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ČASOPIS PODRUŽNICE SRPSKOG LEKARSKOG DRUŠTVA U LESKOVCU

APOLLINEM MEDICUM ET AESKULAPIUM HYGEAMQUE AC PANACEAM IURO DEOSQUE OMNES ITEMQUE DEAS TESTES FACIO ME HOC IUSIURANDUM ET HANC CONTESTATIONEM PRO VERIBUS ET IUDICIO MEO INTEGRE SERVATURUM ESSE…

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Naslovna strana: **Nutritivna terapija kod pacijenata sa inflamatornim bolestima creva**

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ORIGINALNI RADOVI

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PERIOPERATIVNA NUTRITIVNA TERAPIJA KOD PACIJENATA SA INFLAMATORNIM BOLESTIMA CREVA – SKRINING, DIJAGNOSTIKA I TERAPIJA PERIOPERATIVNE MALNUTRICIJE

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SAŽETAK

Uvod: Inflamatorne bolesti creva (IBC) predstavljaju grupu crevnih poremećaja koji dovode do hronične inflamacije gastrointestinalnog trakta. IBC obuhvataju Kronovu bolest i ulcerozni kolitis. Uprkos napretku nehirurškog lečenja, poput biološke, antibiotske i nutritivne terapije, ovi pacijenti zahtevaju hirurški tretman. Dokazano je da je malnutricija glavni faktor rizika za perioperativne komplikacije.

Cilj: uočavanje najvećih izazova u perioperativnom periodu kod pacijenata sa inflamatornim bolestima creva.

Materijal i metode: istraživanje je sprovedeno popunjavanjem anonimnog onlajn upitnika koji se sastoji od dvadeset četiri pitanja. Upitnik je distribuiran onlajn, ciljajući anesteziologe, gastroenterologe i hirurge. Statistička analiza je izvršena korišćenjem SPSS 21.0.

Rezultati: Anesteziolozi su činili 72,9% ispitanika, 20,3% hirurzi i 6,8% gastroenterolozi. Svega 8,6% specijalista redovno koristi alate za skrining malnutricije, dok 12,1% ispitanika obavlja redovnu nutritivnu podršku za pacijente sa IBD. Najčešći alati za procenu nutritivnog statusa su anamneza, fizikalni pregledi, antropometrijska merenja i laboratorijski testovi. U preoperativnom periodu 90,1% nutritivne podrške čini kombinacija enteralne i parenteralne ishrane. Svi ispitanici su se složili da su glavni izazovi u radu nedostatak edukacije, organizacione podrške, vremena i resursa.

Zaključak: Preoperativna nutritivna procena i terapija kod bolesnika sa IBC se još uvek ne koriste rutinski, a metode i vreme trajanja su još uvek različite. Dalji rad na edukaciji, implementaciji i identifikaciji u pravcu nutritivne podrške kod ovih pacijenata je od vitalnog značaja

Ključne reči: inflamatorne bolesti creva, malnutricija, perioperativni period

SUMMARY

Introduction: Inflammatory bowel disease (IBD) encompasses a group of intestinal disorders characterized by chronic inflammation of the gastrointestinal tract. IBD includes Crohn's disease and ulcerative colitis. Despite advances in non-surgical management, including biologics, antibiotics, and nutritional support, patients with IBD commonly require surgical treatment. Malnutrition is found to be a significant risk factor for postoperative complications.

Objective: This review will focus on the role of healthcare professionals in preoperative assessment, the challenges in perioperative care, and management principles for patients with inflammatory bowel disease (IBD).

Methods: This research was conducted by filling out an anonymous online questionnaire consisting of twenty-four questions. The questionnaire was distributed online, targeting doctors, specialists in anesthesiology, gastroenterology, and surgery. Statistical analysis was performed using SPSS 21.0.

Results: The study involved 59 healthcare professionals specializing in different fields. 72.9% of them were anesthesiologists, 20.3% were surgeons, and 6.8% were gastroenterologists. Only 8.6% of specialists use the Malnutrition Screening Tool regularly. Only 12.1% of respondents are performing regular Nutritional support for patients with IBD. The most commonly used tools for nutritional assessment include anamnesis and physical examinations, anthropometric measurements, and laboratory tests. In the preoperative period, 90.1% of nutritional support is a combination of enteral and parenteral nutrition. All of the respondents agreed that the main challenges are a lack of knowledge, organizational support, time, and resources.

Conclusion: No specific preoperative nutritional support is regularly used, and methods and timing remain diverse. Further work on education, implementation, and identifying clinical needs and benefits for nutritional support in patients is vitally needed.

Keywords: Inflammatory bowel disease, malnutrition, perioperative period

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Introduction

Inflammatory bowel diseases (IBD), which include Crohn's disease and ulcerative colitis, are marked by chronic and recurring inflammation of the gastrointestinal tract [1]. The clinical progression of these diseases can vary significantly, but it is most often characterized by periods of activity and remission [2]. Part of their complexity is centered on the fact that, although they originate from the gastrointestinal tract, these diseases often manifest clinically in other organ systems, such as the spine, eyes, and skin, which can worsen systemic inflammation and additionally require immunosuppressive therapy. Chronic inflammation and immunosuppressive therapy hurt the ability of these patients to feed themselves [3]. Although we have seen daily progress in new non-surgical therapeutic methods that have reduced the rate of hospital admission for these patients, the rate of indication for operative care remains high. The course of these diseases is progressive and often requires surgery to remove certain parts of the gastrointestinal tract, whether due to severe colitis, perforation, fistulas, dysplasia, or malignant changes. Certain studies estimate that 26-47% of patients with Crohn's disease will require operative management ten years after diagnosis, and more than 80% twenty years after diagnosis [4, 5].

Malnutrition is a significant independent risk factor for patients with IBDs, affecting up to 70% of this population. Patients who are malnourished and undergo surgical treatment face a particularly high risk of postoperative complications. Malnutrition can lead to delayed recovery from illness and surgery, as well as impaired wound healing, which often results in more extended hospital stays and increased hospital costs [6, 7]. Several factors contribute to the decline in nutritional status among these patients, including reduced food intake, increased gastrointestinal tract losses, nutrient malabsorption, heightened dietary needs due to systemic inflammation, and iatrogenic factors [8, 9]. Since malnutrition is a modifiable risk factor, it's crucial to understand how preoperative assessments of nutritional status can impact surgical outcomes. This understanding highlights the importance of administering perioperative dietary therapy for patients with IBD [10, 11].

The European Society for Clinical Nutrition and Metabolism (ESPEN) recommends that patients be screened for malnutrition at the time of diagnosis, with regular follow-up assessments thereafter [12]. While these patients may appear well-nourished, they are often at risk for micronutrient deficiencies, particularly in vitamin D, zinc, iron, vitamin B6, vitamin B12, and vitamin C. Therefore, it is essential to screen for and address these deficiencies [13]. Diagnosing malnutrition can be challenging, especially in patients with IBD, and no gold standard for diagnosis has been established yet [14]. Standard clinical tools for assessing nutritional status include body mass index (BMI), unintentional weight loss, reduced intake of essential micro- and macronutrients, and the percentage of body fat [13].

Recent recommendations suggest that specific indicators are crucial for identifying severe malnutrition, particularly in patients with inflammatory bowel disease (IBD). These indicators include a weight loss of more than 10–15% within six months, a body mass index (BMI) of less than 18.5 kg/m², and serum albumin levels below 30 g/L [10, 12, 15]. According to the ESPEN guidelines, patients with IBD should be screened for malnutrition using validated nutritional screening tools, similar to protocols for patients undergoing general surgery [16]. The Nutritional Risk Score 2002 (NRS 2002) and the Malnutrition Universal Screening Tool (MUST) are specifically recommended for this purpose [16, 17]. A score of 3 or higher is associated with an increased risk of gastrointestinal surgery and indicates the need for nutritional support [18]. Additionally, other universal nutritional screening tools that may be utilized include the Mini Nutritional Assessment (MNA), the Subjective Global Assessment scale (SGA), the Nutritional Risk Index (NRI), and the Controlling Nutritional Status score (CONUT) [19, 20]. When considering ESPEN recommendations for nutritional support in these patients, energy deli-

very should be set at 30–35 kcal/kg/day, as the energy requirements for individuals with IBD are comparable to those of the healthy population. If there is a clinical suspicion of varying energy needs in specific disease states, individual energy requirements should be assessed using indirect calorimetry along with a personalized physical activity factor. Individuals with active IBD have increased protein requirements, which should be raised to 1.2–1.5 g/kg/d for adults compared to general population recommendations. Every patient with IBD deserves the benefit of personalized counseling from a skilled dietitian [12]. This is an integral part of a comprehensive multidisciplinary approach, not only enriching nutritional therapy but also playing a vital role in safeguarding against malnutrition and related disorders. Prioritizing this support can significantly improve health outcomes and enhance overall well-being. Determining the best approach to medical nutrition in IBD can be complex and depends on several factors. These include the patient's ability to eat, the absorptive capacity of the gastrointestinal tract, the patient's nutritional and inflammatory status, and the therapeutic goals. Oral nutritional supplements are typically the first step and are considered a supportive therapy that complements a regular diet. When possible, enteral nutrition (EN) should be prioritized over parenteral nutrition (PN). However, if EN does not meet more than 60% of a patient's energy needs, it should be supplemented with parenteral nutrition (PN), particularly during the perioperative period [12, 21, 22].

Optimizing the preoperative nutritional status in patients with IBD through a collaborative approach among healthcare specialists is essential for achieving favorable surgical outcomes.

Objective

This review aims to highlight the importance of preoperative nutritional therapy and the involvement of various healthcare professionals in clinical practice during preoperative assessments, addressing challenges in perioperative care, and outlining management principles for patients with inflammatory bowel disease (IBD).

Methods

This study employed an online questionnaire comprising twenty-four questions, designed to assess the knowledge, attitudes, and practices of various medical professionals regarding nutritional support for patients with inflammatory bowel disease. The questionnaire was distributed online through professional associations, targeting doctors who specialize in anesthesiology, surgery, and gastroenterology, who are involved in patient care and nutritional assessment. It's important to note that the study's focus on nutritional support for inflammatory bowel disease is directly relevant to your field. Participants were required to be licensed healthcare professionals with at least one year of clinical experience currently practicing in a hospital. Participation in the study was voluntary and anonymous.

A structured questionnaire was developed based on current clinical guidelines and relevant literature related to nutritional assessment and support. The questionnaire included a combination of multiple-choice and open-ended questions and was divided into several sections:

- Demographics and Professional Background: Age, gender, specialty, years of experience, type of healthcare facility, and previous training in nutritional support.
- Knowledge of Nutritional Assessment Tools: Awareness and utilization of screening tools, including MUST, NRS-2002, and SGA.
- Clinical Practice and Attitudes: Frequency and perceived importance of nutritional assessment, involvement in nutrition therapy planning, and collaboration with other disciplines.
- Barriers and Educational Needs: Reported challenges to providing adequate nutritional support, as well as interest in further training.

The finalized questionnaire was hosted on an online survey platform (Google Forms), and the link was distributed through targeted communication channels. Statistical analysis was performed using SPSS version 21.0.

Results

The study involved 59 healthcare professionals specializing in different fields. 72.9% of them were anesthesiologists, 20.3% were surgeons, and 6.8% were gastroenterologists.

Most respondents (30.5%) reported having between 6 and 10 years of clinical practice. Additionally, 23.5% have more than 20 years of experience, 16.9% have less than 5 years, 15.5% have between 11 and 15 years, and 13.6% possess 16 to 20 years of experience. A total of 83.1% of specialists work in Tertiary Clinical Centers, while 16.9% are employed in secondary hospital centers. Only 8.6% of specialists use the Malnutrition Screening Tools regularly, and the majority of medical professionals work in tertiary care hospitals. The most commonly used screening tools in clinical practice are the Nutritional Risk Screening 2002 (55.9%) and the Mini Nutritional Assessment (23.5%) (Chart 1).

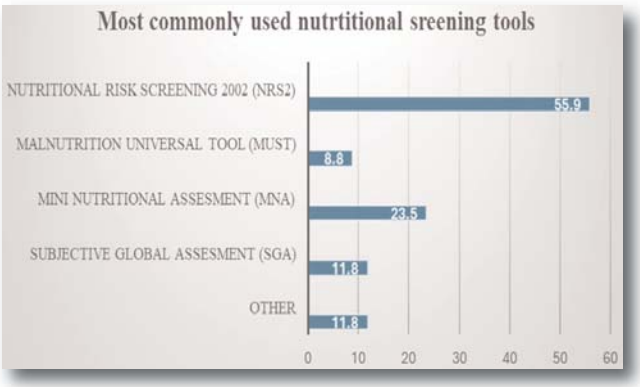

Chart 1. Most commonly used nutritional screening tools

In our facilities, perioperative nutritional support is mainly performed by anesthesiologists (40.7%). Only 12.1% of respondents are performing regular Nutritional support for patients with IBD. The most commonly used tools for nutritional assessment include anamnesis, physical examination, anthropometric measurements, and laboratory tests.

44.1% of respondents are uncertain about how long preoperative nutritional support should last, while 27.1% indicated it should be fewer than 4 days, and 22% suggested a duration of 4 to 7 days before surgery.

Only 12.1% of respondents regularly provide nutritional support for patients with IBD, while 32% do so occasionally, 21% rarely, 20% are unsure how often it is done, and 15% indicated that they do not provide it at all (Chart 2).

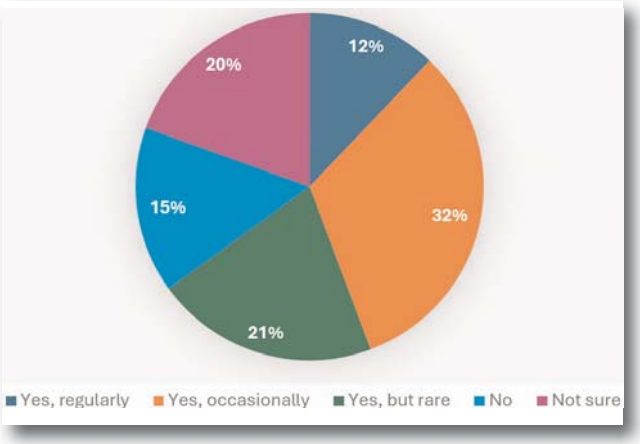

Chart 2. Response percentage for regular nutritional support performance in malnourished patients with inflammatory bowel disease.

In the preoperative period, 91% of nutritional support consists of a combination of enteral and parenteral nutrition, whereas 4.5% relies solely on either enteral or parenteral support. Additionally, 21.1% of patients consume liquid carbohydrates orally before surgery.

All respondents acknowledged that the primary challenges include a lack of knowledge, organizational support, time constraints, and available resources.

Discussion

Nutritional support is integral to the multidisciplinary management of IBD. The collaboration of various medical specialists is essential to ensure comprehensive and individualized care for patients with IBD. Each specialty contributes distinct expertise to address the intricate nutritional requirements associated with this disease [23]. Gastroenterologists should play a central role in diagnosing and managing IBD. They are crucial in assessing disease activity, evaluating the nutritional effects of inflammation, and making decisions regarding enteral or parenteral nutrition [24]. In contrast to our study, gastroenterologists expressed the least interest in managing patients during the perioperative period. Unfortunately, in our study, only 8.6% of specialists regularly use Malnutrition Screening Tools for patients with IBD, and the majority of

medical professionals are based in tertiary care hospitals. What is reasonable to consider is that most of these patients are followed at these level medical centers. Surgical specialists, particularly colorectal surgeons, become critical in cases where surgical intervention is required due to complications such as strictures, fistulas, or refractory disease. Surgeons often rely on nutritional assessments to determine timing and readiness for surgery and collaborate with anesthesiologists and gastroenterologists to implement perioperative dietary strategies [25]. As suggested in some studies, our results indicate that the most commonly used screening tools were NRS 2002 and MNR. Other scores were also utilized, but they were used less frequently [16, 17, 19, 20, 26]. There are limited research papers that examine the specific roles of various healthcare specialists in providing perioperative nutritional support to patients with inflammatory bowel disease (IBD). In our facilities, anesthesiologists are primarily responsible for this support, accounting for 40.7% of the role. However, this responsibility is often shared with surgeons and dietitians. Unfortunately, the role of dietitians in our healthcare system is not well-defined [27, 28]. The duration of total parenteral nutrition can vary based on individual patient needs and the severity of their malnutrition or active Crohn's disease. Some studies suggest that administering TPN for 18 to 90 days before surgery, particularly for patients with moderate to severe Crohn's disease, may lead to improved clinical outcomes and a reduction in postoperative complications. On the other hand, some studies suggest that oral intake may be more effective. Considering these various factors, it is not surprising that 44.1% of our respondents are unsure how long nutritional therapy for these patients should last [12, 29]. Furthermore, due to the unique challenges each faces, several key factors can complicate oral intake in these patients. Our study indicates that a combination of oral and parenteral nutritional therapy is the most commonly used approach. Just like with medical interventions, implementing dietary therapies necessitates careful consideration and discussion. It is essential for patients to work closely with a dietitian and to have clear goals and expectations [12, 30].

As shown in other research, all respondents agreed that the main challenges in this field are a lack of knowledge, inadequate organizational support, insufficient time, and limited resources [31].

Conclusion

The management of perioperative nutrition in patients with IBD undergoing surgery is highly inconsistent. The regular use of specific preoperative nutritional support is lacking, and the methods and timing for such support vary significantly. There is a clear need for further efforts in education, implementation, and the identification of clinical needs and benefits related to nutritional support, as it is crucial for patient care.

References

1. Abraham C., Medzhitov R. Interactions between the host innate immune system and microbes in inflammatory bowel disease. Gastroenterology. 2011;140(6): 1729–37
2. Romberg-Camps MJ, Dagnelie PC, Kester AD, Hesselink-van de Kruijs MA, Cilissen M, Engels LG, et al. Influence of phenotype at diagnosis and of other potential prognostic factors on the course of inflammatory bowel disease. Am J Gastroenterol. 2009; 104:371–83.
3. Ng SC, Shi HY, Hamidi N, Underwood FE, Tang W, Benchimol EI, et al. Worldwide incidence and prevalence of inflammatory bowel disease in the 21st century: a systematic review of population-based studies. Lancet. 2017;390(10114):2769-78.
4. Tsai L, Ma C, Dulai PS, Prokop LJ, Eisenstein S, Ramamoorthy SL, et al. Contemporary Risk of Surgery in Patients with Ulcerative Colitis and Crohn's Disease: A Meta-Analysis of Population-Based Cohorts. Clin Gastroenterol Hepatol. 2021;19(10):3031-45
5. Fiorindi C, Cuffaro F, Piemonte G, Cricchio M, Addasi R, Dragoni G, et al. Effect of long-lasting nutritional prehabilitation on postoperative outcome in elective surgery for IBD. Clin Nutrition. 2021; 40(3):928-35.
6. Mijač D, Janković GL, Jorga J, Krstić MN. Nutritional status in patients with active inflammatory bowel disease: prevalence of malnutrition and methods for routine nutritional assessment. Eur J Intern Med. 2010;21(4):315–19.
7. Yamamoto T, Nakahigashi M, Saniabadi AR. Review article: diet and inflammatory bowel disease--epidemiology and treatment. Aliment Pharmacol Ther. 2009;30:99–112

8. Hartman C, Eliakim R, Shamir R. Nutritional status and nutritional therapy in inflammatory bowel diseases. World J Gastroenterol. 2009;15:2570–8.
9. Balestrieri P, Ribolsi M, Guarino MPL, Emerenziani S, Altomare A, Cicala M. Nutritional Aspects in Inflammatory Bowel Diseases. Nutrients. 020;31 (12):372.
10. Grass F, Pache B, Martin D, Hahnloser D, Demartines N, Hübner M. Preoperative nutritional conditioning of Crohn's patients-systematic review of current evidence and practice. Nutrients. 2017;9(6)562.
11. Okita Y, Araki T, Okugawa Y, Kondo S, Fujikawa H, Hiro J, et al. The prognostic nutritional index for postoperative infectious complications in patients with ulcerative colitis undergoing proctectomy with ileal pouch-anal anastomosis following subtotal colectomy. J Anus Rectum Colon. 2019;3:91-7.
12. Bischoff, Stephan C. et al. ESPEN guideline on Clinical Nutrition in Inflammatory Bowel Disease. Clin Nutr. 2023:42(3):352-7.
13. Schwartz E. Perioperative parenteral nutrition in adults with inflammatory bowel disease: a review of the literature. Nutrition in Clinical Practice. 2016; 31(2):159–70.
14. Wagner I. J., Rombeau J. L. Nutritional support of surgical patients with inflammatory bowel disease. Surgical Clinics of North America. 2011;91(4):787–803
15. Spinelli A., Allocca M., Jovani M., Danese S. Review article: optimal preparation for surgery in Crohn's disease. Alimentary Pharmacology & Therapeutics. 2014;40(9):1009–22.
16. Sandhu A, Mosli M, Yan B, Gregor, J, Chande N, Ponich, T et al. Self-Screening for malnutrition risk in outpatient inflammatory bowel disease patients using the malnutrition universal screening tool (MUST). J. Parenter. Enter. Nutr. 2016;40:507–10.
17. Kondrup, J.; Rasmussen HH Hamberg, O.; Stanga, Z.; An ad hoc ESPEN Working Group. Nutritional risk screening (NRS 2002): A new method based on an analysis of controlled clinical trials. Clin. Nutr. 2003, 22, 321–36.
18. Schiesser, M.; Müller, S.; Kirchhoff, P.; Breitenstein, S.; Schäfer, M.; Clavien, P.-A. Assessment of a novel screening score for nutritional risk in predicting complications in gastro-intestinal surgery. Clin. Nutr. 2008, 27, 565–70.
19. Bamba S, Sasaki M, Takaoka A, Takahashi K, Imaeda H, Nishida A, et al. Sarcopenia is a predictive factor for intestinal resection in admitted patients with Crohn's disease. PLoS ONE 2017, 12, e0180036.
20. Ulíbarri JI, González-Madroño A, de Villar NG, González P, González B, Mancha A, et al. CONUT: A tool for controlling nutritional status. First validation in a hospital population. Nutr. Hosp. 2005;20:38–45.
21. Sood A, Ahuja V, Kedia S, Midha V, Mahajan R, Mehta V, et al. Diet and inflammatory bowel disease: The Asian Working Group guidelines. Indian J Gastroenterol. 2019;38:220–46.
22. Bischoff SC, Escher J, Hébuterne X, Kłęk S, Krznaric Z, Schneider S, et al. ESPEN practical guideline: Clinical Nutrition in inflammatory bowel disease. Clin Nutr. 2020;39:632–53.
23. Istratescu D, Preda CM, Manuc T, Meianu C, Stroie T, Diculescu M. A Comprehensive Review of Dietary Approaches in Maintaining Remission of Inflammatory Bowel Diseases in Adults. Medicina. 2024;60(7): 1068.
24. Gomollón F, Dignass A, Annese V, Tilg H, Van Assche G, et al. 3rd European evidence-based consensus on the diagnosis and management of Crohn's disease. J Crohns Colitis. 2016;11(1):3-25.
25. Walters TD, Griffiths AM, Shaoul R. Nutrition in pediatric inflammatory bowel disease: From etiology to treatment. Nat Rev Gastroenterol Hepatol. 2020;17 (10):662–76.
26. Sokulmez P, Demirbağ, AE, Arslan P, Dişibeyaz S. Effects of enteral nutritional support on malnourished patients with inflammatory bowel disease by subjective global assessment. Turk. J. Gastroenterol. 2014; 25:493–507.
27. Kim DH, Seo JM, Choi MG. Perioperative nutritional practices and attitudes among gastrointestinal oncologic surgeons in Korea: a nation-wide survey study. Ann Clin Nutr Metab. 2023;15(3):81-7.
28. Drover JW, Cahill NE, Kutsogiannis J, Pagliarello G, Wischmeyer P, Wang M, et al. Nutrition therapy for the critically ill surgical patient: we need to do better! JPEN J Parenter Enteral Nutr 2010;34:644-52.
29. Di Caro S, Fragkos KC, Keetarut K, et al. Enteral Nutrition in Adult Crohn's Disease: Toward a Paradigm Shift. Nutrients. 2019;11(9):2222.
30. Reznikov EA, Suskind DL. Current Nutritional Therapies in Inflammatory Bowel Disease: Improving Clinical Remission Rates and Sustainability of Long-Term Dietary Therapies. Nutrients. 2023;15(3):668.

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INTRAMEDULARNA FIKSACIJA TROHANTERIČNOG REGIONA FEMURA: PREDNOSTI I MANE - PREGLED LITERATURE

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SAŽETAK

Prelomi trohanterne regije se svrstavaju u grupu zdravstvenih problema koje za posledicu imaju invaliditet, promenjen kvalitet života kao i povećanje procenta mortaliteta. S obzirom na to da je životni vek produžen, broj starijih osoba je povećan a samim tim i učestalost trohanternih preloma je veća. Naš cilj je da se intramedularna fiksacija preloma trohanterne regije predstavi kao jedna od najsavremenijih metoda lečenja. Mnogobrojna savremena literatura opisuje da je intramedularni klin odličan za operativno lečenje trohanternih preloma femura, kao i da se sastoji od dva cefalična zavrtnja koji su međusobno u integrisanom delovanju. Korišćenjem ovog osteosintetskog materijala postiže se veliki stepen stabilnosti fragmenata a ujedno i eliminišu rotacione sile između glave i vrata femura. Lečenje preloma trohanterne regije femura upotrebom intra i ekstramedularne fiksacije je veliki izazov za operatora kako zbog anatomske specifičnosti regije, teškoća i komplikacija tokom operacije tako i pojave postoperativnih komplikacija. Najidealnije je ono sredstvo koje će se odupreti svim silama koje dovode do rotacije, promene angulacije fragmenata kao i medijalnom pomeranju osovine femura. Intramedularna fiksacija preloma transtrohanterične regije predstavlja savremenu metodu operativnog lečenja sa minimalnim kako intraoperativnim tako i postoperativnim komplikacijama.

Ključne reči: trohanterni prelom, femur, intramedularna fiksacija

SUMMARY

Fractures of the trochanteric region are classified as a group of health problems that result in disability, a changed quality of life, and an increase in the mortality rate. Given that life expectancy has increased, the number of older adults has also increased, and therefore, the frequency of trochanteric fractures is higher. Our goal is to present the intramedullary fixation of fractures of the trochanteric region as one of the most modern methods of treatment. Numerous contemporary studies describe that the intramedullary nail is excellent for the operative treatment of trochanteric femoral fractures, and that it consists of two cephalic screws that are in an integrated action with each other. The use of this osteosynthetic material achieves a high degree of stability of the fragments and at the same time eliminates the rotational forces between the bone and the neck of the femur. Treatment of fractures in the trochanteric region of the femur using both intra- and extramedullary fixation poses a significant challenge for the operator due to the anatomical specificity of the area, the potential difficulties and complications that can arise during surgery, and the risk of postoperative complications. The ideal tool is the one that resists all forces leading to rotation, change in the angulation of the fragments, as well as medial displacement of the femoral shaft. Intramedullary fixation of fractures of the transtrochanteric region represents a modern method of operative treatment with minimal both intraoperative and postoperative complications.

