23.5%	52.4%	24.1%	100.0%	

Legend: Q7: a. very scared, b. scared, but not that much, c. I was not scared; Q8: a. yes, I would take them for a regular check-up, and for emergency intervention, b. no, I would not take them for a regular check-up, but only for emergency intervention; Q9: a. to a state institution, b. to a private dental clinic



Graph 1. Distribution of agreement levels with responses 7a, 7b, and 7c on the Likert scale

erately scared, and only 7.4% were not scared at all. In contrast, among those without a family history of infection, 10.1% were very scared, 56.3% were moderately scared, and 33.6% reported no fear. The difference was highly statistically significant ($p < 0.0001$) (**Table 2**).

The highest average agreement score (Q7) on the Likert scale (3.48 ± 1.525) was recorded for option b (“moderately scared”), while the lowest (2.57 ± 1.636) was for option c (“not scared at all”) (**Graph 1**).

The association between parents’ fear levels (Q7), their attitudes towards the necessity of dental interventions (Q8), and their preferred type of dental institution during the pandemic (Q9) was analyzed using Pearson’s chi-square test (**Table 3**).

When asked about the types of dental intervention they would seek for their children during the pandemic, 75.4% of respondents stated they would go for both regular check-ups and emergency interventions, while 24.6% would go only for emergencies. This choice was not significantly influenced by the level of fear ($p > 0.05$) (**Table 3**).

Regarding the choice of dental institution during the pandemic, 56.7% preferred state institutions, while 43.3% chose private clinics. Again, no statistically significant association was found with the level of fear ($p > 0.05$) (**Table 3**).

Although a correlation was observed between a moderate level of fear (“I was scared, but not too much”) and the choice of institution or decision to pursue regular or emergency dental care (Q8 and Q9), this correlation was not statistically significant.

Discussion

Dental settings are often perceived as stressful environments for both children and their parents. During the Covid-19 pandemic, this fear was notably intensified due to the perceived risk of SARS-CoV-2 transmission, especially in the absence of adequate protective measures [13]. At the onset of the pandemic, parents – motivated by concern for their children’s well-being – were generally more cautious than individuals without parental responsibilities [14].

Approximately half of the surveyed parents in our study reported a moderate level of fear regarding SARS-CoV-2 infection, which some authors suggest

may positively influence behavioral changes related to infection prevention [15]. Taravati et al. in Iran similarly reported that the majority of parents (62.6%) experienced moderate fear, while 26.8% reported strong fear [16]. In Poland, Olszewska et al. [17] found that the proportion of parents with above-average fear levels was over ten times higher than in the pre-pandemic period, correlating closely with children’s fear levels.

Likert scale responses in our study further confirmed a predominance of moderate fear, with few respondents reporting a complete absence of concern. In contrast, Samuel et al. [18] found that parents generally reported high levels of fear, possibly reflecting differences in cultural mentality or prior societal hardships in Serbia – such as wars, economic crisis, or natural disasters – that may influence emotional responses.

Although previous research has shown that mothers were more engaged in their children’s oral health during the pandemic [19], our findings revealed that mothers and fathers expressed similar levels of fear. However, other studies have found that women were generally more fearful than men in dental settings during the pandemic [16]. This discrepancy may stem from mothers heightened emotional burden as primary caregivers, although shared responsibilities with fathers could explain the more balanced levels of fear observed in our study.

Our findings also indicate no significant differences in fear levels based on place of residence. Both urban and rural populations expressed moderate fear, which may reflect relatively stable mental health across regions, despite increased infection risk in densely populated urban areas and widespread exposure to media coverage. While similar national studies are lacking, research in Germany has shown regional variation in fear and mental health based on local infection rates [20].

Education background significantly influenced parental fear. Half of the respondents with only primary education reported no fear of SARS-CoV-2 infection. This may reflect limited understanding of disease transmission or a lack of public health awareness, which could hinder detection and risk assessment [21].

Previous studies have found that lower education levels are associated with greater fear and anxiety during the pandemic [16]. The majority of information about COVID-19 was disseminated through social media, television, and internet platforms [10], and excessive media consumption has been linked to elevated fear and misinformed attitudes, as noted by Garfin et al. [22]. Parents with secondary and higher education levels demonstrated more controlled responses to the threat of infection, likely due

to better knowledge of the virus and its transmission routes. Surme et al. [23] similarly found that parental knowledge about SARS-CoV-2 transmission varies significantly by education level. Notably, 9.6% of respondents with lower education levels in their study reported having no knowledge of transmission pathways, which may indirectly affect fear perception.

As Mertens et al. [24] noted, families who experienced the loss of loved ones during the pandemic were more likely to experience elevated fear. In our study, respondents with a family history of SARS-CoV-2 infection were significantly more fearful compared to those without such experiences. While 36.4% of parents in our sample had a positive family history of infection, Taravati et al. [16] reported slightly lower percentage (25.6%) and found no significant correlation between family infection history and fear.

Access to dental care was also disrupted by government-imposed restrictions and a general lack of understanding about the virus [1]. Parental knowledge, behavior, and attitudes of play an essential role in maintaining children's oral health. Better parental knowledge is associated with better oral health outcomes [10]. The pandemic has highlighted the need to disseminate oral health information through digital platforms, allowing pediatric dentists to offer preventive guidance remotely. Telephone consultations and teledentistry can support parent-dentist-child communication [25], although this approach remains underutilized globally [19] and should be further promoted.

Most surveyed parents acknowledge the importance of both regular dental check-ups and emergency interventions for their children. Only a minority believed dental visits should be reserved for emergencies during the pandemic. This contrasts with findings from Guo et al. [8], who emphasized the need for emergency-only dental treatment due to heightened parental fear. Campagnaro et al. [9] sim-

ilarly observed that parents with greater fear were less likely to bring their children to the dentist. In China, as many as 84% of parents reported they would only take their children for urgent dental care during the pandemic [10]. Ceyhan et al. [26] reported that only a quarter of parents had taken their child to the dentist, despite dental issues being present, while 74.4% had not. Ekinici et al. [27] found that mothers were more proactive, with 81.9% affirming they would take their child to the dentist, compared to only 59.6% of fathers. Additionally, there has been a global increase in interest in self-treatment during the pandemic [28].

Regarding choice of dental institution, preferences were nearly evenly split between public and private clinics. In line with our findings, a similar study reported that 53.19% of parents feared virus transmission during dental visits and preferred private practices [11]. Sahin et al. [29] found that 69.3% of respondents chose private clinics, while 18.8% chose dental faculties and 11.9% opted for public institutions. Trust in the quality of care provided may influence institutional choice [30]. In response to global healthcare disruption, the World Health Organization issued guidelines for both public and private dental sectors, recommending protective measures such as masks, gloves, face shields, hand hygiene, ventilation, disinfection, reduced companions, and spacing between appointments [1].

Conclusion

Although a moderate level of fear regarding Severe Acute Respiratory Syndrome Coronavirus 2 infection in dental settings was confirmed among parents, it did not significantly alter their behavior concerning regular dental check-ups, treatment of their children, or the choice of dental institution. The results of this study offer valuable insights that can inform strategies for public behavior in the context of future pandemics.

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CHARACTERISTICS OF SUPRACONDYLAR FRACTURES IN THE PEDIATRIC POPULATION IN REGARD TO FRACTURE TYPE ACCORDING TO THE GARTLAND CLASSIFICATION

KARAKTERISTIKE SUPRAKONDILARNIH PRELOMA U DEČJEM UZRASTU U POREĐENJU SA TIPOM PRELOMA PO GARTLANDOVOJ KLASIFIKACIJI

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Abstract

Introduction. Supracondylar fractures are among the most common elbow injuries in the pediatric population and represent a significant therapeutic challenge. This study investigates the epidemiological and clinical characteristics of these fractures, with a particular focus on treatment approaches. **Materials and Methods.** A retrospective analysis was conducted on data from 254 patients treated at the Department of Traumatology, Clinic for Pediatric Surgery, from 2019 to 2023. The study was approved by the Ethics Committee of the Institute for Child and Youth Health Care of Vojvodina. Patients were divided into two age groups. Data collected included demographics, fracture type, treatment modality, treatment duration, comorbidities, complications, and outcomes. Statistical analysis was performed using *Jeffrey's Amazing Statistics Program* software, employing the chi-square test and Mann-Whitney U test. **Results.** Of the 254 patients, 56.69% were male and 43.31% female. Among school-aged children, the most common cause of injury was falling from a bicycle, while preschool-aged children most often sustained injuries during play. Type IIA fractures were more frequently associated with right arm injuries, whereas type IIIC fractures were common in the left arm injuries. Orthopedic reduction and percutaneous fixation using Kirschner wires were employed in 97.23% of cases. **Conclusion.** Supracondylar humerus fractures are more frequent in male children. No statistically significant difference was found in fracture incidence between preschool and school-age groups. Left-sided injuries were more common. Neurological complications were the most frequently observed, although no significant association was found between complication rates and fracture type. **Key words:** Elbow Injuries; Humeral Fractures, Distal; Child; Fractures, Bone; Classification; Bone Wires; Sex Factors

Sažetak

Uvod. Suprakondilarni prelomi predstavljaju jedan od najčešćih preloma u zglobu lakta kod pedijatrijske populacije i izazov su u lečenju. Ova studija istražuje epidemiološke i kliničke aspekte ovih preloma, s posebnim fokusom na modalitete lečenja. **Materijal i metode.** Istraživanje je sprovedeno kao retrospektivna analiza podataka pacijenata sa suprakondilarnim prelomom humerusa lečenih na Odeljenju traumatologije Klinike za dečju hirurgiju od 2019. do 2023. godine uz dozvolu Etičke komisije Instituta za zdravstvenu zaštitu dece i omladine Vojvodine. Prema uzrastu, 254 pacijenta su podeljeni u dve grupe. Analizirani su demografski podaci, mehanizam povrede, tip preloma, način lečenja i komplikacije lečenja. Statistička obrada izvršena je korišćenjem softvera *Jeffrey's Amazing Statistics Program*, a razlike među grupama su testirane hi-kvadrat testom i Men-Vitnijevim U-testom. **Rezultati.** 56,69% ispitanika su bili muškog, a 43,31% ženskog pola. Dominantan uzrok povređivanja kod školske dece bio je pad sa bicikla, dok se kod predškolske dece povrede najčešće dešavaju tokom igre. Pacijenti sa povredama desne ruke su češće imali IIA tip preloma, dok su pacijenti sa povredama leve ruke imali IIIC tip. Kod 97,23% pacijenata načinjena je ortopedska repozicija i perkutana fiksacija pomoću Kiršnerovih igala. **Zaključak.** Suprakondilarni prelom humerusa kod pedijatrijskih pacijenata češći je kod muške dece. Nije bilo statistički značajne razlike u učestalosti preloma između predškolske i školske grupe. Dokazano je češće povređivanje leve ruke. Najčešće su neurološke komplikacije, bez statistički značajne povezanosti u odnosu na tip preloma. **Ključne reči:** povrede lakta; suprakondilarni prelomi; dete; prelom kosti; klasifikacija; Kiršnerove igle; pol

Introduction

Supracondylar fractures are the most common type of elbow fracture in children, accounting for up to 70% of all elbow fractures and ranking second only to distal radius fractures in overall pediatric fracture incidence [1,2]. They represent approximately two-thirds of all fracture-related hospitalizations in the pediatric popu-

lation [3], with an estimated incidence of 177.3 per 100,000 children. These fractures are more frequently observed in male children and typically involve the non-dominant arm [1]. The high incidence of supracondylar fractures in children is attributed to several anatomical and developmental factors, including increased laxity of the collateral ligaments, the relative immaturity of the supracondylar region of the humer-

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us, and the biomechanical vulnerability of the elbow joint during hyperextension [2–4]. Supracondylar fractures are classified by the mechanism of injury into two main types: extension and flexion [5].

