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ABOUT JOURNAL

Aim and scope

Annales Medicinae Urgentis (AMU) is a open-access peer reviewed medical journal published by the Croatian Society for Emergency Medicine that aims to improve the care of patients with emergency and critical illness by acquiring, discussing, distributing, and promoting evidence-based information relevant to emergency physicians and intensivists.

It publishes original original articles, reviews, case reports, meta-analysis, comments, methodologies, perspectives/ viewpoints, editorials, images, news, communications, letters to the editor, etc with no restrictions on the maximum length of manuscripts, provided that the text is concise and comprehensive. The AMU uses the Diamond Open Access model. This means that there are NO author processing fees and no fees to access the published papers.

HLZ - HRVATSKO DRUŠTVO ZA HITNU MEDICINU
CMA - CROATIAN SOCIETY OF EMERGENCY MEDICINE

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ANNALES MEDICINAE URGENTIS: *MESSAGE FROM THE EDITORS*

Prof. Višnja Nesek Adam, MD, PhD

Prof. Ivan Gornik, MD, PhD

Dear Colleagues,

With great joy and pride, we are pleased to present the third issue of *Annales Medicinae Urgentis*, the official open-access, peer-reviewed journal of the Croatian Medical Association – Croatian Society of Emergency Medicine (CMA–CSEM). Each new issue is an important milestone in the development of our journal and reflects our ongoing commitment to advancing emergency and critical care medicine.

With every issue, we move closer to meeting the criteria for inclusion in international bibliographic and citation databases. This progress reflects not only the increasing quality and relevance of our published work but also the continuous refinement of our editorial processes and standards.

A major advancement introduced in this issue is the implementation of a fully automated manuscript submission and tracking system, designed to enhance transparency, communication, and efficiency throughout the editorial process. In addition, *Annales Medicinae Urgentis* now operates under a double-blind peer-review system, ensuring impartial evaluation and further strengthening the scientific integrity of the journal. These measures represent an important step forward, elevating the journal to a higher professional and academic level.

This issue features a rich variety of contributions, including original research, reviews, case reports, and other scholarly works relevant to emergency and intensive care practice. Together, these articles showcase the growing scientific engagement of our community and reaffirm the journal's role as a platform for knowledge exchange, evidence-based discussion, and professional development.

We deeply thank our authors for their trust, our reviewers for their careful and constructive evaluations, and our editorial team for their dedication and hard work. Your efforts are essential in shaping *Annales Medicinae Urgentis* into a credible, visible, and internationally recognized journal.

We warmly encourage all members of the emergency and critical care community to actively engage with the journal. Submit your research, share your clinical insights through reviews or case reports, participate in peer review, or simply engage in discussions and spread knowledge. Every contribution, no matter how small it may seem, strengthens the journal, enriches our community, and ultimately helps improve patient care. Your voice, expertise, and experience are vital to shaping the future of emergency medicine.

Looking ahead, we remain confident that with continued commitment to quality, ethical rigor, and collaborative effort, *Annales Medicinae Urgentis* will continue to grow in impact and recognition. Each issue brings us closer to our shared goal of international indexing and visibility, fostering a stronger, more connected, and evidence-driven community.

Thank you for being an active part of this journey. Together, through curiosity, collaboration, and dedication, we can advance the practice of emergency and critical care medicine and make a meaningful difference for patients around the world.

Warm regards,

Prof. Višnja Nesek Adam, MD, PhD
and *Prof. Ivan Gornik, MD,PhD*
Editors-in-Chief, Annales Medicinae Urgentis

ORIGINAL ARTICLE / IZVORNI ZNANSTVENI ČLANAK

CAN THE ADDITION OF A URINE TEST STRIP FACILITATE THE DIAGNOSIS OF AN ACUTE APPENDICITIS? A DIAGNOSTIC ACCURACY STUDY

MOŽE LI DODATAK TEST TRAKICE ZA URIN OLAKŠATI DIJAGNOZU AKUTNE UPALE CRVULJKA? ISTRAŽIVANJE DIJAGNOSTIČKE TOČNOSTI

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Abstract

Background: In our previous case-control retrospective pilot study we concluded that acute appendicitis may be successfully ruled in with high accuracy based on elevated WBCs and negative urine test strip in combination with presented clinical symptoms. We aimed to validate and assess the diagnostic accuracy of a newly proposed scoring system incorporating urinalysis.

Participants and methods: From June 2018 to May 2020, a total of 176 adult patients with suspected acute appendicitis were prospectively enrolled in a diagnostic accuracy study.

Results: The logistic regression on the entire group of patients revealed the significance of the addition of urine test strip results to standard laboratory variables (WBC and neutrophils%) only in the group of male patients.

Conclusion: Future studies should focus on validating the newly proposed scoring system incorporating urinalysis in larger, multicenter cohorts. The ultimate goal remains the development of accurate, practical tools that support timely decision-making while minimizing unnecessary imaging and surgery.

Keywords: acute appendicitis; Alvarado score; diagnostic accuracy study; scoring system; urine test strip

Sažetak

Uvod: U našem prethodnom retrospektivnom pilot-istraživanju s dizajnom slučaj-kontrola zaključili smo da se akutna upala crvuljka može s visokim stupnjem pouzdanosti potvrditi na temelju povišenog broja leukocita te negativne test trake mokraće u kombinaciji s prisutnim kliničkim simptomima. Cilj ovog istraživanja bio je provjeriti i procijeniti dijagnostičku točnost novopredloženog bodovnog sustava koji uključuje analizu mokraće.

Ispitanici i metode: Od lipnja 2018. do svibnja 2020. prospektivno je obuhvaćeno ukupno 176 odraslih bolesnika sa sumnjom na akutnu upalu crvuljka. Postupak je proveden kao ispitivanje dijagnostičke točnosti.

Rezultati: Logistička regresija na cijeloj skupini bolesnika pokazala je da dodavanje nalaza test trake mokraće standardnim laboratorijskim pokazateljima (broj leukocita i udio neutrofila) doprinosi dijagnostičkoj vrijednosti samo u skupini muških bolesnika.

Zaključak: Buduća istraživanja trebala bi biti usmjerena na potvrđivanje vrijednosti novopredloženog bodovnog sustava koji uključuje analizu mokraće u većim, multicentričnim istraživanjima. Cilj ostaje razvoj pouzdanih i praktičnih alata koji podupiru pravodobno donošenje kliničkih odluka uz smanjivanje potrebe za nepotrebnim podvrgavanjima slikovnim tehnikama i kirurškim zahvatima.

Ključne riječi: akutna upala crvuljka; Alvaradov bodovni sustav; bodovni sustav; dijagnostička točnost; test traka mokraće

Introduction

Suspected acute appendicitis is one of the most common indications for emergency surgery in abdominal surgery (1). Given that the procedure itself is technically relatively simple and considering the fact that neglected appendicitis is accompanied by a high morbidity rate, surgeons have a low threshold for operation if there is any suspicion of appendicitis, which results in a relatively high rate of acceptable negative appendectomies (up to about 15%) (2). Imaging methods in terms of ultrasound or MSCT can be of significant use in the diagnosis of acute appendicitis, but with certain limitations. In the adult population, unlike children, ultrasound has very limited value. On the other hand, MSCT has a high sensitivity in the diagnosis of acute appendicitis, but due to the unavailability and cost of the examination, as well as the significant harmful radiation, this examination could not be established as a routine examination in cases of suspected acute appendicitis (3). For all of the above, decision-making in cases of suspected acute appendicitis still relies predominantly on the surgeon's clinical assessment, which is based on data from the physical examination, medical history, and laboratory tests (4). Given the rather wide differential diagnosis of abdominal pain, numerous scoring systems have been proposed with the aim of facilitating the correct decision-making in the diagnosis of acute appendicitis. Unfortunately, none of them has proven to be ideal (5,6). One of the most popular is certainly an Alvarado scoring system (7), designed in 1986, that combines certain clinical and laboratory parameters (Table 1). In our previously published case-control retrospective pilot study, we concluded that acute appendicitis in emergency settings may be successfully ruled in with high accuracy based on elevated WBCs and negative urine test strip in combination with presented clinical symptoms (8). We also observed that CRP did not contribute to the overall diagnostic accuracy, in contrast to previously published studies. Based on our preliminary findings we have prepared a prospective diagnostic accuracy study protocol with two distinct objectives:

(1) To evaluate the diagnostic accuracy of the Alvarado score within our patient population and determine its usefulness as a decision-support tool for surgeons when considering operative management. The results of this objective were published in Acta Chirurgica Belgica Journal in 2024 (9).