Keywords: trochanteric fracture, femur, intramedullary fixation

Introduction

Fractures of the trochanter region are classified as a group of health problems that result in disability, a change in quality of life, and an increase in mortality rates. Given that life expectancy has increased, the number of older adults has also increased, and therefore, the frequency of trochanteric fractures is higher [1]. Fractures of the trochanteric region comprise 50% of all

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hip fractures, of which 40% are unstable. They belong to the group of extracapsular fractures and are most common in the elderly population. Patients are exposed to forces of lower intensity, and it should be emphasized that the bones in women have changed structures due to demineralization resulting from osteoporosis. They mostly occur as a result of falling from the same level, such as from a bed or chair. Of course, since they are older adults, if their health condition is satisfactory, surgery is often the first choice of treatment. The ideal is to operate within the first 24 hours to reduce mortality rates and postoperative complications [2]. Fractures of the trochanteric region of the femur in young people occur as a result of the action of high-energy forces (overturning with a tractor, the effect of a firearm, traffic trauma, etc.)

There are numerous classifications of fractures of the trochanteric region of the femur. They are also divided into stable and unstable fractures. Furthermore, AO/OTA classification is most often used, while Tronz, Evans, and Jensen-Mishaels are some of the other classifications [3]. The most widely used classification today is the AO/OTA classification, created in 1987. This classification divides the trochanteric region 31-A into nine types depending on the degree of comminution. Covers most fractures of the trochanteric region within other classification systems. By classifying fractures into only three groups (A, 1-2-3), the classification itself is highly significant (Figure 1) [4].

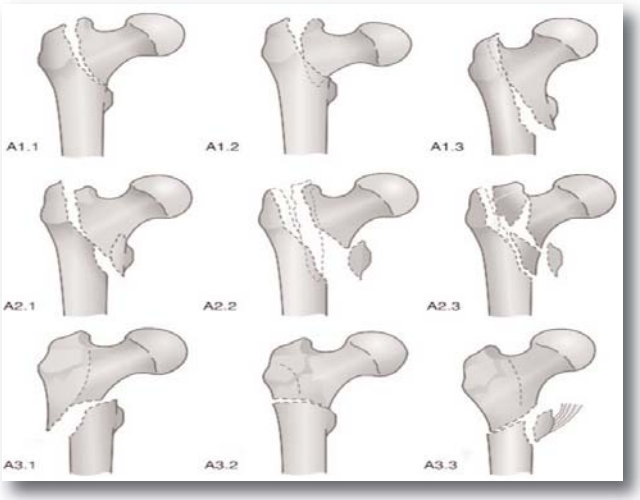

Figure 1. AO/OTA classification and subclassification.

Methods

The methodological framework of the research in the work is subordinated to the subject, the structure of the work, and the achievement of the set goals. The research used a systematic literature review methodology based on the PRISMA Method (Preferred Reporting Items for Systematic Reviews and Meta-Analyses - PRISMA), using clear and predetermined inclusion and exclusion criteria. Databases such as Web of Knowledge, Scholar, and Science Direct will be accessed to search for scientific literature in English and other regional languages.

The research was conducted in January 2025. The literature review includes articles from studies published over the last 15 years. Additionally, the goal is to present intramedullary fixation of trochanter fractures as one of the most modern methods of treatment, as well as to review the experiences of other authors who have applied this technique.

In order to achieve a satisfactory reduction and to facilitate the patients' early recovery, surgical treatment is required for such kinds of fractures [5]. The dynamic hip screw (DHS) implant, which was previously regarded as the gold standard therapy for stable intertrochanteric fractures, was shown to be inadequate for the stabilisation of fractures of the unstable kind (Figure 2), [6]. As opposed to extramedullary devices such as DHS, proximal femoral nails (PFN) have a biomechanical advantage because of their closer location to the vector of force line and shorter moment arm [7]. Moreover, based on the results of several reports, intramedullary fixation may be preferable to extramedullary fixation for patients since there is a lower risk of implant failure and reoperation, and functional scores are higher [8,9,10]. It is possible to implant a PFN with a minimally invasive procedure. By performing a closed reduction of the fracture, the haematoma is maintained, and the surgeon can do a minimally invasive procedure with minimum soft-tissue dissection, thereby minimizing surgical trauma, blood loss, infec-

tion, and wound complications [11,12]. Complications of operative treatment for trochanteric femur fractures with extramedullary and intramedullary fixation include wound dehiscence, infection, pseudarthrosis, device failure, and hip joint arthrosis (Figure 4), [8-12].

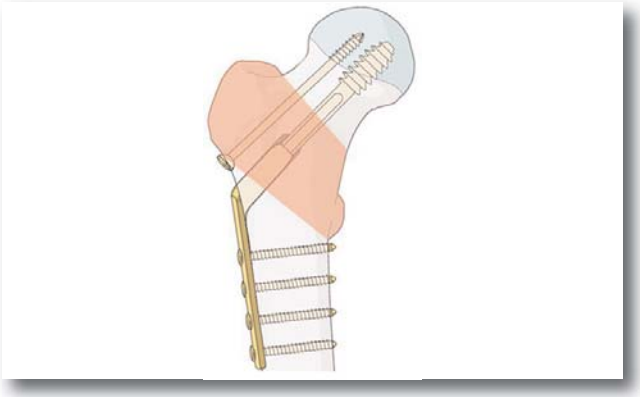

Figure 2. Dynamic hip screw (DHS)

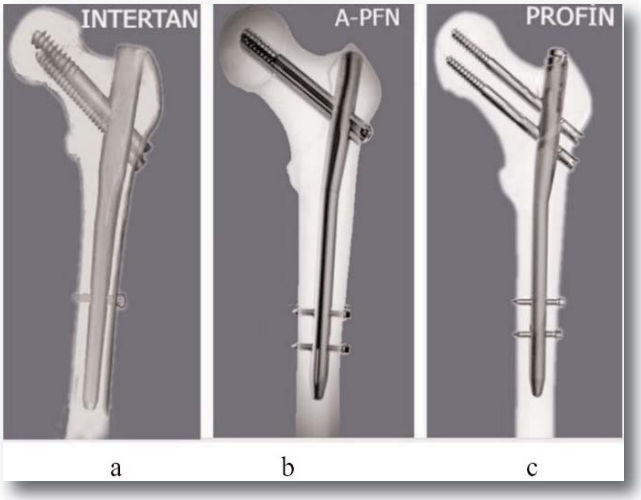

Figure 3. Types of proximal femoral nails (PFN): a) InterTAN (Intertrochanteric Antegrade Nail), b) A-PFN (Antirotational Proximal Femoral Nail), c) PROFIN (Proximal Femoral Intramedullary Nail)

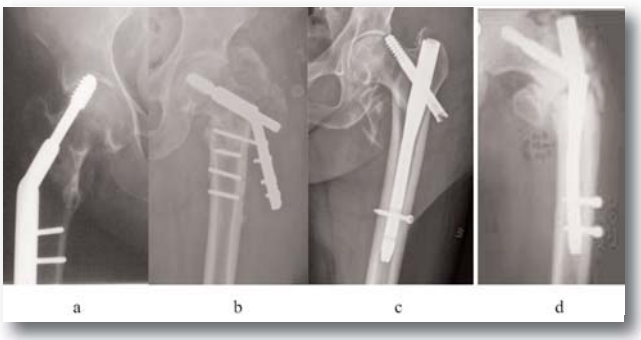

Figure 4. Complications of operative treatment of intertrochanteric fracture: a) Cut – out of DHS b) Broken screws on DHS c) Cut – out of A-PFN d) Broken nail of A-PFN

Characteristics of PFNs

InterTAN (Intertrochanteric Antegrade Nail)

The titanium alloy used in the production of InterTAN PFN allows for a proximal 4° valgus offset. The nail features a trapezoidal cross-section with a 17 mm proximal diameter and a 10 to 11.5 mm grooved distal tip diameter. InterTAN PFNs are available with either a 125° or 130° collodiaphyseal angle (CDA). A lag screw of 11 mm and a compression screw of 7 mm were used. The tip of the nail was secured by a single screw that was locked in either a dynamic or static configuration. With the combined proximal screw system, it was possible to achieve interfragmentary compression of up to 15 mm. The InterTAN nail is designed with an interlocking lag nail system that helps minimise femoral head movement and prevents the femoral head from collapsing[7].

A-PFN (Antirotational Proximal Femoral Nail)

A-PFN is available in two different lengths: 160 and 220 mm. The top portion of the proximal nail features a 6° valgus angle (mediolateral curvature) with a diameter of 15 mm. This nail is available in four different diameters: 9, 10, 11, and 12; it has a lag screw that compresses the fractures and a wedge block that provides rotational stability for femoral fractures. The 10 mm wide thread and 125° angle of the lag screw are consistent with the CDA. The wedge block is in the groove on the lower portion of the lag screw. The distal end of the nail has two locking holes appropriate for either dynamic or static fixations, as well as a slot [13].

PROFIN (Proximal Femoral Intramedullary Nail)

PROFIN PFN is a titanium alloy tube with a cannulated and flat design. It features a proximal valgus offset of 6° and a distal grooved shape, and it is attached with two 8.5 mm lag screws with 135° CDA. The surgical compression of interfragmentary fractures was also possible with this system. The nail has a 16 mm diameter at its

proximal end and three separate distal diameters measuring 10, 11, and 12 mm. Both dynamic and static fixation with 4.5 mm locking screws are possible via the two distal holes [14].

Surgical Management

Before starting the application of the intramedullary nail, it is necessary to perform anatomical reduction of the fracture after introducing the patient to general or regional anesthesia on the extension table, as well as antibiotics and protection against deep vein thrombosis. After that, a 5 cm surgical incision is made above the greater trochanter, and the muscle tissue is layered with a blunt preparation. Kirschner wires - the guide is introduced into the medullary canal from the top of the greater trochanter, where it is the entry point, and the position of the wires is monitored by radiographic recording in LL and AP. Then follows reaming of the proximal femur with a 16 cm diameter reamer. After applying the intramedullary nail and visually confirming whether the anteversion of the nail is appropriate, two screws of the proper length are used in the proximal part of the nail. Proximal screws are integrated with the lower screw, 5 mm shorter than the upper one, to perform compression of the fragments. After visual confirmation that the intramedullary nail is in the appropriate position, the setting of the cortical screw in the distal edge of the nail follows in a static or dynamic position (whether we want compression or not) [15,16,17,18].

Discussion

The anatomical specificity of the proximal femur, the frequent occurrence of complications, as well as the occurrence of difficulties during fracture osteosynthesis, is an excellent challenge for operative treatment. The most adequate device is the one that can prevent medial translation of the femoral shaft, rotation, and, of course, a change in the collodiaphyseal angle. Today, in the official literature, many controversies can be found about the type of apparatus (osteosynthetic material) that is most adequate [17,18]. Meta-analyses show that the intramedullary wedge achieves a short healing period and a low rate of complications compared to extramedullary fixation.

Oliveira et al. did a study with over 230 patients, where the highest number of deaths was in patients over 90 years old. In 118 patients, or 51.3% of patients, death occurred after the completion of operative treatment and implementation of rehabilitation. Only 3.5% (8 patients) died during hospitalization. Out of the total number of patients, 83.5% were women. They also found that there was an association between the duration of surgery and the death of patients after the completion of orthopedic treatment and rehabilitation ($p < 0.05$), as well as between the presence of heart disease in patients and the death of patients during hospitalization [19].

Sharma et al. proved that in the group of patients where intramedullary fixation was performed, the mean length of the incision was 4.9 cm. Still, there was a greater exposure to radiation during the operation ($p < 0.01$). It is statistically significant that the length of the operation itself was shorter when using intramedullary osteosynthesis ($p < 0.01$). Average blood loss as well as postoperative blood replacement was higher in the group operated with the DHS system compared to the group with intramedullary osteosynthesis. Although not statistically significant, the duration of hospitalization was longer in patients with extramedullary versus intramedullary osteosynthesis. They also determined that the cost of the implants themselves in extramedullary osteosynthesis was 55% of the total cost of intramedullary osteosynthesis. Due to the complexity of the instruments and the course of the operation, the incidence of technical errors was higher in the group with intramedullary osteosynthesis, 9.67% compared to the extramedullary group, where it was 3.48%. But that's why the occurrence of infection was higher in the group with extramedullary osteosynthesis. The percentage of mortality was similar in both groups, but it is stated that the cause was not related to the operation itself and occurred three months after the operation [20]. Meniscalo et al. included patients with intramedullary osteosynt-

hesis in their study. The intramedullary wedge they used is a 130° angle screw, 170mm long, and one 10mm diameter screw or two 6mm diameter screws. The percentages of rapid recovery and return to functionality are significantly high during treatment [21]. In the research by Wang et al., which included 924 patients - 486 with intramedullary and 438 with extramedullary osteosynthesis - significant data were obtained. The average age of the patients was 60 years. They found data that during intramedullary osteosynthesis, blood loss was minimal, surgical-traumatic tissue damage was minimal, and the percentage of complications was lower. But they stated that it is statistically significant that comminuted fractures can be resolved only by extramedullary osteosynthesis [22]. Wei Fu et al. compared the treatment outcomes of a patient with an intertrochanteric femoral fracture using intramedullary (PFN) and extramedullary (DHS) osteosynthesis. A retrospective study showed that separate analysis of samples leads to clear indications for operative treatment. Statistical analysis revealed that the method using the PFN device is associated with a shorter operation time and a reduced need for blood and blood product transfusions. Both techniques have demonstrated excellent clinical results [23]. Additionally, the duration of the operation and the postoperative Hip Harris score test show more favorable results with intramedullary fixation compared to extramedullary fixation. Intraoperative blood loss is lower with intramedullary fixation than with extramedullary fixation [24]. Yoo J, et al. showed that in 351 patients surgically treated with intramedullary fixation, surgical and non-surgical complications were few, including anemia and electrolyte imbalance [25]. Liu et al. showed that in 18 patients after intramedullary fixation of the proximal femur, THA was the method of choice for the treatment of arthrosis of the hip joint. The operations were successful with minimal blood loss and good results of functional tests, which is, of course, an indicator of the use of the appropriate method for femur fractures [26]. Yang et al. retrospectively analyzed 216 patients with intertrochanteric fractures treated using intramedullary fixation. They reported minimal blood loss, little deviation from the bone axis, and excellent results on functional tests [27]. Niu E and others presented that the most frequently used method is operative treatment of hip fractures. Simplicity of the surgical technique, minimal blood loss, minimal incision length, as well as shorter duration of surgery, are the features of intramedullary fixation, which makes it the first choice in operative treatment. In their study, 68% used cephalomedullary fracture fixation [28].

Saul et al. reported a success rate of 358 patients with intramedullary wedge application, which was enormous, occurring within 24 hours after the fracture. Out of the total number, as many as 46% of patients had a pertrochanteric fracture. The study showed that the longest delay time was hip surgery (28.3h) [29]. Dekhne et al. reviewed 910 patients, noting the percentage of implants requiring revision. They concluded that only 7% of patients with cephalomedullary nails required revision [30].

Bo Y and colleagues performed a reflexive analysis of unstable intertrochanteric fractures with different subdivisions. In each group, intramedullary fixation showed excellent results. $P < 0.05$ was statistically significant [31].

Kwek et al. showed that patients with unstable intertrochanteric fractures treated with intramedullary fixation had a shorter hospital stay and underwent early fracture fixation ($p < 0.001$) [32]. A group of different authors conducted studies, the results of which showed that intramedullary fixation of fractures minimized blood loss, shortened the duration of surgery, reduced pain intensity to a minimum, and led to almost ideal bone union. Comparing the four main items between different categories of implants, they concluded that the use of intramedullary fixation is the best method of choice for fracture treatment [33-40]. Li XP and co-authors performed a prospective cohort study with patients treated with intramedullary fixation. Comparing the group of patients who died with those who survived, they found that the percentage of comorbidities was higher in patients who died. [31]

Ju JB and co-authors followed 164 patients in their study. Thirty-nine patients died, and the rest were processed for further functional analysis. HHS was 71.8±13.1, and the Barthel index was 80.2±18.1. By associating the functional results with the patient's age, albumin values, and ADL, the group of authors identified the underlying factors. This will help them to modify the variable factors to achieve better outcomes and a better functional prognosis [42].

Zhong G and his co-authors performed an analysis where patients were followed for an average of 24.7 months. The patients had a pertrochanteric fracture and were treated with intramedullary fixation and arthroplasty. Comparing these two groups of patients, the time for revision, and the healing time, intraoperative blood loss, and limb shortening, HHS concluded that the results are far more favorable in patients who were treated with intramedullary fixation [43].

Sezgin EA, with a group of authors, conducted a retrospective study in Lithuania and Turkey, where 100 patients with proximal femur fractures caused by low-energy force participated. Patients were classified into nine subcategories using risk assessment tools. Comparing the functional results, they concluded that intramedullary fixation is the first choice of treatment [44]. Chee YH and co-authors studied 13 publications with 687 patients. They concluded that the average operation time, average hospital stay, and average time to surgery were shorter with intramedullary fixation [45].

Jennison T and co-authors compared the operative time and length of hospital stay in patients with a preprosthetic fracture and a fracture of the trochanteric region of the femur treated operatively with intramedullary fixation. Of course, they concluded that the time of surgery and the time of hospital stay are shorter with intramedullary fixation of proximal femur fractures [46].

Phruetthiphat OA et al found that an integrated scoring system (ISSI score) developed based on surgical and medical techniques, due to its high specificity and sensitivity, its results can be used for the evaluation and treatment of patients with intertrochanteric fractures treated with PFNA fixation [47]. Qin Y and his authors proved that THA is a very effective method of hip salvage after failed intramedullary fixation. However, it should be emphasized that the preoperative risk and complications are high [48].

Su Z, together with his co-authors, conducted a study comparing InterTan and PFN. The study included 75 cases. In the results of the study, no significant difference can be observed in the gender composition, age, fracture site, type of AO, anesthesia method, fracture reduction, and distance from the tip between the InterTan group and the PFNA group. This is an indication that intramedullary fixation (regardless of which osteosynthetic material is used) is the first choice for the treatment of fractures of the proximal end of the femur [49].

Conclusion

Surgically treated fractures of the trochanter region with intramedullary fixation are now the preferred method. The small surgical incision, lower intraoperative blood loss, and reduced complication rates are consistent with this approach.

References

1. Mattisson L, Bojan A, Enocson A. Epidemiology, treatment and mortality of trochanteric and subtrochanteric hip fractures: data from the Swedish fracture register. BMC MusculoskeletDisord. 2018 Oct 12;19(1):369.
2. Selim A, Ponugoti N, Naqvi AZ, Magill H. Cephalomedullary nailing versus dynamic hip screw with trochanteric stabilisation plate for the treatment of unstable per-trochanteric hip fractures: a meta-analysis. J OrthopSurg Res. 2021 Jan 11;16(1):47.
3. Biakto KT, PaturusiI A, Azis HS, Putra LT,Kurniawan, J. A comparison of walking ability between the dynamic hip screw and cephalomedullary nailing fixations in intertrochanteric femur fracture. Bali Medical Journal, 2022 11(1), 368-72.
4. Tucker SM, Wee H, Fox E, Reid JS, Lewis GS. Parametric Finite Element Analysis of Intramedullary Nail Fixation of Proximal Femur Fractures. J Orthop Res. 2019 Nov;37(11):2358-66.
5. Sharma V, Babhulkar S, Babhulkar S. Role of gamma nail in management of pertrochanteric fractures of femur. Indian J Orthop. 2008 Apr;42(2):212-6.

6. Zhang K, Zhang S, Yang J, Dong W, Wang S, Cheng Y, Al-Qwbani M, Wang Q, Yu B. Proximal femoral nail vs. dynamic hip screw in treatment of intertrochanteric fractures: a meta-analysis. Med Sci Monit. 2014 Sep 12;20:1628-33.
7. Lu Y, Uppal HS. Hip Fractures: Relevant Anatomy, Classification, and Biomechanics of Fracture and Fixation. Geriatr Orthop Surg Rehabil. 2019 Jul 3;10:2151459319859139.
8. Zheng XL, Park YC, Kim S, An H, Yang KH. Removal of a broken trigen intertan intertrochanteric antegrade nail. Injury. 2017 Feb;48(2):557-59.
9. Yu X, Wang H, Duan X, Liu M, Xiang Z. Intramedullary versus extramedullary internal fixation for unstable intertrochanteric fracture, a meta-analysis. Acta Orthop Traumatol Turc. 2018 Jul;52(4):299-307.
10. Li AB, Zhang WJ, Wang J, Guo WJ, Wang XH, Zhao YM. Intramedullary and extramedullary fixations for the treatment of unstable femoral intertrochanteric fractures: a meta-analysis of prospective randomized controlled trials. Int Orthop. 2017 Feb;41(2):403-13
11. Mereddy P, Kamath S, Ramakrishnan M, Malik H, Donnachie N. The AO/ASIF proximal femoral nail antirotation (PFNA): a new design for the treatment of unstable proximal femoral fractures. Injury. 2009; 40(4):428-32.
12. Nherera L, Trueman P, Horner A, Watson T, Johnstone AJ. Comparison of a twin interlocking derotation and compression screw cephalomedullary nail (InterTAN) with a single screw derotation cephalomedullary nail (proximal femoral nail antirotation): a systematic review and meta-analysis for intertrochanteric fractures. J Orthop Surg Res. 2018;13(1):46.
13. Karakus O, Ozdemir G, Karaca S, Cetin M, Saygi B. The relationship between the type of unstable intertrochanteric femur fracture and mobility in the elderly. J Orthop Surg Res. 2018;13(1):207.
14. Soylemez MS, Uygur E, Poyanli O. Effectiveness of distally slotted proximal femoral nails on prevention of femur fractures during and after intertrochanteric femur fracture surgery. Injury. 2019;50(11):2022-29.
15. Gursoy S, Simsek ME, Akkaya M, Dogan M, Bozkurt M. Transtrochanteric approach can provide better postoperative care and lower complication rate in the treatment of hip fractures. ClinInterv Aging. 2019;14:137-43.
16. Falaschi P, Marsh D. The Management of Older Patients with Fragility Fractures [Internet]. 2nd ed. Cham (CH): Springer; 2021. Chapter 9..
17. Zhang WQ, Sun J, Liu CY, Zhao HY, Sun YF. Comparing the Intramedullary Nail and Extramedullary Fixation in Treatment of Unstable Intertrochanteric Fractures. Sci Rep. 2018;8(1):2321
18. Ponz-Lueza V, Valle J, Urda AL, García-Coiradas J, León C, Marco F. Estudiocomparativo del tratamiento de lasfracturassubtrocantéreas en pacientesancianos: clavo de reconstrucción T2 v sclavo Gamma largo [Comparative study of the treatment of subtrochanteric fractures in elderly patients: reconstruction nail T2 vs long Gamma nail]. ActaOrtop Mex.2020; 34(4):205-10
19. Oliveira CEN, Feitosa ACC, Falótico GG, Ferreira GF, Durigon TS, Arliani GG. Mortality in patients > 90 years old with proximal femoral fractures subjected to surgery. ActaOrtop Bras. 2022;30(4):e255534.
20. Sharma A, Sethi A, Sharma S. Treatment of stable intertrochanteric fractures of the femur with proximal femoral nail versus dynamic hip screw: a comparative study. Rev Bras Ortop. 2017 Nov 8;53(4):477-81.
21. Maniscalco P, Quattrini F, Ciatti C, Burgio V, Rivera F, Di Stefano G, Pavone V. A preliminary experience with a new intramedullary nail for trochanteric fractures. Acta Biomed. 2020;91(4-S):122-27.
22. Wang ZH, Li KN, Lan H, Wang XD. A Comparative Study of Intramedullary Nail Strengthened with Auxiliary Locking Plate or Steel Wire in the Treatment of Unstable Trochanteric Fracture of Femur. Orthop Surg. 2020;12(1):108-15
23. Fu CW, Chen JY, Liu YC, Liao KW, Lu YC. Dynamic Hip Screw with Trochanter - Stabilizing PMC 7453265 Plate Compared with Proximal Femoral Nail Antirotation as a Treatment for Unstable 2020: 1896935.
24. Huang Y, Zhang C, Luo Y. A comparative biomechanical study of proximal femoral nail (InterTAN) and proximal femoral nail antirotation for intertrochanteric fractures. International Orthopaedics [Internet]. 2013 Oct 5;37(12):2465–73. Available from: http://dx.doi.org/10.1007/s00264-013-2120-1
25. Yoo J, Chang J, Park C, Hwang J. Risk Factors Associated with Failure of Cephalomedullary Nail Fixation in the Treatment of Trochanteric Hip Fractures. ClinOrthop Surg. 2020;12(1):29-36.
26. Liu L, Sun Y, Wang L, Gao Q, Li A, Wang J, Gao Y. Total hip arthroplasty for intertrochanteric fracture fixation failure. Eur J Med Res. 2019;24(1):39
27. Yang S, Yang Y, Huo Y, Yu J, Sheng L, Sun X, Liu X, Yin J, Yin Z. Effect of the degree of displacement of the third fragment on healing of femoral shaft fracture treated by intramedullary nailing. J Orthop Surg Res. 2022;17(1):380
28. Niu E, Yang A, Harris AH, Bishop J. Which Fixation Device is Preferred for Surgical Treatment of Intertrochanteric Hip Fractures in the United States? A Survey of Orthopaedic Surgeons. Clin Orthop Relat Res. 2015;473(11):3647-55
29. Saul D, Riekenberg J, Ammon JC, Hoffmann DB, Sehmisch S. Hip Fractures: Therapy, Timing, and Complication Spectrum. Orthop Surg. 2019;11(6): 994-1002.
30. Dekhne MS, Thomas HM, Haider T, Mortensen S, Rodriguez EK, Weaver MJ, von Keudell A. Treatment and outcomes of basicervical femoral neck fractures: A systematic review. J Orthop Surg (Hong Kong). 2021 Jan-Apr;29(1):23094990211003344.
31. Bo Y, Qin Y, Zang Y, Yang H. The suitable fixation for unstable intertrochanteric fractures: A protocol of comparative clinical study. Medicine (Baltimore). 2020 Oct 30;99(44):e23046.
32. T J, Kwek EBK. Are Intertrochanteric Fractures Evolving? Trends in the Elderly Population over a 10-Year Period. Clin Orthop Surg. 2022;14(1):13-20.
33. Li M, Li ZR, Li JT, Lei MX, Su XY, Wang GQ, Zhang H, Xu GX, Yin P, Zhang LC, Tang PF. Three-dimensional mapping of intertrochanteric fracture lines. Chin Med J (Engl). 2019;132(21):2524-33.