Fractures in this study were categorized based on radiological findings using the modified Gartland classification system [6]. Due to the high frequency of Gartland type III fractures, we propose a supplementary subclassification to provide a more detailed assessment: Type IIIA – posteromedial displacement of the distal fragment, Type IIIB – posterolateral displacement of the distal fragment, Type IIIC – posterior cortical displacement less than 2 mm on lateral radiograph.

Despite being common, the treatment of supracondylar fractures remains a topic of debate. One major area of uncertainty lies in choosing between conservative and surgical management, especially for type II fractures, where treatment decisions depend on the degree of displacement, fracture stability, and the presence of neurovascular complications [7]. Another ongoing discussion concerns the optimal timing of surgical intervention – whether immediate operative management is superior to delayed treatment after a short observation period [8]. Additionally, attention must be given to the risk of postoperative complications such as residual deformity, joint contractures, and nerve injury [9].

The aim of this study is to analyze the characteristics of supracondylar humeral fractures in children treated at a single healthcare institution, with attention special focus on gender, age, side and mechanism of injury, treatment methods, and associated complications, in relation to the modified fracture classification.

Material and Methods

The retrospective study analyzed data from medical records of pediatric patients diagnosed with supracondylar humerus fractures who were hospitalized and treated at the Department of Traumatology, Clinic for Pediatric Surgery, Institute for Child and Youth Health Care of Vojvodina, between 2019 and 2023.

Patient data were retrieved from the *Heliant* health information system and the digital radiological database (Picture Archiving and Communication System – PACS).

A total of 254 patients were included in the study and categorized into two age-based groups: preschool children (1–6 years) and school-aged children (7 years and older). The following parameters were extracted from the medical records: demographic data, fracture type, treatment method, duration of treatment, essence of comorbidities, complications, and treatment outcomes.

Statistical analysis was performed using *JASP* software version 0.18.3.0. Descriptive statistics for nu-

merical variables were reported as means and standard deviations, while categorical (nominal) variables were summarized as percentages and frequencies. Group differences in categorical (nominal) variables were analyzed using the Chi-square test or Fisher’s exact test, as appropriate. The Mann–Whitney U test was used to compare numerical variables between groups. The predictive value of selected variables for the occurrence of neurological complications was assessed using binary logistic regression. A p-value < 0.05 was considered statistically significant. All results were summarized and presented in tabular form.

Results

A total of 254 participants with supracondylar humerus fractures were included in the study. Of these, 239 children (94.09%) were classified as extension-type fractures, and 15 (5.91%) as flexion-type (**Figure 1**). Of all participants, 56.69% were male and 43.31% were fe-

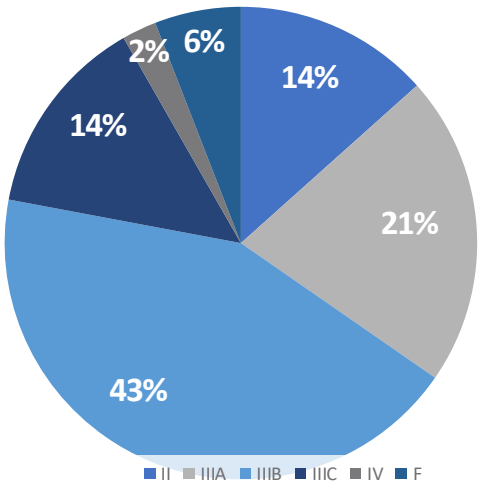


Figure 1. Distribution of supracondylar fractures

male. The age of participant ranged from 1 to 17 years. The preschool–age group comprised 49.21%, while 50.78% were older than 7 years (**Table 1**). There was no statistically significant difference in the distribution of fracture types by age group or sex ($p > 0.05$).

The common mechanism of injury in school-aged children was falling while riding a bicycle or engaging

Table 1. Distribution by gender and age group

Gender	
Male	144 (56.69%)
Female	110 (43.31%)
Age group	
Preschool	125 (49.21%)
School	129 (50.78%)

Table 2. Age distribution of injury mechanisms by patient gender

Injury Mechanism	Age group		Total	Fisher's exact	P
	Preschool	School			
Sports injury	3	14	17	19.973	0.001
	8.39%	8.60%	6.69%		
Unknown/other	55	61	116		
	56.81%	58.18%	45.66%		
Bicycle-related injury	12	21	33		
	16.30%	16.69%	12.99%		
Injury during play	47	31	78		
	38.53%	39.46%	30.71%		
Fall from the height	8	1	9		
	4.44%	4.55%	3.54%		
Traffic accident	0	1	1		
	0	0.50%	0.39%		
Total	125	129	254		
	100%	100%	100%		

in sports activities. In contrast, injuries in the preschool group most frequently occurred during play or due to falls from height. This difference in injury mechanism between age groups was statistically significant ($p < 0.05$) (**Table 2**).

Regarding the side of injury, left arm fractures were more prevalent ($n = 144$, 56.69%) compared to right arm fractures (43.31%).

Among the extension type fractures, 34 (13.39%) had type II fractures, 54 (21.26%) had type IIIA, 110 (43.31%) had type IIIB, 35 (13.78%) had type IIIC, and 6 patients (2.36%) had type IV fractures (**Table 3**).

Type IIA fractures were more frequently observed in right arm injuries, while type IIIC fractures were more common in left arm injuries. Although this difference was not statistically significant, the p-value

was borderline ($p = 0.058$), warranting cautious interpretation.

Treatment most commonly involved closed (orthopedic) reduction followed by percutaneous fixation using Kirschner wires, performed in 97.23% of patients. Open reduction and Kirschner wire fixation were necessary in six cases (2.37%). One patient (0.40%) was treated with closed reduction and cast immobilization. There was no statistically significant association between the side of injury and the treatment method ($p > 0.05$). The Kirschner wire sizes ranged from 1.4 mm to 2.0 mm. Crossed pin placement was the most frequently used technique, applied in 226 cases (88.97%), while lateral pinning was used in 27 cases. No statistically significant association was found between the method of pin placement and the

Table 3. Fracture classification according to the side of the injured arm

Fracture classification	Side		Total	Fisher's exact	p
	Right arm	Left arm			
II	15	19	34	10.503	0.058
	13.64%	13.29%	13.44%		
IIIA	27	27	54		
	24.55%	18.88%	21.34%		
IIIB	49	61	110		
	44.55%	41.96%	43.31%		
IIIC	10	25	35		
	9.09%	17.48%	13.83%		
IV	0	6	6		
	0	4.20%	2.37%		
F	9	6	15		
	8.18%	4.20%	5.93%		
Total	110	144	254		
	43.31%	56.69%	100%		

severity of the fracture. Similarly, there were no significant differences in the time to cast removal or hardware extraction in relation to sex or age ($p > 0.05$).

Neurological complications were documented in 10 patients at initial emergency evaluation. Three patients exhibited median nerve (n. medianus) involvement, two had ulnar nerve (n. ulnaris) injuries, and two had radial nerve (n. radialis) deficits. Two children had combined deficits involving the ulnar and median nerves, and one child presented with a combination of ulnar and radial nerve involvement. The majority of neurological injuries occurred in type IIIB fractures ($n = 5$), followed by type IIIA ($n = 4$), and type IV ($n = 1$). All neurological deficits resolved over time, with complete recovery in all affected children within 6 to 12 months. No vascular injuries were recorded in the patient cohort.

Discussion

Supracondylar humerus fractures represent one of the most frequent and clinically significant pediatric fractures [1]. In our study, extension-type fractures predominated (94%), which aligns with existing literature [5,6]. Using our proposed subclassification of Gartland type III fractures into IIIA, IIIB, and IIIC, we found that type III accounted for 78.4% of all cases. Among these, type IIIB (posterolateral displacement) was the most common (43.3%), followed by type IIIA (posteromedial displacement, 21.3%), and type IIIC (minimal posterior cortical displacement, 13.8%). Type II fractures constituted 13.4% of cases, while type IV fractures – associated with multidirectional instability – were rare (2.4%). Flexion-type fractures accounted for 5.9% of the total. This high frequency of type III fractures is consistent with prior studies reporting that type III fractures comprise 60–70% of supracondylar fractures requiring hospitalization, while types I and II are less common (each about 15–20%) [10]. The elevated proportion of type III fractures in our cohort likely reflects a referral bias, as our institution serves as a regional trauma center. The rarity of type IV fractures also mirrors previous reports [6,11]. However, the predominance of subtype IIIB contrasts with some studies that report equal or greater frequencies of IIIA fractures [12, 13], suggesting the need for further research.

We observed higher overall incidence of fractures in boys (56.7%) compared to girls (43.3%), consistent with literature attributing this to increased physical activity and risk-taking behaviors in boys [1,14]. However, there was no statistically significant difference in the distribution of fracture types by sex ($p=0.623$), indicating that while boys are more likely to sustain fractures, the severity distribution across fracture

types II through IV, including flexion types, is comparable between sexes. This aligns with prior studies noting sex as a risk factor for fracture occurrence but not for fracture type or severity [10,12,15].

The age distribution in our study showed a mean of 6.73 ± 2.52 years, consistent with the established peak incidence between 5 and 7 years [10,15]. Dividing patients into preschool (1–6 years) and school-age (7 years and older) groups, we found no significant difference in the distribution of specific Gartland fracture ($p = 0.129$). Although flexion-type and type IV fractures appeared more frequent in older children, and type IIIA fractures were more frequent in younger children, these differences were not statistically significant. This suggests that fracture severity is more strongly influenced by injury mechanics – such as fall height, angle, and impact force – than by age alone. Most studies highlight age as a general risk factor for fracture but not as a determinant of fracture severity [16]. Future research should examine fracture type distribution in broader age ranges, such as toddlers under three years or adolescents over 12, or analyze age as a continuous variable to identify subtle patterns.

Left arm injuries were more common (56.7%) than right arm fractures (43.3%), which is consistent with reports that supracondylar fractures more frequently affect the non-dominant arm [14]. Our analysis by Gartland fracture type revealed a borderline significant difference ($p = 0.058$), with type IIIA and flexion-type fractures more common on right arm injuries, and type IIIC and all type IV fractures observed exclusively on the left. These findings may reflect underlying biomechanical factors and warrant further investigation [17]. There was a statistically significant difference in the mechanism of injury between age groups ($p = 0.001$). Pre-school children typically sustained injuries from play or falls from height, while school-age children more often sustained fractures while riding bicycles or doing sports. Most injuries (94%) were caused by falls onto an outstretched hand (FOOSH), resulting in extension-type fractures [10, 18]. Higher-energy mechanisms, such as falls from height or bicycle accidents, are more likely to result in complete displacement (Gartland types III and IV), while lower-energy falls tend to cause less severe injuries (type II) [19]. This corresponds with the high proportion of type III fractures (78.4%) in our study.