(2) To validate and assess the diagnostic accuracy of a newly proposed scoring system incorporating urinalysis in addition to other clinical and laboratory parameters (Table 2).

This study was built upon a previously published case-control pilot study, aiming to validate its preliminary findings.

Table 1. Alvarado score for diagnosis of acute appendicitis (7)

	Alvarado Score	Point*
Symptoms	Migratory right iliac fossa pain	1
	Anorexia	1
	Nausea/vomiting	1
Signs	Tenderness in right iliac fossa	2
	Rebound tenderness	1
	Elevated temperature	1
Laboratory findings	Leukocytosis (WBC >10x109/L)	2
	Shift to the left of neutrophils (>70%)	1
Total		**10**

* For each of the present symptoms, signs or laboratory findings, an adequate number of points is assigned. A score of 5 or 6 is compatible with the diagnosis of acute appendicitis. A score of 7 or 8 indicates a probable appendicitis. A score of 9 and 10 indicates a very probable appendicitis.

Table 2. A newly proposed score for diagnosis of acute appendicitis, including urinalysis

	Alvarado Score	Point*
Symptoms	Migratory right iliac fossa pain	1
	Anorexia	1
	Nausea/vomiting	1
Signs	Tenderness in right iliac fossa	2
	Rebound tenderness	1
	Elevated temperature	1
Laboratory findings	Leukocytosis (WBC >10x109/L)	2
	Shift to the left of neutrophils (>70%)	1
	Urine test strip negative	1
Total		**11**

* For each of the present symptoms, signs or laboratory findings, an adequate number of points is assigned. A score of 8 or 9 indicates a probable appendicitis.

Materials and Methods

Subjects

From June 2018 to May 2020, a total of 176 adult patients with suspected acute appendicitis were prospectively enrolled in a diagnostic accuracy study.

During the study period, all patients presenting to the Emergency Surgical Department of University Hospital Sveti Duh with right lower quadrant abdominal pain—and without a history of appendectomy—were evaluated by a single surgeon (author Branko Bakula, BB). Those deemed to have suspected appendicitis were included. The study received approval from the Hospital Ethics Committee, and written informed consent was obtained from all participants. The current paper addresses the second objective of the prospective study.

Methods

All patients underwent standard diagnostic evaluation, including a physical examination and collection of all variables required for the calculation of the Alvarado score (total white blood cell count (WBC), percentage of neutrophils). Additionally, the C-reactive protein concentrations (CRP) (immunoturbidimetry method on Beckman Coulter AU680 analyzer (Beckman Coulter, Brea, California, US) and urine test strip results (iChem Velocity Urine Chemistry Strips for in vitro use with the automated iChemVELOCITY System (Beckman Coulter, Brea, California, USA)) were also recorded. Positive findings of blood (≥0.3 mg/L) and/or leukocytes (≥25 WBC/μL) on the test strip were considered as a „positive“ result.

However, neither the Alvarado score nor the newly proposed scoring system incorporating urinalysis were not calculated during the initial assessment as surgical decision-making was based exclusively on clinical judgment and entirely independent of any scoring systems.

Urinalysis, traditionally used to exclude urinary tract pathology, may also play a complementary role in appendicitis assessment when integrated into structured diagnostic models.

Statistical analysis

Normality of data distribution was assessed using the Kolmogorov–Smirnov test. Patients were classified into groups with either confirmed or excluded acute appendicitis. Differences between the two groups were evaluated with the Mann–Whitney test for continuous variables and Fisher's exact test for categorical variables. Diagnostic accuracy metrics—sensitivity, specificity, positive predictive value, negative predictive value, and positive and negative likelihood ratios—were derived from 2×2 contingency tables. Logistic regression analysis was performed to evaluate if the CRP concentrations and urine test strip results were significant predictors of acute appendicitis, among other laboratory parameters already included in the Alvarado score. Statistical analyses were conducted using MedCalc Statistical Software version 16.2.0 (MedCalc Software bvba, Ostend, Belgium). A p-value of <0.05 was considered statistically significant.

Results

Comparison of basic demographic characteristics, as well as clinical and laboratory parameters between groups of patients with and without appendicitis was described in details in the previously published article that addressed the first objective of the prospective study (9). The comparison of additional laboratory parameters (urine test strip analysis and CRP) between groups of patients with and without appendicitis is shown in Table 3. CRP was significantly higher in acute appendicitis groups (68.0 vs 6.0 mg/L, P<0.0001). The comparison of proportions of

Table 3. Comparison of additional laboratory parameters between groups of patients with and without appendicitis

	APPENDICITIS NEGATIVE (N=126)	APPENDICITIS POSITIVE (N=50)	P*
CRP (mg/L) (median/IQR)	6.0 (1.4 – 28.7)	68.0 (29.9 – 131.0)	<0.0001
Urine test strip positive (N/proportion)	66 (0.52)	21 (0.42)	0.2813

*P<0.05 is considered statistically significant

positive findings of the urinalysis between groups revealed no statistically significant difference (P=0.2813).

Table 4.

The logistic regression on the entire group of patients revealed significance of all four included laboratory variables. However, when dividing patients according to gender, positive urine test strip remained statistically significant only in the group of male patients (Table 4). CRP, although significant in the whole group of selected patients, lost its significant in subgroups of patients stratified according to gender.

Table 5.

Considering the fact that urine test strip addition revealed significant in male subgroup of patients, a diagnostic accuracy study was performed for classical Alvarado scoring system and for a newly proposed scoring system including urinalysis. The comparison of diagnostic accuracy metrics is shown in Table 5.

Discussion

In this prospective study, we evaluated whether the addition of urinalysis could improve diagnostic accuracy for acute appendicitis beyond the parameters included in the traditional Alvarado score. Although the presence of blood and/or leukocytes on urine test strip analysis did not differ significantly between groups of patients with confirmed/rejected diagnosis of acute appendicitis, the logistic regression revealed the urine test strip analysis as a statistically significant negative variable in predicting acute appendicitis. While microscopic hematuria or pyuria can theoretically occur due to irritation of the ureter or bladder by an inflamed appendix (10), these findings

Table 4. The logistic regression in identifying the clinical relevance of the expanded panel of laboratory variables that will contribute to the diagnosis of acute appendicitis

Significant variable	Coefficient	P	Odds ratio	95% CI	Percent of cases correctly classified
All patients (N=176)					
WBC, 109*L	0.20230	0.0017	1.2242	1.0792 – 1.3888	**86.36 %**
Neutrophils, %	0.10733	0.0007	1.1133	1.0461 – 1.1848	
CRP, mg/L	0.00911	0.0109	1.0092	1.0021 – 1.0163	
Urine test strip positive	-0.95009	0.0502	0.3867	0.1494 – 1.0009	
Female patients (N=103)					
WBC, 109*L	0.22363	0.0061	1.2506	1.0658 – 1.4674	**86.41 %**
Neutrophils, %	0.00849	0.0370	1.0887	1.0051 – 1.1791	
Male patients (N=73)					
WBC, 109*L	0.02332	0.0043	1.0236	1.0073 – 1.0401	**93.15 %**
Neutrophils, %	0.26302	0.0006	1.3008	1.1197 – 1.5113	
Urine test strip positive	-4.03151	0.0029	0.0177	0.0012 – 0.2521	

WBC – white blood cell count
CRP – C-reactive protein
The three-step logistic regression was performed to identify the optimal combination of the expanded panel of laboratory variables in predicting the dichotomous outcome: the presence/absence of acute appendicitis.
Step 1: All laboratory variables included in the original Alvarado score (WBC + neutrophils%) plus the expanded panel (CRP and urine test strip) were tested in the whole group of enrolled patients which identified the statistically significant ones.
Step 2: All laboratory variables included in the original Alvarado score (WBC + neutrophils%) plus the expanded panel (CRP and urine test strip) were tested only in the group of female patients which identified the statistically significant ones.
Step 3: All laboratory variables included in the original Alvarado score (WBC + neutrophils%) plus the expanded panel (CRP and urine test strip) were tested only in the group of male patients which identified the statistically significant ones.