34. Guo J, Dong W, Jin L, Yin Y, Zhang R, Hou Z, Zhang Y. Treatment of basicervical femoral neck fractures with proximal femoral nail antirotation. J Int Med Res. 2019;47(9):4333-43.
35. Li C, Zhao D, Xu X, Ding J, Guo Y, Liao L, Li G. Three-Dimensional Computed Tomography (CT) Mapping of Intertrochanteric Fractures in Elderly Patients. Med Sci Monit. 2020 Oct 12;26:e925452.
36. Lewis SR, Macey R, Eardley WG, Dixon JR, Cook J, Griffin XL. Internal fixation implants for intracapsular hip fractures in older adults. Cochrane Database Syst Rev. 2021 Mar 9;3(3):CD013409.
37. Le QT. Effectiveness in the Treatment of Intertrochanteric Fracture in Geriatric Patients by A Novel Prototype Carbon Composite External Fixator. Med Arch. 2021;75(2):122-132
38. Zhang X, Zhang A, Yang X. Clinical study on the effect of intramedullary fixation and extramedullary fixation on unstable intertrochanteric fractures. Ann Palliat Med. 2021 Dec;10(12):12857-12866. doi: 10.21037/apm-21-3635. Retraction in: Ann Palliat Med. 2023;12(3):658
39. Tian RH, Zhang QM, Chu FL, Li XY, Jiang Z, Han L, Sun P, Wang HB, Chi YL, Wu B. Comparison of two methods of locating proximal femoral nail anti-rotation in the treatment of femoral intertrochanteric fractures. J Orthop Surg Res. 2020;15(1):108.
40. Cheng YX, Sheng X. Optimal surgical methods to treat intertrochanteric fracture: a Bayesian network meta-analysis based on 36 randomized controlled trials. J Orthop Surg Res. 2020;15(1):402.
41. Li XP, Zhang P, Zhu SW, Yang MH, Wu XB, Jiang XY. All-cause mortality risk in older patients with femoral neck fracture. BMC Musculoskelet Disord. 2022;23(1):941.
42. Ju JB, Zhang PX, Jiang BG. Risk Factors for Functional Outcomes of the Elderly with Intertrochanteric Fracture: A Retrospective Cohort Study. Orthop Surg. 2019;(4):643-52.
43. Zhong G, Teng L, Li HB, Huang FG, Xiang Z, Cen SQ. Surgical Treatment of Internal Fixation Failure of Femoral Peritrochanteric Fracture. Orthop Surg. 2021;13(6):1739-47
44. Sezgin EA, Markevičiūtė V, Širka A, Tarasevičius Š, Raina DB, Isaksson H, Tägil M, Lidgren L. Combined fracture and mortality risk evaluation for stratifying treatment in hip fracture patients: A feasibility study. Jt Dis Relat Surg. 2020;31(2):163-8.
45. Chee YH, Foo JHX, Hui SJ, Tan KI. Hip Fracture Management Using External Fixation-A Systematic Review. Ann Acad Med Singap. 2020 Jul;49(7):477-88.
46. Jennnison T, Yarlagadda R. A case-control study of 30-day mortality in periprosthetic hip fractures and hip fractures. Ann R Coll Surg Engl. 2020;102(3):229-31.
47. Phruetthiphat OA, Pinijprapa P, Satravaha Y, Kitcharanant N, Pongchaiyakul C. An innovative scoring system for predicting an excellent Harris hip score after proximal femoral nail anti-rotation in elderly patients with intertrochanteric fracture. Sci Rep. 2022;12(1):19939
48. Qin Y, Zhou K, Wang D, Zhou Z, Yang J, Kang P, Pei F, Shen B. [Safety and efficacy of total hip arthroplasty following failed internal fixation of intertrochanteric fractures]. Zhongguo Xiu Fu Chong Jian Wai Ke Za Zhi. 2019;33(2):160-5. Chinese.
49. Su Z, Yang M, Luo G, Liang L, Hao Y. Treatment of Elderly Femoral Intertrochanteric Fracture by InterTan Intramedullary Nail and PFNA. Evid Based Complement Alternat Med. 2022;2022:5020960.

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HEPATORENALNI SINDROM

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SAŽETAK

Hepatorenalni sindrom (HRS) se definiše kao pojava renalne insuficijencije u pacijenata sa odmaklom hroničnom bolešću jetre, ali se može javiti i u akutnoj insuficijenciji jetre, na primer u fulminatnom hepatitisu. HRS se klasifikuje u dva tipa. Tip 1 HRS-AKI (hepatorenalni sindrom sa akutnim zatajivanjem bubrega) ima brz početak, često precipitiran bakterijskom infekcijom, gastrointestinalnom hemoragijom, paracentezom velikog volumena tečnosti bez administracije albumina, kao i usled intenzivne primene diuretika. Brzo dolazi do dekompenzacije, uključujući renalnu i hepatičnu insuficijenciju, kao i encefalopatiju. Tip 2 HRS-CKD (heparorenalni sidrom sa hroničnom bolešću bubrega) se razvija spontano i ima sporu progresiju, a najčešće je primarna klinička prezentacija refraktarni ascites. Pojava AKI (akutno zatajivanje bubrega) kod pacijenata sa cirozom ukazuje na lošu prognozu. Prognoza zavisi od stadijuma, prema kriterijumima Međunarodnog kluba ascitesa (ICA) i etiologije AKI. Preživljavanje u stadijumu 1 je bolje od preživljavanja u stadijumu 2 i 3. Dijagnoza HRS-AKI postavlja se na bazi revidiranih ICA kriterijuma. Primenom novih biomarkera, pre svega uNGAL (lipokalin povezan sa neutrofilnom želatinazom u urinu) može se poboljšati rana identifikacija HRS-AKI i bolje predvideti odgovor na terapiju. Terapija HRS-AKI uključuje primenu terlipresina (analoga vazopresina), sa albuminima, terapiju zamene bubrežne funkcije, TIPS (transjugularni intrahepatički portosistemski šanat) i transplantaciju jetre ili simultanu transplantaciju jetre i bubrega. Zbog sve veće učestalosti ciroze povezane sa MASLD (metabolični uzrokovana masna bolest jetre) fokus je na izučavanju mera prevencije i lečenja HRS koji se razvija kod ovih pacijenata.

Ključne reči: hepatorenalni sindrom, etiopatogeneza, dijagnoza, terapija

SUMMARY

Hepatorenal syndrome (HRS) is defined as the occurrence of renal insufficiency in patients with advanced chronic liver disease, but it can also occur in acute liver insufficiency, for example in fulminant hepatitis. HRS is classified into two types. Type 1 HRS-AKI (hepatorenal syndrome with acute renal failure) has a rapid onset, often precipitated by bacterial infection, gastrointestinal hemorrhage, paracentesis of a large volume of fluid without administration of albumin, and due to intensive use of diuretics. Decompensation occurs quickly, including renal and hepatic failure, as well as encephalopathy. Type 2 HRS-CKD (heparorenal syndrome with chronic kidney disease) develops spontaneously and has a slow progression, and most often the primary clinical presentation is refractory ascites. The occurrence of AKI (acute renal failure) in patients with cirrhosis indicates a poor prognosis. The prognosis depends on the stage, according to the criteria of the International Ascites Club (ICA) and the etiology of AKI. Survival in stage 1 is better than survival in stages 2 and 3. The diagnosis of HRS-AKI is based on the revised ICA criteria. Using new biomarkers, especially uNGAL (urinary neutrophil gelatinase-associated lipocalin), can improve the early identification of HRS-AKI and better predict the response to therapy. Treatment of HRS-AKI includes administration of terlipressin (a vasopressin analog), with albumins, renal replacement therapy, TIPS (transjugular intrahepatic portosystemic shunt), and liver transplantation or simultaneous liver and kidney transplantation. Due to the increasing incidence of cirrhosis associated with MASLD (metabolic associated steatotic liver disease), the focus is on studying measures to prevent and treat the HRS that develops in these patients.

Key words: hepatorenal syndrome, etiopathogenesis, diagnosis, therapy

Uvod

Hepatorenalni sindrom (HRS) se definiše kao pojava renalne insuficijencije u pacijenata sa odmaklom hroničnom bolešću jetre, ali se može javiti i u akutnoj insuficijenciji jetre, na primer u fulminatnom hepatitisu. Smatra se da će najmanje 40% pacijenata sa cirozom jetre i ascitesom razviti HRS tokom evolucije bolesti. Još u 19.

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veku opisuje se oligurija u pacijenata sa hroničnom bolešću jetre u odsustvu proteinurije, povezujući abnormalnost bubrežne funkcije sa abnormalnošću sistemske cirkulacije. Kod HRS histološki izgled bubrega je normalan i bubrezi često nastavljaju normalnu funkciju nakon transplantacije jetre. Ovo čini HRS jedinstvenim patofiziološkim poremećajem koji podstiče proučavanje interakcije između vazokonstriktornih i vazodilatatornih sistema u renalnoj cirkulaciji. HRS ima 3 glavne karakteristike: 1. markantna redukcija glomerularne filtracije (GFR) koja se dešava u odsustvu značajne alteracije histologije bubrega; 2. potencijalna reverzibilnost pod uticajem farmakološke terapije ili transplantacije jetre; 3. udruženost sa čestom insuficijencijom drugih organa i sistema kao što je cirkulatorni i koagulacioni sistem [1]. HRS se tradicionalno klasifikuje u dva tipa. Tip 1 HRS-AKI (hepatorenalni sindrom sa akutnim zatajivanjem bubrega) ima brz početak, često precipitiran bakterijskom infekcijom, gastrointestinalnom hemoragijom, paracentezom velikog volumena tečnosti bez administracije albumina, kao i usled intenzivne primene diuretika. Brzo dolazi do dekompenzacije, uključujući renalnu i hepatičnu insuficijenciju, kao i encefalopatiju. Ovde dolazi do pada glomerularne filtracije (eGFR) <60 ml/min/1,73 m2 za manje od 3 meseca. Tip 2 HRS-CKD (heparorenalni sidrom sa hroničnom bolešću bubrega) se razvija spontano i ima sporu progresiju, a najčešće je primarna klinička prezentacija refraktarni ascites. Tip 2 se naziva i non-AKI (bez akutnog oštećenja bubrega) i ovde dolazi do pada glomerularna filtacije eGFR <60 ml/min/1,73 m2 za više od 3 meseca [2, 3, 4, 5].

U ovom revijskom radu cilj je prikazati savremeni aspekt etiopatogeneze, dijagnostike i tretmana HRS.

Etiopatogeneza HRS

AKI predstavlja ozbiljnu komplikaciju u pacijenata sa cirozom jetre. Definicija AKI je povećanje sCr ≥0,3 mg/dL (≥26.5 mmol/L) u roku od 48 sati ili procentualno povećanje sCr ≥50% od početne vrednosti za koje se zna ili pretpostavlja da se dogodilo u prethodnih 7 dana. Stadijumi AKI, prema Međunarodnom klubu ascitesa (ICA), koji imaju prognostički značaj, prikazani su na tabeli 1 [1].

Tabela 1. Stadijumi AKI

Stadijumi AKI
AKI 1A - Povećanje sCr≥ 0,3 mg/dL (26,5 mmol/l), ali manje od 2 puta, od početne vrednosti do vrednosti <1,5 mg/dL (133 mmol/L)
AKI 1B - Povećanje sCr ≥0,3 mg/dL (26,5 mmol/L), ali manje od 2 puta, od početne vrednosti do vrednosti ≥1,5 mg/dL (133 mmol/L)
AKI 2 - Povećanje sCr >2 do 3 puta u odnosu na početnu vrednost
AKI 3 - Povećanje sCr >3 puta od početne vrednosti ili sCr >4,0 mg/dL (353,6 mmol/L) sa akutnim povećanjem >0,3 mg/dL (26,5 mmol/L) ili započinjanje RRT

AKI, acute kidney injury; RRT, renal replacement therapy; sCr, serum creatinine

Nedavne studije su, koristeći nove dijagnostičke kriterijume, pokazale da je prevalencija AKI u pacijenata hospitalizovanih zbog komplikacija ciroze jetre između 27% i 53%. Glavni etiološki faktor AKI predstavlja hipovolemija, akutna tubularna nekroza (ATN-AKI) i HRS-AKI. Hipovolemija je najčešći etiološki faktor AKI, u skoro polovine slučajeva, uglavnom uzrokovana gubitkom tečnosti usled ekscesivne diureze, dijarejom ili gastrointestinalnim krvarenjem. Bakterijske infekcije, poput spontanog bakterijskog peritonitisa (SBP) su čest rizični faktor razvoja HRS-AKI. Incidencija HRS-AKI u pacijenata sa SBP iznosi preko 30%. Mehanizam kojim bakterijska infekcija, posebno SBP, dovodi do HRS-AKI najverovatnije je putem sistemskog inflamatornog odgovora koji vodi u povećanje vazodilatatornih medijatora, koji dovode do hemodinamskih promena u dekompenzovanoj cirozi jetre sa posledičnim smanjenjem renalnog krvnog protoka i glomerularne filtracije (GFR). Pored bakterijske infekcije, paracenteze velikog volumena, bez administracije albumina, mogu dovesti do HRS-AKI [6, 7].

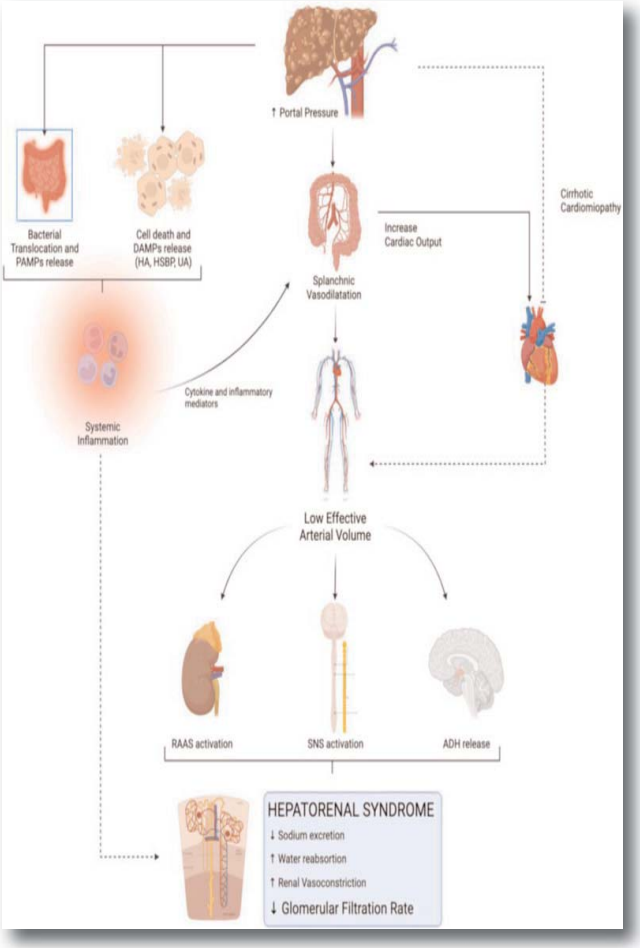
Pojava AKI kod pacijenata sa cirozom ukazuje na lošu prognozu. Prognoza zavisi od stadijuma i etiologije AKI. Preživljavanje u stadijumu 1 je bolje od preživljavanja u stadijumu 2 i 3. Devedesetodnevno preživljavanje je bilo 84%, 56%, 48% i 43% u pacijenata sa stadijumom 1A, 1B, 2 i 3, respektivno. U zavisnosti od etiologije AKI kod pacijenata sa hipovolemijom

indukovanim AKI bolja je prognoza u poređenju sa pacijentima sa HRS-AKI i ATN-AKI [8, 9].

Uobičajeno pojavu HRS-AKI trebalo bi razmotriti kao odmaklu manifestaciju cirkulatorne disfunkcije karakteristične za dekompenzovanu cirozu jetre sa ascitesom i edemima. Ali i druge patogenetske abnormalnost treba uzeti u obzir kao što je sistemska inflamacija i oštećena kardijalna funkcija.

Cirkulatorna disfunkcija dovodi do poremećaja renalne perfuzije. Naime, u cirozi jetre zbog prisustva ekstenzivne fibroze i portalne hipertenzije dolazi do produkcije vazodilatatornih supstanci kao što je azot-oksid (NO), ugljen-monoksid i endokanabinoidi u splanhničkoj cirkulaciji. Ovi vazodilatatorni medijatori dovode do splanhničke arterijske vazodilatacije i efektivne arterijske hipovolemije. Kako srednja vrednost arterijskog pritiska pada aktiviraju se kompenzatorni mehanizmi kao što je renin-angiotenzin-aldosteron sistem (RAAS), simpatički nervni sistem i arginin vazopresin, kako bi se održao arterijski pritisak, efektivan arterijski krvni volumen i renalna perfuzija. Konačno, sa iscrpljenjem kompenzatornih mehanizama i razvojem splanhničke vazodilatacije dolazi do vazokonstrikcije aferentnih arteriola glomerula i oštećenja renalnog krvnog protoka što vodi u HRS-AKI [1].

Cirotična kardiomiopatija nastaje u odmakloj fazi bolesti jetre. U ranoj fazi ciroze jetre sa srednje teškom portalnom hipertenzijom postoji hiperdinamično cirkulatorno stanje, koje se karakteriše povećanjem »cardiac output«, frekvencije srca i plazma volumena. Ovi mehanizmi kompenzuju redukovanu sistemsku vaskularnu rezistenciju u cirozi, održavajući arterijski pritisak i perfuziju bubrega na zadovoljavajućem nivou. Međutim, u odmakloj fazi ciroze dolazi do redukcije »cardiac output« zbog pada kontraktilnog odgovora na stres, elektrofizioloških poremećaja i alteracije dijastolne relaksacije što se označava kao cirotična kardiomiopatija. Sa njenim nastankom dolazi do smanjenja efektivnog arterijskog krvnog volumena i redukcije renalnog krvnog protoka što uzrokuje nastanak HRS-AKI [10, 11].



Slika 1. Patogeneza HRS-AKI (ADH, antidiuretic hormone; DAMPS, damage-associated molecular patterns; HA, hyaluronic acid; HSBP, heat shock binding protein; PAMPs, pathogen-associated molecular patterns; RAAS, renin-angiotensin-aldosteron system; SNS, sympathetic nervous system) [1].

Sistemska inflamacija u dekompenzovanoj cirozi manifestuje se povećanim nivoom proinflamatornih citokina, kao što je intrerleukin (IL) 6, tumor necrosis factor (TNF) α i C-reaktivni protein. Nivo ovih citokina je veći u pacijenata sa HRS-AKI. Povećan nivo citokina najverovatnije nastaje bakterijskom translokacijom iz creva u portalnu cirkulaciju. Prepoznavanje od strane imunog sistema pojedinih molekularnih struktura u bakterijama, poznato kao »sa patogenom povezane molekularne strukture« može dovesti do aktivacije imunog sistema. Oštećenje ćelija jetre izazvano različitim uzrocima, kao što su alkohol ili taloženje masti, izazvalo bi oslobađanje molekula kao što su mokraćna kiselina, S100 proteini, adenozin trifosfat (ATP) ili proteini toplotnog šoka (heat-shock proteins), poznati kao »molekularni obrasci povezani sa

oštećenjem«, koje takođe prepoznaju ćelije urođenog imuniteta. Studije su pokazale da nivo u plazmi TNFα i IL 6 je u korelaciji sa oštećenjem bubrega kod pacijenata SBP. Ovi nalazi pokazuju da sistemska inflamacija dovodi do arterijske vazodilatacije, oštećenja sistemske hemodinamike i pogoršanja bubrežne perfuzije. Štaviše, postoji pretpostavka da bi proinflamatorni citokini mogli direktno da oštete pojedine organe, kao što je bubreg [12, 13, 14]. Na slici 1 prikazani su različiti patogeni faktori potencijalno uključeni u patogenezu HRS-AKI [1].

Rizični faktori nastanka HRS-AKI su odmakla ciroza jetre sa visokim MELD (model of end stage liver disease) skorom, C klasa Child-Pugh-Turcotte skora, prisustvo ascitesa, sepse i varicealnog krvarenja. Prevencija hipovolemije kod infekcije, posebno kod SBP, upotreba antibiotika sa infuzijama albumina i sprečavanje cirkulatorne disfukcije nakon paracenteze velikog volumena (>5L) smanjuje učestalost HRS-AKI [1].

Dijagnoza HRS

Većina osoba sa cirozom jetre koje razviju HRS imaju nespecifične simptome, kao što su umor, malaksalost ili disgeuzija (izmenjeni osećaj ukusa). Razvoj HRS se obično zapaža kada pacijenti primete smanjeno izlučivanje urina i kada rezultati analize krvi pokažu pad bubrežne funkcije. HRS nema specifične znake. Međutim, otkrivanje stigmata hronične bolesti jetre je važno, jer većina pacijenata sa rizikom od HRS ima cirozu.

U diferencijalnoj dijagnozi treba razmotriti prerenalnu azotemiju sa deplecijom volumena, lekovima indukovanu nefrotoksičnost (NSAIL, aminoglikozidi, kontrasti koji sadrže jod i drugi), glomerulonefritis, postrenalnu azotemiju sa izlaznom opstrukcijom, renalnu vaskularnu bolest i posebno akutnu tubularnu nekrozu (ATN).

Smernice Britanskog društva za gastroenterologiju (BSG), Evropskog udruženja za proučavanje jetre (EASL) i Američkog udruženja za proučavanje bolesti jetre (AASLD) preporučuju upotrebu abdominalne ultrasonografije, dijagnostičke paracenteze i kulturu ascitne tečnosti u obradi pacijenata sa sumnjom na HRS. Mada nivo serumskog kreatinina je loš marker renalne funkcije u pacijenata sa cirozom jetre, ne postoje drugi pouzdani neinvazivni markeri za monitoring renalne funkcije u ovih pacijenata [8, 15].

Međunarodni klub ascitesa (ICA) je predložio revidirane dijagnostičke kriterijume za HRS-AKI koji uključuju sledeće [3]:

- Dijagnoza ciroze i ascitesa
- Dijagnoza AKI prema ICA-AKI kriterijumima (tabela 1)
- Nema odgovora nakon 2 uzastopna dana povlačenja diuretika i povećanja volumena plazme albuminom 1 g/kg telesne težine
- Odsustvo šoka
- Nema trenutne ili nedavne upotrebe nefrotoksičnih lekova (NSAIL, aminoglikozidi, jodirana kontrastna sredstva, itd.)
- Nema makroskopskih znakova strukturne insuficijencije bubrega, definisanih kao odsustvo proteinurije (>500 mg/dan), odsustvo mikrohematurije (>50 crvenih krvnih zrnaca na polju velikog uvećanja), normalni nalazi na ultrazvuku bubrega

Novi biomarkeri u dijagnozi HRS-AKI mogu poslužiti pre svega u diferencijalnoj dijagnozi AKI, odnosno razlikovanju ATN-AKI i HRS-AKI. Ovi novi biomarkeri su obično supstance koje su pojačano luče u uslovima povrede bubrežnih tubula i stoga su povećane kod ATN-AKI. Smernice AASLD preporučuju diferencijalnu dijagnozu zasnovanu na kliničkoj proceni, zajedno sa upotrebom lipokalina povezanog sa neutrofilnom želatinazom u urinu (uNGAL) i natrijuma u urinu. Visoki nivoi uNGAL i visoko frakciono izlučivanje natrijuma (>1%) ukazuju na ATN-AKI, dok niski nivoi uNGAL i nisko frakciono izlučivanje natrijuma (<1%) ukazuju na HRS-AKI. EASL smernice daju slične preporuke zasnovane na kliničkoj proceni uz uNGAL. NGAL nije odobren od strane FDA kao marker tubularne nekroze, ali nedavno je zatraženo odobrenje za ovu indikaciju. Drugi biomarkeri, kao što su IL18, molekul oštećenja bubrega-1(KIM-1), protein koji vezuje L-masne

kiseline (L-FABP) ili albumin, su izučavani, ali nijedan od njih nije imao prednost u odnosu na uNGAL [15, 16, 17].

Tretman HRS

Uspešno lečenje HRS-AKI zavisi od dijagnostikovanja osnovnog uzroka bubrežne disfunkcije. Kad je dijagnoza HRS-AKI utvrđena odmah se preduzima specifična terapija.

Farmakološka terapija

Primarna strategija u lečenju HRS-AKI uključuje upotrebu vazoaktivnih lekova u kombinaciji sa infuzijama albumina kako bi se izazvala vazokonstrikcija splanhničkih arterijskih krvnih sudova. Ovaj pristup deluje protiv vazodilatacije izazvane cirozom i portalnom hipertenzijom i povećava srednji arterijski pritisak, čime se poboljšava bubrežni protok krvi [18]. Metaanalize i sistematske revije su pokazale efikasnost terlipresina, sintetičkog analoga vazopresina, u kombinaciji sa albuminima u tretmanu HRS-AKI, i preporuče se kao prva linija tretmana u svim publikovanim vodičima. Terlipresin se može primenjivati kao bolus od 1 mg svakih 6 sati, a doza se zatim može povećati na 2 mg svakih 6 sati nakon 48–72 sata ako ne dođe do smanjenja serumskog kreatinina (<25–30% od vrednosti pre tretmana). Kontinuirana infuzija od 2 mg/dan, sa maksimalnim postepenim povećanjem do 12 mg/dan, jednako je efikasna kao i bolusi, ali je u nižoj dnevnoj dozi i ima manje neželjenih efekata [19].

Norepinefrin, koji pretežno deluje na alfa adrenergičke receptore, potom Midodrin, alfa 1 adrenergički agonist i oktreotid, analog somatostatina koji deluje na smanjenje splanhničke vazodilatacije, pokazali su manji efekat u HRS-AKI od terlipresina [18].

Tekući vodiči preporučuju 20-40 gr dnevno 20-25% albumina tokom tretmana HRS-AKI. U slučaju pulmonalnog edema treba prekinuti infuziju albumina. Pacijenti koji dobijaju vazokonstriktore trebaju biti monitirani zbog eventualnih neželjenih efekata, prevashodno ishemičnih epizoda, što zahteva isključivanje leka. Veća učestalost respiratorne insuficijencije i pulmonalnog edema od primene terlipresina zabeležena je u odnosu na placebo [20].

Primena vazokonstriktora nije definitivna terapija već most ka transplantaciji jetre. Reverzija HRS-AKI vazokonstriktorima smanjuje potrebu za terapijom zamene bubrežne funkcije (ili tzv renal replacement tharepy, RRT), kako pre tako i posle transplantacije i smanjuje rizik od hronične bolesti bubrega nakon transplantacije [21].

Terapija zamene bubrežne funkcije

Terapiju zamene bubrežne funkcije trebalo bi indikovati kod nedostatka odgovora na vazokonstriktore i albumin, što se manifestuje nastankom uremije, teške metaboličke acidoze, elektrolitskog dizbalansa i edemom pluća. Ovi pacijenti imaju nizak srednji arterijski pritisak i često ne tolerišu intermitentnu dijalizu, te bi trebalo sprovesti kontinuiranu zamenu bubrežne funkcije. Pacijenti podvrgnuti zameni bubrežne funkcije imaju lošu prognozu sa mortalitetom preko 80% za 180 dana, tako da ona predstavlja samo most do transplantacije jetre. Ukoliko pacijenti pogodni za transplantaciju dobiju graft preživljavanje je preko 70% za godinu dana. Kod pacijenata kod kojih je transplantacija jetre kontraindikovana, terapija zamene bubrežne funkcije može biti neefikasna i njena upotreba treba da se razmatra od slučaja do slučaja. Takođe, postoji mogućnost smanjenja potencijala za oporavak bubrega nakon transplantacije jetre [1, 22].