Surgical management was the predominant treatment approach. Closed reduction and percutaneous fixation with Kirschner wires (CRIF) was used in 97.2% of cases, while open reduction (ORIF) was required in only 2.4%. Conservative treatment with cast immobilization (CRIM) was used in one patient (0.4%). Most surgical interventions were performed

within 24 hours, although patients initially managed conservatively who required surgery were treated after an average of 3.3 days later due to secondary displacement. This treatment pattern aligns with clinical guidelines recommending surgery for displaced fractures (Gartland types II-IV), and conservative management for stable, non-displaced fractures (type I) [10,20–23]. Cross-pin fixation (medial and lateral wires) was used in 88.97% of surgical cases, while lateral-only pinning was applied in 10.62%. There was no significant correlation between fracture type and pin configuration ($p > 0.05$), indicating that the choice of pinning technique was likely based on intraoperative stability and surgeon preference. Although cross-pin fixation offers greater rotational stability, it carries a higher risk of ulnar nerve injury, whereas lateral pinning is safer but potentially less stable for more severe fractures [10,20,24]. Our institution's preference for cross-pin fixation differs from emerging trends favoring lateral pinning for nerve safety. However, we observed no significant difference in outcomes, consistent with the findings of Kocher et al. [24].

The diameter of Kirschner wires ranged from 1.4 mm to 2.0 mm, as recommended based on patient age and bone thickness [13,20]. The average immobilization period was approximately 3.5 weeks (23–24 days), consistent with pediatric protocols. There were no statistically significant differences in immobilization duration by age or sex ($p > 0.05$). While not analyzed in our study, immobilization length may also correlate with fracture severity. Standard practice suggests 3–4 weeks of immobilization due to children's rapid bone healing, although recent studies explore shorter durations depending on fixation quality [25].

Neurovascular complications occurred in 3.9% of patients (10/254), most frequently involving the median and ulnar nerves, with fewer radial nerve injuries. Although anterior interosseous nerve palsy is often cited as most common in literature, our findings align with those of Tomaszewski et al. [15]. The relatively higher incidence of ulnar nerve injury may be associated with the prevalent use of cross-pin fixation [24]. Neurological deficits were observed only in displaced fractures, though no statistically significant association was found ($p = 0.174$), possibly due to small sample size. No vascular injuries were reported, a fa-

vorable result compared to literature noting radial pulse absence in 6–20% of cases and vascular compromise in 6–7% of displaced fractures [8,15,16]. This underscores the importance of timely surgical intervention and careful operative technique.

This study has several limitations. As a retrospective analysis, it was based on medical records, which may contain inconsistent or incomplete data, potentially affecting reliability. Conducted in a single institution, the findings may not be generalizable to other settings. Additionally, long-term outcomes – particularly regarding functional recovery and late complications such as malunion or neurological deficits – were not assessed. Variability in surgeon expertise and intraoperative technique was also not considered, which may influence outcomes. Future research should multicenter studies with prospective follow-up to evaluate long-term results and validate these findings in more diverse populations.

Conclusion

This study provides valuable insights into the relationship between age, gender, injury mechanism, and treatment modality in pediatric supracondylar humerus fractures.

A higher incidence of fractures was observed in male patients, indicating greater susceptibility compared to females. The side of the injury (left vs. right arm) and fracture type did not significantly influence treatment duration, suggesting that these factors are not major determinants in recovery time. However, the choice of treatment was strongly correlated with fracture type, with most displaced fractures managed successfully through closed reduction and internal fixation.

The exceptionally low rate of neurological complications underscores the effectiveness of the treatment approaches used at our institution.

In summary, the findings highlight the importance of a timely diagnosis and appropriate treatment selection, particularly for older patients. They also support the need for individualized treatment planning based on patient characteristics and fracture severity. Further research is essential to refine therapeutic protocols and ensure optimal long-term outcomes in the treatment of fractures.

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REVIEW ARTICLES PREGLEDNI ČLANCI

HEALTH IMPLICATIONS AND SAFETY OF ARTIFICIAL SWEETENERS

ZDRAVSTVENE IMPLIKACIJE I BEZBEDNOST VEŠTAČKIH ZASLAĐIVAČA

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Pregledni članak

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Abstract

Introduction. Non-nutritive sweeteners allow for the enjoyment of sweet-tasting foods with minimal calorie intake. Their growing popularity is driven by increased health awareness and efforts to reduce sugar consumption, particularly among individuals at higher risk of obesity and diabetes. **Results.** Artificial sweeteners vary in chemical structure and mechanisms of action, providing intense sweetness even at low concentrations. Their metabolism in the human body depends on the specific compound, and their safety is rigorously assessed by global regulatory agencies. While most are approved for use and considered safe within recommended intake levels, emerging data suggest potential long-term effects, including alternations in gut microbiota, impaired glucose metabolism, and increased risk of certain diseases. Despite these concerns, sugar substitutes play a significant role in modern nutrition by enabling reduced caloric intake without compromising taste. **Conclusion.** Continued research is essential to fully understand the health benefits and risks of non-nutritive sweeteners, supporting informed choices regarding their inclusion in everyday diets.

Key words: Sweetening Agents; Health Impact Assessment; Safety; Risk Factors; Drug-Related Side Effects and Adverse Reactions; Food Additives

Sažetak

Uvod. Veštački zaslađivači predstavljaju široko korišćene prehrambene aditive koji omogućavaju unos hrane sa slatkim ukusom, uz minimalan unos kalorija. Njihova popularnost raste usled sve veće svesti o zdravlju i potrebe za smanjenjem unosa šećera, posebno kod populacije sa povećanim rizikom od gojaznosti i dijabetesa. **Rezultati.** Veštački zaslađivači poseduju različite hemijske strukture i mehanizme delovanja, koji omogućavaju postizanje intenzivnog slatkog ukusa pri malim koncentracijama. Metabolizam ovih jedinjenja u ljudskom organizmu varira u zavisnosti od vrste zaslađivača, a njihova bezbednost je predmet pažljive procene regulatornih tela na globalnom nivou. Iako su mnogi odobreni za upotrebu i smatraju se bezbednim kada se koriste u preporučenim količinama, dostupni podaci ukazuju na potencijalne dugoročne rizike, uključujući uticaj na mikrobiom creva, metabolizam glukoze i rizik od određenih poremećaja. Veštački zaslađivači imaju značajnu ulogu u modernoj ishrani, omogućavajući smanjenje unosa šećera i kalorija bez kompromisa u pogledu ukusa. **Zaključak.** Ipak, potrebne su dodatne analize kako bi se dodatno razjasnile zdravstvene koristi i rizici, čime bi se omogućilo, uz potpunu informisanost, donošenje odluka o njihovoj upotrebi i integraciji u svakodnevnu ishranu.

Glavne reči: zaslađivači; procena uticaja na zdravlje; sigurnost; faktori rizika; neželjeni efekti i neželjene reakcije na lekove; prehrambeni aditivi

Introduction

Sweetening agents are widely used as sugar substitutes in foods, beverages, pharmaceuticals, and hygiene products across the globe [1]. Research on newborns has demonstrated that human preference for sweet-tasting foods is innate [2].

The U.S. Food and Drug Administration (FDA) has approved several non-nutritive sweeteners (NNS) for consumption within the limits of the acceptable daily intake (ADI). These include acesulfame-K, saccharin, sucralose, neotame, aspartame, and stevia. The ADI represents the quantity of a substance that

can be safely consumed daily over a lifetime without posing significant health risks and is expressed in milligrams per kilogram of body weight [3]. Other commonly used sweeteners include alitame – approved for use in South America, China, and Australia – and cyclamate, which is permitted in 50 countries, though not in the U.S. [4].

In the European Union, sweetener alternatives are also approved as food additives [5]. Their safety is assessed by national regulatory authorities, the European Food Safety Commission (EFSA), and the Joint FAO/WHO Expert Committee on Food Additives (JECFA), ensuring that only sweet-

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Abbreviations

NNS	– non-nutritive sweeteners
FDA	– Food and Drug Administration
ADI	– acceptable daily intake
EU	– European Union
T2D	– type 2 diabetes
SCFAs	– short-chain fatty acids

eners with established safety profiles are authorized for public use [6].

However, excessive consumption of these additives may lead to adverse effects, and it is essential to raise consumer awareness of potential risks [4]. Studies have associated artificial sweeteners with gastrointestinal disturbances, neurological symptoms (such as headaches and altered taste perception, and an increased risk of cardiovascular disease and type 2 diabetes (T2D) [7].

A large-scale prospective cohort study recently found that individuals with higher consumption of artificial sweeteners had an increased risk of developing T2D compared to non-consumers, with particularly strong association observed for aspartame and acesulfame-K [8].

Due to their widespread use in a dietary, processed, and cosmetic products, complete avoidance of artificial sweeteners is nearly impossible. Nevertheless, certain populations should exercise caution, including children, individuals with diabetes, pregnant or breastfeeding women, and patients with migraines or epilepsy [4].

Children are especially vulnerable, as they tend to consume more food and beverages per kilogram of body weight. The American Dietetic Association advises against the use of artificial sweeteners in children under the age of two years of age and recommends minimal or no consumption during pregnancy and lactation, despite FDA approval. Some evidence also suggests a potential link between sweetener intake during pregnancy and an increased risk of premature birth [9,10].

This study focuses on aspartame and other commonly used FDA-approved sweeteners, which have undergone extensive safety evaluations and are widely incorporated into food and beverage products.

Acesulfame Potassium (E950)

Acesulfame potassium (Ace-K) is a non-caloric artificial sweetener that is over 200 times sweeter than sucrose and is among the most widely used sugar substitutes worldwide [11]. When used alone, Ace-K can produce a slightly bitter aftertaste; therefore, it is often blended with other sweeteners such as sucralose or aspartame. After oral ingestion, Ace-K is rapidly and

completely absorbed in the gastrointestinal tract. It is quickly distributed throughout the body and primarily excreted unchanged in the urine, with no evidence of tissue bioaccumulation. At peak plasma concentrations, the highest levels are found in the gastrointestinal tract, bile, kidneys, and bladder [12]. One of the Ace-K's by-products, acetoacetamide, has shown toxic effects in high concentrations. Animal studies demonstrated that a diet containing 1% acetoacetamide over three months induced tumor growth in the thyroid gland. However, human exposure to this compound is considered negligible, and the FDA has concluded that Ace-K is safe for human consumption [13]. The diabetogenic potential of Ace-K has been examined in various studies with findings suggesting a stronger association with impaired glucose metabolism than sucralose. Elevated doses of Ace-K have been linked to disrupted insulin regulation and glucose homeostasis, which could contribute to the development of type 2 diabetes and metabolic disease. One study reported a 36% higher relative risk of developing metabolic syndrome in individuals who consumed Ace-K-sweetened beverages compared to non-consumers [13]. Notably, even low doses of Ace-K (around 1-4% of the ADI) have been associated with earlier onset of puberty in girls [13]. Furthermore, a large cohort study involving 10,388 participants found a significant association between total consumption of artificial sweeteners – specifically Ace-K – and an increased risk of cardiovascular diseases [13]. In animal models, Ace-K has also been shown to alter the composition of the gut microbiota. Mice treated with Ace-K exhibited an increased abundance of the *Bacteroides* genus compared to controls. *Bacteroides* species have the capability of degrading complex glycans and producing short-chain fatty acids (SCFAs), which are vital for host metabolism [14]. Additionally, Ace-K administration led to a significant rise in pyruvate levels, a central metabolite in energy pathways that can serve as a precursor to SCFAs [14].