Table 5. Comparison of diagnostic accuracy metrics for Alvarado score and newly proposed urinalysis scoring system, in a subgroup of male patients

N=73	Criterion	Se (%) (95% CI)	Sp (%) (95% CI)	LR+ (95% CI)	LR- (95% CI)	PPV (95% CI)	NPV (95% CI)
Alvarado score	≥7	84.6 (65.1 – 95.6)	87.2 (74.3 – 95.2)	6.63 (3.08 – 14.25)	0.18 (0.07 – 0.44)	78.6 (59.1 – 91.7)	91.1 (78.8 – 97.5)
Urinalysis score	≥8	76.9 (56.4 – 91.0)	91.5 (79.6 – 97.6)	9.04 (3.46 – 23.62)	0.25 (0.12 – 0.51)	83.3 (62.6 – 95.3)	87.8 (75.2 – 95.4)

Criterion - This value corresponds with the number of positive findings in the scoring systems presented in Tables 1 and 2

Se – Sensitivity; Sp – Specificity; LR+ - Positive Likelihood Ratio; LR- - Negative Likelihood Ratio; PPV – Positive Predictive Value; NPV – Negative Predictive Value

are nonspecific and commonly seen in urinary tract infections or other causes of abdominal pain (11). As such, urinalysis has traditionally been used more as a tool to exclude urinary tract pathology (12) rather than to confirm appendicitis, which could explain the observed negative correlation. Interestingly, our gender-stratified logistic regression analysis showed that a negative urine dipstick result remained a significant predictor only among male patients. The inclusion of urinalysis increased specificity in diagnosis of acute appendicitis, however the sensitivity was being reduced. This finding may reflect gender-specific differences in the prevalence of alternative diagnoses (13).

Women more frequently present with gynecological or urinary conditions that can produce positive urine dipstick results, potentially obscuring any association with appendicitis (14). In contrast, men have fewer common alternative causes of abnormal urinalysis, which may make positive findings more specific in this subgroup. Although this observation is clinically relevant, it should be interpreted with caution, as it may be influenced by sample size and requires further validation in larger cohorts. As recommended by Kollias et al., further research should evaluate the influences that can predict postoperative outcomes following appendectomies between sexes and how to prevent/reduce their occurrence as it has been shown that women had a higher rate of negative appendectomies (13, 15).

Consistent with existing literature, CRP was significantly elevated in patients with appendicitis, reinforcing its role as a useful inflammatory marker in the diagnostic workup (16). However, as we already showed in our preliminary pilot study (8), the logistic regression did not identify CRP concentration as a significant contributor to the acute appendicitis diagnosis in our study, when stratified into subgroups according to gender. Perhaps the underlying cause includes the same information that WBC and CRP offer, and thus one variable becomes redundant. It is worth mentioning that CRP spanned up to remarkably high 416 mg/L in the group of patients without the diagnosis of acute appendicitis, while some acute appendicitis patients had normal CRP values. The observed is in line with the study performed by Atema et al. Who concluded that no WBC count or CRP level can safely and sufficiently confirm or exclude the suspected diagnosis of acute appendicitis in patients who present with abdominal pain of 5 days or less in duration (17). Hallan et al. cautions that CRP is a test of „medium accuracy“ with significant variability accross studies (18). Critically, Shakhatreh et al. Concluded that while CRP is helpful, it does not replace clinical surgical expertise (19). The test is most valuable as a complementary diagnostic tool, not a standalone diagnostic method.

Incorporating urinalysis into a modified scoring system may support more precise clinical decision-making and help reduce unnecessary imaging and surgery, although further validation in larger multicenter cohorts is required.

The strengths of our study include its prospective design, the inclusion of consecutive patients evaluated by the same surgeon, and the independent assessment of clinical decision-making without influence from scoring systems. These features reduce selection bias and increase internal validity. However, several limitations should be acknowledged. First, this was a single-center study, which may limit generalizability. Second, the number of patients within gender subgroups may not have been sufficient to fully assess interaction effects. Third, urine dipstick analysis, while rapid and inexpensive, lacks the precision of microscopic urinalysis or urine culture, which might have provided additional insight.

Future studies should focus on validating the newly proposed scoring system incorporating urinalysis in larger, multicenter cohorts. The ultimate goal remains the development of accurate, practical tools that support timely decision-making while minimizing unnecessary imaging and surgery.

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ORIGINAL ARTICLE / IZVORNI ZNANSTVENI ČLANAK

PHYSICIANS' AND NURSES' SATISFACTION WITH THE QUALITY AND EFFECTIVENESS OF PHYSIOTHERAPY CARE IN INTENSIVE CARE UNITS IN CROATIA

ZADOVOLJSTVO LIJEČNIKA I MEDICINSKIH SESTARA KVALITETOM I UČINKOVITOŠĆU FIZIOTERAPEUTSKE SKRBI U JEDINICAMA INTENZIVNE MEDICINE U HRVATSKOJ

Marko Martinović[2], *Snježana Benko Meštrović[1,2,3], Martin Ivanović[1], Antea Marković[4]

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Abstract

Introduction: Intensive Care Units (ICUs) provide advanced, evidence-based care for critically ill patients. Physiotherapy is a vital component of ICU care but is often unavailable or insufficiently standardized. This study examined physicians' and nurses' satisfaction with physiotherapy care in Croatian ICUs and identified potential areas for improvement.

Methods: A 26-item digital questionnaire was disseminated throughout Croatian ICUs to physicians and nurses. The items addressed included physiotherapy availability, equipment accessibility, satisfaction with the quality and effectiveness of care, and their perspectives on improvement. Responses were rated on a 5-point Likert scale or by selecting predefined options. Data analysis was performed using descriptive statistics in R Studio.

Results: In total, 120 participants from 12 Croatian counties were included. The majority of responses (105) were from nurses/technicians, and only 15 from physicians. Physiotherapists were available in all ICUs, mainly on a consultative basis and mostly during morning shifts. Participants reported that physiotherapy interventions were effective in reducing pain, improving joint mobility, and enhancing respiratory function. Despite high overall satisfaction, participants emphasized the need for extended physiotherapist availability, improved ICU-specific training, and greater professional autonomy.

Conclusion: Physicians and nurses expressed general satisfaction with ICU physiotherapy care but suggested improvements in physiotherapy availability and staff competence. Implementing standardized physiotherapy practices across ICUs could improve treatment outcomes and contribute to earlier patient discharge.

Keywords: availability; intensive care unit; physiotherapy; quality; satisfaction.

Sažetak

Uvod: U Jedinicama intenzivne medicine (JIM) zbrinjavaju se kritično bolesnici primjenom naprednih metoda liječenja temeljenih na dokazima. Fizioterapija ima ključnu ulogu u skrbi u JIM-u, no često je nedostupna ili nedovoljno standardizirana. Cilj istraživanja bio je analizirati zadovoljstvo liječnika i medicinskih sestara kvalitetom i učinkovitošću fizioterapeutske skrbi u JIM-ovima u Hrvatskoj te ispitati kako se ista može poboljšati.