Transjugularni intrahepatički portosistemski šant (TIPS)

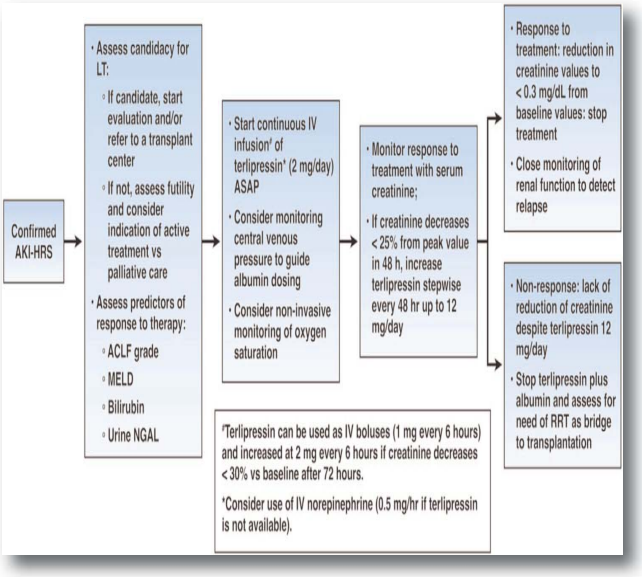
TIPS se primarno koristi kod refraktarnog ascitesa ili varicealnog krvarenja, jer efikasno redukuje portalnu hipertenziju. Pojedine studije su ispitivale efekat TIPS u lečenju HRS. U studiji Ponzo i saradnika [23] kod 41 pacijenta sa HRS-CKD je primenjen TIPS i došlo je do popravke renalne funkcije za nedelju dana sa stabilnim održavanjem tokom praćenja od 12 meseci. Nedavni pregled Cochrane baze podataka

dva randomizovana klinička ispitivanja pokazao je neizvesnost u pogledu smanjenja mortaliteta od svih uzroka sa primenom TIPS kod pacijenata sa HRS-CKD [24]. Randomizovano kontrolisano kliničko ispitivanje (Liver-HERO) sprovedeno je radi procene pacijenata sa HRS-AKI koji se leče terlipresinom i albuminom u odnosu na tretman sa TIPS. Rezultati su pokazali prednost TIPS u pogledu preživljavanja [25].

Transplantacija jetre i simultana transplantacija jetre i bubrega

Transplantacija jetre je difinitivan tretman HRS-AKI. Ne može se predvideti koliko vremena je potrebno da traje HRS-AKI da nakon tog vremena ne bi bio više moguć oporavak bubrega posle transplantacije jetre. Takođe, ne može se dobro proceniti uticaj postojećih komorbiditeta kao što je dijabetes, starost, neprepoznata hronična bubrežna bolest, etiologija AKI, perioperativni događaji i posttransplantaciona imunosupresija na pojavu disfunkcije bubrega nakon transplantacije jetre [26]. MELD skor se koristi u proceni indikacije za transplantaciju jetre kod pacijenata sa HRS-AKI. Međutim, treba naglasiti, pri formiranju liste čekanja za transplantaciju jetre, da je za bilo koji dati MELD skor mortalitet veći kod pacijenata sa HRS-AKI nego kod drugih pacijenata sa cirozom bez HRS-AKI [27].Oporavak bubrežne funkcije je glavni cilj kod pacijenata sa HRS-AKI koji se podvrgavaju transplantaciji. Retrospektivne studije su pokazale da je odgovor na lečenje terlipresinom i albuminom pre transplantacije jetre povezan sa boljom funkcijom bubrega i kliničkim ishodima nakon transplantaciie jetre [28].Važno je napomenuti da je duže trajanje terapije zamene bubrežne funkcije pre transplantacije jetre povezano sa manjom verovatnoćom oporavka bubrega nakon transplantacije jetre, što je povezano sa većim rizikom od smrtnosti nakon transplantacije. Na osnovu ovih nalaza, tema koja zaslužuje posebno razmatranje je indikacija za istovremenu transplantaciju jetre i bubrega u odnosu na samo transplantaciju jetre kod pacijenata sa HRS-AKI [29]. Kriterijumi za formiranje liste za transplantaciju uključuju trajanje AKI i terapije zamene bubrežne funkcije, kao i prisustvo hroničnog oboljenja bubrega. Pored toga, daje se prednost pacijentima koji razviju tešku bubrežnu disfunkciju (eGFR <20 ml/min po 1,73 m2 ili zavisnost od dijalize) između 60 i 365 dana nakon transplantacije jetre da prime transplantaciju bubrega u prvoj godini[18].

Na slici 2 prikazan je algoritam tretmana HRS [1].



Slika 2. Algoritam tretmana HRS (LT, liver transplantation; AKI, acute kidney injury; HRS, hepatorenal syndroma; ACLF, Acute-on-chronic liver failure; MELD, model for and stage liver disease; uNGAL, urine neutrophil gelatinase-associated lipocalin; RRT, renal replacement therapy) [1].

HRS u cirozi uzrokovanoj MASLD (steatoza jetre povezana sa metaboličkom bolešću)

U poslednjih nekoliko godina izmenila se etiologija ciroze jetre, odnosno došlo je do povećanja broja pacijenata sa cirozom povezanom sa MASLD (ranije poznatom kao NAFLD - nealkoholna masna bolest jetre). Pacijenti sa cirozom povezanom sa MASLD imaju neke karakteristike koje su posebno važne u pogledu funkcije bubrega. Pacijenti sa MASLD su stariji i imaju veću učestalost kardiovaskularnih komorbiditeta u poređenju sa pacijentima sa drugim etiologijama ciroze, što može izmeniti odgovor na farmakološku terapiju HRS-AKI i/ili smanjiti njenu izvodljivost. Isto tako, ovi pacijenti imaju veću učestalost hronične bolesti bubrega u poređenju sa pacijentima sa drugim etiologijama

ciroze, što može biti povezano sa godinama, nekim komorbiditetima, kao što su arterijska hipertenzija ili dijabetes melitus tipa 2, ili samim MASLD. Prisustvo hronične bolesti bubrega povećava teškoće u dijagnozi i lečenju HRS-AKI zbog koegzistencije organskih i funkcionalnih uzroka AKI kod istog pacijenta. Trenutni dijagnostički kriterijumi za HRS-AKI isključuju pacijente koji već imaju strukturnu bolest bubrega, ali i oni mogu razviti HRS-AKI. Oskudni su podaci o učestalosti, kliničkom toku i odgovoru na terapiju HRS-AKI kod pacijenata sa cirozom uzrokovanom MASLD. To je zato što je većina objavljenih studija urađena pre trenutne epidemije ciroze povezane sa MASLD. Naime, terapijske studije koje procenjuju efikasnost vazokonstriktora kod pacijenata sa HRS-AKI obuhvatile su manje od 10% ili 20% slučajeva sa cirozom povezanom sa MASLD [30, 31]. Postojeće informacije mogu se sumirati na sledeći način: (1) kod pacijenata sa cirozom povezanom sa MASLD lečenih transplantacijom jetre, upotreba terapijke zamene bubrežne funkcije i sinhrone transplantacije jetre i bubrega je verovatnija nego kod pacijenata sa drugim etiologijama ciroze; [2] Ciroza povezana sa MASLD je najbrže rastuća indikacija za sinhronu transplantaciju jetre i bubrega; (3) MASLD je nezavisni prediktivni faktor hronične bolesti bubrega nakon transplantacije jetre. Potrebna su dalja istraživanja kako bi se procenila epidemiologija, dijagnoza, tok i odgovor na različite terapije za AKI kod pacijenata sa cirozom povezanom sa MASLD [1, 32].

Zaključak

Pojavu HRS-AKI trebalo bi razmotriti kao odmaklu manifestaciju cirkulatorne disfunkcije karakteristične za dekompenzovanu cirozu jetre sa ascitesom i edemima. Ali i druge patogenetske abnormalnost treba uzeti u obzir kao što je sistemska inflamacija i oštećena kardijalna funkcija. Ove promene dovode do kompromitovanja renalne perfuzije ali i direktnog oštećenja bubrega. Pored klasične dijagnostike, upotrebom novih biomarkera može se poboljšati rana identifikacija HRS-AKI, bolje predvideti odgovor na terapiju, kao i poboljšati diferencijalna dijagnoza pre svega prema ATN-AKI. Usavršavanje farmakoterapije, prvenstveno vazokonstriktornih agenasa, kao što su selektivni agonisti vazopresina može poboljšati efikasnost lečenja. Potom, primena lekova za snižavanje portalne hipertenzije i kombinacija vazokonstriktora sa drugom terapijom, kao što je terapija zamene bubrežne funkcije, očekuje se da poveća preživljavanje pacijenata i smanji potrebu za simultanom transplantacijom jetre i bubrega. Rastuća incidencija ciroze povezane sa MASLD dovela je do razvoja mera prevencije, dijagnostike i lečenja HRS-AKI kod ovih pacijenata.

Literatura

1. Pose E, Piano S, Juanola A, Gines P. Hepatorenal syndrome in cirrhosis. Gastroenterology 2024; 166: 588-604.
2. Ginès P, Solà E, Angeli P, Wong F, Nadim MK, Kamath PS. Hepatorenal syndrome. Nat Rev Dis Primers 2018; 4: 23.
3. Angeli P, Ginès P, Wong F, Bernardi M, Boyer TD, Gerbes A, et al. Diagnosis and management of acute kidney injury in patients with cirrhosis: revised consensus recommendations of the International Club of Ascites. Gut 2015; 64: 531-7.
4. Angeli P, Garcia-Tsao G, Nadim MK, Parikh CR. News in pathophysiology, definition and classification of hepatorenal syndrome: a step beyond the International Club of Ascites (ICA) consensus document. J Hepatol 2019; 71:811–22.
5. Tonon M, Rosi S, Gambino CG, Piano S, Calvino V, Romano A, et al. Natural history of acute kidney disease in patients with cirrhosis. J Hepatol 2021; 74: 578–83.
6. Fagundes C, Barreto R, Guevara M, Garcia E, Solà E, Rodrigez E, et al. A modified acute kidney injury classification for diagnosis and risk stratification of impairment of kidney function in cirrhosis. J Hepatol 2013; 59: 474–81.
7. Huelin P, Piano S, Solà E, Stanco M, Solé C, Moreira R, et al. Validation of a staging system for acute kidney injury in patients with cirrhosis and association with acute-on-chronic liver failure. Clin Gastroenterol Hepatol 2017; 15: 438–45.e5.
8. European Association for the Study of the Liver. EASL Clinical Practice Guidelines for the management of patients with decompensated cirrhosis. J Hepatol 2018; 69: 406–60.
9. Patidar KR, Cullaro G, Naved MA, Kabir S, Grama A, Orman ES, et al. Prognostic significance of acute kidney injury stage 1B in hospitalized patients with cirrhosis: a US nationwide study. Liver Transpl 2024; 30: 244–53.
10. Møller S, Bendtsen F. The pathophysiology of arterial vasodilatation and hyperdynamic circulation in cirrhosis. Liver Int 2018; 38: 570–80.

11. Nazar A, Guevara M, Sitges M, Terra C, Solà E, Guigou C, et al. LEFT ventricular function assessed by echocardiography in cirrhosis: relationship to systemic hemodynamics and renal dysfunction. J Hepatol 2013; 58: 51–7.
12. Solé C, Solà E, Huelin P, Carol M, Moreira R, Cereijo U, et al. Characterization of inflammatory response in hepatorenal syndrome: relationship with kidney outcome and survival. Liver Int 2019; 39:1246–55.
13. Albillos A, Martin-Mateos R, Van der Merwe S, Wiest R, Jalan R, Alvares-Mon M. Cirrhosis-associated immune dysfunction. Nat Rev Gastroenterol Hepatol 2022; 19: 112–34.
14. Albillos A, de Gottardi A, Rescigno M. The gut-liver axis in liver disease: pathophysiological basis for therapy. J Hepatol 2020; 72: 558–77.
15. Biggins SW, Angeli P, Garcia-Tsao G, Ginès P, Ling SC, Nadim MK, et al. Diagnosis, Evaluation, and Management of Ascites, Spontaneous Bacterial Peritonitis and Hepatorenal Syndrome: 2021 Practice Guidance by the American Association for the Study of Liver Diseases. Hepatology 2021; 74:1014-48.
16. Allegretti AS, Solà E, Ginès P. Clinical Application of Kidney Biomarkers in Cirrhosis. Am J Kidney Dis 2020; 76(5): 710-9.
17. Juanola A, Ma AT, Pose E, Ginès P. Novel Biomarkers of AKI in Cirrhosis. Semin Liver Dis 2022;42 (4): 489-500.
18. Khemichian S, Nadim MK, Terrault NA. Update on hepatorenal syndrome: from pathophysiology to treatment. Annu Rev Med 2025; 76: 373-87.
19. Pitre T, Kiflen M, Helmeczi W, Dionne JC, Rewa O, Bagshaw SM, et al. The Comparative Effectiveness of Vasoactive Treatments for Hepatorenal Syndrome: A Systematic Review and Network Meta-Analysis. Crit Care Med 2022; 50(10):1419-29.
20. Pichler RH, Swenson ER, Leary PJ, Paine CH. Terlipressin: Hopes Fulfilled or Dashed? Clin J Am Soc Nephrol 2022;17(1):140-2.
21. Velez JCQ, Wong F, Reddy KR, Sanyal AJ, Vargas HE, Curry MP, et al. The Effect of Terlipressin on Renal Replacement Therapy in Patients with Hepatorenal Syndrome. Kidney360. 2023; 4(8):1030-8.
22. Staufer K, Roedl K, Kivaranovic D, Drolz A, Horvatits T, Rasoul-Rockenschaub S, et al. Renal replacement therapy in critically ill liver cirrhotic patients-outcome and clinical implications. Liver Int 2017; 37(6): 843-50.
23. Ponzo P, Campion D, Rizzo M, Roma M, Caviglia GP, Giovo I, et al. Transjugular intrahepatic porto-systemic shunt in cirrhotic patients with hepatorenal syndrome - chronic kidney disease: Impact on renal function. Dig Liver Dis 2022; 54(8): 1101-8.
24. Gonzalez-Garay AG, Serralde-Zúñiga AE, Velasco Hidalgo L, Flores García NC, Aguirre-Salgado MI. Transjugular intrahepatic portosystemic shunts for adults with hepatorenal syndrome. Cochrane Database Syst Rev 2024; 18;1(1):CD011039.
25. Ripoll C, Platzer S, Franken P, Aschenbach R, Wienke A, Schuhmacher U, et al. Liver-HERO Study Group. Liver-HERO: hepatorenal syndrome-acute kidney injury (HRS-AKI) treatment with transjugular intrahepatic portosystemic shunt in patients with cirrhosis-a randomized controlled trial. Trials 2023; 24(1): 258.
26. Nadim MK, Durand F, Kellum JA, Levitsky J, O'Leary JG, Karvellas CJ, et al. Management of the critically ill patient with cirrhosis: A multidisciplinary perspective. J Hepatol 2016; 64 (3):717-35.
27. Alessandria C, Ozdogan O, Guevara M, Restuccia T, Jiménez W, Arroyo V, et al. MELD score and clinical type predict prognosis in hepatorenal syndrome: relevance to liver transplantation. Hepatology 2005; 41(6): 1282-9.
28. Piano S, Gambino C, Vettore E, Calvino V, Tonon M, Boccagni P, et al. Response to Terlipressin and Albumin Is Associated With Improved Liver Transplant Outcomes in Patients With Hepatorenal Syndrome. Hepatology 2021; 73(5): 1909-19.
29. Sharma P, Goodrich NP, Zhang M, Guidinger MK, Schaubel DE, Merion RM. Short-term pretransplant renal replacement therapy and renal nonrecovery after liver transplantation alone. Clin J Am Soc Nephrol 2013; 8 (7): 1135-42.
30. Bassegoda O, Rivera-Esteban J, Serra I, Morillas R, Broquetas T, Vergara M, et al. High frequency of acute decompensation and cancer in patients with compensated cirrhosis due to nonalcoholic fatty liver disease: A retrospective cohort study. Hepatol Commun 2022; 6(11): 3212-22.
31. Byrne CD, Targher G. NAFLD as a driver of chronic kidney disease. J Hepatol 2020; 72(4): 785-801.
32. Patidar KR, Belcher JM, Regner KR, St Hillien SA, Simonetto DA, Asrani SK, et al: from the HRS-HARMONY consortium. Incidence and outcomes of acute kidney injury including hepatorenal syndrome in hospitalized patients with cirrhosis in the US. J Hepatol 2023; 79(6): 1408-17.

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PROCENA ZNANJA I STAVOVA ADOLESCENATA O REPRODUKTIVNOM ZDRAVLJU

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SAŽETAK

Uvod: Reproduktivno zdravlje predstavlja ključan segment ukupnog zdravlja adolescenata. Uprkos dostupnosti informacija, brojna istraživanja ukazuju na nedovoljno znanje mladih o ovoj temi.

Cilj: Procena znanja i stavova adolescenata o reproduktivnom zdravlju, kao i ispitivanje povezanost tih varijabli sa sociodemografskim faktorima.

Materijal i metode: Sprovedena studija uključivala je 958 učesnika, a podaci su prikupljeni pomoću anonimnog anketnog upitnika koji se sastojao iz tri grupe pitanja: demografske karakteristike, testa znanja i pitanja o sredstvima informisanja. Rezultati su analizirani deskriptivnim i inferencijalnim statističkim metodama.

Rezultati: Sprovedena studija brojala je 958 učenika. Prosečna starost svih ispitanih pri stupanju u prvi seksualni odnos bila je 16,4 godine. Muški ispitanici statistički značajno ranije stupaju u seksualne odnose. Viša prosečna starost pri prvom stupanju u seksualne odnose prisutna je kod većeg uspeha u školi. Po sopstvenoj proceni, većina ispitanika smatra da ima sve potrebne informacije o kontracepciji. Devojke su pokazale statistički značajno veće znanje i odgovorniji stav prema sopstvenom reproduktivnom zdravlju. Kontraceptivna sredstva koriste 87% onih koji su imali polne odnose. Sa problemom neželjene trudnoće susrelo se 1% ispitanih. Samo 42% ispitanika je posetilo ginekologa, urologa ili savetovalište za mlade. U najvećem broju slučajeva ispitanici se u slučaju problema mogu obratiti roditeljima (86%).

Zaključak: Rezultati ukazuju na potrebu za sistematskom sveobuhvatnom seksualnom edukacijom koja će biti prilagođena uzrastu. Neophodna je veća uključenost porodice, škole i zdravstvenih radnika u obrazovanje mladih o reproduktivnom zdravlju, radi podizanja nivoa znanja i osnaživanja adolescenata da donose informisane i odgovorne odluke.

Ključne reči: reproduktivno zdravlje, kontracepcija, adolescenti, seksualna edukacija

SUMMARY

Introduction: Reproductive health, a crucial component of adolescents' overall well-being, is a topic that continues to spark interest and concern. Despite the abundance of information available, a number of studies have pointed to a significant gap in young people's knowledge in this area.

Objective: to assess the knowledge and attitudes of adolescents about reproductive health, and to examine the connection of these variables with sociodemographic factors.

Materials and Methods: The study involved 958 participants. Data were collected through an anonymous survey questionnaire comprised of three groups of questions: demographic characteristics, a knowledge test, and questions regarding information sources. The results were analyzed using descriptive and inferential statistical methods.

Results: The study revealed that the average age of all respondents at the time of their first sexual intercourse was 16.4 years. Male respondents statistically entered sexual relationships earlier. A higher average age at first sexual intercourse is linked to greater success in school. Most respondents believe they have all the necessary information about contraception. Girls demonstrated statistically significantly greater knowledge and a more responsible attitude toward their reproductive health. Contraceptives are used by 87% of those who have had sex. Only 1% of the respondents faced the issue of unwanted pregnancy. Only 42% of respondents visited a gynecologist, urologist, or youth counseling center. In most cases, respondents can turn to their parents in times of trouble. These findings shed light on the current state of adolescent reproductive health and can guide future interventions.

Conclusion: The results underscore the need for systematic, comprehensive sex education that is tailored to the age and needs of adolescents. This education should not only focus on the biological aspects of reproductive health but also on the social and emotional aspects. It is crucial to involve families, schools, and health workers in this education. Their active participation is necessary to ensure that young people are equipped with the knowledge and skills to make responsible decisions about their reproductive health.

Keywords: reproductive health, contraception, adolescents, sexual education.

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Introduction

Adolescence is a period of rapid growth and sexual maturity that occurs between the ages of 10 and 19, marking the beginning of adulthood with numerous changes in a person's physical, psychological, emotional, and social well-being [1, 2]. During this period, adolescents can have serious health and social consequences. According to the World Health Organization (WHO), the most serious problems among adolescents are early pregnancy, childbirth, HIV, depression, the presence of violence, drug and alcohol abuse, intentional injuries, malnutrition, overweight, and tobacco use. These problems are increasingly recognized as serious global public health problems and are all associated with increased maternal mortality among pregnant adolescents and increased suicide rates among adolescent males [3]. One example is that a significant number of adolescents have some risky sexual behavior, and they do not receive appropriate treatment for the sexual health problems they face [4].

Reproductive health is a fundamental component of the general health and well-being of an individual, especially in the period of adolescence and early adulthood. According to the World Health Organization (WHO) definition, reproductive health refers to a state of complete physical, psychological, and social well-being in all aspects related to the reproductive system, encompassing not only the absence of disease or weakness but also the ability to have a satisfying and safe reproductive life. Preserving the reproductive health of young people is crucial for the prevention of unwanted pregnancies, sexually transmitted infections (STIs), as well as for building healthy attitudes towards sexuality, partnership, and responsibility [5].

Adolescent sexual and reproductive health is one of the most critical components of the global problem of PPI prevalence. Early sexual intercourse, often without adequate protection, increases the risk of numerous issues, from unwanted pregnancies to infections such as HPV, chlamydia, and HIV. At the same time, young people's attitudes towards contraception, abortion, and sexual education are shaped under the strong influence of peers, media, family, and the educational system. These attitudes are often accompanied by risky habits that can have long-term consequences for reproductive and psychological health [6]. Today, international associations and agencies increasingly focus on improving sexual and reproductive health and provide numerous funding programs. In 2002, the Special Session of the United Nations General Assembly on Children acknowledged the need for the development and implementation of health policies and programs for adolescents to promote their physical and mental well-being [7].

The sexual and reproductive health of adolescents is strongly related to their social, cultural, and economic environment. In addition to regional variations, experiences vary by age, gender, education, residence, sexual orientation, and socioeconomic status [8, 9]. Access to healthcare and sources of education, information, and support also varies significantly across regions. These differences necessitate country-level research; however, despite these variations, key issues, barriers, and challenges, as well as potential solutions, can be identified at all levels [10].

Considering all of the above, it is necessary to systematically investigate the level of information among young people regarding reproductive health, as well as their attitudes and behaviors, to identify critical points and formulate guidelines for improving preventive programs and educational content.

Objective

The goal of this research is to provide insight into the current situation among young people, identify differences based on gender, age, and education, and highlight potential factors that shape their decisions and behaviors in the realm of sexual and reproductive health. Also, the goal is to examine the level of knowledge of young people about the fundamental aspects of reproductive health, as well as to analyze attitudes and habits related to sexual behavior.

Methods

For the research, a questionnaire consisting of three groups of questions was used. The first group of questions related to questions about basic demographic characteristics, the second group of questions (knowledge test) related to the questions associated to topics such as puberty, menstrual cycle, pregnancy, contraception and PPI, while the third group of questions included questions about who they would turn to for advice regarding problems in their sexual life, from whom they get the most information on this topic, as well as things related to communication with their partner when entering into sexual relations.

The data were collected anonymously and voluntarily between June 1, 2023, and June 1, 2025, with the consent of educational institutions. The aim of the research was explained to the participants, and participation was anonymous and voluntary, with no charge.

The research was conducted by the ethical principles for research involving minors, and all data were collected with full respect for the anonymity and confidentiality of the participants.

The data were processed using the software package SPSS (Statistical Package for the Social Sciences), version 21.0. Methods of descriptive statistics (average values, percentages, standard deviations) and inferential statistics were used - t-test for independent samples and Pearson's correlation, depending on the nature of the data and the goal of the analysis. Statistical significance was determined at the level of $p < 0.05$.

Results

A total of 958 adolescents, aged 17 to 19 (III and IV grades of high school), participated in the research. Of the total number of respondents, 595 (62%) were girls, and 363 (38%) were boys. The average age of the participants was 17.8 years.

Of the total number of respondents, 61% stated that they had sexual relations. About gender, statistically significantly more male respondents (65%) than female respondents (59%) entered sexual relations.

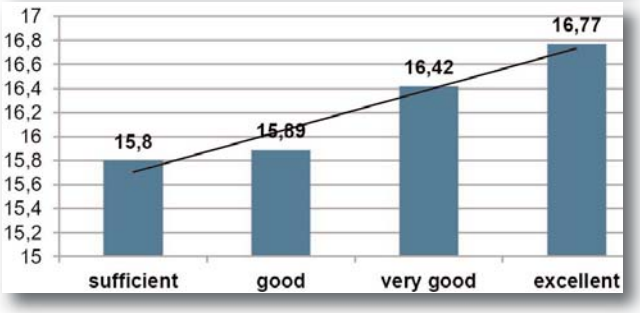
When asked when they had sexual intercourse for the first time, the most significant number of surveyed students answered at the age of 17 - 35%, then at the age of 16 - 25%, and at the age of 18 - 18%.

The average age of all surveyed students when they had their first sexual relationship was 16.40 years. The average age of the male respondents was 15.80 years, while the average age of the female respondents was statistically significantly later, 16.77 years. Male respondents enter into sexual relations statistically significantly earlier than female respondents.

We also compared the average age at first sexual intercourse with success in school. A higher average age at first sexual intercourse is present in a greater number of cases with greater success in school (Table 1 and Graph 1). Among adolescents, there is no statistically significant difference in the average age at entering sexual relations for the first time according to success at the end of the last school year, while there are statistically significant differences among adolescent girls.

Table 1. Age at first sexual intercourse, by success

Sufficient	15,80
Good	15,89
Very good	16,42
Excellent	16,77



Graph 1. Age at first sexual intercourse, by success level

According to their assessment, the majority of respondents (90% - 88% of girls and 94% of boys) believe that they have all the necessary information about contraception. 96% of respon-

dents had heard of at least one method of contraception, while only 36% knew exactly which methods were reliable. The most frequently mentioned forms of protection were condoms (77%) and contraceptive pills (32%), while long-term methods such as IUDs or implants were rarely known (<2%).

Older respondents (IV grade of high school) showed statistically significantly better overall knowledge compared to younger respondents (III grade of high school). Girls showed statistically substantially greater understanding and a more responsible attitude towards their reproductive health compared to boys. Only 42% of respondents knew precisely when the fertile days in the menstrual cycle are, while only 35% of respondents answered questions about sexually transmitted infections correctly.

Contraceptives are used by 87% of those who have had sex, of which 91% of male and 85% of female respondents. 62% use some protection in every relationship. Condom, as a means of contraception, is the most frequently used contraceptive method, 77% of respondents. 1% of the respondents encountered the problem of unwanted pregnancy.

Only 42% of respondents visited a gynecologist, urologist, or youth counseling center. Statistically significant, a greater number of adolescent girls who have had sexual relations go to gynecological examinations.

In the majority of cases, respondents can turn to their parents in case of problems (86%). Regarding the conversation with their parents, 42% of respondents state that they have openly discussed sexuality with their parents at least once, while 58% have never done so.