Ace-K is currently approved for use in over 50 countries, including Canada, Switzerland, Norway, Japan, the United States, Australia, and various EU member states [15]. The FDA initially approved Ace-K for use in carbonated beverages in 1988, followed by a broader approval for general use in 2003 [16]. The acceptable daily intake (ADI) established by the FDA is 15 mg/kg of body weight [17].

Aspartame (E951)

Aspartame is a low-calorie artificial sweetener approximately 200 times sweeter than sucrose. In Europe, it is approved as a food additive and is widely used to sweeten beverages, desserts, confectionery,

dairy products, chewing gum, low-calorie and weight management products, and as a tabletop sweetener [18]. Chemically, aspartame is a methyl ester composed of two amino acids: L-aspartic acid and L-phenylalanine, combined with methanol through esterification. Upon digestion, these components are released in the following proportions: phenylalanine (50%), aspartic acid (40%), and methanol (10%), all of which are readily absorbed through the intestinal mucosa. While these metabolites are naturally occurring in many foods, in high doses they may exert harmful effects, particularly with chronic consumption [19]. Methanol, once absorbed, is gradually metabolized in the liver into formaldehyde, a known neurotoxin, and subsequently into formic acid via the enzyme alcohol dehydrogenase [12]. Formic acid can inhibit cytochrome oxidase, a critical enzyme in the mitochondrial respiratory chain, leading to increased anaerobic metabolism and lactate accumulation. Elevated plasma levels of phenylalanine – another aspartame metabolite – may inhibit tyrosine hydroxylase and tryptophan hydroxylase, enzymes essential for the synthesis of neurotransmitters such as serotonin and dopamine. These neurotransmitters are involved in regulating mood, cognition, motor activity, appetite, sleep, and cardiovascular function. Therefore, individuals with phenylketonuria – a genetic disorder resulting in the inability to metabolize phenylalanine into tyrosine – must strictly avoid aspartame consumption due to the risk of neurotoxicity [19].

Several studies have suggested a potential link between aspartame intake and disturbances in glucose metabolism, including associations with obesity, insulin resistance, and alterations in the gut microbiota, particularly in animal models [19].

Research has also explored potential neurotoxic effects of aspartame and its breakdown products. Some findings point to a possible association with the pathogenesis of neurodegenerative disorders, including multiple sclerosis, Alzheimer's disease, Parkinson's disease, and brain tumors [19].

In terms of renal safety, frequent high-dose intake of aspartame has demonstrated nephrotoxic effects in experimental studies. Long-term exposure led to a dose-dependent increase in free radical formation in kidney tissues and a significant reduction in the activity of key antioxidant enzymes such as catalase, superoxide dismutase, glutathione reductase, and glutathione peroxidase in both liver and kidney tissues of rats [20].

Aspartame was first approved by the U.S. FDA in 1981 for use as a tabletop sweetener, and in 1996, it received approval for general use in food and beverages [2]. The acceptable daily intake (ADI) of aspar-

tame is 50 mg/kg of body weight per day, as specified by FDA [17].

Saccharin (E954)

Saccharin is an artificial sweetener derivative from toluene sulfonamide, chemically known as osulfabenzamide (2,3-dihydro-3-oxobenzisulfonazole). It is approximately 200-700 times sweeter than sucrose and is commonly used in combination with other sweeteners such as cyclamate or aspartame to mask its characteristic bitter or metallic aftertaste [15,17]. Saccharin is often employed to enhance the palatability of food, beverages, and pharmaceuticals without increasing their caloric value [15]. Pharmacokinetically, saccharin is not metabolized by the human body and is excreted unchanged in the urine. However, its use is not recommended during pregnancy or breastfeeding due to its potential to cross the placenta barrier and appear in breast milk [2].

Historically, saccharin was considered suitable for individuals with diabetes, as it does not undergo metabolic processing and does not elevate blood glucose levels [21]. However, more recent studies have raised concerns about its potential effects on glucose homeostasis. Evidence suggests that saccharin may interfere with glucose regulation, impair insulin sensitivity, and influence glucose absorption, potentially contributing to hyperinsulinemia, insulin resistance, and adipose tissue accumulation [22]. One study demonstrated a positive correlation between saccharin intake and an increased body weight, attributed to the appetite-regulation centers in the brain. In animal studies, saccharin-sweetened water resulted in increased hunger compared to glucose-sweetened water [15]. Furthermore, saccharin and other non-nutritive sweeteners may enhance sweet cravings, thereby promoting overconsumption of high-calorie foods and contributing to weight gain [21]. Artificial sweeteners like saccharin may also induce an insulin response due to their sweet taste, despite the absence of increased blood glucose levels. This mismatch may result in hypoglycemia, which can further stimulate hunger and lead to increased caloric intake. In long-term animal studies, mice fed a mixture of saccharin and cyclamate gradually increased their caloric intake, resulting in weight gain and greater fat deposition [23].

Saccharin is currently approved in over 100 countries and is generally recognized as safe when used within recommended limits. Nonetheless, due to conflicting findings regarding its metabolic effects, caution is advised, particularly in vulnerable populations [24]. The acceptable daily intake (ADI) established by the U.S. FDA is 15 mg/kg of body weight per day [17].

Sucralose (E955)

Sucralose is a synthetic non-nutritive sweetener derived from sucrose through a process that involves substituting three hydroxyl groups with chlorine atoms. This structural modification produces a compound that is approximately 600 times sweeter than sucrose [3,17]. Sensory studies show that sucralose does not have the bitter aftertaste associated with some other non-nutritive sweeteners [25].

The human body does not metabolize sucralose as a carbohydrate, and thus does not provide energy or elevate blood glucose levels. Most of the ingested sucralose passes through the gastrointestinal tract unchanged and is excreted in the feces. A smaller fraction (11–27%) is absorbed and excreted via the urine, without evidence of tissue accumulation [2, 25]. Importantly, sucralose does not cross the placenta or the blood-brain barrier, further supporting its favorable safety profile [25].

However, animal studies have raised concerns regarding the impact of sucralose on gut microbiota. In a study conducted on mice, low-dose sucralose administration led to significant alternations in the microbial composition of the ileum, jejunum, and colon, with a notable increase in pathogenic bacteria [21].

A study involving dietary inclusion of 5% sucralose reported a reduction in thymic weight in animal models. However, further investigation indicated that the observed effect may be attributable to nutritional imbalances rather than sucralose's inherent toxicity [11]. While most clinical studies indicate that sucralose does not significantly alter glucose metabolism, emerging evidence suggest that concurrent intake of sucralose with carbohydrates may impair insulin sensitivity in healthy individuals [21].

The FDA classifies sucralose as safe for human use when consumed in amounts not exceeding the ADI, which is 5 mg/kg body weight [17].

Neotame (E961)

Neotame is the one of the most recent NNS approved for human consumption. It is obtained derivative of aspartame, produced through N-alkylation, resulting in a compound that is chemically similar to aspartame but significantly more potent [2].

Neotame is approximately 7,000 to 13,000 times sweeter than sucrose, making it one of the most intense sweeteners available. In addition to its use as a non-caloric sweetener, it is also employed as a flavor enhancer, particularly in sour fruit flavors [2].

It is minimally absorbed by the body, does not accumulate in tissues, and is excreted unchanged [11].

In a study involving rats, a reduction in body weight was noted during exposure to neotame. However, this weight loss was not attributed to the toxic effects of neotame, but rather to reduced food intake due to its unpleasant taste at high concentrations [2]. In a separate four-week animal study, neotame exposure was associated with changes in gut microbiota composition, including an increase in *Bacteroides* genus, which is involved in polysaccharide fermentation, and a decrease in *Lachnospiraceae* and *Ruminococcaceae*, bacterial families known for their production of short-chain fatty acids (SCFAs). SCFAs are crucial for energy homeostasis, lipid and fatty acid absorption, and bile acid metabolism [26]. Human studies have shown that neotame does not raise blood glucose levels. It may cause headaches and loss of appetite, while excessive consumption may affect the liver [27]. Neotame is not metabolized by oral bacteria, which means it does not contribute to dental caries [28].

The FDA has established an acceptable daily intake (ADI) for neotame of 0.3 mg/kg of body weight [17]. Safety studies have not demonstrated any adverse effects in clinical trials, physical examinations, or histopathological evaluations [11].

Advantame (E969)

Advantame is a non-nutritive artificial sweetener and a chemical derivative of aspartame, composed of 3-hydroxy-4-methoxyphenylpropane, aspartic acid, and the methyl ester of phenylalanine [29]. It has a sweetening power approximately 20,000 times greater than that of sucrose [17]. It does not have a bitter or sour aftertaste [11].

It is suitable for use in iced tea, coffee, and powdered drink mixtures, chewing gums, and yogurts [11].

Toxicological studies have demonstrated that advantame does not exhibit teratogenic potential. Animal toxicity studies and data from human studies have confirmed that it is safe for use in food products [11]. The FDA approved advantame for general use in foods and beverages in 2014. It is considered safe for the population, including individuals with diabetes, as it does not affect blood glucose levels [29]. According to FDA guidelines, the ADI for advantame is 32.8 mg/kg body weight per day [17].

Steviol Glycosides (E960)

Stevia rebaudiana (Asteraceae) is a small perennial herb native to South America, traditionally used to sweeten beverages such as mate tea. Out of approximately 150–300 species of the *Stevia* genus, only 18 possess sweetening properties, with *S. rebaudiana* being

the most potent. The primary sweet components are steviol glycosides, predominantly stevioside (9.1%) and rebaudioside A (3.8%) [30]. Rebaudioside A is approximately 450 times, and stevioside 300 times sweeter than sucrose. Despite their intense sweetness, both stevioside and rebaudioside A may produce a bitter or metallic aftertaste, which is reduced with increased compound purity or when the two are used in combination [15,30]. The European Food Safety Authority (EFSA) has established an acceptable daily intake (ADI) of 4 mg/kg of body weight for steviol glycosides. Clinical evidence indicates that, when consumed within this limit as sweeteners, steviol glycosides exert no significant pharmacological effects. Steviol glycosides are non-caloric, non-cariogenic, non-allergenic, and considered a natural alternative to sucrose [30]. Unlike other artificial sweeteners, they pass through the upper digestive tract unchanged and are fermented only in the large intestine by intestinal microbiota [15]. Preclinical and clinical studies suggest that stevioside lowers blood glucose levels without altering glucagon concentrations. It slows glucose absorption in the small intestine by approximately 40% and suppresses gluconeogenesis by downregulating the gene encoding phosphoenolpyruvate carboxykinase – an enzyme involving hepatic glucose production. These effects are observed only under hyperglycemic conditions [15, 31]. There is evidence of stevioside and rebaudioside A inducing vasodilation, diuresis, and natriuresis, ultimately reducing plasma volume and lowering arterial blood pressure. However, these effects occur only at doses higher than the ADI and are not observed in normotensive individuals [Pau-car]. Furthermore, stevia leaf extract has demonstrated antimicrobial and antifungal activities, effectively inhibiting pathogens such as *Staphylococcus aureus*, *Salmonella typhi*, *Escherichia coli*, *Aeromonas hydrophila*, *Bacillus cereus*, *Klebsiella pneumoniae* and *Vibrio cholerae*, as well as fungi such as *Penicillium chrysogenum* and *Aspergillus niger* [15]. Additionally, steviol glycosides are non-cariogenic, helping to prevent the development of dental caries [15].