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Metode: Liječnici i medicinske sestre/tehničari zaposleni u JIM-ovima diljem Hrvatske ispunili su digitalni upitnik od 26 pitanja vezanih za dostupnost i kvalitetu fizioterapeutske skrbi i opreme, te mogućnosti poboljšanja iste. Odgovori su uključivali odabir ocjene slaganja s jednom od ponuđenih tvrdnji u rasponu od 1 do 5 (Likertova skala) ili odabir jednog od ponuđenih odgovora. Dobiveni odgovori analizirani su deskriptivnom statistikom u programu R studio.

Rezultati: U istraživanju je sudjelovalo 120 ispitanika (105 medicinskih sestara i tehničara, 15 liječnika) iz 12 županija u RH. Fizioterapeuti su bili dostupni u svim JIM-ovima, uglavnom radeći konzilijarno ili u jutarnjoj smjeni. Ispitanici smatraju da fizioterapijske intervencije doprinose ublažavanju boli, povećanju pokretljivosti zglobova i poboljšanju respiracijske funkcije. Unatoč visokom stupnju zadovoljstva, izrazili su potrebu za boljom dostupnošću, te učinkonvitijim treningom i edukacijom fizioterapeuta.

Zaključak: Temeljem dobivenih rezultata može se zaključiti kako su liječnici i medicinske sestre zadovoljni pruženom fizioterapeutskom skrbi u JIM-ovima, ali da svakako postoji prostor za njeno poboljšanje, osobito u dostupnosti i educiranosti fizioterapeuta. Standardizacija fizioterapeutske skrbi u JIM-ovima mogla bi poboljšati ishode liječenja i doprinjeti ranijim otpustima bolesnika.

Ključne riječ: dostupnost; fizioterapija; jedinica intenzivne medicine; kvaliteta; zadovoljstvo.

Introduction

Intensive Care Units (ICUs) are specialized hospital departments responsible for treating critically ill patients with acute, life-threatening conditions. These units use advanced medical technologies and therapeutic strategies to stabilize vital functions and prevent or minimize possible complications (1).

Among the leading causes of ICU admission are respiratory diseases, which often require mechanical ventilation that increases the risk of ventilator-associated pneumonia (VAP). Complications associated with VAP further prolong hospitalization and increase healthcare costs (2,3). Another common complication of ICU management is intensive care unit-acquired weakness (ICUAW), which develops in 50–80% of patients mechanically ventilated for more than 48 hours (4,5). ICUAW causes structural and functional impairments that have lasting impacts on quality of life (5). Skeletal muscle atrophy develops rapidly within hours of intubation, while ocular and facial muscles typically remain unaffected. Moreover, prolonged mechanical ventilation contributes to weakness of the diaphragm and other respiratory muscles, thereby extending ICU stays and increasing the risk of VAP (6).

A fundamental physiotherapeutic strategy for the prevention and treatment of ICU-acquired weakness is early mobilization. By definition, it is initiated within 72 hours of ICU admission and involves a progression of activities from passive and active range of motion to full ambulation (7,8).

Respiratory physiotherapy and early mobilization in the Intensive Care Unit (ICU) are essential components in the management and recovery of critically ill patients.

Equally important in critical care is the preservation of mucociliary transport function through effective secretion management. This includes techniques such as postural drainage combined with manual percussion and expiratory vibrations, followed by forced coughing and expectoration (9,10,11). Additionally, positive expiratory pressure (PEP) devices, typically set at 10–20 cm H_2O, and mechanical insufflation-exsufflation devices generating alternating positive and negative pressures are frequently employed to assist coughing and expectoration (12,13).

In the ICU setting, maintaining respiratory and peripheral muscle function demands a coordinated, multidisciplinary approach. Physiotherapists, as essential members of the team, need to possess specialized skills and a profound understanding of mechanical ventilation principles, its modes, variations, and possible complications (14). Such an approach has been shown to shorten the duration of mechanical ventilation and reduce the length of hospital stay (15).

Despite increasing evidence supporting early rehabilitation strategies, their uptake and delivery in Europe have been variable. Physiotherapy care is often not standardized, and official data on physiotherapists'

availability in ICUs remains limited (2). To address the lack of a standardized ICU physiotherapy framework, the European Respiratory Society developed the Harmonised Education in Respiratory Medicine for European Specialists (HERMES) curriculum, which defines essential knowledge and competencies for managing critically ill patients (16,17).

Standardisation of physiotherapy care in the ICU is necessary to ensure consistency, quality, and evidence-based practice across healthcare institutions.

According to the Regulation on Norms and Standards for the Provision of Healthcare Services in Croatia, ICU teams are formally composed of physicians and nurses/technicians (18). Although physiotherapists are not formally included in these regulations, they are often a part of ICU teams across Croatia, as their interventions significantly contribute to improved clinical outcomes and earlier patient discharge. While their role in ICUs is well documented, Croatia still lacks a formal training program for respiratory physiotherapists, who primarily acquire their skills through informal training.

This study assessed physicians' and nurses' satisfaction with physiotherapy care in Croatian ICUs and explored opportunities for improvement.

Methods

The study was conducted in June 2024 using an electronic survey distributed across Croatia. Participants included physicians and nurses employed in Intensive Care Units (ICUs). Inclusion criteria required participants to be between 20 and 64 years of age and have sufficient proficiency in the Croatian language. Participation was voluntary, and respondents were informed that they could withdraw from the study at any time.

Methods and Instruments

Data were collected through a specifically designed digital questionnaire (MS Office Forms), which participants accessed via a link or QR code (Appendix 1). Prior to distribution, department heads received an invitation to participate, including an explanation of the study's purpose, assurance of anonymity, and a statement of voluntary participation. The questionnaire consisted of 26 items, comprising 8 questions on socio-demographic characteristics and employment, 6 on the availability of physiotherapy services, 6 addressing access to physiotherapy equipment, and 6 on satisfaction with physiotherapy care in the ICU. The latter section was further supplemented with a structured question on potential improvements to physiotherapy services and the most commonly applied interventions according to participants. Responses were recorded using a 5-point Likert scale (1-strongly disagree, 5-strongly agree) or as categorical selections.

Statistical Analysis

For the analysis of questionnaire data, descriptive statistics were applied, and the results are presented both descriptively and in tabular form. For all numerical variables, basic statistical measures were calculated, including mean, median, standard deviation, minimum, maximum, and quartiles. For all categorical variables, frequencies, relative frequencies (percentages), and the most common values were determined. Likert-scale items were analyzed using descriptive statistics, including frequency distribution, most frequent rating, and median.

All statistical procedures were performed using R Studio (RStudio version 4.0.4., Posit, PBC).

Results

A total of 120 participants (100 women and 20 men) were included in the study, with a mean age of 36.66 years (range 20-64, SD = 10.69). The participants took approximately 9 minutes to complete the survey.

As presented in Table 1, most participants were nurses, and the largest educational group consisted of bachelor's degree holders.

Table 1. Participants' occupation and educational level

	Category	Freq
1	Physician in training/resident	5
2	Specialist physician	10
3	Nurse/technician (Master's degree, MSc)	13
4	Nurse/technician (Bachelor's degree, BSc)	54
5	Nurse/technician (Secondary school)	38

The length of participants' work experience in the ICU is presented in Table 2. More than half of the participants had at least five years of experience, which adds to the credibility of their responses.7

Table 2. Length of participants' professional experience

	Category	Freq
1	1-5 years	43
2	5-10 years	31
3	10-15 years	12
4	More than 15 years	33

Tables 3 and 4 divide participants by location and type of healthcare institution they work at. The majority were employed in Clinical Hospital Centers, with the highest representation from Split-Dalmatia County, the City of Zagreb, and Zagreb County.

Table 3. Number of participants by healthcare institution category

	Category	Freq
1	Clinical Hospital	7
2	University Hospital Center	92
3	General Hospital	17
4	County General Hospital	3
5	Specialized Hospital	1

Table 4. Number of participants by healthcare institution location

	Counties	**Freq**
1	Bjelovar-Bilogora	1
2	City of Zagreb and Zagreb County	34
3	Istria	1
4	Karlovac	10
5	Krapina-Zagorje	1
6	Osijek-Baranja	6
7	Primorje-Gorski Kotar	11
8	Split-Dalmatia	47
9	Varaždin	6
10	Vukovar-Srijem	1
11	Zadar	1

Table 5 provides an overview of ICU physiotherapists' working hours, reflecting physiotherapy service availability and continuity in Croatia. The findings indicate a lack of standardized schedules, predominance of morning shift coverage, and absence of 24-hour physiotherapy services in all ICUs.