Discussion

The results of this research indicate that the knowledge of adolescents about reproductive health is not at a satisfactory level, which mainly refers to the understanding of fundamental biological processes, contraceptive methods, and PPIs. It was observed that, although most adolescents have basic information, it is often based on incorrect or incomplete information and can have serious consequences for the health of young people, as well as for their future reproductive decisions. These findings are consistent with previous studies conducted in the region and around the world, which indicate a lack of comprehensive sexuality education in educational systems [11, 12]. For example, research in Serbia and neighboring countries has shown that young people often acquire information from unreliable sources, such as the Internet and peers, which can contribute to the spread of wrong beliefs. This was also demonstrated in earlier research conducted in the region's countries, where authors highlighted the low awareness among adolescents of reproductive health and the need for systematic education [13, 14]. For example, research in secondary schools in Croatia showed that more than 60% of students were not entirely sure how the menstrual cycle works, and only 35% of respondents correctly identified the correct use of condoms [15]. These findings are consistent with our results, confirming the existence of a broader problem in access to reproductive health education.

Within our analysis, significant differences in knowledge levels were observed among different subgroups of respondents. Girls showed a higher level of knowledge compared to their male peers, especially in areas related to the menstrual cycle, contraception, and the importance of regular gynecological examinations. This is in line with the work of Kirby [16], who pointed out that girls generally show a higher level of interest in reproductive health information, often due to more immediate physiological experiences and greater social pressure to behave responsibly about sexual activities. Grammar school students had significantly better results than vocational school students, which may be a consequence of differences in curricula and a possible greater focus on general educational content in grammar schools. These results indicate the existence of educational inequality in access to key information on reproductive health.

Of particular concern is the fact that a significant percentage of respondents express conser-

vative attitudes towards the topics of sexuality, especially regarding open conversations with parents and health professionals. Respondents repeatedly stated that they felt shame, fear of judgment, or considered the topics "not appropriate for their age," which may indicate deep-rooted cultural taboos that make it challenging to create a safe and open environment for learning and discussion. Such attitudes can lead to avoidance of health examinations, non-use of contraception, and increased risk of unwanted pregnancies and sexually transmitted diseases [17, 18].

By WHO recommendations, comprehensive sexual education must be part of the school curriculum, starting with early adolescence. It must be adapted to the age, cultural context, and real needs of young people. Education must include topics such as physiological changes in puberty, menstruation, pregnancy, contraception, protection against sexually transmitted infections, emotional aspects of sexual relations, as well as the rights of young people to access information and health services [11, 12].

Limitations of our study include the fact that it is a cross-sectional study conducted in a limited geographic area, which may affect the overall representativeness of the data. Additionally, a questionnaire with a self-assessment component was used, which carries the risk of subjective bias and the potential for socially desirable answers. Additionally, the research did not include parents, teachers, or health workers, who play a crucial role in shaping the knowledge and attitudes of adolescents. For future research, it is recommended to incorporate qualitative methods to gain a deeper understanding of the reasons behind certain attitudes and behaviors [19].

Based on the findings, it is clear that there is a need for the systematic introduction of comprehensive sex education into the school curriculum, grounded in scientific evidence and tailored to each age group. Additionally, it is crucial to enhance the capacities of the school and health system to provide adolescents with easier access to counseling and reproductive health services.

Conclusion

The results of this research indicate the existence of significant gaps in adolescents' knowledge of reproductive health, as well as pronounced variations in attitudes that reflect the influence of education, social environment, and cultural norms. Of particular concern is that a large number of respondents demonstrate limited understanding of important aspects of sexual health, including contraception, prevention of sexually transmitted infections, and access to health services. Identified differences in knowledge and attitudes depending on demographic characteristics indicate the need for a more targeted approach in education. Girls and high school students showed a higher level of information, which suggests that certain groups of adolescents remain systematically neglected when it comes to access to adequate information about reproductive health.

These findings confirm the urgent need to introduce comprehensive, scientifically based, and age-appropriate sex education into the formal education system. In addition to school education, it is essential to involve parents, healthcare workers, and the broader community to create a supportive environment that fosters the development of knowledge and healthy attitudes in young people. Further research should incorporate qualitative methods and a wider geographical distribution of respondents to gain a deeper understanding of the factors that shape adolescents' knowledge, behavior, and attitudes towards reproductive health. A systematic and integrated approach in education is a key step towards improving the health and well-being of young generations.

References

1. Rondini S, Krugu JK. Knowledge, attitude and practices study on reproductive health among secondary school students in Bolgatanga, upper east region, Ghana. Afr J Reprod Health. 2009;13(4):51–66.
2. Sarfo EA, Salifu Yendork J, Naidoo AV. Understanding Child Marriage in Ghana: The Constructions of Gender and Sexuality and Implications for Married Girls. Child Care Pract [Internet]. 2020;0(0):1–14.
3. Ndayishimiye P, Uwase R, Kubwimana I, Niyonzima JDLC, Dzekem Dine R, Nyandwi JB, et al. Availability, accessibility, and quality of adolescent

Sexual and Reproductive Health (SRH) services in urban health facilities of Rwanda: A survey among social andhealthcare providers. BMC Health Serv Res. 2020;20(1):1–11.
4. Govender D, Naidoo S, Taylor M. Knowledge, attitudes and peer influences related to pregnancy, sexual and reproductive health among adolescents using maternal healthservices in Ugu, KwaZulu-Natal, South Africa. BMC Public Health. 2019;19(1):1–16.
5. United Nations. Resolution adopted by the General Assembly [on the report of the Ad Hoc Committee of the Whole (A/S-27/19/Rev.1 and Corr.1 and 2)] S-27/2. A worldfitfor children 2002. 11 October 2002 Twenty-seventh special session
6. Haque SE, Rahman M, Itsuko K, et al. The effect of a school-based educational intervention on menstrual health: an intervention study among adolescent girls in Bangladesh. BMJ Open 2014;4:e004607.
7. United Nations. Convention on the Rights of the Child. General Comment No. 4 (2003). Adolescent health and development in the context of the Convention on the Rights of the Child. CRC/GC/2003/4 http://daccess-dds-ny.un.org/doc/UNDOC/GEN/G03/427/24/PDF/G0342724.pdf?OpenElement.
8. Bearinger LH, Sieving RE, Ferguson J, Sharma V. Global perspectives on the sexual and reproductive health of adolescents: patterns, prevention, and potential. Lancet 2007;369(9568):1220–31.
9. Chandra-Mouli V, McCarraher DR, Phillips SJ, Williamson NE, Hainsworth G. Contraception for adolescents in low and middle income countries: needs, barriers, and access. Reprod Health 2014;11(1):1.
10. Morris JL, Rushwan H. Adolescent sexual and reproductive health: The global health challenges. Int J Gynaecol Obstet. 2015;131(1):40-42.
11. UNESCO. International technical guidance on sexuality education: An evidence-informed approach. Paris: United Nations Educational, Scientific and Cultural Organization; 2018.
12. World Health Organization. Standards for sexuality education in Europe: A framework for policy makers, educational and health authorities and specialists. Copenhagen: WHO Regional Office for Europe; 2022.
13. Đurić O, Petrović D, Pavlović M. Znanje i stavovi adolescenata o seksualnom i reproduktivnom zdravlju u Srbiji. Medicinski pregled. 2020;73(3-4):101–7.
14. Vuković M, Jovanović S, Lukić A. Adolescenti i seksualno zdravlje: analiza znanja i ponašanja. Zdravstvena zaštita. 2021;50(2):123–30.
15. Marušić A, Novak I, Petrović I. Poznavanje kontracepcije među srednjoškolcima u Hrvatskoj. Društvena istraživanja. 2019;28(1):155–73.
16. Kirby D. Emerging Answers 2007: Research Findings on Programs to Reduce Teen Pregnancy and Sexually Transmitted Diseases. Washington (DC): National Campaign to Prevent Teen and Unplanned Pregnancy; 2007.
17. Ingham R, Hirst J. Promoting sexual health. In: Detels R, Gulliford M, Karim QA, Tan CC, editors. Oxford Textbook of Global Public Health. Oxford: Oxford University Press; 2010. p. 1475–87.
18. Bearinger LH, Sieving RE, Ferguson J, Sharma V. Global perspectives on the sexual and reproductive health of adolescents: Patterns, prevention, and potential. Lancet. 2007;369(9568):1220–31.
19. Pound P, Langford R, Campbell R. What do young people think about their school-based sex and relationship education? A qualitative synthesis of young people's views and experiences. BMJ Open. 2017; 6(9):e011329.

Citation:

Katanić F, Katanić Vico N, Kalember S, Kopitović V, Milatović S, Katanić T, Kopitović A, Havrljenko J, Lalić I. Assessment of Knowledge and Attitudes of Adolescents Regarding Reproductive Health. Apoll med et Aesc. 2025 jul-septembar vol 23 (3):

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MAGNETNA REZONANTNA KOGNITIVNO VOĐENA TRUS BIOPSIJA PROSTATE: PROSPEKTIVNA STUDIJA NA 24 PACIJENTA - ISKUSTVO IZ JEDNOG CENTRA

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SAŽETAK

Uvod: Multiparametrijska magnetna rezonanca prostate (mpMRI) značajno je unapredila dijagnostiku karcinoma prostate. Kognitivno vođena MRI-TRUS biopsija pruža praktičnu tehniku za centre sa ograničenim mogućnostima fuzione biopsije.

Cilj: Proceniti dijagnostičku tačnost kognitivno vođene MRI-TRUS biopsije u otkrivanju klinički značajnog karcinoma prostate nakon prethodnih neuspešnih standardnih TRUS biopsija.

Materijali i metode: Prospektivna studija koja je do sada obuhvatila dvadeset četiri muškarca u Zdravstvenom centru Prokuplje. Pacijenti sa povišenim prostata-specifičnim antigenom (PSA) i/ili abnormalnim digitalnim rektalnim pregledom podvrgnuti su mpMRI, a zatim kognitivno vođenoj TRUS biopsiji. Ciljane biopsije su izvršene na sumnjivim mpMRI lezijama (PI-RADS ≥3) sa dodatnim standardnim sistematskim biopsijama od 12 jezgara. Histopatološki rezultati su analizirani naknadno.

Rezultati: Klinički značajan karcinom prostate (Glison ≥7) je otkriven kod 20 od 24 pacijenta. Kognitivno vođenom biopsijom otkriveno je 85,3%, pozitivnih rezultatata sa osetljivošću od 75%. Dva klinički značajna slučaja bolesti su propuštena ciljanom biopsijom, ali su otkrivena standardnom sistematizovanom biopsijom u toku iste procedure.

Zaključak: Kognitivno vođena MRI-TRUS biopsija omogućava dobre dijagnostičke performanse u ovoj prospektivnoj kohorti. Njena tačnost naglašava njenu ulogu kao isplative alternative u centrima koji nemaju resurse za softverske fuzione procedure.

Ključne reči: karcinom prostate; multiparametrijska magnetna rezonanca (mpMRI); transrektalna ultrazvučna biopsija (TRUS); kognitivno vođena biopsija; PI-RADS; dijagnostička tačnost

SUMMARY

Multiparametric magnetic resonance imaging (mpMRI) has improved the diagnostics of prostate cancer. Cognitive-guided MRI-TRUS biopsy provides a hands-on technique for centers with limited fusion biopsy capabilities.

Objective: To evaluate the diagnostic accuracy of cognitive-guided MRI–TRUS biopsy in detecting clinically significant prostate cancer after previously failed standard TRUS biopsies.

Methods: Twenty-four men with elevated prostate-specific antigen (PSA) and/or abnormal digital rectal examination underwent mpMRI followed by cognitive-guided TRUS biopsy. Targeted biopsies were performed on suspicious mpMRI lesions (PI-RADS ≥3) with additional standard systematic 12-core biopsies. Histopathological results were analyzed afterwards.

Results: Clinically significant prostate cancer (Gleason ≥7) was detected in 18 of 24 patients. Cognitive-guided biopsy found 85.3%, positive results with sensitivity of 75% . Two clinically significant cases were missed on targeted biopsy but detected by systematic cores at the same procedure.

Conclusions: Cognitive-guided MRI–TRUS biopsy allows us a good diagnostic performance in this prospective cohort. Its accuracy emphasises its role as a cost-effective alternative in centers without resources for software based fusion procedures.

Keywords: prostate cancer; multiparametric magnetic resonance imaging (mpMRI); transrectal ultrasound biopsy (TRUS); cognitive-guided biopsy; PI-RADS; diagnostic accuracy

Introduction

Prostate cancer is the most commonly diagnosed malignancy in men and remains a leading cause of cancer-related death worldwide [1]. European guidelines recommend performing mpMRI before biopsy and targeting suspicious lesions in appropriate clinical scenarios [2]. Multiparametric MRI (mpMRI) enables precise lesion localization and targeted sam-

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pling, improving prostate cancer diagnostics [3]. Traditional systematic TRUS-guided biopsy is associated with limitations, including sampling error, under-detection of clinically significant cancer, and over-diagnosis of indolent disease. Cognitive-guided biopsy, though physicians dependent experience, offers a simple and very cost-effective approach for centers without dedicated fusion technology [4].

Multiparametric MRI (mpMRI) has transformed prostate cancer diagnostics, enabling lesion localization and targeted biopsy [5]. Systematic analyses and comparative studies show that MRI-targeted biopsies increase detection of clinically significant cancer relative to standard approaches [6]. Cognitively guided targeted biopsy, in the hands of a trained urologist, can achieve results comparable to software fusion with lower costs and better accessibility [7]. MRI–TRUS fusion biopsy can be performed via software-based platforms, in-bore MRI guidance, or cognitively by clinicians mental mapping of MRI lesions and their match on ultrasound exams [8]. The AUA/SAR consensus underscores the role of an MRI-targeted approach and consideration of combining it with systematic sampling to reduce missed significant disease [9]. Head-to-head evaluations suggest that cognitively targeted biopsies can achieve detection rates for clinically significant prostate cancer comparable to software fusion approaches in appropriately selected patients [10].

Any biopsy strategy must also account for procedure related complications. Although generally infrequent, they include: infection, bleeding, and urinary retention. These risks should inform patient counseling and involve prophylaxis protocols that are well established [11].

Epidemiologic trends, including age related burden and regional variation in incidence, underscore the need for streamlined diagnostic pathways that minimize unnecessary procedures while prioritizing clinically significant disease [12]. Prospective studies as ours can demonstrate that pre-biopsy mpMRI provides high diagnostic accuracy and substantial negative predictive value, allowing biopsy avoidance in appropriately selected men [13]. Meta analyses evidence are showing that MRI-targeted biopsy improves detection of clinically significant cancer compared with standard systematic TRUS guided byopsies, [14]. Multicenter validation of PI-RADS v2 confirms that higher category scores correlate with a greater incidence of clinically significant prostate cancer, supporting risk stratification and precise targeting [15]. Finally, when combining targeted with systematic cores, clinicians should balance the incremental diagnostic field against the cumulative complications reported across systematic, random, and image-guided techniques [16].

This study aimed to evaluate the diagnostic accuracy of cognitive-guided MRI–TRUS biopsy in a prospective cohort of 24 patients.

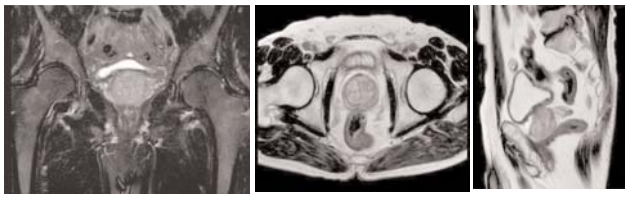
Materials and Methods

Prospective study from January 2024 and August 2025. (so far) included 24 men with clinical suspicion of prostate cancer. Patients were admited and prepared for medical procedure at General hospital “Aleksa Savić” (Health Center Prokuplje). Inclusion criteria were: elevated PSA between 4-14.3 ng/mL and/or abnormal digital rectal examination. Inclusion criteria was least one suspicious lesion on mpMRI (PI-RADS ≥3) with minimum one prior standard negative TRUS biopsy. Exclusion criteria were previous prostate surgery, contraindications to MRI, and active urinary tract infection. All patients gave their informed consent.

Imaging and Biopsy Protocol

All mpMRI examinations were performed on a 3T scanner using standard T2-weighted, diffusion-weighted, and dynamic contrast-enhanced sequences. Lesions were scored according to PI-RADS v2. All patients included for biopsy were PIRADS 2/3 and higher.

After examination of MR results under TRUS guidance, combined topical and local anaesthesia, targeted biopsies (2–4 cores per lesion) were performed cognitively by urologist. A systematic 12-core biopsy was also obtained in each case in the same time of procedure.



Picture 1. 3T Multiparametric prostate MRI with prostatic lesion of peripheral zone PIRADS 4 in left lobe marked as a targeted lesion for biopsy.

Histopathology and Data Analysis

Biopsy specimens were reviewed by specialized uropathologists. Clinically significant prostate cancer was defined as Gleason score ≥7. Diagnostic accuracy, sensitivity, specificity, PPV, and NPV of cognitive-guided biopsy were calculated against the combined reference standard (systematic + targeted biopsy). Clinically insignificant prostate cancer is left for active surveillance.

Results

Median patient age was 66 years (range 52–78). Median PSA was 9.1 ng/mL (range 4–14.3).A total of 28 lesions were identified across 24 patients: 20 PI-RADS 4–5 and 8 PI-RADS 3. Among the 24 patients included in the study, lesions were stratified according to PI-RADS classification. PI-RADS 3 lesions were observed in 4 patients (16.7%), PI-RADS 4 in 10 patients (41.7%), and PI-RADS 5 in 10 patients (41.7%). The detection rate of clinically significant prostate cancer increased proportionally with higher PI-RADS categories, with the majority of Gleason ≥7 cancers identified in PI-RADS 4 and 5 groups.

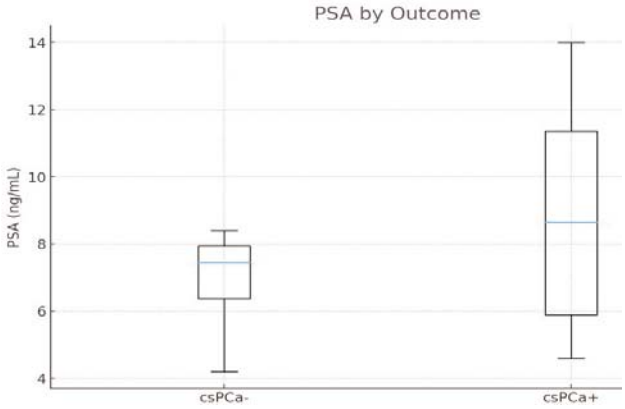


Figure 1. PSA (ng/ml) distribution within clinically significant (csPCa+) and clinically insignificant csPCa- finings.

20 clinically significant cancers with Gleason >7. 2 cases missed by targeted biopsy were detected by concomitant systematic biopsy. Prostate cancer detected in 20/24 patients (83,33%) with targeted lesion biopsies accuracy of 75% (18 of 24 patients). Two cases were detected only by systematic biopsy represent clinically significant prostate cancer missed by targeted but caught on systematic biopsy. PSA values ranged from 4.0 to 14.3 ng/mL, with overlap between men with and without clinically significant prostate cancer.

Table 1. Biopsy Results Summary. Summarizes results of targeted and systematic biopsy, of prostate cancers detected by MRI-targeted biopsy, cases missed but captured by systematic biopsy, and patients with negative findings.

Metric	*Value*
Overall csPCa detection	20/24 (83.3%)
Targeted-only detection rate	18/24 (75.0%)
Systematic-only added positive result	8.3%
Targeted positives	18
csPCa total	20
Missed by targeted/ caught by systematic	2

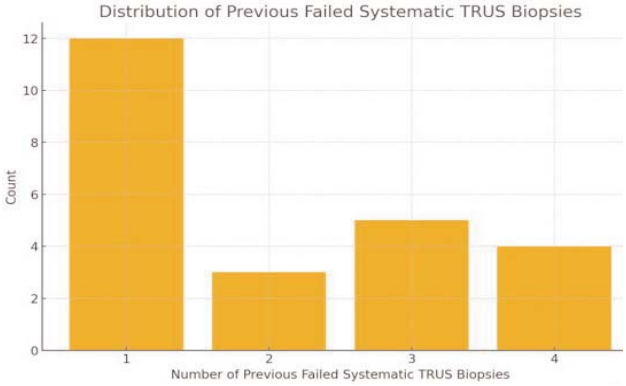
Abnormal DRE findings were more common among patients with clinically significant prostate cancer, although this association did not reach statistical significance. The number of prior negative TRUS biopsies ranged from one to four.

Table 2. DRE (Digital Rectal Exam) distribution. Clinically significant prostate cancer was detected even in patients with multiple prior negative procedures (1 to 4 prior biopsies).

DRE Status	csPCa+	csPCa-	Total
Abnormal	7	1	8
Normal	13	3	16
Total	20	4	24

Table 3/Figure 2. Distribution of previous failed TRUS biopsies.

Prev Failed TRUS Biopsies	Count	Proportion
1.0	12	0.500
2.0	3	0.125
3.0	5	0.208
4.0	4	0.167



Overall, the combination of targeted and systematic biopsy minimized false negatives and maximized csPCa detection in this cohort.

Discussion

This study demonstrates that MRI cognitive TRUS-guided biopsy achieved a high detection rate of clinically significant prostate cancers (83.3%) in a small prospective series. While most cases were detected by targeted biopsy alone, systematic cores contributed with rescuing two cases of significant disease. This difference was not statistically significant ($p = 0.12$), but it highlights the combined role of systematic sampling in minimizing the risk of failure. This supports the concept matching with prior reports, that targeted biopsy enhances detection but systematic sampling remains clinically valuable to avoid missed diagnoses. [11,16].The analysis of PI-RADS categories revealed a clear increase in cancer detection with higher scores [15,16]. When comparing PI-RADS 3 lesions to PI-RADS 4 and 5, the difference in clinically significant prostate cancer detection reached statistical significance ($p <0.05$, Chi-square test). This finding emphasizes the predictive value of the PI-RADS system in clinical decision-making.

PSA levels also demonstrated clinical relevance, with a median of 9.1 ng/mL. Patients above the median PSA were significantly more likely to have clinically significant disease compared with those below the median ($p< 0.05$, M/W U test). This suggests that PSA continues to be an important marker especially when crossmatched with MRI findings.

Observed association between abnormal DRE and csPCa shows relevance of this simple physician's exam, though its predictive power remains weak compared to modern imaging. Furthermore, csPCa was identified even among men with up to four prior negative systematic biopsies as within our so in other centers, highlighting the diagnostic advantage of MRI-based targeting in repeat biopsy procedures.

Our findings compared to existing literature match the detection rates of 70–85% for csPCa using MRI-targeted techniques. Though our present analysis is limited by its small sample size and single-center experience. Future studies with larger, multi-center cohorts are needed to confirm these results and optimize patient selection criteria.

The technique has several advantages: accessibility, lower cost, and shorter procedure time compared with software-based fusion platforms. However, it remains physician-dependent and may miss smaller or anteriorly located lesions either on MRI detection or at very biopsy procedure time, as demonstrated by the two missed clinically significant cancers in our series.

Systematic biopsy remains necessary to be combined with targeted sampling, particularly for patients with negative or equivocal mpMRI lesions.

Conclusion

Cognitive-guided MRI–TRUS biopsy demonstrated good diagnostic accuracy in detecting clinically significant prostate cancer in this prospective cohort of 24 patients. With its accuracy it represents a viable and cost-effective al-

ternative in centers without access to advanced fusion platforms. Larger multicenter studies are required to validate these findings.

Prospective study, as mentioned will include, in future, pathohistological findings of radical prostatectomy and correlation as a gold standard. Nonetheless, our findings support the feasibility of cognitive fusion biopsy in routine practice.

References

1. Siegel RL, Miller KD, Wagle NS, Jemal A. Cancer statistics, 2023. CA Cancer J Clin. 2023; 73(1): 17-48. doi:10.3322/caac.21763
2. Mottet N, et al. EAU-EANM-ESTRO-ESUR-SIOG Guidelines on Prostate Cancer. Eur Urol. 2023.
3. Turkbey B, Rosenkrantz AB, Haider MA, Padhani AR, Villeirs G, Macura KJ, Tempany CM, Choyke PL, Cornud F, Margolis DJ, Thoeny HC, Verma S, Barentsz J, Weinreb JC. Prostate Imaging Reporting and Data System Version 2.1: 2019 Update of Prostate Imaging Reporting and Data System Version 2. Eur Urol. 2019 Sep;76(3):340-351. doi: 10.1016/j.eururo.2019.02.033. Epub 2019 Mar 18. PMID: 30898406.
4. Khoo CC, Eldred-Evans D, Peters M, van Son M, van Rossum PSN, Connor MJ, et al. A Comparison of Prostate Cancer Detection between Visual Estimation (Cognitive Registration) and Image Fusion (Software Registration) Targeted Transperineal Prostate Biopsy. Journal of Urology [Internet]. 2021 Apr 1 [cited 2025 Sep 2];205(4):1075–81. Available from: https://doi.org/10.1097/JU.0000000000001476
5. Kasivisvanathan V, Rannikko AS, Borghi M, Panebianco V, Mynderse LA, Vaarala MH, Briganti A, Budäus L, Hellawell G, Hindley RG, Roobol MJ, Eggener S, Ghei M, Villers A, Bladou F, Villeirs GM, Virdi J, Boxler S, Robert G, Singh PB, Venderink W, Hadaschik BA, Ruffion A, Hu JC, Margolis D, Crouzet S, Klotz L, Taneja SS, Pinto P, Gill I, Allen C, Giganti F, Freeman A, Morris S, Punwani S, Williams NR, Brew-Graves C, Deeks J, Takwoingi Y, Emberton M, Moore CM; PRECISION Study Group Collaborators. MRI-Targeted or Standard Biopsy for Prostate-Cancer Diagnosis. N Engl J Med. 2018 May 10;378(19):1767-1777. doi: 10.1056/NEJMoa1801993. Epub 2018 Mar 18. PMID: 29552975; PMCID: PMC9084630.
6. van der Leest M, Cornel E, Israël B, Hendriks R, Padhani AR, Hoogenboom M, Zamecnik P, Bakker D, Setiasti AY, Veltman J, van den Hout H, van der Lelij H, van Oort I, Klaver S, Debruyne F, Sedelaar M, Hannink G, Rovers M, Hulsbergen-van de Kaa C, Barentsz JO. Head-to-head Comparison of Transrectal Ultrasound-guided Prostate Biopsy Versus Multiparametric Prostate Resonance Imaging with Subsequent Magnetic Resonance-guided Biopsy in Biopsy-naïve Men with Elevated Prostate-specific Antigen: A Large Prospective Multicenter Clinical Study. Eur Urol. 2019 Apr;75(4):570-578. doi: 10.1016/j.eururo.2018.11.023. Epub 2018 Nov 23. PMID: 30477981.
7. Wegelin O, van Melick HHE, Hooft L, Bosch JLHR, Reitsma HB, Barentsz JO, Somford DM. Comparing Three Different Techniques for Magnetic Resonance Imaging-targeted Prostate Biopsies: A Systematic Review of In-bore versus Magnetic Resonance Imaging-transrectal Ultrasound fusion versus Cognitive Registration. Is There a Preferred Technique? Eur Urol. 2017 Apr;71(4):517-531. doi: 10.1016/j.eururo.2016.07.041. Epub 2016 Aug 25. PMID: 27568655.
8. Sonn GA, Chang E, Natarajan S, Margolis DJ, Macairan M, Lieu P, Huang J, Marks LS. Value of Targeted Prostate Biopsy Using Cognitive Guidance with mpMRI. Eur Urol. 2014;65(4):809-815. doi:10.1016/j.eururo.2013.03.030.
9. Bjurlin MA, Carroll PR, Eggener S, Fulgham PF, Margolis DJ, Pinto PA, et al. Update of Prostate mpMRI and MRI-Targeted Biopsy Guidelines: AUA/SAR Consensus Statement. J Urol. 2020;203(4):706-712. doi:10.1097/JU.0000000000000617.
10. Pepe P, Garufi A, Priolo G, Pennisi M. Cognitive targeted vs Fusion targeted prostate biopsy: Detection rate for clinically significant prostate cancer. World J Urol. 2016;34(4):425-430. doi:10.1007/s00345-015-1635-7.
11. Loeb S, Vellekoop A, Ahmed HU, Catto J, Emberton M, Nam R, et al. Systematic Review of Complications of Prostate Biopsy. Eur Urol. 2013;64(6):876-892. doi:10.1016/j.eururo.2013.05.049.
12. Rawla P. Epidemiology of Prostate Cancer. World J Oncol. 2019;10(2):63-89. doi:10.14740/wjon1191.
13. Ahmed HU, Bosaily AE, Brown LC, Gabe R, Kaplan R, Parmar MK, et al; PROMIS Study Group. Diagnostic accuracy of multiparametric MRI and TRUS biopsy in prostate cancer (PROMIS): a paired validating confirmatory study. Lancet. 2017;389(10071):815-822. doi:10.1016/S0140-6736(16)32401-1.
14. Schoots IG, Roobol MJ, Nieboer D, Bangma CH, Steyerberg EW, Hunink MG. MRI-targeted biopsy may enhance detection of clinically significant prostate cancer vs standard TRUS biopsy: systematic review and meta-analysis. Eur Urol. 2015;68(3):438-450. doi:10.1016/j.eururo.2014.11.037.
15. Hansen NL, Barrett T, Kesch C, Pepdjonovic L, Bonekamp D, Oprea-Lager DE, et al. Multicentre evaluation of PI-RADS v2. Eur Radiol. 2017;27(9):4124-4133. doi:10.1007/s00330-017-4787-6.
16. Borghesi M, Ahmed H, Nam R, Schaeffer E, Schiavina R, Taneja S, Weidner W, Loeb S. Complications After Systematic, Random, and Image-guided Prostate Biopsy. Eur Urol. 2017;71(3):353-365. doi:10.1016/j.eururo.2016.08.004.