Conclusion

In contemporary diets, non-nutritive sweeteners play an essential key role in reducing calorie and sugar intake – an essential strategy for the prevention and management of obesity and metabolic disorders. Their ability to provide intense sweetness without contributing to caloric intake makes them an appealing option for health-conscious consumers. However, despite approval from regulatory agencies, the long-term safety and health implications of artificial sweeteners remain incompletely understood, warranting further investigation.

Emerging evidence suggests that certain artificial sweeteners may be associated with adverse health outcomes, including alterations in glucose metabolism, modulation in the gut microbiota, enhanced appetite, and potential neurodegenerative changes.

Use of artificial sweeteners is particularly prevalent among specific population groups, notably women, individuals with higher body mass index, and those with higher education and income levels. These compounds are most commonly found in dietary beverages, sugar-free chewing gums, low-calorie dairy products, and tabletop sweeteners. Consumption trends show increasing use of sweeteners such as sucralose and saccharin, while the use of others, like cyclamate, has declined due to shifting consumer preferences and regulatory guidance.

Public education is vital in promoting informed choices regarding artificial sweeteners. Consumers must be made aware of potential individual sensitivities, such as phenylketonuria, and the need for special caution in vulnerable populations, including children, pregnant women, and individuals with chronic health conditions. Enhancing food literacy, particularly in the interpretation of nutrition labels, can empower consumers to make healthier dietary choices and better understand the potential effects of artificial sweeteners on overall health.

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CASE REPORTS PRIKAZI SLUČAJEVA

DIAGNOSTIC IMAGING OF GIANT CHROMOPHOBE RENAL CELL CARCINOMA – CASE REPORT

RADIOLOŠKA DIJAGNOSTIKA GIGANTSKOG HROMOFOBNOG KARCINOMA BUBREŽNIH ČELIJA – PRIKAZ SLUČAJA

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Case report

Prikaz slučaja

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Abstract

Introduction. Renal cell carcinoma is the most common kidney malignancy, accounting for approximately 3% of all adult malignancies. Chromophobe renal cell carcinoma, a relatively rare subtype, comprises about 5% of all renal cell carcinoma cases and is generally associated with a more favorable prognosis compared to other subtypes. Only 10% of patients present with the classic triad of hematuria, pain, and a flank mass, and more than 40% are asymptomatic. Early detection and appropriate management are crucial for improving patient outcomes. **Case Report.** A 57-year-old female presented with an anemic syndrome (erythrocytes $3.05 \times 10^{12}/L$, hemoglobin 71 g/L) and weakness over a 10-day period. She reported no weight loss and maintained a normal appetite. Abdominal ultrasound revealed a heterogeneous mass in the right epigastrium, inseparable from the right kidney. Subsequent computed tomography imaging confirmed a mass in the upper pole of the right kidney measuring $13.7 \times 11.3 \times 17$ cm, with necrotic areas and microcalcifications. Radical nephrectomy was performed, and histopathological analysis confirmed chromophobe renal cell carcinoma and chronic pyelonephritis. Despite postoperative treatment, the patient died one year later due to tumor recurrence and multiorgan failure. **Conclusion.** Although chromophobe renal cell carcinoma is less aggressive than other subtypes, it still presents significant challenges. In this particular case, the outcome was fatal because the patient failed to present symptoms in time, making this case unique. Regular check-ups and early diagnostic evaluation are crucial to facilitate timely intervention and improve outcomes.

Key words: Diagnostic Imaging; Tomography, X-Ray Computed; Carcinoma, Renal Cell; Early Diagnosis

Introduction

Renal cell carcinoma (RCC) is the most common malignant tumor of the kidney, accounting for ap-

Sažetak

Uvod. Karcinom bubrežnih ćelija je najčešći maligni tumor bubrega i čini otprilike 3% svih karcinoma kod odraslih. Hromofobni karcinom bubrežnih ćelija, relativno redak podtip, čini oko 5% slučajeva i generalno je povezan sa boljom prognozom u poređenju sa drugim podtipovima. Samo 10% osoba sa karcinomom bubrežnih ćelija ima klasičnu trijadu simptoma: hematuriju (prisustvo krvi u mokraći), bol i masu u slabinskoj regiji, dok više od 40% obolelih ne pokazuje nijedan od ta tri simptoma. Rano otkrivanje i odgovarajuće lečenje su ključni za poboljšanje ishoda kod pacijenata. **Prikaz slučaja.** Pacijentkinja starosti 57 godina dolazi kod hematologa sa anemičnim sindromom (eritrociti $3,05 \times 10^{12}/L$, hemoglobin 71 g/L) i slabosti tokom poslednjih 10 dana. Nije imala gubitak telesne mase i imala je očuvan apetit. Daljim ispitivanjem, ultrazvuk abdomena je pokazao heteroehogenu masu u desnom epigastrijumu, neodvojivu od desnog bubrega. Kompjuterizovana tomografija je potvrdila prisustvo mase u gornjem polu desnog bubrega dimenzija $13,7 \times 11,3 \times 17$ cm, sa nekrozama i mikrokalcifikacijama. Patohistološki nalaz nakon radikalne nefrektomije potvrdio je dijagnozu hromofobnog karcinoma bubrežnih ćelija i hroničnog pijelonefritisa. Nažalost, godinu dana nakon nefrektomije, pacijentkinja je preminula usled recidiva karcinoma i kasnijeg multiorganskog otkazivanja. **Zaključak.** Hromofobni karcinom bubrežnih ćelija, iako manje agresivan u odnosu na druge podtipove, i dalje predstavlja značajne izazove. U ovom konkretnom slučaju, ishod je bio fatalan jer pacijentkinja nije imala rane simptome, na vreme, što čini ovaj slučaj specifičnim. Redovne kontrole i rana dijagnoza su ključni za pravovremeno prepoznavanje bolesti i poboljšanje ishoda.

Ključne reči: dijagnostički imidžing; CT; karcinom bubrežnih ćelija; rana dijagnoza

proximately 3% of all adult cancers and represents about 90% of kidney malignancies [1]. Clinical presentation varies widely, ranging from asymptomatic cases to those with severe symptoms. The classic

Abbreviations

RCC – Renal Cell Carcinoma
CT – Computed Tomography
MRI – Magnetic Resonance Imaging

triad of hematuria, pain, and a flank mass is present in only 10% of cases, often indicating advanced disease. Over 40% of RCC cases present with none of the three symptoms [2].

RCC includes several histological subtypes, the most common being clear cell RCC (70-90%), followed by papillary RCC (10-15%) and chromophobe RCC (~ 5%) [3]. Chromophobe RCC is thought to originate from the intercalated cells of the collecting duct system [4]. Compared to clear cell RCC, chromophobe RCC typically exhibits less aggressive behavior, with a lower rate of metastasis and better overall prognosis [5]. It is more common in older individuals and has been associated with chronic kidney diseases, including end-stage renal disease and dialysis dependence [6].

Diagnosis relies on clinical evaluation, imaging (such as CT and MRI), and definitive histopathological analysis [7,8]. Surgical management, including partial or radical nephrectomy, remains the primary treatment modality. In select cases, adjuvant therapies such as immunotherapy may be employed [9].

Case Report

A 57-year-old female presented for a routine annual medical examination. Laboratory tests revealed an anemic syndrome (erythrocytes $3.05 \times 10^{12}/L$, hemoglobin 71 g/L). The patient reported a 10-day history of generalized weakness but denied weight loss or

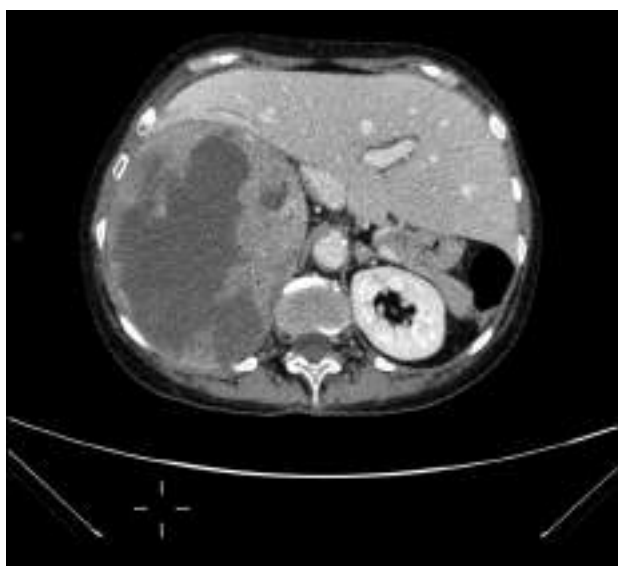


Figure 1. Axial CT scan of the abdomen – Renal cell carcinoma

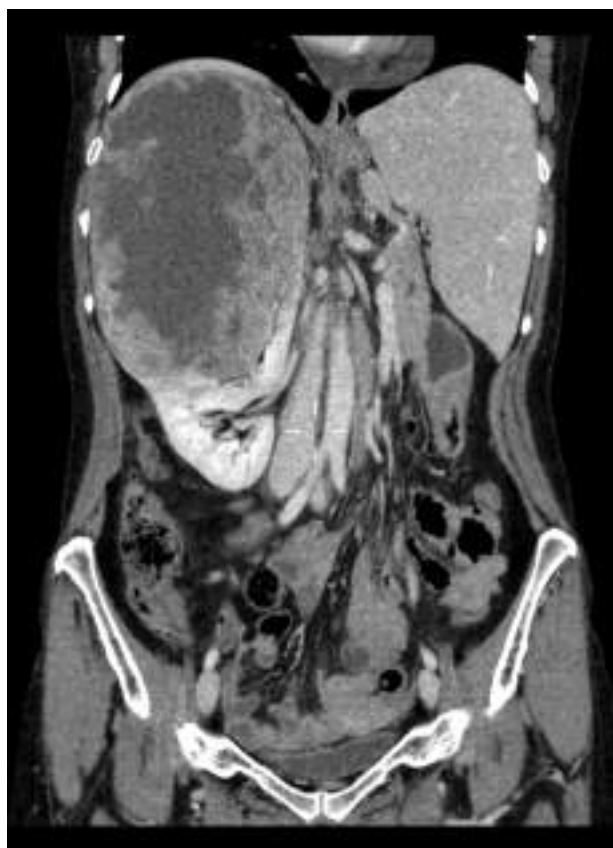


Figure 2. Coronal CT scan of the abdomen – Renal cell carcinoma

appetite changes. Physical examination by a hematologist revealed a palpable mass in the right lower abdomen, prompting referral to an abdominal ultrasound.