Table 5. ICU physiotherapists' working hours and availability

	Category	**Freq**
1	Attends on a consultative basis (upon request, according to referral)	36
2	Present continuously during the morning/day shift	52
3	Present continuously during the morning and afternoon shifts	31
4	Present continuously 24 hours a day	0

Table 6 details participants' assessments of physiotherapists' competence, effectiveness, overall satisfaction, and the perceived quality of ICU physiotherapy.

Table 7 presents participants' views on the most frequently performed physiotherapy interventions in their ICUs.

Table 6. Assessment of physiotherapists' performance, effectiveness, and satisfaction in ICUs

	Statement	**Grade (N)**	**Median grade**
1	A physiotherapist is trained to work with critically ill patients	1(2), 2(5), 3(21), 4(36), 5(54)	4
2	The physiotherapist is familiar with ICU medical equipment used in patient care	1(6), 2(13), 3(24), 4(37), 5(40)	4
3	The role of the physiotherapist in the treatment process is important for faster recovery of critically ill patients	1(1), 2(2), 3(4), 4(10), 5(103)	5
4	The physiotherapist contributes to pain reduction in patients	1(2), 2(5), 3(16), 4(38), 5(59)	4
5	The physiotherapist contributes to improved mobility in patients	1(0), 2(1), 3(4), 4(19, 5(96)	5
6	The physiotherapist contributes to prevention of pressure ulcers in patients	1(1), 2(8), 3(8), 4(34), 5(69)	5
7	The physiotherapist has access to various therapy aids in the ICU	1(6), 2(22), 3(38), 4(32), 5(22)	3
8	The physiotherapist improves patients' respiratory status in the ICU	1(0), 2(4), 3(6), 4(31), 5(79)	5
9	Nurses/technicians perform physiotherapy procedures when a physiotherapist is unavailable in the ICU	1(10), 2(20), 3(39), 4(28), 5(23)	3
10	The physiotherapist plans and implements physiotherapy procedures in consultation with ICU doctors	1(2), 2(3), 3(16), 4(38), 5(61)	5
11	I am satisfied with the knowledge and skills the physiotherapist demonstrates in the ICU	1(3), 2(9), 3(17), 4(34), 5(57)	4
12	The physiotherapist actively participates in the application of noninvasive mechanical ventilation	1(22), 2(23), 3(26), 4(17), 5(32)	3
13	The physiotherapist independently carries out bronchial secretion aspiration procedures	1(45), 2(17), 3(20), 4(9), 5(29)	3
14	The physiotherapist uses various aids such as mobility and respiratory therapy equipment	1(7), 2(10), 3(25), 4(27), 5(51)	4
15	How would you rate the overall satisfaction with the work of the physiotherapists in your ICU?	1(2), 2(10), 3(21), 4(46), 5(40)	4

Table 7. Reported frequency of physiotherapy interventions in ICUs (only one answer allowed)

	Category	Freq
1	Gait training	1
2	Passive joint mobilization	43
3	Patient positioning	2
4	Interventions for secretion mobilization	9
5	Patient verticalization	18
6	Breathing exercises	31
7	Peripheral muscle strengthening exercises	16

When asked how ICU physiotherapy could be improved, most participants emphasized the need for longer physiotherapist presence in the unit. Other suggestions included better training on ICU equipment and procedures, improved communication with staff and patients, and greater professional autonomy. A full overview of responses is presented in Table 8.

Table 8. Identified areas for improvement in ICU physiotherapy practice

	Category	Freq
1	Better education on devices and procedures performed in the ICU	15
2	Longer presence of physiotherapists in the ICU	89
3	Communication with doctors and nurses/technicians	6
4	Communication with patients	1
5	Greater professional autonomy	8

Discussion

Implementing continuous physiotherapy in the ICU has been shown to significantly improve patient outcomes by preventing respiratory infections, reducing the duration of mechanical ventilation, shortening ICU stays, and thereby lowering overall treatment costs (19,20). Early rehabilitation is associated with an increase in functional capacity and muscle strength, an improvement in walking distance and a better perception of health-related quality of life (21).

Despite clear evidence of its benefits, physiotherapy care in Croatia remains inconsistently accessible, lacks continuity and is not standardized across healthcare settings. Furthermore, physicians and nurses tend to associate physiotherapy primarily with passive patient mobilization, whereas essential ICU interventions such as noninvasive mechanical ventilation and bronchial secretion aspiration are rarely recognized as part of the physiotherapists' role. Although overall satisfaction with physiotherapy care was high, participants identified key areas for improvement, including greater ICU presence, enhanced professional training, and increased autonomy in clinical practice.

In Croatia, there is a need for additional formal education and specialization in ICU physiotherapy to enhance professional competence and clinical outcomes.

The availability and competence of physiotherapists vary internationally. In Western Europe, 25% of hospitals report no dedicated ICU physiotherapists, 34% provide coverage during night shifts, and 85% provide coverage during weekends (22). However, some European Union countries reflect the situation in Croatia. One study reported physiotherapists' presence in 76% of surveyed ICUs, primarily during daytime hours (60.9%). In 39% of ICUs, physiotherapists were available for less than three hours per day, 65% provided interventions as needed, and only 4.3% offered weekend coverage (23). In a scoping review of 1121 titles from South Africa and United States of America, variability in physiotherapist to patient ratio was observed, ranging from 1:4 to 1:50 physiotherapist to critical care beds, while 11–40% ICUs reported daily physiotherapist presence (24). Unlike in some European countries, where physiotherapists are integrated into ICU teams and often present during daytime hours or available 24/7, Croatia lacks official data on the availability of physiotherapy services in ICUs (19).

The effectiveness of physiotherapy and early mobilization in the ICU was evaluated at University Hospital Centre Rijeka by comparing 8-hour and 12-hour physiotherapy programs. The study included 437 patients with ICU stays of more than 24 hours, assigned to either an experimental group (12-hour care) or a control group (8-hour care). In the experimental group, 44% of patients achieved sitting and 21% standing, compared with the control group, where only 26% achieved sitting and 6% standing. Patients receiving 12-hour care were also weaned from mechanical ventilation sooner and transferred to the ward more quickly (25).

A study of patients with amyotrophic lateral sclerosis (ALS) assessed tolerance to non-invasive ventilation (NIV) before and after the employment of a respiratory physiotherapist (RT). At follow-up, NIV tolerance reached 73% in the RT group, compared with 22% in the group without RT involvement. These findings demonstrate that active involvement of respiratory physiotherapists in optimizing NIV can increase patient tolerance by up to 50%, resulting in significantly improved outcomes (26).

To ensure optimal patient care, the European Society of Intensive Care Medicine advises one physiotherapist for every five patients, available seven days a week (20). A study conducted in Chile found that 70% of ICUs have physiotherapists available 24/7, with coverage in 87% of public and 46% of private hospitals. In 41% of

hospitals, one physiotherapist manages up to five patients during the week, while 23% of ICUs employ specialized physiotherapists, predominantly in the private sector. Continuous physiotherapy care is essential for managing ICU patients, yet the availability of specialized education and training remains limited (27).

A study involving 815 mechanically ventilated patients showed that continuous 24-hour physiotherapy coverage resulted in shorter ventilation periods, reduced ICU stays, and lower treatment costs compared to care limited to 12 hours per day (28).

A study conducted in Malaysia investigated nurses' perceptions of physiotherapists in the ICU, surveying 33 nurses with a minimum of six months of ICU experience. A 19-item questionnaire assessed physiotherapist availability, roles, and interventions. Patient mobilization was identified as a primary role, contributing to faster weaning from mechanical ventilation and shorter ICU stays (29).