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SLEEP APNEA U EVROPI, KINI I SJEDINJENIM AMERIČKIM DRŽAVAMA

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SAŽETAK

Sleep apnea je ozbiljan poremećaj spavanja koji se karakteriše ponavljanim prekidima disanja zbog delimične ili potpune opstrukcije gornjih disajnih puteva. Postoje tri osnovna tipa: opstruktivna, centralna i mešovita. Najčešći oblik je opstruktivna sleep apnea (OSA), koja je povezana sa povećanim rizikom od kardiovaskularnih bolesti, hipertenzije, moždanog udara i dijabetesa. Faktori rizika uključuju gojaznost, starije životno doba, muški pol i anatomske anomalije disajnih puteva. Dijagnoza se postavlja polisomnografijom, dok je zlatni standard u terapiji upotreba CPAP aparata, koriste se još, oralni preparati i u težim slučajevima hirurške intervencije. Sleep apnea ima značajan uticaj na kvalitet života, uzrokujući dnevnu pospanost, smanjenu kognitivnu funkciju i povećan rizik od saobraćajnih nesreća. Rano prepoznavanje simptoma, pravovremena dijagnostika i adekvatan tretman ključni su za prevenciju komplikacija i poboljšanje ukupnog zdravlja pacijenata. Sleep apnea predstavlja ozbiljan zdravstveni problem, što zahteva povećanu svest među lekarima i pacijentima.

Klučne reči: sleep apnea, gojaznost, polisomnografija, CPAP

SUMMARY

Sleep apnea is a serious sleep disorder characterized by repeated interruptions of breathing due to partial or complete obstruction of the upper airways. There are three main types: obstructive, central, and mixed. The most common form is obstructive sleep apnea (OSA), which is associated with an increased risk of cardiovascular diseases, hypertension, stroke, and diabetes. Risk factors include obesity, older age, male gender, and anatomical abnormalities of the airways. Diagnosis is established through polysomnography, while the gold standard for therapy is the use of CPAP devices; oral appliances and, in more severe cases, surgical interventions are also utilized. Sleep apnea significantly impacts quality of life, causing daytime sleepiness, reduced cognitive function, and an increased risk of traffic accidents. Early recognition of symptoms, timely diagnosis, and appropriate treatment are crucial for preventing complications and improving overall patient health. Sleep apnea represents a major health issue, necessitating greater awareness among both physicians and patients.

Keywords: sleep apnea, obesity, polysomnography, CPAP

Uvod

Sleep apnea je ozbiljan poremećaj spavanja koji se karakteriše ponovljenim prekidima disanja tokom noći. Ovi prekidi, poznati kao apneje, mogu trajati od nekoliko sekundi do nekoliko minuta, i mogu se ponoviti stotine puta tokom jedne noći. Sleep apnea negativno utiče na kvalitet sna i dovodi do ozbiljnih zdravstvenih problema, uključujući povišen krvni pritisak, srčane bolesti, moždani udar, dijabetes tipa 2, respiratornih (plućnih) problema, pa čak i smanjenje životne dobi. Osobe sa sleep apnejom često ne shvataju ozbiljnost svog stanja jer simptomi, poput hrkanja ili povremenih buđenja tokom noći, mogu biti blagi ili neprimetni [1].

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Najčešći oblik sleep apnee je opstruktivna sleep apnea (OSA). Ovaj oblik nastaje kada se mišići u zadnjem delu grla opuste tokom sna, blokirajući disajne puteve i ometajući normalno disanje, pri čemu dolazi do kolapsa gornjih disajnih puteva. Kako se disanje prekida, mozak reaguje i šalje signal da se osoba probudi, često u trenutku kada nije ni svesna toga, čime dolazi do čestih buđenja tokom noći. Zbog ovih buđenja, osoba ne ulazi u duboke faze sna, što ometa odmor i regeneraciju organizma.

Pored opstruktivne sleep apnee, postoji i centralna sleep apnea, koja je mnogo ređa i nastaje kada mozak ne šalje pravilne signale mišićima koji kontrolišu disanje što dovodi do privremenog prestanka disanja tokom sna. U ovom slučaju, problem nije fizička blokada disajnih

puteva, već disfunkcija u regulaciji disanja od strane mozga. Kompleksna sleep apnea, ili kombinovana sleep apneja, uključuje elemente oba oblika – opstruktivnog i centralnog, i zahteva specifičan pristup lečenju. Nastaje kada se kod pacijenta sa opstruktivnom sleep apneom pojave epizode centralne apnee nakon uvođenja CPAP terapije [2, 3, 4].

Simptomi sleep apnee mogu biti različiti tokom noći i dana i često uključuju hrkanje, nesanicu, suvoću usta pri buđenju, umor tokom dana, probleme sa koncentracijom, glavobolje, pa čak i depresiju. Mnoge osobe sa sleep apnejom nemaju svesnost o tome da pretrpljuju problem jer se apneje javljaju tokom sna, dok sam poremećaj može imati ozbiljne dugoročne posledice na zdravlje. Osobe koje ne leče sleep apneju mogu razviti druge ozbiljne bolesti, kao što su povišen krvni pritisak, srčane bolesti, moždani udar, poremećaji u metabolizmu, smanjenje sposobnosti za koncentraciju i povećan rizik od nesreća zbog dnevnog umora.

Dijagnoza sleep apnee obuhvata nekoliko koraka, uključujući analizu simptoma, faktori rizika, fizikalni pregled i različite dijagnostičke testove. Najprecizniji test je polisomnografija (zlatni standard), koja se obavlja u laboratoriji za spavanje (noćno testiranje), gde se prate telesne funkcije tokom spavanja, uključujući disanje, otkucaje srca, pokrete tela i nivo kiseonika u krvi [5, 7]. Takođe, postoje i uređaji za kućno testiranje spavanja koji mogu pružiti osnovne informacije, ali ne mogu zameniti stručnu dijagnozu.

Lečenje: sleep apnea se može uspešno konrolisati i zavisi od težine poremećaja i obuhvata promene životnih navika, kao što su mršavljenje, prestanak pušenja i smanjenje konzumacije alkohola, ali i upotrebu specijalizovanih uređaja. Najčešće korišćen uređaj za lečenje opstruktivne sleep apnee je CPAP (Continuous Positive Airway Pressure)-zlatni standard, koji koristi blagi pritisak vazduha kako bi sprečio opuštanje mišića u grlu i održao disajne puteve otvorenima tokom spavanja. Takođe, u nekim slučajevima, kada je poremećaj ozbiljan, razmatraju se hirurške intervencije ako postoje jasne anatomske prepreke, poput uklanjanja uvećanih tonzila ili operacija na nosnim šupljinama [8].

Bez obzira na vrstu sleep apnee, važno je prepoznati simptome i potražiti pomoć. Pravovremena dijagnoza i lečenje mogu značajno poboljšati kvalitet života i smanjiti rizik od ozbiljnih zdravstvenih komplikacija. Cilj ovog rada je istražiti uzroke, dijagnozu, lečenje i uticaj sleep apnee na zdravlje, sa posebnim akcentom na razlike u prevalenci i lečenju sleep apnee u različitim regionima sveta, uključujući Kinu, SAD i Evropu [9, 10].

Cilj rada

Cilj istraživanja je bio da se uporede: prevalenca, dijagnostičke metode, terapija sleep apneje na u različitim regionima sveta.

Materijali i metode

U ovom radu, fokusirali smo se na analizu opstruktivne sleep apnee u različitim regionima sveta, uključujući Kinu, SAD i Evropu. Da bismo sproveli sveobuhvatnu analizu, koristili smo podatke iz različitih izvora, uključujući medicinsku literaturu, epidemiološke studije, izveštaje o prevalenci sleep apnee, kao i kliničke smernice za dijagnozu i lečenje ovog poremećaja. Podaci koji su analizirani obuhvataju poslednje dostupne statističke izveštaje, međunarodne medicinske studije, kao i naučne radove koji se bave specifičnostima dijagnostike i lečenja sleep apnee u različitim geografskim i socijalnim uslovima [10].

1. Pregled literature: Kao osnovni metod, sproveden je temeljni pregled relevantne literature. Literatura je pretraživana u naučnim bazama podataka kao što su PubMed, Google Scholar, Scopus, i Web of Science. Izabrani su radovi koji se bave epidemiologijom sleep apnee, razlikama u prevalenci u različitim delovima sveta, kao i pristupima u dijagnostici i lečenju. Prvenstveno su odabrani radovi koji su obuhvatili studije u Kini, SAD-u i Evropi, kako bi se dobio uvid u globalne razlike u pristupu ovom poremećaju.

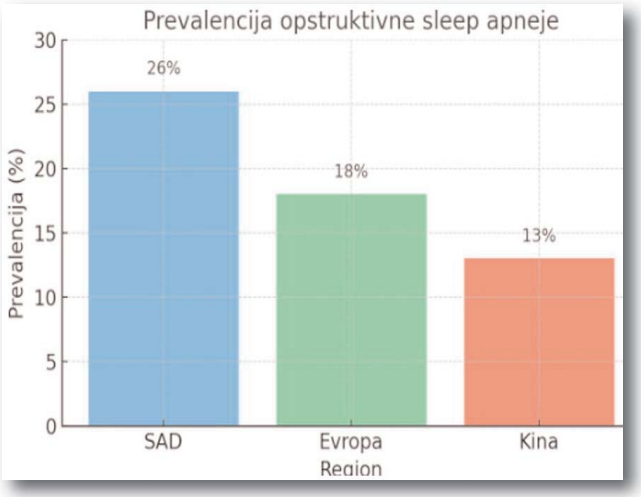
2. Epidemiološke studije: Za analizu prevalencije sleep apnee u različitim regionima, analizirane su epidemiološke studije koje pružaju statističke podatke o učestalosti sleep apnee. Ove studije su pružile uvid u to koliko je sleep apneja rasprostranjena u različitim delovima sveta, kao i koje su specifične grupe u većem riziku, na osnovu demografskih, genskih, socijalnih i životnih faktora. Takođe, analizirane su studije koje se bave odnosom između socioekonomskih faktora, životnih navika (kao što su pušenje i konzumacija alkohola), telesne mase, i učestalosti sleep apnee.
3. Kliničke smernice i protokoli lečenja: S obzirom na to da je sleep apneja ozbiljan poremećaj koji zahteva lečenje, analizirani su postojeći klinički protokoli za dijagnozu i lečenje opstruktivne sleep apnee u različitim zemljama. Ove smernice su uključivale upotrebu različitih dijagnostičkih alata, kao što su polisomnografija, kućno testiranje spavanja i praćenje nivoa kiseonika u krvi, kao i preporučene terapije, uključujući CPAP uređaje, lekove i hirurške intervencije. Posebna pažnja posvećena je razlikama u pristupu lečenju u različitim zemljama i njihovim zdravstvenim sistemima.
4. Statističke metode: Podaci koji su prikupljeni iz literature i epidemioloških studija analizirani su pomoću deskriptivnih statističkih metoda, uključujući izračunavanje prosečnih vrednosti, standardnih devijacija, i udelima u populaciji. Takođe, korišćeni su testovi za upoređivanje razlika između različitih regiona (npr. t-test i analiza varijanse), kako bi se procenile značajne razlike u prevalenci sleep apnee i metodama lečenja u Kini, SAD-u i Evropi.
5. Kvalitativna analiza: Osim kvantitativnih podataka, sprovedena je i kvalitativna analiza koja se bavila specifičnostima dijagnostike i lečenja sleep apnee u različitim kulturnim i društvenim kontekstima. Analizirani su intervjui sa lekarima i stručnjacima iz oblasti spavanja, kao i mišljenja pacijenata o tretmanima i terapijama. Kroz ovu analizu, cilj je bio da se istraže potencijalne razlike u pristupu lečenju, kao i prepreke u dijagnostici i lečenju sleep apnee u različitim zemljama.

Rezultati rada

U okviru ovog istraživanja analizirana je prevalencija, dijagnostika, metode lečenja i prisustvo komorbiditeta kod pacijenata sa opstruktivnom sleep apnejom u Kini, Sjedinjenim Američkim Državama i Evropi. Rezultati su prikazani kroz više grafikona i uporednih analiza.

1. Prevalencija sleep apneje u različitim regionima

Rezultati pokazuju da postoji značajna razlika u učestalosti opstruktivne sleep apneje među regionima. U SAD-u prevalencija iznosi približno 26% odrasle populacije, u Evropi između 15% i 20%, dok je u Kini nešto niža i kreće se oko 10% do 15%. Faktori poput stope gojaznosti, životnih navika i starosne strukture populacije doprinose ovim razlikama.

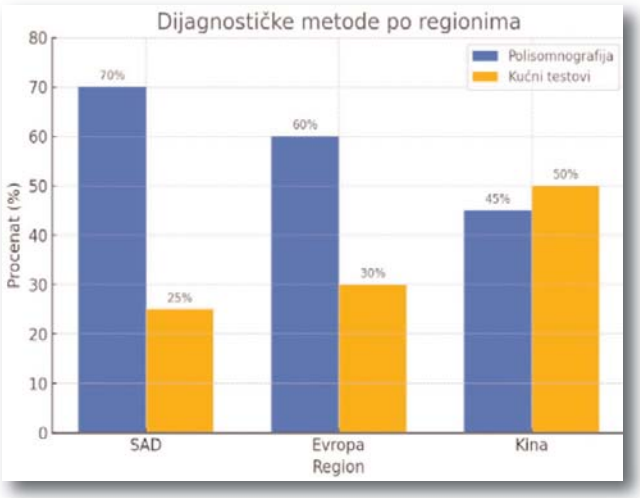


Grafikon 1: Prevalencija opstruktivne sleep apneje

2. Najčešće korišćene dijagnostičke metode

Dijagnostika sleep apneje najčešće se oslanja na polisomnografiju, ali postoje razlike u dostupnosti i primeni različitih metoda:

- U SAD-u, 70% pacijenata se dijagnostikuje polisomnografijom.
- U Evropi, 60% koristi polisomnografiju, dok 30% koristi kućne testove.
- U Kini, samo 45% koristi polisomnografiju, dok 50% koristi jednostavnije kućne testove.

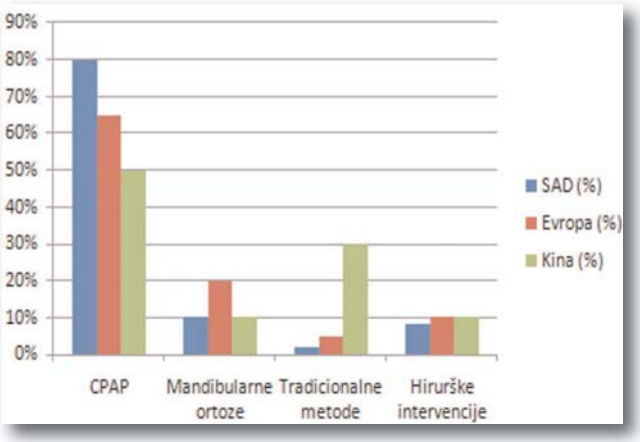


Grafikon 2: Dijagnostičke metode po regionima

3. Najčešće metode lečenja

U lečenju sleep apneje dominiraju CPAP uređaji, ali postoje i regionalne razlike u pristupu:

- U SAD-u, 80% pacijenata koristi CPAP uređaj kao primarnu terapiju.
- U Evropi, 65% koristi CPAP, dok 20% koristi mandibularne ortoze.
- U Kini, 50% pacijenata koristi CPAP, dok značajan broj (30%) koristi kombinaciju tradicionalnih terapija i savremenih metoda.

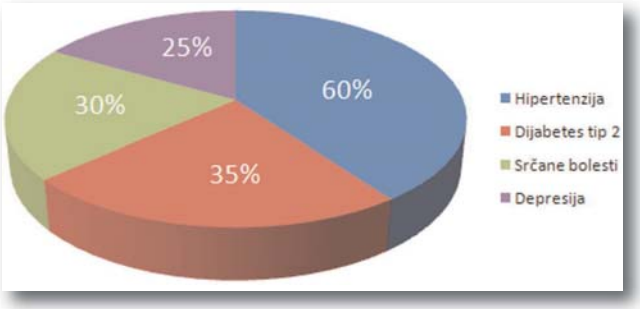


Grafikon 3: Terapije za sleep apneju po regionima

4. Komorbiditeti kod pacijenata sa sleep apnejom

Sleep apneja je snažno povezana sa povećanim rizikom od raznih hroničnih bolesti. Analizom podataka utvrđeno je sledeće:

- 60% pacijenata sa sleep apnejom ima hipertenziju.
- 35% ima dijabetes tipa 2.
- 30% ima bolesti srca.
- 25% pokazuje simptome depresije.



Grafikon 4: Učestalost komorbiditeta kod pacijenata sa sleep apnejom

Diskusija

Opstruktivna sleep apneja (OSA) predstavlja jedan od najznačajnijih poremećaja spavanja sa ozbiljnim posledicama po zdravlje i kvalitet života pacijenata. Rezultati istraživanja pokazuju da je OSA globalni zdravstveni problem, ali sa značajnim varijacijama u prevalenciji, dijagnostičkim metodama i pristupima lečenju u zavisnosti od regiona. Ova diskusija analizira moguće uzroke ovih razlika, njihove posledice, kao i potencijalne pravce za unapređenje dijagnostike i terapije [11, 12].

Prevalencija opstruktivne Sleep Apnee je najviša u Sjedinjenim Američkim Državama, što je u skladu sa poznatim faktorima rizika kao što su visok stepen gojaznosti, nezdrav način života i starija struktura populacije. U poređenju sa SAD-om, Evropa pokazuje nešto nižu prevalenciju, što može biti posledica razlika u načinu ishrane, većoj fizičkoj aktivnosti i različitim zdravstvenim politikama usmerenim na prevenciju hroničnih bolesti. Kina, s druge strane, ima relativno nižu prevalenciju uloga kraniofacijalne anatomije, ali treba napomenuti da su poslednjih godina faktori rizika kao što su prekomerna telesna masa i smanjena fizička aktivnost u porastu, što bi u budućnosti moglo dovesti do povećanja učestalosti OSA u toj zemlji.

Dijagnostika sleep apneje značajno zavisi od dostupnosti zdravstvenih resursa. U razvijenim zemljama poput SAD-a i većine evropskih država, polisomnografija (PSG) je široko dostupna i

smatra se zlatnim standardom za dijagnostikovanje OSA. Međutim, i pored široke dostupnosti, visoki troškovi ovih testova i potreba za specijalizovanim centrima mogu predstavljati prepreku za sve pacijente. U Kini se, zbog ograničenih resursa i velikog broja stanovnika, češće koriste jednostavniji kućni testovi spavanja, što može dovesti do manje precizne dijagnoze (imaju osetljivost do 80%) [2, 4, 10]. Ove razlike ukazuju na potrebu za razvojem ekonomičnijih, ali dovoljno preciznih metoda za dijagnozu koje bi bile dostupne i pristupačne širom sveta.

Kada je reč o terapiji, CPAP uređaji ostaju najefikasnija terapijska opcija za većinu pacijenata sa OSA. Visok stepen upotrebe CPAP uređaja u SAD-u i Evropi pokazuje visok nivo svesti o važnosti kontinuirane terapije. Ipak, i pored efikasnosti, mnogi pacijenti teško se prilagođavaju CPAP terapiji zbog nelagodnosti, što može dovesti do loše adherencije. U Kini, pored modernih terapija, i dalje postoji značajno oslanjanje na tradicionalne metode lečenja, što je kulturno ukorenjeno, ali postavlja pitanje efikasnosti tih metoda u odnosu na standardizovane medicinske tretmane [7, 8]. Zanimljivo je da Evropa pokazuje fleksibilniji pristup lečenju, uključujući široku primenu alternativnih terapija kao što su mandibularne ortoze, koje mogu biti korisne kod pacijenata sa blagom do umerenom sleep apnejom.

Prisustvo komorbiditeta kod pacijenata sa sleep apnejom dodatno komplikuje kliničku sliku i povećava zdravstvene rizike. Visoka učestalost hipertenzije, dijabetesa i kardiovaskularnih bolesti među obolelima jasno ukazuje na potrebu za sveobuhvatnim pristupom u lečenju, koji ne bi smeo da se fokusira samo na tretman apneje, već i na prevenciju i upravljanje pratećim bolestima. Ovo dodatno potvrđuje važnost ranog otkrivanja OSA i adekvatnog lečenja, kako bi se smanjio rizik od ozbiljnih komplikacija.

Takođe, značajan izazov predstavlja niska svest javnosti o sleep apneji. Mnogi pacijenti nisu ni svesni da imaju ovaj poremećaj, jer simptomi poput hrkanja i umora često nisu prepoznati kao ozbiljan zdravstveni problem. Zato su edukacija populacije, kontinuirano stručno usavršavanje zdravstvenih radnika i jačanje preventivnih programa ključni koraci u borbi protiv OSA na globalnom nivou [6].

Iako su ostvareni značajni pomaci u dijagnostici i terapiji sleep apneje, rezultati ukazuju da je potrebno dalje unapređivati pristup ovom poremećaju, naročito u zemljama u razvoju. Standardizacija protokola dijagnostike i terapije, razvoj novih, dostupnijih tehnologija za praćenje spavanja i povećanje ulaganja u javnozdravstvene kampanje mogli bi imati dugoročan pozitivan uticaj na smanjenje učestalosti i posledica sleep apneje.

Zaključno, iako se sleep apneja sve više prepoznaje kao ozbiljan zdravstveni problem širom sveta, ostaju značajne razlike između regiona koje zahtevaju pažljivo prilagođene strategije za unapređenje ranog otkrivanja, dijagnostike i lečenja. Dalja istraživanja, globalna saradnja i inovacije u terapijskim pristupima biće ključni faktori za bolje upravljanje ovim poremećajem u budućnosti [5, 7].

Zaključak

Sleep apneja je ozbiljan i često potcenjen poremećaj spavanja sa značajnim posledicama po zdravlje pojedinca i šire društvo. Analiza prevalencije, dijagnostičkih metoda, terapijskih pristupa i komorbiditeta jasno ukazuje da Sleep Apnea nije samo individualni problem, već i važno javnozdravstveno pitanje koje zahteva sistematski pristup.

Rezultati istraživanja pokazali su da postoje značajne razlike između regiona u učestalosti i upravljanju ovim poremećajem. Visoka prevalencija u Sjedinjenim Američkim Državama ukazuje na potrebu za još jačim preventivnim programima, dok situacija u Kini osvetljava izazove u dostupnosti savremenih dijagnostičkih i terapijskih sredstava. Evropa, sa relativno uravnoteženim pristupom, može služiti kao model za integraciju različitih metoda u cilju povećanja dostupnosti i efikasnosti lečenja.

Iako CPAP terapija ostaje zlatni standard u tretmanu sleep apneje, potreba za razvojem novih, pacijentu prihvatljivijih terapijskih opcija

je očigledna. Takođe, prisustvo komorbiditeta kao što su hipertenzija, dijabetes i kardiovaskularne bolesti dodatno naglašava značaj sveobuhvatnog i multidisciplinarnog pristupa lečenju.

Jedan od ključnih izazova ostaje niska svest o sleep apneji među opštom populacijom, što odlaže dijagnozu i povećava rizik od komplikacija. Samo kroz kombinaciju edukacije zdravstvenih radnika I javnosti, rani skrining u populacijama visokog rizika, promociju zdravih životnih navika, dostupne dijagnostike i individualizovanih terapijskih pristupa moguće je efikasno smanjiti teret koji ovaj poremećaj nosi.

Dalja istraživanja bi trebalo da se fokusiraju na razvijanje jeftinijih i lakše dostupnih metoda dijagnostike, kao i na razvoj novih terapijskih rešenja koja će povećati adherenciju pacijenata. Pored toga, međunarodna saradnja u razmeni znanja i iskustava može značajno doprineti unapređenju borbe protiv sleep apneje na globalnom nivou.

Zaključno, iako su postignuti značajni pomaci u razumevanju i lečenju sleep apneje, predstoji još mnogo posla kako bi se ovaj ozbiljan poremećaj adekvatno prepoznao, lečio i sprečio, čime bi se unapredilo zdravlje miliona ljudi širom sveta. Dijagnoza i terapija sleep apneje je nužnost za očuvanje zdravlja i kvaliteta života.