Ultrasound imaging showed a well-demarcated *heterogeneous* mass in the right epigastric region, measuring approximately 16.2 x 14.5 cm, inseparable from the parenchyma of the right kidney and compressing the liver parenchyma. A complementary CT scan of the abdomen and pelvis confirmed a mass in the upper pole of the right kidney, measuring 13.7 x 11.3 x 17 cm, with areas of necrosis and microcalcifications (**Figure 1**). The mass compressed adjacent structures but showed no evidence of infiltration (**Figure 2**). Delayed-phase imaging demonstrated loss of function in the right kidney. The mass was classified as RCC (Renal Cell Carcinoma). No signs of dissemination in the abdomen and pelvis were found. The patient underwent a radical right nephrectomy three days later. Histopathological examination confirmed chromophobe renal cell carcinoma and chronic pyelonephritis. Postoperative therapy with sunitinib (Sutent) was initiated.

Despite initial treatment, the patient developed tumor recurrence and multiorgan failure, ultimately resulting in death one year after surgery.

Conclusion

This case illustrates the diagnostic and therapeutic challenges posed by chromophobe renal cell carcinoma, despite its typically favorable prognosis. In

this instance, the absence of specific symptoms led to a delayed diagnosis, contributing to a fatal outcome. Regular check-ups and early diagnosis are crucial for the timely identification of the disease and improving outcomes.

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SPONTANEOUS VAGINAL DELIVERY THROUGH A POSTERIOR BUCKET-HANDLE CERVICAL TEAR WITHOUT CERVICAL OS DILATATION – A CASE REPORT

SPONTANI VAGINALNI POROĐAJ KROZ ZADNJU CEVIKALNU RUPTURU PO TIPU „DRŠKA KOFE“ BEZ DILATACIJE SPOLJAŠNJEG MATERIČNOG UŠĆA – PRIKAZ SLUČAJA

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Abstract

Introduction. Cervical tears represent a significant cause of postpartum hemorrhage and maternal morbidity, particularly at term. Among these, bucket-handle cervical tears – characterized by a circumferential laceration of the anterior or posterior cervical lip resembling a bucket handle – are extremely rare. This case highlights the clinical presentation, management, and outcome of such an injury. **Case Report.** A 29-year-old Serbian primiparous woman at 40 weeks of gestation was admitted for fetal monitoring following detection of bradycardia during contractions. She had no history of cervical procedures. Artificial rupture of membranes was performed upon admission, triggering strong uterine contractions and leading to spontaneous vaginal delivery of a healthy male neonate within four hours. No cervical prostaglandins were used, and oxytocin was administered for only five minutes prior to fetal expulsion. Postpartum examination revealed a posterior bucket-handle cervical tear, which served as the point of fetal exit and was the source of significant hemorrhage. No injuries to the uterine body or signs of hemoperitoneum were observed. The cervical tear was surgically repaired. The patient experienced a drop in hemoglobin and was treated with iron supplementation. Follow-up examinations confirmed normal healing of the cervix and vaginal tissues. **Conclusion.** This case underscores the importance of considering cervical tears as a potential complication, even in the absence of traditional risk factors. Appropriate management includes intrapartum monitoring, surgical repair when indicated, and consideration of elective cesarean delivery and cervical length surveillance in future pregnancies. Standardized protocols for diagnosis and management are essential to improve maternal outcomes and inform future obstetric care.

Key words: Cervix Uteri; Rupture; Lacerations; Delivery, Obstetric; Postpartum Hemorrhage; Surgical Procedures, Operative; Risk Factors

Introduction

Cervical tears are a known cause of postpartum hemorrhage and can result in serious maternal complications, including mortality, if not promptly diagnosed and managed [1]. Documented types of cervical trauma during childbirth include lateral

Sažetak

Uvod. Rupture grlića materice predstavljaju značajan rizik za postpartalno krvarenje i morbiditet majke, naročito u terminskim trudnoćama. Ruptura grlića u obliku „drške kofe“ – retka laceracija prednje ili zadnje usne grlića koja podseća na polukružnu dršku – predstavlja najređi oblik ove povrede. Prikazani slučaj ilustruje ovako izraženu povredu. **Prikaz slučaja.** Pacijentkinja, 29 godina starosti, primipara, u 40. gestacijskoj nedelji, hospitalizovana je zbog fetalne bradikardije tokom kontrakcija. Anamneza je bila bez prethodnih cervikalnih intervencija. Po prijemu je sprovedena veštačka ruptura plodovih ovojnica – amniotomija, što je indukovalo jake kontrakcije i rezultovalo vaginalnim porođajem zdravog muškog novorođenčeta u roku od četiri sata. Cervikalna primena prostaglandina nije bila indicirana, a oksitocinska infuzija trajala je svega pet minuta pre ekspulzije ploda. U postpartalnom periodu dijagnostikovana je zadnja ruptura grlića materice u obliku „drške kofe“, koja je predstavljala izlaznu putanju za fetus i uzrokovala obilno krvarenje. Nisu uočene lezije uterineg korpusa niti znaci hemoperitoneuma. Hirurška revizija i sanacija su sprovedene uspešno. Registrovan je pad nivoa hemoglobina, te je ordinirana peroralna suplementacija gvožđem. Na postpartalnoj kontroli zabeležen je uredan lokalni oporavak. **Zaključak.** Ovaj prikaz ističe složenost i potencijalne komplikacije cervikalnih ruptura, čak i bez predisponirajućih faktora. U budućim graviditetima preporučuju se pažljivo intrapartalno praćenje, razmatranje elektivnog carskog reza i serijsko transvaginalno merenje dužine cerviksa. Standardizacija protokola za dijagnostiku i lečenje ovih povreda od suštinskog je značaja za optimizaciju maternalnih ishoda.

Ključne reči: grlić materice; rupture; laceracije; porođaj; postpartalno krvarenje; operativne hirurške procedure; faktori rizika

tears, bucket-handle tears, and annular detachment of the cervix [2]. These injuries are more frequently observed in term deliveries and are often associated with risk factors such as cervical cerclage, labor induction, maternal youth, assisted vaginal delivery, prostaglandin use, a scarred cervix, and precipitous labor. Among these, a bucket-handle tear – characterized by

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Abbreviations

CTG – cardiotocography
CD&C – cervical dilatation and curettage
ARM – artificial rupture of the membranes

a circumferential laceration of either the anterior or posterior cervical lip that forms a bridge-like structure resembling a bucket handle - is particularly uncommon [3,4]. We present a rare case of spontaneous vaginal delivery through a posterior bucket-handle cervical tear in the absence of identifiable risk factors. To the best of our knowledge, this specific presentation has not previously been reported in literature.

Case Report

A 29-year-old primiparous Serbian woman, gravida 2 para 1, at 40 weeks' gestation, was admitted for continuous fetal monitoring due to recurrent fetal bradycardia (heart rate as low as 100 bpm) during prolonged uterine contractions. Her obstetric history included one previous uncomplicated full-term vaginal delivery. She had no history of cervical surgical procedures (e.g., loop excision, conization, curettage, or dilatation of the cervix) that could cause fibrotic changes or stenosis of the cervical canal. Routine speculum and digital examinations during the pregnancy were normal. Her medical and surgical was unremarkable, and the pregnancy had progression without complications under regular parental care. At admission, the cervix was effaced and dilated to 1 cm with cephalic presentation and intact amniotic sac. No cervical prostaglandins were employed in the procedure. The patient received a 5% glucose solution intravenously. No enema or additional induction measures were applied. One hour later, artificial rupture of membranes (ARM) was performed, with clear amniotic

fluid noted. Despite more frequent contractions, cervical dilation remained minimal two hours later. Analgesia and intravenous fluids were administered. Approximately 3.5 hours after admission, the patient experienced a strong urge to push. Digital examination suggested full cervical dilatation with the fetal head at station +2. An oxytocin infusion (0.9% NaCl 500 ml with 5 IU oxytocin, at 30 ml/min) was administered for five minutes, resulting in the spontaneous vaginal birth of a healthy male neonate weighing 3800 g and measuring 52 cm. Apgar scores were 9 and 10 at 1 and 5 minutes, respectively. Following placental expulsion – during which macroscopic placental defects were observed – a manual uterine revision was performed. Examination below the vaginal retractors revealed that the anatomical cervical os remained only 1 cm dilated (**Figure 1**). Simultaneously, a bleeding posterior cervical tear extending from 3 to 8 o'clock was discovered. This tear, resembling a bucket-handle lesion, had served as the passage through which the fetus was delivered (**Figure 2**). The vaginal fornices were intact, and the tear did not extend into them. The possibility of a substantial uterine corpus lesion was dismissed upon recognizing the tear boundaries. The absence of hemoperitoneum was confirmed both clinically and by transabdominal ultrasound, which showed no free fluid. The patient was transferred to the operating room for surgical repair. Hemostasis was achieved using a combination of simple interrupted and figure-of-eight sutures (Polysorb® 2, Covidien, Medtronic, USA). Intraoperative management included administration of uterotonics (synthetic oxytocin, methylergonovine maleate, and carboprost tromethamine) and prophylactic antibiotics (cefazolin and metronidazole). Total estimated blood loss was 700 ml, with a drop in hemo-



Figure 1. Dilatation of external cervical os after delivery



Figure 2. Bucket-handle cervical posterior lip tear after delivery

globin from 114 g/L to 99 g/L, managed conservatively with iron supplementation. The patient was monitored in the intensive care unit for 24 hours and discharged on the third postpartum day. At the three-week follow-up, vaginal and cervical healing were progressing normally.