The studies referenced above emphasize the importance of continuous physiotherapy in achieving favorable treatment outcomes. Limitations of this study include uneven regional representation (nine regions unrepresented), disproportionate participation by nurses and technicians (87%) compared with physicians (13%), and a realatively short study duration.

Despite these limitations, responses from 120 participants across more than half of Croatia's regions provided valuable insights, supporting the essential role of physiotherapists in ICU teams and highlighting the benefits of extended physiotherapy availability in critical care.

Conclusion

Physiotherapy care in ICUs is essential for the multidisciplinary management of critically ill patients, contributing to improved functional outcomes and preventing complications associated with prolonged hospitalization. The integration of physiotherapists into ICU teams significantly enhances patient outcomes and overall treatment effectiveness. In Croatia, however, continuous and standardized physiotherapy care remains underdeveloped, despite clear evidence of its significance. While healthcare professionals express satisfaction with physiotherapist involvement in ICUs, they emphasize the need for improved staffing coverage and advanced clinical competence. Future research should aim for a more balanced representation of physicians and nurses, with broader regional participation, to achieve a comprehensive evaluation of physiotherapy care and promote the standardization of ICU practices across Croatia.

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APPENDIX 1

Questionnaire: "Perception and Availability of Physiotherapy in Intensive Care Units in the Republic of Croatia"

1.	**Your age**	_____ (fill in)
2.	**Your gender**	a) M b) F c) I prefer not to disclose
3.	**Your level of education**	a) Secondary school b) Bachelor's degree (BSc) c) Master's degree (MSc)
4.	**Your occupation**	a) Nurse/technician (Secondary school) b) Nurse/technician (BSc) c) Nurse/technician (MSc) d) Physician in training/resident e) Specialist physician
5.	**Category of healthcare facility where you are employed**	a) University Hospital Center b) Clinical Hospital c) General Hospital d) County General Hospital e) Specialized Hospital
6.	**County in which your facility is located**	List of counties in Croatia
7.	**Category of ICU where you work**	a) General b) Surgical c) Internal medicine d) Pediatric e) Urology f) Neurology g) Other
8.	**How long have you been working at your current workplace?**	a) 1-5 years b) 5-10 years c) 10-15 years d) More than 15 years

9.	**How much time per day is the physiotherapist present in your ICU?**	a) Present continuously during morning or day shifts b) Present continuously during morning and afternoon shifts c) Present continuously 24 hours a day d) Attends on a consultative basis (upon request, according to referral)
	For the following questions, indicate your answer on a scale from 1 to 5 (1 – strongly disagree, 5 – strongly agree)	
10.	**The physiotherapist is trained to work with critically ill patients**	1 – 2 – 3 – 4 – 5
11.	**The physiotherapist is familiar with the medical equipment available in the ICU and used in treating critically ill patients**	1 – 2 – 3 – 4 – 5
12.	**The physiotherapist's role in the treatment process is important for faster recovery of critically ill patients**	1 – 2 – 3 – 4 – 5
13.	**The physiotherapist's interventions reduce pain in patients**	1 – 2 – 3 – 4 – 5
14.	**The physiotherapist's interventions improve patient mobility**	1 – 2 – 3 – 4 – 5
15.	**The physiotherapist's interventions prevent the development of pressure ulcers in patients**	1 – 2 – 3 – 4 – 5
16.	**The physiotherapist has access to various aids for conducting therapy in the ICU**	1 – 2 – 3 – 4 – 5
17.	**The physiotherapist's interventions improve respiratory status in ICU patients**	1 – 2 – 3 – 4 – 5
18.	**Nurses/technicians perform physiotherapy procedures when the physiotherapist is not present in the ICU**	1 – 2 – 3 – 4 – 5
19.	**The physiotherapist independently plans and carries out physiotherapy procedures in consultation with physicians in the ICU**	1 – 2 – 3 – 4 – 5
20.	**I am satisfied with the knowledge and skills that the physiotherapist applies in their work in the ICU**	1 – 2 – 3 – 4 – 5
21.	**The physiotherapist actively participates in the application of NIV (non-invasive ventilation)**	1 – 2 – 3 – 4 – 5
22.	**The physiotherapist independently performs bronchial secretion aspiration procedures**	1 – 2 – 3 – 4 – 5
23.	**The physiotherapist uses various aids (mobility aids, respiratory therapy aids, ADL aids, etc.) in their work**	1 – 2 – 3 – 4 – 5
24.	**Which physiotherapy intervention do you think is performed most frequently in your ICU?**	a) Patient verticalization b) Gait training (with/without mobility aids) c) Breathing exercises d) Peripheral muscle strengthening exercises e) Patient positioning f) Interventions for secretion mobilization g) Passive joint mobilization
25.	**In which aspect could the physiotherapists' work in your ICU be improved?**	a) Communication with patients b) Communication with doctors and nurses/technicians c) Greater professional autonomy d) Better education on devices and procedures performed in the ICU e) Longer presence of physiotherapists in the ICU
26.	**How would you rate your overall satisfaction with the physiotherapist's work in your ICU?**	1 – 2 – 3 – 4 – 5

PRIKAZ SLUČAJA / CASE REPORT

VEXUS KAO KLINIČKI KOMPAS U HITNOM BOLNIČKOM PRIJAMU

VEXUS AS A CLINICAL COMPASS IN THE EMERGENCY DEPARTMENT

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Sažetak

Uvod: Procjena volumskog statusa i venske kongestije u bolesnika s uznapredovalim srčanim popuštanjem ostaje klinički izazov. VExUS protokol (engl. *Venous Excess Ultrasound Score*) temelji se na ultrazvučnoj procjeni venskog sustava i omogućava neinvazivnu, brzu i lako ponovljivu procjenu kongestije.

Prikaz slučaja: Prikazujemo 92-godišnju bolesnicu s brojnim pridruženim bolestima i terminalnim srčanim popuštanjem, zaprimljenu zbog dispneje, hipoksije i znakova kongestije. Ultrazvučni pregled trbuha izveden je konveksnom sondom (2–5 MHz) u skladu s važećim tehničkim preporukama, u supiniranom položaju s desne lateralne strane. Nalaz je pokazao redukciju bubrežnog parenhima, povišeni rezistivni indeks (RI 0,78) te izrazitu dilataciju donje šuplje vene (4,5 cm) i hepatalnih vena s dominacijom D vala (VExUS gradus 2). Početno ciljano vođena terapija prema nalazu VExUS-a dovela je do privremene stabilizacije. Bolesnica je otpuštena nakon privremene stabilizacije temeljem ciljano vođene terapije, no dva puta se vratila u bolnicu, a pri trećem dolasku preminula unatoč poduzetim mjerama liječenja..

Zaključak: Prikaz potvrđuje kliničku vrijednost VExUS-a u hitnoj medicinskoj službi te podupire sustavnu primjenu u praćenju bolesnika visokog rizika od srčanog popuštanja.

Ključne riječi: hitna medicina; srčano popuštanje; ultrazvuk; venska kongestija; VExUS protokol

Abstract

Background: Assessment of volume status and venous congestion in advanced heart failure remains challenging. The Venous Excess Ultrasound Score (VExUS) is a non-invasive protocol enabling rapid bedside evaluation of congestion.

Case presentation: We present a 92-year-old female with multimorbidity and end-stage heart failure, admitted with dyspnea, hypoxia, and clinical signs of congestion. Abdominal ultrasound was performed using a convex 2–5 MHz probe in accordance with current technical recommendations, with the patient in supine position and approached from the right lateral side. Findings included reduced renal parenchyma, elevated resistive index (RI 0.78), and marked dilatation of the inferior vena cava (4.5 cm) and hepatic veins with D-wave predominance (VExUS grade 2). Initial targeted therapy based on VExUS findings led to temporary stabilization. The patient was discharged but returned twice; VExUS was not repeated. She died during her third emergency department visit

Conclusion: This case highlights the clinical value of VExUS in emergency settings and supports its systematic use in monitoring high-risk heart failure patients.