Literatura

1. Punjabi, N. M. (2008). The epidemiology of adult obstructive sleep apnea. Proceedings of the American Thoracic Society, 5(2), 136–143.
2. Peppard, P. E., Young, T., Barnet, J. H., Palta, M., Hagen, E. W., & Hla, K. M. (2013). Increased prevalence of sleep-disordered breathing in adults. American Journal of Epidemiology, 177(9), 1006–1014.
3. Senaratna, C. V., Perret, J. L., Lodge, C. J., Lowe, A., Campbell, B. E., Matheson, M. C., Hamilton, G. S., & Dharmage, S. C. (2017). Prevalence of obstructive sleep apnea in the general population: A systematic review. Sleep Medicine Reviews, 34, 70–81.
4. Sullivan, C. E., Issa, F. G., Berthon-Jones, M., & Eves, L. (1981). Reversal of obstructive sleep apnea by continuous positive airway pressure applied through the nares. The Lancet, 317(8225), 862–865.
5. Young, T., Palta, M., Dempsey, J., Skatrud, J., Weber, S., & Badr, S. (1993). The occurrence of sleep-disordered breathing among middle-aged adults. New England Journal of Medicine, 328(17), 1230–1235.
6. Jordan, A. S., McSharry, D. G., & Malhotra, A. (2014). Adult obstructive sleep apnoea. The Lancet, 383(9918), 736–747.
7. Franklin, K. A., & Lindberg, E. (2015). Obstructive sleep apnea is a common disorder in the population—A review on the epidemiology of sleep apnea. Journal of Thoracic Disease, 7(8), 1311–1322.
8. Gami, A. S., Caples, S. M., Somers, V. K. (2003). Obesity and obstructive sleep apnea. Endocrinology and Metabolism Clinics of North America, 32(4), 869–894.
9. Malhotra, A., & White, D. P. (2002). Obstructive sleep apnoea. The Lancet, 360(9328), 237–245.
10. Strollo, P. J., & Rogers, R. M. (1996). Obstructive sleep apnea. New England Journal of Medicine, 334(2), 99–104.
11. Lavie, L. (2015). Oxidative stress in obstructive sleep apnea and intermittent hypoxia—Revisited—the bad ugly and good: Implications to the heart and brain. Sleep Medicine Reviews, 20, 27–45.
12. Somers, V. K., White, D. P., Amin, R., Abraham, W. T., Costa, F., Culebras, A., Daniels, S., Floras, J. S., Hunt, C. E., Olson, L. J., Pickering, T. G., Russell, R., Woo, M., & Young, T. (2008). Sleep apnea and cardiovascular disease: An American Heart Association/American College of Cardiology Foundation Scientific Statement. Circulation, 118(10), 1080–1111.

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PREVENTIVNI PREGLED ŠTITASTE ŽLEZDE U DOMU ZDRAVLJA BELA PALANKA

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SAŽETAK

Uvod: Štitasta žlezda je najveća endokrina žlezda. Sastoji se od dva režnja spojena istmusom, smeštena je ispred i kaudalno od hrskavice larinksa ispod kože, i zato je dostupna kliničkom pregledu. Njena osnovna funkcija je da produkuje tiroksin (T4) i trijodtironin (T3) koji imaju niz metaboličkih uloga. Najveći deo cirkulišućeg hormona je T4, a dominantan intracelularni je T3 koji se lakše se vezuje za receptore hormona. Bolesti štitne žlezde su u sekreciji hormona ili uvećanju same žlezde ili oba. Poremećaji u sekreciji hormona su hipotireoza i hipertireoza, a poremećaji u građi štitaste žlezde su Grejvs-Bazedovljeva bolest, nodusna toksična struma i tiroiditisi.

Cilj istraživanja: Cilj rada je procena stanja štitaste žlezde i hormonskog statusa pacijenata koji su se sasvim dobrovoljno javili na organizovani ultrazvučni pregled štitaste žlezde.

Materijal i metode: Istraživanje je sprovedeno u Domu zdravlja Bela Palanka u toku organizovanog pregleda štitastee žlezde 21.10. i 22.10. 2023. godine. Hormonske analize nivoa TSH i FT4 su određivane samo onim pacijentima kojima je nalaz na ultrazvuku ukazivao na poremećaj u strukturi. U obradi podataka je korišćen SPSS. Za prikazivanje razultata je korišćen Microsoft Word i Excel.

Rezultati: Oba dana skrininga se javilo 144 pacijenata. Muškaraca je bilo 11, a žena 133. Prosečna starost je bila 56,86±6,24 godina. Ultrazvučni nalazi pacijenata su podeljeni u 8 grupa. Najviše njih je imalo uredan nalaz i to 60 (41,66%), a najmanje je bilo pacijenata sa smanjenom štitastom žlezdom dva (1,38%). Noduse je imalo 35 pacijenata (24,31%), a difuzno uvećanu žlezdu 5,55% ispitanika. Nivo TSH hormona se kod njih kretao od niskog, preko normalnog do blago povišenog. Samo dva pacijenta su imala nizak nivo, normalan je imalo 85 pacijenata, a blago povišene vrednosti TSH je imalo 5 pacijenata. Nivo FT4 se normalno kreće od 12-22 ρmol/L. Ukupno je bilo 18 pacijenata u tom opsegu, a svi ostali su imali snižen nivo ispod 12 ρmol/L (74 njih).

Zaključak: Naše istraživanje je ukazalo da ima više pacijenata sa poremećajima u strukturi štitaste žlezde nego onih sa urednim nalazom. Zato treba ukazivati na što raniju kontrolu ultrazvukom, jer supkliničke forme hipotireoidizma mogu proći neopaženo.

Ključne reči: štitasta žlezda, hormoni, ultrazvuk

SUMMARY

Introduction: The thyroid gland is the largest endocrine gland. It consists of two lobes connected by an isthmus. It is located anterior and caudal to the laryngeal cartilage under the skin, and is therefore accessible to de clinical review.Its main function is to produce thyroxine T4 and threeiodthyronine T3 which have a series metabolic roles. Most of the circulating hormone is T4, and predominant intracellular is T3 which binds more easily to hormone receptors. Diseases of the thyroid gland are in the in secretion of hormones or enlargement of the gland itself or both.

Disorders in the secretion of hormones are hypothyroidism and hare hyperthyroidism, and disorders in the structure of the thyroid gland are Graves –Basedov disease, nodular toxic goiter and thyroiditis.

Research objective: The aim of the investigation is to assess the state of the thyroid gland and the hormonal status of patiens who came to organized ultrasound examination of the thyroid gland and hormone.

Material and methods: The research was conducted in the Bela Palanka Health Center on organized examination of the thyroid gland on 21. and 22. Ocober 2023 year. Hormone analyzes of TSH and FT4 levels were determined only for those patients who werw found ultrasonic indicated disturbance in the structure. SPSS was used in data processing Microsoft Word and Exel were used to present the results.

Results: 144 patients showed up on both screening days. There were 11 men and 133 women. Average age was 56,86±6,24 years. The ultrasound findings of the patients were divided into 8 groups. The most of them (41,66%) had normal findings, and the fewest with reduce immunty gland (1,38%). 35 (24,31%) patiens had nodules and 5,55% of subjects had a diffusely enlarged gland. TSH level ranged from low to slidhtly elevated. Only two patients had a low level, 85 patients had a normal level, and 5 had slightly elevated. The FT4 level normally ranges from 12-22ρmol/L. There were a total of 18 patients in thet volume range, and all others had a lowere level below 12 ρmol/L (74 of them).

Conclusion: Our research indicated that there are more patients with disorders in the structure of the gland then those with normal findings. That is why is necessary to indicate zhe earliest ultrasound control, because subclinical forms of hypothyreoidism can go unnoticed.

Keywords: thyroid gland, hormones, ultrasound

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Uvod

Štitasta žlezda je najveća endokrina žlezda. Sastoji se od dva režnja spojena istmusom, i smeštena je ispred i kaudalno od hrskavice larinksa ispod kože, i zato je dostupna kliničkom pregledu. Njena osnovna funkcija je da produkuje tiroksin (T4) i trijodtironin (T3) koji imaju niz metaboličkih uloga.

Osnovna jedinica građe štitaste žlezde je folikul koji okružuje šupljinu ispunjenu koloidom.

Glavni protein koloida je tireoglobulin (TG). Za normalnu funkciju štitaste žlezde je neophodno uneti jod hranom i vodom, u obliku jodida. Nakon transporta iz cirkulacije u tireocite, jod se može koncentrisati u 50 puta većoj koncentaciji u odnosu na krv, a pod uticajem peroksidaze jodid se oksiduje do joda. Takav se vezuje za tirozin iz TG (jodinacija) i nastaju tironini. Na taj način u štitastoj žlezdi unutar TG se nalaze velike rezerve tiroidnih hormona koji omogućuju normalnu funkciju štitaste žlezde i do par meseci nakon prestanka sinteze.

Sinteza hormona štitaste žlezde je pod kontrolom tireostimulišućeg hormona (TSH) iz prednjeg režnja hipofize. On ubrzava rast tireocita, transport joda, peroksidaciju, jodinaciju, endocitozu TG i oslobađanje T4 i T3 u cirkulaciji.

Najveći deo cirkulišućeg hormona je T4, a dominantan intracelularni je T3 koji se lakše se vezuje za receptore hormona [1].

Bolesti štitaste žlezde se manifestuju kao poremećaji u sekreciji hormona ili uvećanju same žlezde (struma) ili oba.

Poremećaji u sekreciji hormona su hipotireoza i hipertireoza, a poremećaji u građi štitaste žlezde su Grejvs-Bazedovljeva bolest (MGB), nodusna toksična struma i tiroiditisi [2]. Kod MGB nivo TSH je nizak ili nemerljiv, a FT4 i FT3 je povišen. Postoji i difuzna mekana struma, uz postojanje oftalmopatije i kožnih promena. Ukoliko se ne leči adekvatno, dovodi do komplikacija na srcu, tireotoksičnog srca i do tireotoksične krize, oluje. Nodusna toksična struma je drugi po učestalosti oblik hipertireoze. Može postojati multinodusna toksična struma kada se u pojedinim nodusima ekscesivno prozvode hormoni. Može se javiti eutireoidna polinodusna struma koja u sklopu nekog autoimunog procesa počne da proizvodi hormone u višku. Promena zvana solitarni nodus u štitnoj žlezdi je u stvari benigni tumor, adenom, koji autonomno proizvodi hormone [3].

Tireoiditisi su grupa oboljenja koja najčešće započinju usled infekcije iz okoline. Hronični tireodoitis (Hašimoto) je autoimuno zapaljenje sa limfocitnom infiltracijom štitaste žlezde i njenim uvećanjem u vidu difuzne, elastične, gumaste strume [4, 5].

Cilj rada

Cilj rada je procena stanja štitaste žlezde i hormonskog statusa pacijenata koji su se sasvim dobrovoljno javili na organizovani ultrazvučni pregled štitaste žlezde.

Materijal i metode

Istraživanje je sprovedeno u Domu zdravlja Bela Palanka u toku prvog vikenda organizovanog pregleda štitaste žlezde 21.10. i 22.10. 2023. godine. Sugerisano je pacijentima preko sredstava javnog informisanja da bi trebalo da se jave oni bez ranije dijagnostikovanih poremećaja štitaste žlezde. Zatim je beležen, pored imena i prezimena, datum rođenja i ultrazučni nalaz.

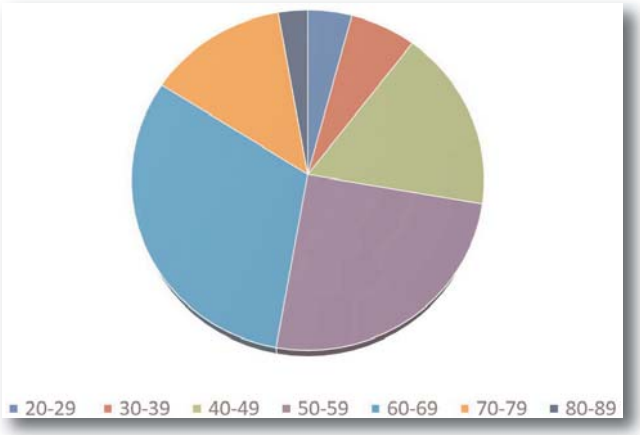
Hormonske analize nivoa TSH i FT4 su određivane samo onim pacijentima kojima je nalaz na ultrazvuku ukazivao na poremećaj u strukturi. Te analize su rađene u laboratoriji Doma zdravlja.

Za analizu starosne strukture pacijenata, aritmetičke sredine, standarne devijacije, standardizovanog odstupanja (Z vrednost) kao i za analizu ostalih podataka dobijenih u ovom istraživanju je korišćen SPSS.

Za prikazivanje razultata je korišćen Microsoft Word i Excel.

Rezultati

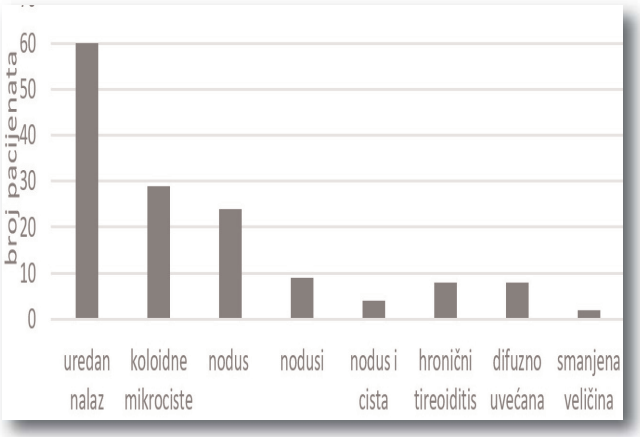
Oba dana skrininga se javilo 144 pacijenata. Muškaraca je bilo 11, a žena 133. Prosečna starost je bila 56,86±6,24 godina (grafikon 1).



Grafikon 1 Starosna struktura ispitanika

Najviše je bilo ispitanika u dobnoj grupi između 60 i 69 godina. Pacijenata iznad 80 godina je bilo četvoro.

.Na grafikonu broj 2 je prikazan nalaz ultrazvukom.



Grafikon 2 Nalaz štitaste žlezde ultrazvukom

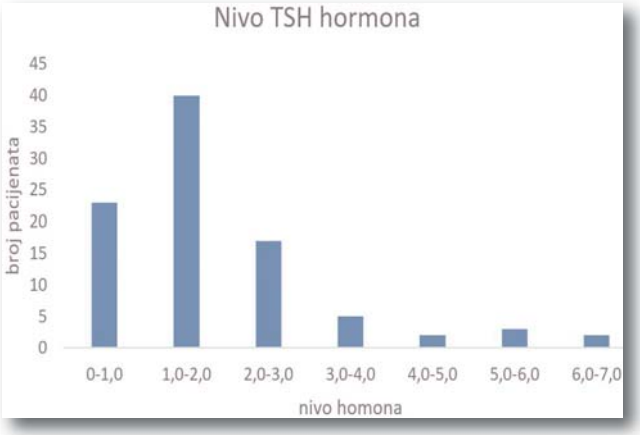
Ultrazvučni nalazi pacijenata su podeljeni u 8 grupa. Najviše pacijenata je imalo uredan nalaz i to 60 (41,66%), a najmanje je bilo pacijenata sa smanjenom štitastom žlezdom dva (1,38%).

Noduse je imalo 35 pacijenata (24,31%), a difuzno uvećanu žlezdu 5,55% ispitanika.

Sledeći korak u ovom skriningu je bila provera hormonskog statusa samo kod onih pacijenata sa poremećajem u strukturi žlezde.

Određivan je nivo TSH i FT4 hormona. Takvih pacijenta je bilo 92 (63, 88%) ukupnog broja pacijenata koji su se javili na preventivni pregled. Bilo je 6 muškatraca i 86 žena.

Na grafikonu br. 3 prikazan je nađen nivo TSH hormona kod ispitanika.



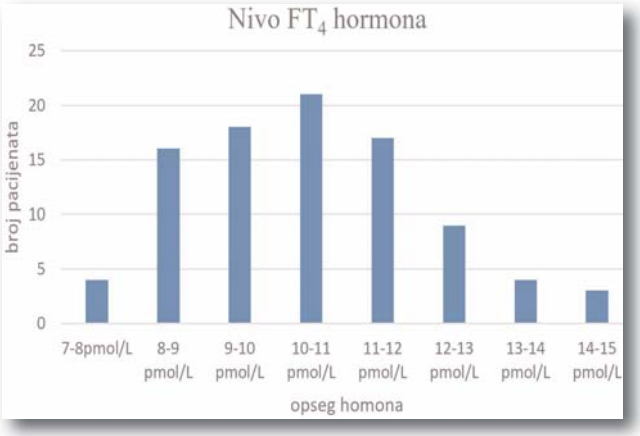
Grafikon 3 Nivo TSH hormona

Nivo TSH hormona se kod njih kretao od niskog, preko normalnog do blago povišenog. Samo dva pacijenta su imala nizak nivo TSH (0-0,4 μIU/ml), normalan je imalo 85 pacijenata (0,4-4,5 μIU/ml), a blago povišene vrednosti TSH (4,5-10 μIU/ml)je imalo 5 pacijenata.

Interval varijacije je 7,50 μIU/ml. To je razlika između najviše i najniže izmerene vrednosti hormona TSH.

Srednja vrednost hormona je 1,84 ± 2,91 μIU/ml.

Z test za nivo značajnosti testa od p=0,05 je 2,1 i nema statistički značajne razlike između Z vrednosti hipotetičkog osnovnog skupa i ispitivanog uzorka. Dobijene vrednosti hormona TSH nisu statistički signifikantne i samo su izraz slučajnog varijabiliteta uzorka.



Grafikon 4 Nivo FT4 hormona

Nivo FT4 se normalno kreće od 12-22 ρmol/L. Ukupno je bilo 18 pacijenata u tom opsegu, a svi ostali sui mali snižen nivo FT4 ispod 12 ρmol/L (74 njih).

Interval varijacije je 7,20 ρmol/L.

Srednja vrednost je 10,47 ± 1,66 ρmol/L,

Prema podacima sa grafikona 4 se uočava da je najveći broj pacijenata u klasi 10-11 ρmol/L, i tu se nalazi 21 pacijent (22,8%).

Z test za p=0,05 je 54,7 i postoji statistički značajna razlika između Z vrednosti hipotetičkog osnovnog skupa i ispitivanog uzorka. Zato su dobijene vrednosti hormona FT4 statistički signifikantne i uzorak ispitanika je reprezentativan.

Diskusija

Ispitivanje građe štitaste žlezde ultrazvukom je u porastu poslednjih godina. U tome možda ima malo i straha koji natera ljude da ispituju svoje zdravlje. Zato treba iskoristiti ovakve preglede u najbližem domu zdravlja, jer se bolesti tiroideje pojavljuju u svim uzrastima.

Starost pacijenta je u našem istraživanju bila najzastupljenija u dobnoj grupi od 60 do 69 godina. Mlađih od 20 godina nije bilo. Bolesti štitaste žlezde su češte po učestalosti kod starije populacije u Evropi [6, 7].

Kada je u pitanju pol obolelih u literaturi, više je žena u odnosu na muškarce [8]. I u našem

istraživanju su prednjačile žene 12 puta više.

Prema rezultatima prikazanih u ovom radu, nalaz UZ štitaste žlezde je ukazao da više ima onih sa otkrivenim poremećajem građe nego sa urednim nalazom, Čvorića u štitastoj žlezdi je bilo kod 37 pacijenata. Koloidne mikrociste su nađene kod 29 ispitanika. Difuzno uvećanu žlezdu je imalo 8 pacijenata, a smanjenu veličinu 2 pacijenta. Hronični tireoiditis je nađen kod 8 ispitanika. Sličnih podataka ima i u medicinskoj literaturi [9, 10, 11].

Kada je u pitanju hormonski status, nizak nivo TSH je uočen kod 2 pacijenta. Nizak nivo TSH (0 – 0,4 μIU/ml (hipertireoza) može ukazati na povećano lučenje formona štitaste žlezde, FT4 i FT3. Najveći broj pacijenata je imao uredan nalaz (0,4 – 4,5 μIU/ml), a samo 5 ispitanika blago povišene vrednosti do 10 μIU/ml (blagi hipotireoidizam). Povišen nivo TSH može biti posledica povećanog FT4 koji se luči u samoj žlezdi (hipotireoza). Normalan TSH praktično isključuje poremećaj funkcije žlezde [12, 13].

Nivo FT4 hormona se normalno kreće od 12-22 ρmol/L. Ukupno je bilo 18 pacijenata u tom opsegu, a svi ostali su mali snižen nivo FT4 ispod 12ρmol/L (74 njih). Povišene vrednosti nije imao niko [13]. FT4 analiza ili test slobodnog tiroksina koristi se u proceni pravilnog rada, odnosno funkcije štitaste žlezde, kada postoje indikacije da je tireoidna žlezda zahvaćena određenim oboljenjem. FT4 analiza koristi se u dijagnostici hipertireoze (povećane funkcije štitaste žlezde) kada povišeni nivoi FT4 mogu ukazivati na prekomerno aktivnu štitastu žlezdu sa gubitkom težine, povećane nervoze, aritmije, ubrzan rad srca, tremor itd. Hipotireoza (smanjena funkcija štitaste žlezde) je stanje sa smanjenim nivoom FT4 što može ukazivati na neaktivnu štitastu žlezdu. Simptomi su povećanje telesne težine, umor, slaba cirkulacija, osećaj hladnoće, usporen rad srca, suvu kožu itd. Autoimuni poremećaj štitaste žlezde se mogu pratiti preko ovog hormona poput Hašimoto tireoiditisa (koji dovodi do hipotireoze) ili Gravesove bolesti (koja dovodi do hipertireoze) [14].

FT4 analiza se često sprovodi kod procene opšteg zdravlja štitaste žlezde kao što je to slučaj u našem istraživanju, a što su sproveli i drugi autori [15].

U Evropi ima mnogo slučajeva neprepoznate snižene funkcije štitaste žlezde [16].

Zato treba posebno obratiti pažnju na supkliničke manifestacije oboljenja štitaste žlezde na koje su ukazivali i drugi autori [17, 18, 19, 20].

Zaključak

Ovo istraživanje koje je bilo sasvim dobrovoljno je ukazalo je da ima više pacijenata sa poremećajima u strukturi štitaste žlezde nego onih sa urednim nalazom.

Treba ukazivati na što raniju kontrolu UZ štitaste žlezde, dostupnog u domovima zdravlja.

U budućnosti se može ispitati i komorbiditet ovih ispitanika i u svetlu tih podataka tumačiti rezultate. Supkliničke forme hipotireoidizma mogu proći neopaženo; zato posebno treba po-

vesti računa o svim simptomima kod pacijenta. Nalaz hormona može pomoći u rasvetljavanju ovih problema.

Potrebno je kroz oblike edukacije upotpuniti znanja izabranog lekara iz oblasti oboljenja štitaste žlezde i ohrabtiti ih na aktivnije učešće u tretmanu svojih pacijenata.

Literatura

1. Ilić S. Interna medicina. Prosveta Niš, 2004. 307-319.
2. Seferović P. et al. Interna medicina. Medicinski fakultet Beograd, 2023.280-350.
3. Fiore V, Barucca A, Barracio S. et all. Hypothyreoidism in older adults: A narrative Review. Endocr Metab Immune Disord Drug Targets. 2024;24(8):879-884.
4. Troshina EA, Panfilova EA, Mikhina MS et all.Clinical practice guidelines for acute and chronic thyroiditis (excluding autoimmune thyroiditis).Probl Endokrinol (Mosk). 2021. 12;67(2):57-83.
5. Martinez Quintero B, Yazbeck C, Sweeney LB. Thyroiditis: Evaluation and Treatment. Fam Physician. 2021: 1;104(6):609-617.
6. Dedon J. Thyroid Disease in Aging.Mo Med. 2022;119(4):351-353.
7. Duntas LH, Yen PMDiagnosis and treatment of hypothyroidism in the elderly. Endocrine. 2019;66(1): 63-69.
8. Wémeau JL, Klein M, Sadoul JL et all.Graves' disease: Introduction, epidemiology, endogenous and environmental pathogenic factors Ann Endocrinol.2018; 79(6):599-607.
9. Blank W, Müller T, Braun B. Thyroid nodles-how to proceed?Praxis (Bern 1994). 2012;5;101(18):1167-73.
10. Sheth S. Role of ultrasonography in thyroid disease.Otolaryngol Clin North Am. 2010;43(2):239-55.
11. Aribon PA, Teope E, Egwolf AL, Diagnostic Accuracy of American College of Radiology Thyroid Imaging Reporting Data System: A Single-center Cross-sectional Study. J ASEAN Fed Endocr Soc 2024;39 (1):61-68.
12. Pirahanchi Y, Toro F, JialalI. Physiology, Thyroid Stimulating Hormone. StatPearls, 2025.
13. Sheehan MT.Biochemical Testing of the Thyroid: TSH is the Best and, Oftentimes, Only Test Needed - A Review for Primary Care. Clin Med Res. 2016;14 (2):83-92.
14. Antonelli A, Fallahi P, Elia G, Ragusa F, Paparo SR, Ruffilli I, Patrizio A, Gonnella D, Giusti C, Virili C, Centanni M, Shoenfeld Y, Ferrari SM.Graves' disease: Clinical manifestations, immune pathogenesis (cytokines and chemokines) and therapy. Best Pract Res Clin Endocrinol Metab. 2020;34(1):101388.
15. Kostoglou-Athanassiou I, Ntalles K. Hypothyroidism - new aspects of an old disease.Hippokratia. 2010;14 (2):82-7.
16. DE Hellman.The thyroid gland. Contemp Anesth Pract. 1980:3:109-45.
17. Carlé A, Karmisholt JS, Knudsen N. et all.Does Subclinical Hypothyroidism Add Any Symptoms? Evidence from a Danish Population-Based Study. Am J Med. 2021 Sep;134(9):1115-1126.
18. Dizdarevic-Bostandzic A, Surkovic I, Balic S, Karlovic-Beslic V. Reasons for Referring Patients for Determining the Hormonal Status of the Thyroid Gland From the Level of Primary Health Care in Sarajevo Canton.Mater Sociomed. 2024;36(1):14-17.
19. Maldjian PD, Chen T.Is visual assessment of thyroid attenuation on unenhanced CT of the chest useful for detecting hypothyroidism?.Clin Radiol. 2016 Nov;71(11):1199.
20. Díez JJ, Iglesias P. Spontaneous subclinical hypothyroidism in patients older than 55 years: an analysis of naturalcourse and risk factors for the development of overt thyroid failure. J Clin Endocrinol Metab. 2004 Oct;89(10):4890-7.

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EDUKACIONI RADOVI

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KONTRASTNA MAMOGRAFIJA

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SAŽETAK

Kontrastna mamografija predstavlja slikovnu rendgenološku endografsku dijagnostičku metodu pregleda dojke uz pomoć jodnog kontrastnog sredstva (JKS) aplikovanog intravenskim (iv.) putem. Izvodi se na isti način kao i standardna mamografija, samo što se iv. putem aplikuje JKS. Kontrastna mamografija se primenjuje u cilju procene i detekcije poznatih i suspektnih lezija na dojci kao dodatak mamografiji sa ultrazvukom ili bez ultrazvuka, ili kao alternativa oslikavanju magnetnom rezonancijom, kada je magnetna rezonancija kontraindikovana ili nedostupna. BIRADS klasifikacija olakšava tumačenje nalaza kontrastne mamografije. U literaturi se sreće pod sinonimima: kontrastno pojačana mamografija, intravenska mamografija (IVM), engleski: Contrast-enhanced mammography (CEM).