Discussion

Clinically significant cervical lacerations are reported in approximately 0.2-1.7% of vaginal deliveries. Although uncommon, they are important causes of postpartum hemorrhage [4]. Among various risk factors, cervical tears are most commonly associated with labor induction – particularly the use of intra-vaginal prostaglandins – and operative vaginal deliveries. The growing global trend toward labor induction in recent years has further highlighted this concern [5]. While prostaglandins facilitate cervical ripening and fetal passage, their use has also been associated with an increased risk of uterine rupture in women with a history of uterine surgery [6]. Qurashi et al. described a series of bucket-handle cervical tears following labor induction with prostaglandins, identifying key contributing factors [7]. Operative vaginal deliveries using vacuum or forceps have long been associated with higher rates of soft tissue injury, including cervical lacerations. Additionally, cervical fibrosis from prior trauma or procedures – such as loop excision, cerclage, or curettage – can predispose to intrapartum cervical tears during labor [8]. In a study of 251 women with previous cervical cerclage, the incidence of intrapartum cervical lacerations during labor was 14%, significantly higher than the 2% observed in the control group [9]. Djokovic et al. reported that prior cervical dilation and curettage (CD&C), often performed for pregnancy termination, may result in subclinical cervical injury. While the most patients with a history of CD&C have uneventful future deliveries, this procedure has been linked to an increased risk of postpartum hemorrhage [10]. In the present case, none of the commonly reported risk factors were identified. The patient had no history of cervical procedures, labor induction agents (prostaglandins or oxytocin), or assisted delivery. Interestingly, Neri et al. proposed that digital cervical examination – frequently used to assess labor progress – may pose a risk, particularly in edematous cervixes, possibly leading to trauma and tears such as the bucket-handle type. However, our patient underwent only three digital cervical exams over a four-hour course, making this an unlikely cause. Precipitate labor remains the only possible contributing factor in our case. It is characterized by rapid cervical

dilation and fetal descent and has been linked to cervical lacerations in previous studies [11]. Several pathophysiological mechanisms for intrapartum bucket-handle and other cervical tears have been proposed. These include strong uterine contractions (spontaneous or induction-enhanced), premature bearing down against and incompletely dilated cervix, and sustained pressure by the fetal presenting part, which may compromise local blood circulation, leading to cervical edema, necrosis, and eventual avulsion. In posterior bucket-handle tears, as seen here, tone theory suggests that anterior displacement of the cervix during labor causes excessive pressure on the posterior cervical lip, resulting in tear [12]. Fibrotic changes may alter the distribution of pressure, resulting in unbalanced pressure on either the anterior or posterior cervical lip. Another proposed mechanism involves cervical edema and necrosis due to compression between the vertex and the pubic symphysis. However, relative prominence of posterior over anterior tears remains incompletely understood [13]. Because of their rarity, there is no standardized approach to repairing bucket-handle cervical tears. Nonetheless, large tears, particularly those associated with hemorrhage, clearly require surgical repair. Tears extending beyond the internal os or involving the lower uterine segment should prompt laparotomy for proper visualization and managed. The choice of suture material is critical. It must provide sufficient tensile strength to resist uterine contractions while minimizing the risk of tissue injury. In our case, we used Polysorb® 2, a multifilament braided absorbable suture, which has been recommended in the literature [13]. The technique also matters. While some advocate for continuous or mattress sutures, we opted for a combination of simple interrupted or figure-of-eight interrupted sutures [8]. Additionally, cervical closure with the suture should be monitored carefully considering its position and potential access difficulties. Some authors recommend using tools like a swab-on-a-stick or sigmoidoscope to avoid patency, though we did not use any such devices in our case [13]. In rare cases, repair may not be feasible, requiring partial cervical amputation or even hysterectomy [14]. Fortunately, primary repair was possible in our patient, with successful healing confirmed on follow-up. The implications of cervical tears for future pregnancies remain uncertain. A large retrospective cohort study reported a 4.9% recurrence rate of cervical lacerations compared to 0.1% in controls, along with an increased incidence of cervical insufficiency (1.9% vs. 0.3%) and potentially higher rates of spontaneous miscarriage [15, 16]. Although some women with prior cervical avulsion or partial cervical excision have subsequently had term deliveries, others have experienced preterm birth or

miscarriage. To mitigate risk, some obstetricians opt for elective cesarean delivery in future pregnancies [8, 11]. Currently, there is no evidence-based guideline on the use of cervical cerclage following a bucket-handle tear. However, serial transvaginal cervical length measurement during pregnancy, combined with clinical judgment regarding cerclage or planned cesarean section, may help reduce recurrence risk [12]. Importantly, characteristics and changes in the cervix during labor should be closely monitored. Rigid persistence of the external cervical os may justify early cesarean section delivery to prevent trauma [14].

Conclusion

This report presents a rare case of spontaneous vaginal delivery through a posterior bucket-handle

cervical tear, without dilation of the external cervical os. Prompt surgical management was successful, and the patient recovered well. Cervical lacerations – though rare – can lead to serious maternal morbidity and should be carefully considered as there are, currently, no standardized protocols for managing such injuries or guiding care in future pregnancies. We recommend comprehensive clinical evaluation of the cervical integrity at delivery, along with serial prenatal ultrasound transvaginal cervical length surveillance in future pregnancies. Elective cerclage and cesarean delivery may be considered in select cases. Although rare, bucket-handle cervical tear should be carefully considered in patients undergoing labor induction, operative delivery, having a history of previous cervical trauma such as loop excision, cervical dilatation, and curettage or cerclage, or experiencing precipitate labor.

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RADIOLOGICAL EVALUATION OF BERTOLOTTI SYNDROME – CASE REPORT

RADIOLOŠKA EVALUACIJA BERTOLOTTI SINDROMA – PRIKAZ SLUČAJA

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Abstract

Introduction. Bertolotti syndrome is an anatomical variation characterized by the presence of a lumbosacral transitional vertebra, typically involving an enlarged transverse process of the L5 vertebra (>19 mm). It most commonly presents with lower back pain and is classified into four types according to the Castellvi classification, with further subclassification based on the degree of pseudoarticulation. The estimated prevalence in the general population ranges from 4% to 35%. Standard pelvic or lumbosacral spine X-rays are usually sufficient for initial diagnosis, while Magnetic Resonance Imaging and/or computerized tomography imaging is required for definitive diagnosis and classification. Treatment options range from conservative management to surgical intervention, depending on the extent of pseudoarticulation and presence of nerve compression. **Case Report.** We present the case of an elderly female patient with lower back pain and discomfort in the hip region. Following clinical examination, a standard pelvic X-ray was performed, revealing a bony oval formation approximately 30 mm in size in the left paravertebral and suprasacral region. This finding likely correspond to a hypertrophic transverse process of the L5 vertebra or a cranial extension of the S1 lateral mass. Based on radiographic findings and clinical presentation, the primary diagnosis was Bertolotti syndrome. **Conclusion.** This case underscores the clinical utility of plain of radiography as a rapid, cost-effective diagnostic tool in the evaluation of lower back pain, particularly for identifying structural anomalies such as Bertolotti syndrome.

Key words: Low Back Pain; Sacrum; Spine; Radiography; Anatomy; Lumbosacral Region; Diagnosis; Differential

Introduction

Bertolotti syndrome (BS) is a clinical entity characterized by localized lower back pain with altered sagittal mobility of the lumbosacral spine. It arises due to an anatomical variation involving a lumbosacral transitional vertebra (LSTV), most commonly presenting as an enlarged transverse process of the L5 vertebra (>19 mm) that may pseudoarticulate or fuse with the sacrum – with or without associated nerve root involvement. This condition is most frequently observed in older individuals, with a predilection for the left side, and occurs more commonly in males [1–3]. The condition was first described in 1917 by Mario Bertolotti [4].

Sažetak

Uvod. Bertolotti sindrom predstavlja anatomska varijaciju postojanja lumbosakralnog premošćavajućeg pršljena, u vidu uvećanog procesus transversus L5 pršljena (> 19 mm). Najčešće se javlja u vidu bola u donjem delu leđa. Bertolotti sindrom se prema stepenu pseudoartikulacije klasifikuje u četiri grupe prema *Castellvi* klasifikaciji i u dve podgrupe. Prevalencija se kreće 4–35% u opštoj populaciji. Za postavljanje dijagnoze najčešće je dovoljan RTG snimak karlice ili lumbosakralnog dela kičme u standardnim položajima. Radi postavljanja definitivne dijagnoze i klasifikacije Bertolotti sindroma koriste se dijagnostika magnetnom rezonancijom i/ili kompjuterizovanom tomografijom. Lečenje Bertolotti sindroma svodi se na konzervativni tretman, pa sve do hirurškog lečenja, u zavisnosti od stepena pseudoartikulacije i kompromitacije nerava. **Prikaz slučaja.** Pacijentkinja starije životne dobi, sa bolom u donjem delu leđa i u predelu kukova. Nakon fizikalnog pregleda, načinjen je standardni rendgenski snimak karlice. Uočava se koštana ovalna formacija levo paravertebralno i suprasakralno visine oko 30 mm. Može odgovarati voluminoznom procesus transversus L5 pršljena ili kranijalnoj ekstenziji voluminozne bočne mase S1 pršljena. U prvom redu diferencijalno-dijagnostički dolazi u obzir Bertolotti sindrom. **Zaključak.** U ovom prikazu slučaja želeli smo da naglasimo važnost rendgenske dijagnostike u svakodnevnom radu, kao brzu i relativno jednostavnu dijagnostičku proceduru u diferencijalnoj dijagnostici hroničnog lumbalnog sindroma, sa osvrtom na Bertolotti sindrom.

KLjučne reči: lumbalni sindrom; krsna kost; kičma; radiografija; anatomija; lumbosakralna regija; diferencijalna dijagnoza

The condition is classified according to Castellvi classification, which divides LSTV into four main types based on the fusion at the L5/S1 level, with additional two subgroups based on the extent of pseudoarticulation.

- Type I – transverse process >19 mm
- Type II – presence of a false joint
- Type III – complete fusion of processes
- Type IV – A combination of type II on one side and type III on the contralateral side. Each type is further subdivided into A (unilateral) and B (bilateral) (Figure 1).

The reported prevalence of BS in the general population ranges from 4% to 35%, although up to 13% of

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Abbreviations

BS	– Bertolotti syndrome
MRI	– Magnetic Resonance Imaging
CT	– computerized tomography
LSTV	– lumbosacral transitional vertebra

individuals with LSTV remain asymptomatic [2,3,5]. Pain associated with BS is attributed to the enlarged transverse process, osteoarthritic changes between the affected bones, associated disc degeneration, spinal canal stenosis, or varying degrees of nerve compression [1,3,4].

Radiographic evaluation using a standard pelvic or lumbosacral spine X-ray is often sufficient for an initial diagnosis. For a definitive classification and assessment of BS, Magnetic Resonance Imaging (MRI)

and/or computerized tomography (CT) imaging is recommended. However, advanced imaging techniques come with certain limitations: CT involves a high radiation dose approximately 4-10 times greater than that of standard X-rays, and MRI may be uncomfortable for some patients, and more costly, thus posing an economic challenge to healthcare systems [6].

Treatment options for Bertolotti syndrome range from conservative management to surgical interventions, depending on the severity of pseudoarticulation and nerve involvement [2,3].

Case Report

A 76-year-old female patient (Visual Analogue Scale (VAS) > 5, body mass index (BMI) 24.46 kg/m²) presented with chronic pain localized in lower back and hip region. The pain was described as persistent with fluctuating intensity, aggravated by specific movements. Her medical history included anemia, osteoporosis, type 2 diabetes mellitus, hemorrhoidal disease, and the use of a pessary for uterine prolapse. She had previously undergone coronary artery bypass grafting twice. On physical examination, the patient exhibits an anterior trunk inclination and restricted range of motion in both hip joints. The Lasegue test was negative. There were no clinical signs of synovitis in the peripheral joints. Neurological and circulatory function in the lower extremities was preserved, with no evidence of muscle weakness. Ethical approval for the case was obtained from the Ethics Committee of the Special Hospital for Rheumatic Diseases in Novi Sad, Serbia (Approval No. 14/03-1/1-25), and the patient provided written informed consent.