Keywords: emergency medicine; heart failure; ultrasound; venous congestion; VExUS protocol

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Uvod

Procjena volumskog statusa i venske kongestije u bolesnika s uznapredovalim srčanim popuštanjem predstavlja značajan klinički izazov. Klasični pokazatelji često nisu dovoljni za razlikovanje bolesnika s relativnim nedostatkom intravaskularnog volumena od onih s venskom preopterećenošću (tkz. "suhe" od "kongestivne" slike). VExUS protokol (Venous Excess Ultrasound Score) temelji se na ultrazvučnoj procjeni venskog sustava i omogućava neinvazivnu, brzu i lako ponovljivu procjenu kongestije (1,2). Integracijom procjene donje šuplje vene, te Doppler analize hepatičnih, portalnih i intrarenalnih vena, VExUS pruža detaljniji uvid u stupanj sistemske venske kongestije i njezin hemodinamski učinak na ciljne organe, čime se olakšava individualizacija terapije, osobito u prilagodbi doziranja diuretske i vazodilatacijske terapije, te se potencijalno smanjuje rizik od pogoršanja bubrežne funkcije i drugih komplikacija povezanih s prekomjernom ili nedovoljnom dekongestijom.

Vexus protokol

VExUS protokol uključuje dopplersku procijenu (slika 1):

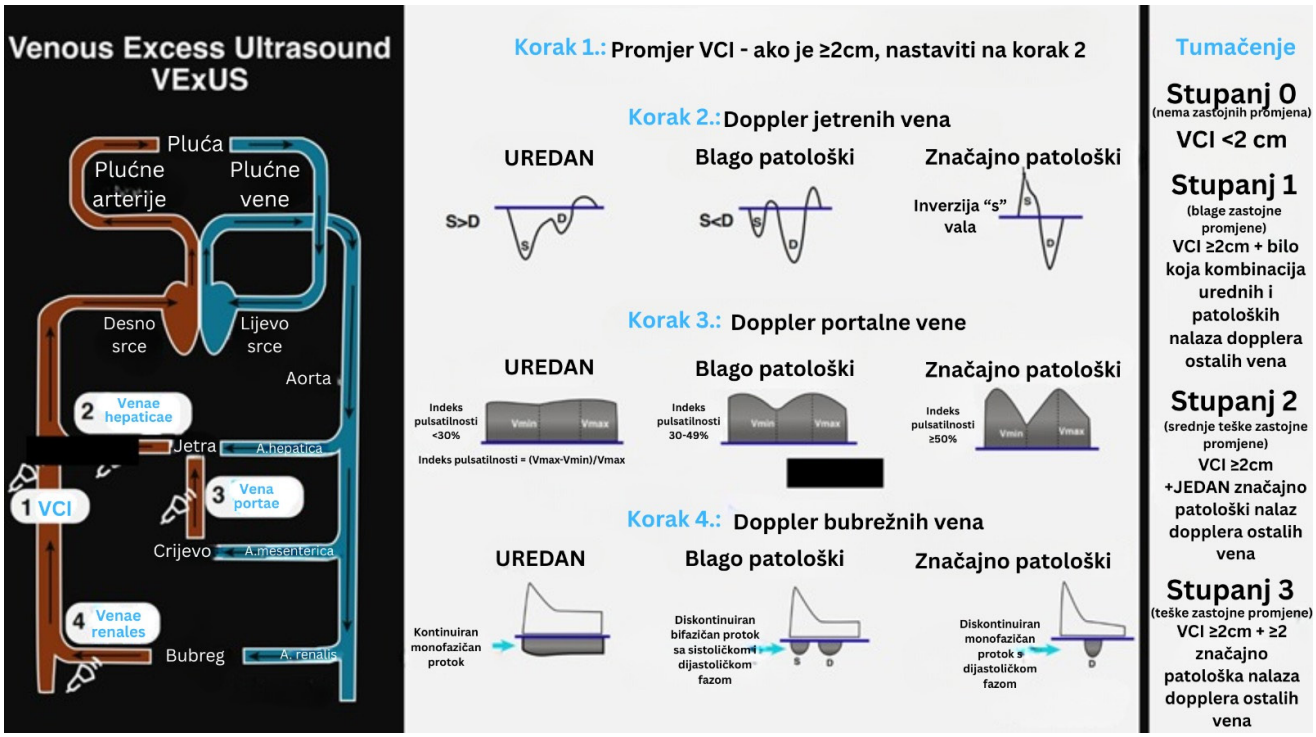
1. donje šuplje vene (lat. v. cava inferior VCI): procjena širine i respiracijske varijabilnosti
2. hepatalnih vena: analiziraju se visina te pozicija S i D valova; denivelacija i inverzija S vala ukazuju na kongestiju
3. portalne vene: procjena širine žile, spektar te indeks pulsatilnosti koji fiziološki mora biti manji do 30% (PI index)
4. bubrežnih vena: fiziološki se mora prikazati kontinuirani monofazični spektar, dok se diskontinuirani oblici s prikazom sistole ili dijastole kategoriziraju u umjerenu i uznapredovalu varijantu

Prema širini VCI i broju ostalih patoloških nalaza kategoriziramo nalaz bolesnika u stupanj kongestije (slika 1):

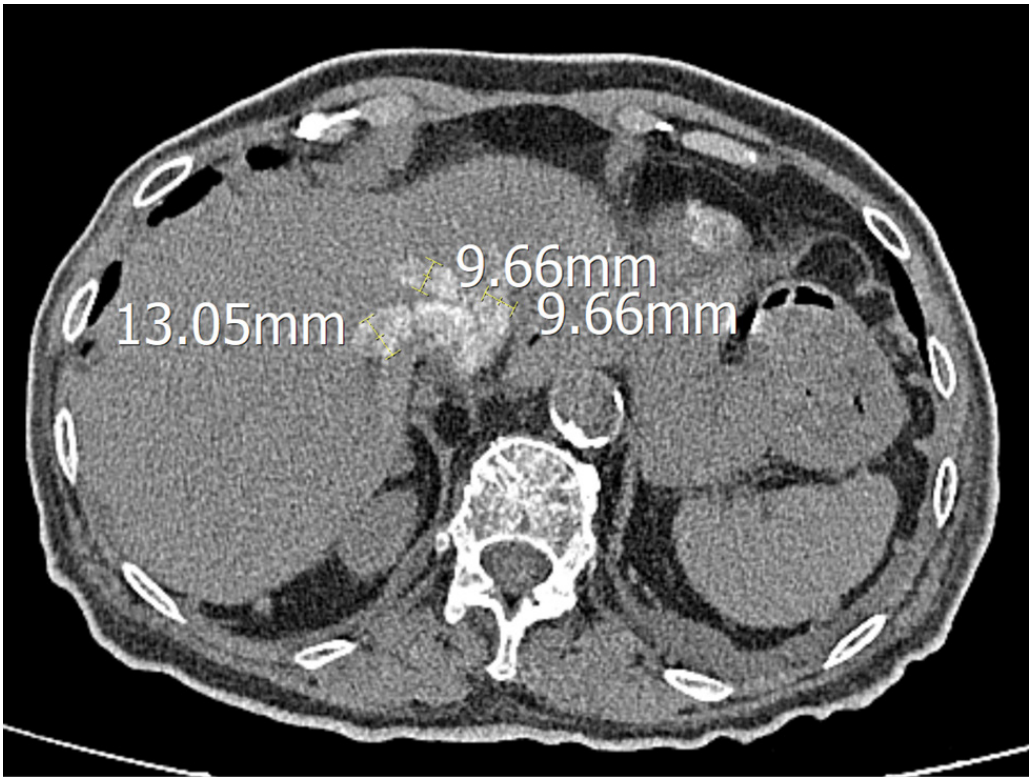
- Stupanj 0: IVC <2 cm, svi nalazi normalni, bez znakova sistemske venske kongestije
- Stupanj 1: IVC ≥2 cm + normalni ili blago patološki nalazi, blaga venska kongestija
- Stupanj 2: IVC ≥2 cm + 1 teški patološki nalaz, umjerena sistemska venska kongestija
- Stupanj 3: IVC ≥2 cm + ≥2 teška patološka nalaza, teška sistemska venska kongestija s visokim rizikom organske disfunkcije