Ključne reči: kontrastna mamografija, jodno kontrastno sredstvo

SUMMARY

Contrast mammography is an image roentgenological endographic diagnostic method of breast examination with the help of iodine contrast medium (JKS) applied intravenously (iv). It is performed in the same way as standard mammography, except that JKS is applied through the iv route. Contrast mammography is used to evaluate and detect known and suspected breast lesions as an addition to mammography with or without ultrasound, or as an alternative to magnetic resonance imaging, when magnetic resonance is contraindicated or unavailable. The BIRADS classification facilitates the interpretation of contrast mammography findings. In the literature, it is found under synonyms: contrast-enhanced mammography, intravenous mammography (IVM), English: Contrast-enhanced mammography (CEM).

Key word: contrast mammography, iodine contrast medium

Uvod

Kontrastna mamografija predstavlja slikovnu rendgenološku endografsku dijagnostičku metodu pregleda dojke uz pomoć jodnog kontrastnog sredstva (JKS) aplikovanog intravenskim (iv) putem. Izvodi se na isti način kao i standardna mamografija, samo što se iv putem aplikuje JKS. Dakle, jednim pregledom objedinjuju se nativna i kontrastna mamografija. Kontrastna mamografija bazira na činjenici da tumor tokom rasta razvijaja svoju prokrvljenost, koja doprinosi da se tumor preboji JKS. Intravenski aplikovano JKS pojačava kontrast tumorske lezije u odnosu na okolno tkivo dojke.

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Sinonimi: kontrastno pojačana mamografija, kontrastna spektralna mamografija, intravenska mamografija (IVM) (engleski: Contrast-enhanced mammography-CEM).

BIRADS klasifikacija olakšava tumačenje nalaza kontrastne mamografije [1-12].

Za izvođenje kontrastne mamografije neophodna je primena JKS. U primeni je rendgensko mamografsko hidrosolubilno nejonsko jodno kontrastno sredstvo jopromid u koncentraciji od 300 i 370 mg /ml joda, koje se u prometu nalazi pod imenom Ultravist 300® i 370® (Bayer).

Intravenska injekcija jodnog kontrasta za mamografiju zahteva slične mere opreza koje se preduzimaju kod drugih endografskih pregleda [4].

Za odraslu osobu kod kontrastne mamografije doza Ultravist-a® iznosi 1,5 ml/kg telesne težine.

Kontrastno sredstvo se aplikuje iv. putem preko plasirane i fiksirane braunile ručno u vidu bolusa ili putem injektora, po mogućnosti putem automatskog injektora.

Vreme pregleda je kratko, sveukupno oko 10 minuta.

Nakon dva minuta od davanja iv injekcije JKS, bolesnica se dovodi do mamografskog aparata, postavlja i pozicionira kao za standardnu nativnu mamografiju. U kojih 10 minuta, čine se uobičajeni kraniokaudalni (CC) i mediolateralni kosi (MLO) mamogrami obe dojke (pri čemu je svaki mamogram sastavljen od nisko- i visoko energetskog mamograma). Kombinacijom ova dva mamograma softverskim putem omogućava se dobijanje novog kontrastnog mamograma na kojem se lako uočava prisustvo kontrasta.

Tokom kontrastne mamografije, tokom jedne iste kompresije, potrebna su nam dve ekspozicije po projekciji. Dakle, svaka ekspozicija sa drugačijom energijom x-zraka, a to je tehnički moguće uz primenu digitalnih mamografskih jedinica. Ovo poslednje rezultuje niskoenergetskim mamogramom (što je identično nativnom mamogramu), i visokoenergetskim mamogramom (koji raspolaže informacijama o distribuciji JKS u dojkama).

Ovakvo korišćenje različitih energija x-zraka je nazvana spektralna mamografija.

Kontrastna mamografija pokazuje visoku dijagnostičku efektivnost i senzitivnost u otkrivanju karcinoma dojke. Između ostalog, kontrastna mamografija pokazuje sličnost u efektivnosti i senzitivnosti tumora dojke u poređenju sa magnetnom rezonancom dojke (MRD), uz manje procenat lažno pozitivnih rezultata. Zato, primena kontrastne mamografije zahteva sve veću primenu u svakodnevnom radu, od potencijalne primene u skriningu kod žena sa gustim tkivom dojke do određivanja stadijuma malignita dojke. Ovo poslednje činjenice ukazuju na dobro poznavanje ove metode pregleda dojke i njenu svakodnevnu implementaciju.

Kontrastna mamografija se primenjuje u cilju procene i detekcije poznatih i suspektnih lezija na dojci kao dodatak mamografiji sa ultrazvukom ili bez ultrazvuka, ili kao alternativa oslikavanju magnetnom rezonancijom, kada je magnetna rezonancija kontraindikovana ili nedostupna.

Klinička vrednost kontrastne mamografije se ogleda u činjenici da služi kao alat praćenju i pojašnjavanju kliničkih sumnjivih i nejasnih nalaza nakon mamografskih pregleda, u prethirurškoj proceni i određivanju stadijuma raka dojke, kada je magnetna rezonanca kontraindikovana i nedostupna.

Bolesnice kod kojih nalazimo vidljive mase, mikrokalcifikacije, asimetriju ili arhitektonska izobličenja mogu imati koristi od dodatnog rendgengrafiranja kontrastnom mamografijom.

Kontrastna mamografija ima potencijal da potvrdi ili isključi leziju, ili da otkrije dodatne lezije sa visokom specifičnošću.

Kontrastna mamografija u prethirurškoj proceni i određivanju stadijuma raka dojke pre svake operacije ključno i jasno otkriva razumevanje obima i mesta lezije u dojci.

Kontrastna mamografija pokazuje bolju procenu opsega bolesti u upoređivanju sa standardnom nativnom mamografijom, sličnu tačnost kao i magnetna rezonancija dojke u prethiruškoj proceni i određivanju stadijuma bolesti kod bolesnica sa rakom dojki, visoku čitljivost i izmenu hirurškog plana u gotovo 20% bolesnica.

Kontrastna mamografija može biti alternativa oslikavanju magnetnom rezonancijom kod žena sa srčanim pejsmejkerima, metalnim implantatima, klaustrofobijom, ili kada je magnetna rezonancija dojke nedostupna.

Međutim, kada je reč o zračenju kod kontrastne mamografije, može se reći da u zavisnosti od strukture i debljine tkiva dojke, kontrastna mamografija uzrokuje povećanje doze zračenja od oko 20%, ali (i tada) oba snimka i dalje nose dozu zračenja koja je manja od preporučene [6, 7].

Doza zračenja zavisi od gustoće dojke i vrste uređaja za mamografiju.

Ukupna doza zračenja kod kontrastne mamografije manja je od granice definisane međunarodnim smernicama za mamografiju (ispod 3 mGy).

Zaključak

Kontrastna mamografija predstavlja slikovnu rendgenološku endografsku dijagnostičku metodu pregleda dojke uz pomoć jodnog kontrastnog sredstva (JKS) aplikovanog intravenskim (iv.) putem. Izvodi se na isti način kao i standardna mamografija, samo što se iv. putem aplikuje JKS.

Jednim pregledom objedinjena je nativna i kontrastna mamografija.

Kontrastna mamografija bazira na činjenici da tumor tokom rasta razvija svoju prokrvljenost, koja doprinosi da se tumor preboji JKS. Intravenski aplikovano JKS pojačava kontrast tumorske lezije u odnosu na okolno tkivo dojke.

Kontrastna mamografija ima potencijal da potvrdi ili isključi leziju, ili da otkrije dodatne lezije sa visokom specifičnošću.

Klinička vrednost kontrastne mamografije se ogleda u činjenici da služi kao alat praćenju i pojašnjavanju kliničkih sumnjivih i nejasnih nalaza nakon mamografskih pregleda, u prethirurškoj proceni i određivanju stadijuma raka dojke, kada je magnetna rezonanca kontraindikovana i nedostupna.

BIRADS klasifikacija olakšava tumačenje nalaza kontrastne mamografije.

Literatura:

1. Babić R: Tumačenje mamografija po BI-RADSU. Apollenum Medicum et Aesculapium 2023: 21(1);40-51.
2. Babić R, Babić S, Stankov S, Mitrović K, Babić N, Jevremović A: Mamografski kardinalni znaci. Apollenum Medicum et Aesculapium 2023:21(2);79-83.
3. Babić R: Dopunske dijagnostičke mamografske procedure. Apollenum Medicum et Aesculapium 2023:21(2);84-86.
4. Babić RR: Neželjene pojave od kontrastnih sredstava pri urografiji sa predlogom mera za smanjenje rizika. Doktorska disertacija. Univerzitet. Beograd. 1998.
5. Mamografija: Preporuke evropskog udruženja za imidžing dojke o informisanju žena. https://www.europadonna.org.rs/sr/aktuelnosti/eusobi/27-mamografija-preporuke-evropskog-udruzenja-za-imidzing-dojke-o-informisanju-zena (poslednje otvaranje: mart 2025)
6. Jeukens CRLPN, Lalji UC, Meijer E et al. Radiation exposure of contrast-enhanced spectral mammography compared with full-field digital mammography. Invest Radiol. 2014; 49:659–665.
7. Tagliafico AS, Bignotti B, Rossi F et al. Diagnostic performance of contrast-enhanced spectral mammography: systematic review and meta-analysis. Breast. 2016; 28:13–19
8. Luczynska E, Piegza T, Szpor J, Heinze S, Popiela T, Kargol J, et al. Contrast-Enhanced Mammography (CEM) Capability to Distinguish Molecular Breast Cancer Subtypes. Biomedicines. 2022;10(10):2384.
9. Sung H, Ferlay J, Siegel R.L, Laversanne M, Soerjomataram I, Jemal A, et al.. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J. Clin. 2021;71:209–249.
10. Grigoryants NF, Sass S, Alexander J. Novel Technologies in Breast Imaging: A Scoping Review. Cureus. 2023;15(8):e44061.
11. Steyerova P, Burgetova A. Current imaging techniques and impact on diagnosis and survival —a narrative review. Annals of Breast Sur. 2022; 6: 25.
12. Matas A: Kontrastna mamografija. Diplomski rad. Sveučilište u Splitu. 2022.

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UTICAJ GOJAZNOSTI NA KRVNI PRITISAK

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SAŽETAK

Epidemija gojaznosti je širom sveta u stalnom porastu,pa se gojaznost svrstava među vodeće bolestisavremene civilizacije. Svako povećanje telesne težine za 10 % i više od idealne označava se kao gojaznost. Povećanje telesne mase za 10 kg dovodi do viših nivoa sistolnog krvnog pritiska u proseku za 4,5 mmHg. Osim što spada u glavne faktore rizika za nastanak široke lepeze kardiovaskularnih oboljenja, ona deluje i indirektno, uzrokujući druge bolesti. Pri tome se 70% novootkrivenih slučajeva sa esencijalnom hipertenzijom povezuje sa viškom telesne mase. Gojaznost povećava verovatnoću pojave raznih oboljenja, naročito srčanih oboljenja, dijabetesa tipa 2, opstruktivne apneje tokom sna, određenih vrsta raka, artroze i astme. Gojaznost se pored pušenja, dislipidemije, dijabetesa, fizičke neaktivnosti, starosti preko 60 godina i dr. ubraja u glavne faktore rizika u razvoju arterijske hipertenzije.

Ključne reči: gojaznost, faktori rizika, krvni pritisak

SUMMARY

The obesity epidemic is constantly increasing all over the world, so obesity ranks among the leading diseases of modern civilization. Any increase in body weight by 10 %more than ideal is marked as obesity. An increase in body weight by 10 kg (22.046 Ib) leadsto higher levels of systolic blood pressure by an average of 4,5 mmHg. Apart from being one of the main risks factors for a wide rang of cardiovascular diseases, it also acts indirectly, causing other illness. According to this 70 % of newly discovered cases with essential hypertension are associated with excess body weight. Obesity increases the possibilityof various diseases, especially theat diseases, type 2 diabetes, obstructive sleep apnea, certain type of cancer, arthrosis and asthma. Along with smoking, dyslipidemia, diabetes, physical inactivity, age over 60, obesity is one of the leading risk factors in the development of arterial hypertension.

Key words: obesity, risk factors, blood pressure

Uvod

Gojaznost (lat.obesitas) je hronična bolest, patološko stanje i sindrom koji se ispoljava prekomernim nakupljanjem masti u organizmu i povećanje telesne težine. Na osnovu podataka The Framingham Heart Study prevalenca hipertenzija među gojaznim osobama iznosi oko 50%.

Svetska zdravstvena organizacija (SZO) objavila je svoj prvi izveštaj o razarajućem globalnom uticaju viskog krvnog pritiska. Hipertenzija pogađa jednu od tri odrasle osobe. Broj ljudi sa hipertenzijom (krvni pritisak od 140/90 mmHg ili viši) udvostručio se između 1990. i 2019. godine, sa 650 miliona na 1,3 milijarde [1].

Veliki broj studija ukazuje na porast stopa morbiditeta i mortaliteta od kardiovaskularnih bolesti već od nivoa 115/75 mmHg, pri čemu svako povećanje krvnog pritiska za 20/10 mmHg duplira taj rizik [2].

Povišeni krvni pritisak kod gojaznih osoba nastaje zbog povećanja vaskularnog prostora tj. novostvorenih krvnih sudova u masnom tkivu što dovodi ido značajno većeg udarnog volumena srca .Međutim, hipertenzija ovde ne nastaje sama po sebi, jer bi u tom slučaju sve gojazne osobe imale visok krvni pritisak. Mehanizam pomoću kojih gojaznost indukuje hipertenziju su multifaktorijelni i kompleksni. Neki od najznačajnijih patofizioloških zbivanja su povećana reapsorcija soli, povećanje ekstracelularne tečnosti ,promene u natriurezi [3].

Postoje dva osnovna tipa gojaznosti: visceralna (centralna, abdominalna, muška) androidni ili (oblik jabuke) tip gojaznosti i ginoidna (gojaznost donjeg dela tela, periferna, ženska) ili

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gojaznost tipa kruške [4]. Odlučujuću ulogunaštetnost po zdravlje ima centralni tip gojaznosti. Zato pri utvrđivanju gojaznosti treba meriti obim struka i ukoliko je on preko 88 cm kod žena ili preko 102 cm kod muškaraca govori se o centralnoj gojaznosti [4]. Centralni tip gojaznosti koji praćen insulinskom rezistencijom dovodi do niza metaboličkih procesa i poremećaja, povećavajući time rizik od nastanka kardiovaskularnih oboljenja. Između ostalog hiperinsulinemija aktivira osovinu renin-angiotenzin-aldosteron koji dovodi do povećanja perifernog otpora i hipervolemije, što rezultuje arterijskom hipertenzijom [5, 6].

Hiperinsulinemija povećava tubulsku reapsorciju natrijuma u bubrezima, stimuliše simpatički nervni sistem, povećava lučenje kateholamina i remeti transmembranski transport jona, čime dovodi do porasta intracelularnog kalcijuma. Kateholamini, i to posebno norepinefrin, imaju snažno vazokonstriktorno dejstvo na periferiji, naročito u mišićima, što zajedno sa ubrzanim procesima ateroskleroze vodi ka smanjivanju volumena samih krvnih sudova i povećanju perifernog otpora. Dokazi za ovo leže u činjenici da su kod gojaznih osoba pronađeni značajno veći nivoi i renina i norepinefrina. Dokazano je da promena stila života i dijeta sa redukcijom soli, bogata voćem i dijetnim vlaknima a siromašna zasićenim mastima, dovode do značajne redukcije vaskularnog rizika. Pri tome se pulsni pritisak pojavljuje kao jak prediktor tog rizika I često označava markerom ateroskleroze [5, 6]. Takođe su i rezultati pomenute Framinghamske studije ukazali na visoku linearnu relaciju između hipertenzije, povećane telesne mase i nastanka koronarne smrti. Ovaj rizik značajno raste kod žena čiji je IMT>25, a kod muškaraca>26,5 kg/m2 [7]. Istovremeno veliki broj studija je pokazao da redukcija telesne mase dovodi kako do sniženja krvnog pritiska tako i nivoa lipida, bolje regulacije glikemije, otklanjanja simptoma depresije i anksioznosti tj. povezanosti sa psihopatologijom jedenja. Prosečan gubitak na telesnoj masi od 6,5% smanjuje arterijski pritisak za 11,1/5,8 mmHg, nivo triglicerida za 94 mg/L, glukoze za 17 mg/L i ukupnog holesterola za 37 mg/L [8, 9].

Osobe se smatraju gojaznim kada njihov indeks telesne mase (engleski: body mass index, BMI), mera koja se dobija kada se telesna masa osobe u kilogramima podeli kvadratom visine te osobe u metrima, prekorači 30 kg/m^2.

BMI(kg/m^2)s	Stanje uhranjenosti
<20	Nedovoljna uhranjenost
20-24,9	Normalna uhranjenost
25-29,9	I stepen gojaznosti
30-39,9	II stepen gojaznosti
>40 III	stepen gojaznosti

Cilj

Najvažniji ciljevi kod većine istraživanja o uticaju gojaznosti na krvni pritisak u bolesnika sa viškom telesne mase su sledeći:

- Prikaz uticaja vrednosti indeksa mase tela, holesterolemije, trigliceremije i glikemije kod predgojaznih i gojaznih hipertenzičara.
- Prikaz uticaja pola i godina života na zastupljenost I karakteristike arterijske hipertenzije.

Metod

Istraživanje i rad o uticaju gojaznosti na krvni pritisak zasnovan je na osnovu sprovedene “Studije otklanjanja i supresije gojaznosti” na krvni pritisak, kod bolesnika sa viškom telesne mase. Studija je sprovedena (2003-2004) na teritoriji opštine Lebane u trajanju od 6 meseci. Studijom je obuhvaćeno 61 bolesnik oba pola, starosti 25-64 godina, kod kojih je na prvom pregledu nađeno povećanje telesne mase tj. IMT>26 kg/m^2.

Rezultati

Rezultati tokom interventne “Studije otklanjanja i supresije gojaznosti” na krvni pritisak pokazuju da je od 61 bolesnika oba pola 44 (72,13 %) bilo žena. Prosečna starost iznosila je 49,7 + -9,2 godina, s tim da su žene nešto starije životne dobi od muškaraca (50,8+-8,4 prema 46,7+-10,7). Od ukupnog broja predgojaznih i gojaznih bolesnika 63,93% već boluje od povišenog krvnog pritiska. Posebno je zastupljenost

ovog komorbiteta izražena kod žena (75,50% prema 35,29%). Najviše zastupljena je sistolno-dijastolna (42,26%) a zatim slede izolovana sistolna (16,39%) i izolovana dijastolna hipertenzija (1,64%).Više od polovine žena boluje od kombinovane sistolne-dijastolne hipertenzije (52,27%) dok muškarci pokazuju podjednaku zastupljenost te izolovane sistolne hipertenzije (po 17,65%). Sa godinama života dolazi do postepenog povećanja učestalosti sistolne i dijastolne hipertenzije tako da je ona najveća kod osoba starosti 55-64 godina. Najveći broj osoba sa viškom telesne mase imao je sistolni krvni pritisak >160 mmHg (40,98%). Zastupljenost osoba sa viškom telesne mase imao je dijastolni krvni pritisak>91 mmHg (31,15%).

Diskusija

Gojaznost se pored pušenja, dislipidemije, dijabetesa, fizičke neaktivnosti, starosti preko 60 godina i dr. ubraja u glavne faktore rizika u razvoju arterijske hipertenzije [5, 6]. Pri tome povećanje telesne mase za 10 kg dovodi do viška novoa sistolnog krvnog pritiska u proseku za 4,5 mmHg [3]. S druge strane povećanje krvnog pritiska za 20/10 mmHg duplira rizik za porast stopa morbiditeta i mortaliteta od kardiovaskularnih bolesti [2]. Takođe je dokazano da promena stila života i dijeta sa redukcijom soli, bogata voćem i dijetnim vlaknima a siromašna zasićenim mastima, dovode do značajne redukcije vaskularnog rizika [5, 6]. Veliki broj studija je pokazao da redukcija telesne mase dovodi kako do sniženja krvnog pritiska tako i nivoa lipida, bolje regulacije glikemije, otklanjanja simptoma depresije i anksioznosti [8, 9]. Najviše je zastupljena sistolno-dijastolna (42,62%), a zatim izolovana sistolna (16,39%) i izolovana dijastolna hipertenzija (1,64%). Više od polovine žena boluje od kombinovane sistolno-dijastolne hipertenzije (52,27%) dok muškarci pokazuju podjednaku zastupljenost te i izolovano sistolne hipertenzije (po17,65%). Posle primenjenih dijetskih mera i poboljšanjem aktivnosti prvenstveno s ciljem smanjivanja i otklanjanja gojaznosti kao oboljenja i faktora rizika, došlo je do signifikantne redukcije broja bolesnika sa povišenim vrednostima krvnog pritiska što su rezultati koji se poklapaju sa objavljenim svetskim studijama [5, 7]. Dokazano je da sa godinama života dolazi do postepenog povećanja učestalosti sistolne i dijastolne hipertenzije tako da je ona najveća kod osoba starosti 55-64 godina. Uticaj starosti na prosečne vrednosti krvnog pritiska je očigledan samo kod sistolnog krvnog pritiska, što verovatno ukazuje na čvršću korelaciju gojaznosti i povišene dijastolne tenzije.

Zaključak

Arterijska hipertenzija je značajan problem osoba sa viškom telesne mase s obzirom na to da gotovo dve trećine njih već boluje od ovog komorbiteta gojaznosti. Ovo ukazuje na visoku korelaciju između ova dva oboljenja. Povišeni krvni pritisak je signifikantno više zastupljen kod predgojaznih i gojaznih žena što je posledica činjenice da je kod njih i prekomerena telesna masa značajniji problem u odnosu na muškarce. Sa godinama života dolazi do postepenog povećanja učestalosti sistolne i dijastolne hipertenzije kao i prosečnih vrednosti sistolnog krvnog pritiska .Kod osoba sa viškom telesne mase najviša je zastupljenost kombinovane sistolno-dijastolne hipertenzije. Više od dve trećine osoba sa viškom telesne mase je imalo sistolni krvni pritisak >140 mmHg. Polovina predgojaznih i gojaznih osoba je imalo dijastolni krvni pritisak >91 mmHg.

Literatura

1. First WHO report details devastating impact of hypertension and ways to stop ithttps://www.who.int/news/item/19-09-2023-first-who-report-details-devastating-impact-of-hypertension-and-ways-to-stop-it
2. Brookes L: The seyenth report of the Joint National Committee on prevention, detection, evaluation, and the treatment of high blood pressure-the NHLBI JNS 7 Press conference. MEDSCAPE CARDIOLOGY,7(1),2003.(http://www.medscape.com/viewarticle/455849).
3. Wofford M R, Davis M M, Harkins K G and all: Therapeutic consideration in thetreatment of obesity hypertension. JOURNAL of CLINICAL HYPERTENSION,4 (3):189-196, 2002.
4. Ilić S, urednik. Interna medicina. Niš: Medicinski fakultet Univerziteta u Nišu;2023.1136

5. Žigić D, Ivanković D Lapčević M: Arterijska hipertenzija i Kardiologija u radu porodičnog lekara. Sekcija opšte medicine SLD-a i Katedra opšte medicine Medicinskog fakulteta Univerziteta u Beogradu, Beograd 2002.
6. Basile J N, Johnson R H: Hypertension 2001: How will JNC VII be different from JNC VI SOUTHERN MEDICAL JOURNAL, 94 (9) 889-890 2001.
7. Rashid M N, Fuentes F, Touchon R S and P. Wehner P S: Obesity and the risk for cardiovascular disease. PREVENTIVE CARDIOLOGY, 6 (!): 42-47,2003-
8. Bevoni L: Management of adult obesity. CLINICAL REVIEWS,13 (5):5 6-62, 2003.
9. Ivković L: Gojaznost, Novi Sad, 2004.

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UPUTSTVO AUTORIMA

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Struktura rada. Svi podnaslovi se pišu velikim slovima i boldovano. Originalni rad treba da ima sledeće podnaslove: Uvod, Cilj rada, Metode rada, Rezultati, Diskusija, Zaključak, Literatura. Prikaz bolesnika čine: Uvod, Prikaz bolesnika, Diskusija, Literatura. Ne treba koristiti imena bolesnika ili inicijale, brojeve istorije bolesti, naročito u ilustracijama.

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Organizacija kao autor:

Diabetes Prevention Program Research Group. Hypertension, Insulin, and proinsulin in participants with impaired glucose tolerance. Hypertension. 2002; 40 (5): 679-86.

Nijedan autor nije dat:

21st century heart solution may have a sting in the tall. BMJ. 2002; 325 (7357): 184.

Volumen sa suplementom:

Glauser TA. Integrating clinical trial data into clinical practice. Neurology. 2002; 58 (12 Supll 7): S6-12.

Knjiga:

Murray PR, Rosenthal KS, Kobayashi GS, Pfaller MA. Medical microbiology 4th ed. St Louis: Mosby; 2002.

Poglavlje u knjizi:

Meltzer PS, Kalloiniemi A, Trent JM. Chromosome alterations in human solid tumors. In: Vogelstein B, Kinzler KW, editors. The genetic basis of human cancer. New York : McGraw-Hill; 2002. p. 93-113

Disertacija:

Borkowsky NM. Infant sleep and feeding: a telephone survey of Hispanic Americans [dissertation].

Mount Pleasant (MI): Central Michigan University; 2002.

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Eatright.org [Internet], Chicago: Academy of Nutrition and Dietetics; c2016 [cited 2016 Dec 27]. Available from: https:// www.eatright.org/

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Tabele. Tabele se označavaju arapskim brojevima po redosledu navođenja u tekstu. Tabele raditi isključivo u Wordu. Korišćene skraćenice u tabeli treba objasniti u legendi ispod tabele. Svaku tabelu odštampati na posebnom listu papira i dostaviti po jedan primerak uz svaku kopiju rada.

Skraćenice. Koristiti samo kada je neophodno i to za veoma dugačke nazive hemijskih jedinjenja, odnosno nazive koji su kao skraćenice već prepoznatljivi (standardne skraćenice, kao npr. DNK, sida, HIV, ATP). Za svaku skraćenicu pun termin treba navesti pri prvom navođenju u tekstu, sem ako nije standardna jedinica mere. Ne koristiti skraćenice u naslovu. Izbegavati korišćenje skraćenica u kratkom sadržaju, ali ako su neophodne, svaku skraćenicu ponovo objasniti pri prvom navođenju u tekstu.

Decimalni brojevi. U tekstu rada decimalne brojeve pisati sa zapetom. Kad god je to moguće, broj zaokružiti na jednu decimalu.

Jedinice mera. Dužinu, visinu, težinu i zapreminu izražavati u metričkim jedinicama (metar -m, kilogram - kg, litar - l) ili njihovim delovima. Temperaturu izražavati u stepenima Celzijusa (°C), količinu supstance u molima (mol), a pritisak krvi u milimetrima živinog stuba (mm Hg). Sve rezultate hematoloških, kliničkih i biohemijskih merenja navoditi u metričkom sistemu, prema Međunarodnom sistemu jedinica (SI).

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- sve margine 2,5 cm
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- uvlačenje pasusa 10 mm
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- Conclusion
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