A standard anteroposterior X-ray of the pelvis in the supine position (**Figure 2**), performed using a Philips DuraDiagnost F30 system, revealed an oval-shaped bony structure measuring approximately 30

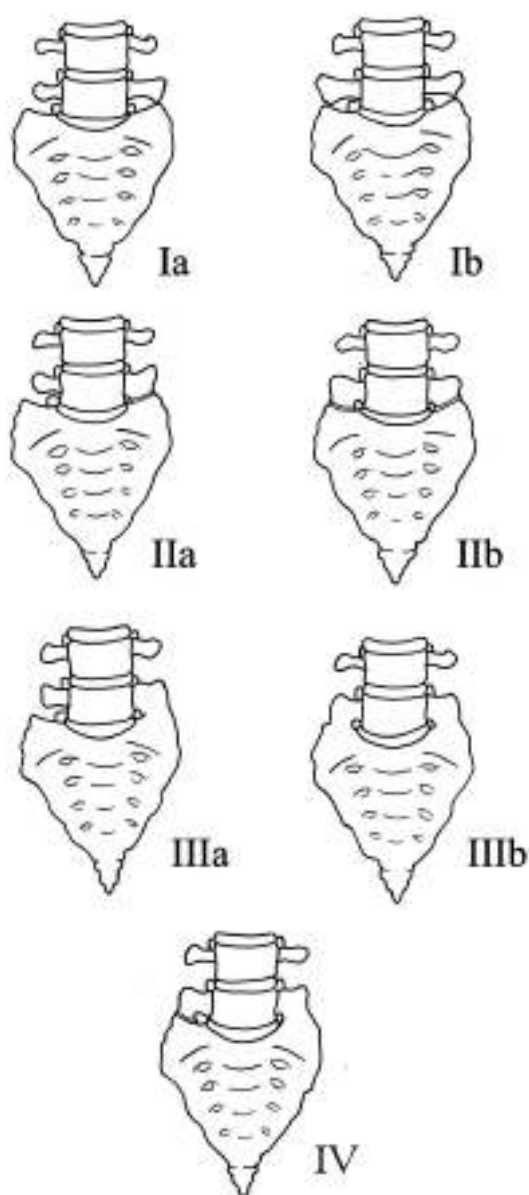


Figure 1. Castellvi's classification (URL: <https://www.ajnr.org/content/31/10/1778>)



Figure 2. Arrow points on enlarged processus transversus



Figure 3. Arrow points on enlarged processus transversus mm in height, located in the left paravertebral and suprasacral region. This finding was suggestive of either a prominent transverse process of the L5 vertebra or a cranial extension of a voluminous lateral mass of the S1 vertebra. Based on the absence of pseudoarticulation, the primary differential diagnosis was BS, Castellvi type IIIa. Laboratory investigations showed mildly elevated acute-phase reactants: C-reactive protein at 11.2 mg/L (reference range: 0–6 mg/L) and erythrocyte sedimentation rate at 45 mm/h (reference range: 0–15 mm/h).

To confirm the diagnosis, a CT scan of lumbosacral spine was performed. Imaging confirmed the presence of a transitional L5 vertebra with a prominent left transverse process that was fused to the sacral bone, consistent with Castellvi type IIIa (**Figure 3**). Additionally, degenerative changes were noted in the intervertebral disc, most prominent at the L4/L5 level, where disc bulging into the spinal canal and intervertebral foramina was observed, accompanied by mild to moderate spinal canal stenosis.

Based on clinical and radiological findings, the BS was confirmed.

Conservative treatment was initiated, consisting of oral analgesics and physical therapy, along with ergonomic education and counseling on protective movement strategies. The patient was referred to her primary care physician for continued follow-up.

Discussion

Bertolotti syndrome is an anatomical variation at the lumbosacral spine level. This anomaly results in a reduced interspace between the L5 transverse processes and the lateral mass of the S1 vertebra, which normally measures between 2 and 3 cm [1].

When L5 is fused with the sacrum, only four lumbar vertebrae remain, while in cases of S1 lumbariza-

tion, six lumbar vertebrae are present, contributing to postural changes and hyperlordosis [4]. The BS often presents with pain localized in the sacral region, hips, lower back, and along the L5 dermatome [1–3]. A genetic predisposition is suspected to play a role in its development [3,4].

Several studies have associated BS with adjacent segment disc degeneration. This may be partially due to a thinner iliolumbar ligament and altered positioning of the conus medullaris - lower in cases of lumbarized S1 and higher in sacralized L5 – possibly contributing to the onset of neurological symptoms [4]. Nonetheless, the precise mechanisms underlying symptom development remain unclear and warrant further research involving larger cohorts.

Standard pelvic or lumbosacral spine radiographs are typically sufficient to raise clinical suspicion of BS. However, advanced imaging such as CT or MRI is required for definite diagnosis and classification based on Castellvi criteria, especially to assess the degree of pseudoarticulation or bony fusion [4]. Literature suggests that diagnostic confirmation can be aided by fluoroscopically guided corticosteroid and local anesthetic injection into the articulation site between the L5 vertebra and iliac wing area, which often results in immediate pain relief. However, due to lack of standardized diagnostic and treatment protocols, BS often goes unrecognized [1–3,5].

Interestingly, some reported cases of lower back pain in younger individuals fall outside the established Castellvi classification but were nevertheless managed as BS [1].

Initial treatment is conservative and includes non-steroidal analgesic therapy and physical therapy. Depending on the extent of structural involvement and the presence of radiculopathy, surgical intervention may be considered [3,7]. Prognosis is generally favorable, with most patients – especially younger ones - returning to normal activities with substantial symptom relief [1,8].

Conclusion

This case highlights the clinical significance of X-ray imaging as a rapid, accessible, and cost-effective tool for diagnosing Bertolotti syndrome when applied appropriately and interpreted in the context of clinical findings. While advanced imaging modalities such as computerized tomography and Magnetic Resonance Imaging remain indispensable for definitive diagnosis and classification, pose also an economic challenge, causing patient discomfort, and requiring longer result interpretation times, standard X-ray imaging retains considerable diagnostic value.

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IN MEMORIAM IN MEMORIAM



**Prof. dr MARIJA
KNEŽEVIĆ POGANČEV
(1958–2024)**

Sa pijetetom se opraštamo od uvažene kolegice Marije Knežević Pogančev, redovnog profesora Medicinskog fakulteta u Novom Sadu.

Marija Knežević rođena je u Kikindi u kojoj se školovala do upisa na Medicinski fakultet u Beogradu. Diplomirala je 1982. godine, a tokom studija je više puta nagrađivana kao student sa najvišim prosekom. Profesionalnu karijeru započela je u rodnoj Kikindi. Specijalizaciju iz pedijatrije završila je 1988. godine, nakon čega je nastavila sa stručnim usavršavanjem. Užu specijalizaciju iz Neurologije i psihijatrije razvojnog doba završava 1990. godine, a 2005. godine i užu specijalizaciju iz Kliničke neurofiziologije i epileptologije. Od 1992. godine zaposlena je u Institutu za zdravstvenu zaštitu dece i omladine Vojvodine, najpre kao šef kabineta za elektroencefalografiju, da bi 2000. godine osnovala Odeljenje razvojne neurologije i epileptologije, na čijem čelu je bila do odlaska u penziju. Magistarske studije završila je na Medicinskom fakultetu u Novom Sadu 1988. godine. Zvanje doktora medicinskih nauka stekla je 2000. godine na Medicinskom fakultetu u Novom Sadu odbranivši doktorsku tezu pod naslovom *Epidemiologija i genetika migrene kod dece*.

U okviru dodatnog usavršavanja prof. Knežević Pogančev je pohađala Internacionalnu školu neuro-nauka Venecijanskog internacionalnog univerziteta, San Servolo, 2007. godine, kao i virtuelne edukacije Evropske akademije za epilepsiju (VIREPA) od 2006. do 2010. godine. U više navrata je bila na studijskim boravcima u Engleskoj i Austriji.

U zvanje asistenta na Katedri za pedijatriju Medicinskog fakulteta u Novom Sadu izabrana je 1994. godine, a zvanje redovnog profesora stekla je 2011. godine. Bila je mentor za osam magistarskih, sedam master radova i tri doktorske disertacije.

Publikovala je više poglavlja u udžbenicima iz pedijatrije, kao i tri monografije u Srbiji (*Epidemiologija i genetika migrene kod dece*; *Elektroencefalografija u pedijatriji*; *Neurogija u pedijatriji*) i jednu u inostranstvu (*Dissociation factors and specific triggers of migraine headache in adolescents*). Autor je preko 100 naučnih publikacija. Kao glavni istraživač vodila je više kliničkih studija. Bila je šef edukacionog tima i predavač u brojnim programima kontinuirane edukacije.

U zasluženu penziju otišla je 28. 9. 2023. godine.

Potpuno posvećena, uvek smirena, razborita, požrtvovana u odnosu na svoje pacijente i njihove roditelje, svojom neumornošću motivisala nas je svakog dana. Visokoorganizovana, stručna i kolegijalna, uvek spremna da prenese svoje znanje i bogato iskustvo studentima i mlađim kolegama, ostavila je neizbrisiv trag u Institutu za zdravstvenu zaštitu dece i omladine Vojvodine i na Katedri za pedijatriju.

Večna joj slava!

*Prof. dr Gordana Vilotijević Dautović
Prof. dr Slobodan Spasojević*



**Dr ALEKSANDAR
ZONJIĆ
(1972–2025)**

Opraštamo se od kolege i načelnika Odeljenja za anesteziiju, reanimatologiju i intenzivnu terapiju dr Aleksandra Zonjića. Rođen je 1972. godine u Beranama u Republici Crnoj Gori. Medicinski fakultet završio je u Beogradu 2003. godine. Nakon završenog fakulteta nastanjuje se u Somboru i zapošljava kao lekar opšte prakse na Odeljenju za prijem, trijažu i zbrinjavanje urgentnih stanja. Specijalizaciju iz anesteziologije završava 2011, a 2018. godine imenovan je za načelnika Odeljenja za prijem, trijažu i zbrinjavanje urgentnih stanja. U toku pandemije COVID-19, 2020. godine preuzima funkciju kovid-koordinatora Bolnice i postaje pomoćnik direktora za organizaciju zdravstvene službe. Od 2022. godine je načelnik Odeljenja za anesteziiju, reanimatologiju i intenzivnu terapiju. Za zasluge u borbi protiv kovida primio je *Zlatnu medalju za zasluge* od predsednika Republike i *Priznanje grada Sombora*, za koje je nesebično ponavljao da ih je primio u ime svih nas koji smo se borili sa njim.

Bolest ga maja 2024. pronalazi na radnom mestu, na dežurstvu, posle anestezije u operacionoj sali. Usledila je desetomesečna borba za život i opstanak. Ovom prilikom zahvaljujemo i kolegama Klinike za anesteziiju, intenzivnu terapiju i terapiju bola UKC Vojvodine koji su dali sve od sebe da pomognu kolegi i saborcu. Borba je trajala dalje i u njegovoj matičnoj kući, na našem odeljenju, gde je negovan s ljubavlju i poštovanjem. Četvrtog marta 2025. stigla je vest da je borba ipak izgubljena, da je dr Aleksandar Zonjić preminuo.

Opraštamo se od čoveka, lekara i prijatelja koji je ostavio dubok trag u našim životima, ličnim i profesionalnim. Ne treba da osećamo tugu što smo ga izgubili već radost što smo ga poznavali.

Slava mu!

*Kolege Odeljenja za anesteziiju,
reanimatologiju i intenzivnu terapiju
Opšte bolnice „Dr Radivoj Simonović“ Sombor*

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