Prikaz slučaja

Bolesnica, 92 godine, s brojnim pridruženim bolestima uključujući šećernu bolest tip 2, hipotireozu, kroničnu opstrukcijsku plućnu bolest te akutizaciju prethodno neprepoznate kronične bubrežne bolesti, klasificirane kao G3a/A1 prema KDIGO smjernicama (umjereno smanjena bubrežna funkcija s normalnom ili blago povišenom albuminurijom) i anamnezom kroničnog srčanog popuštanja s umjereno smanjenom ejekcijskom frakcijom (engl. *Heart Failure with mildly Reduced Ejection Fraction,* HFmrEF), nakon transkateterske implantacije aortnog zaliska (engl. *Transcatheter Aortic Valve Implantation,* TAVI) i implantacije elektrostimulatora, prvotno je pregledana u travnju 2025. godine u hitnoj



Slika 1. Shematski prikaz VExUS protokola (uređeno prema ref. 4)



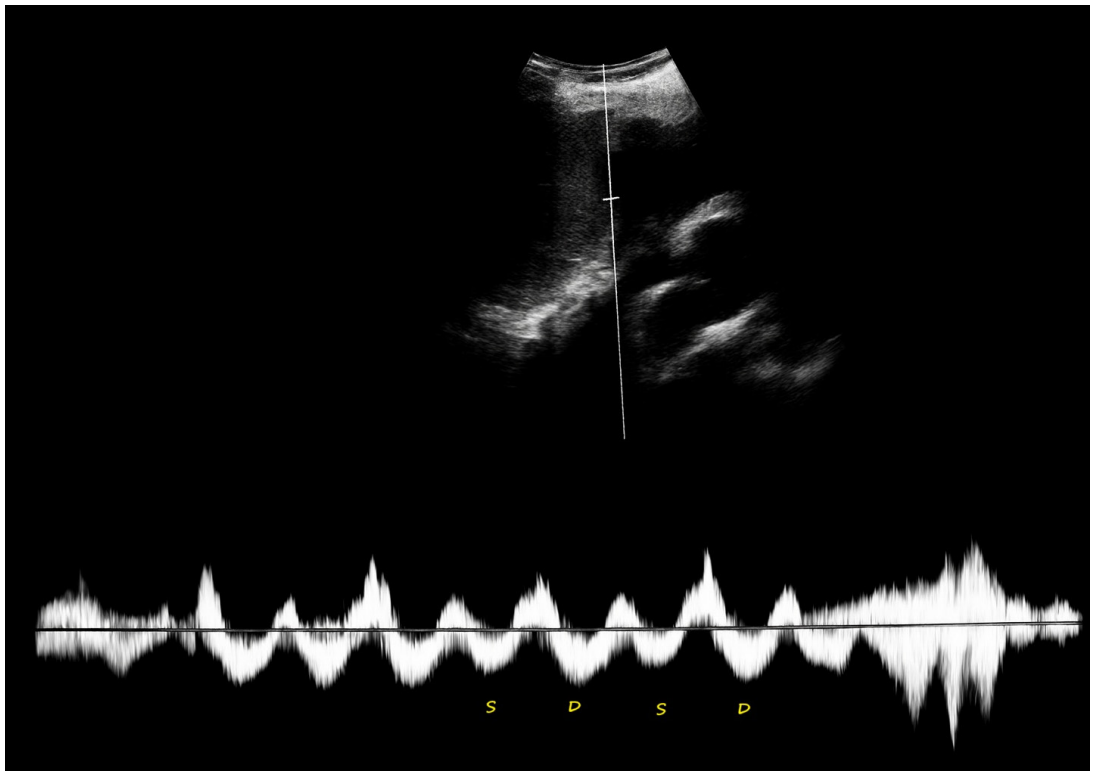
Slika 2. CT prikaz dilatiranih hepatalnih vena s refluksom kontrasta (vidljivo opterećenje desnog srca)

medicinskoj službi Kliničke bolnice Merkur zbog dispneje sa sniženom saturacijom (SpO_2 80 % na sobnom zraku), tahikardije, očuvanog arterijskog tlaka (120/80 mmHg), znakova zastojne jetre, edema potkoljenica, opće slabosti i smanjene diureze. Od patoloških laboratorijskih nalaza isticali su se povišeni N-terminalni fragment pro-B-type natriuretskog peptida (engl. *N-terminal pro–B-type natriuretic peptide,* NT-proBNP) (>4800 pg/mL), visokoosjetljivi troponin I (hTnI 173 ng/L), kreatinin 120 µmol/L uz procijenjenu glomerularnu filtraciju (eGFR 37 mL/min/1,73 m^2), što je odgovaralo kroničnoj bubrežnoj bolesti stadija G3b/A1. kroničnoj bubrežnoj bolesti stadija G3b/A1 (prema KDIGO smjernicama: eGFR 30–44 ml/min/1,73 m^2 uz normalnu ili blago povišenu albuminuriju). Zabilježene su izrazito povišene vrijednosti jetrenih enzima (AST 5054 U/L, ALT 1867 U/L), te hiperglikemija (GUK 23 mmol/L). Pri dolasku bolesnica je bila na terapiji diuretikom Henleove petlje (furosemid) uz suplementaciju kalija (Kalinor), ACE-inhibitorom (perindopril 2 mg), beta-blokatorom (nebivolol 2,5 mg), atorvastatinom 20 mg, levotiroksinom, ipratropijevim bromidom (Atrovent) te inzulinom. Zbog izražene dispneje i tahikardije uz sniženu saturaciju učinjena je MSCT angiografija pluća, kojom je isključena plućna embolija. Nalaz je, međutim, pokazao obostrane plućne infiltrate, pleuralne izljeve te refluks kontrasta u hepatalne vene, što je upućivalo na izraženu kongestivnu komponentu srčanog popuštanja (slika 2).

U hitnoj medicinskoj službi učinjen je ultrazvučni pregled trbuha konveksnom sondom frekvencijskog raspona 2–5 MHz, koja osigurava optimalan odnos penetracije i prostorne rezolucije za procjenu trbušnih struktura, osobito donje šuplje vene, hepatalnih i portalne vene. Pregled je proveden u skladu s važećim tehničkim preporukama za procjenu venske kongestije, uz pristup s desne lateralne strane u ležećem položaju, što se smatra standardnim pristupom za procjenu donje šuplje vene i hepatalnih vena. Ovakav položaj smanjuje pojavu artefakata i omogućuje pouzdaniju dopplersku analizu venskog protoka (3). Uočen je reduciran bubrežni parenhim uz povišen doplerski pokazatelj koji opisuje otpor protoku krvi u arteriji, rezistivni indeks (RI 0,78. Nalazom je dominirala izrazito proširena donja šuplja vena do 4,5 cm uz proširene hepatalne vene. Dopplerski spektar hepatalnih vena pokazivao je dominaciju D-vala nad S-valom, dok je portalna vena bila uredne širine, bez značajne pulzatilnosti (slika 3). Nalaz je u skladu s VExUS gradusom 2.

VExUS protkol oomgućava brzu neinvazivnu procjenu venske kongestije uz krevet bolesnika u hitnoj medicinskoj službi.

Započeto je liječenje kontinuiranom parenteralnom diuretskom terapijom i antibiotskim protokolom. Uveden je mineralokortikoidni antagonist (MRA, eplerenon) u dozi od 12,5 mg, uz oksigenoterapiju 2–3 L/min, čime je bolesnica privremeno stabilizirana i postignuta je odgovarajuća diureza. Uvođenje inhibitora SGLT2 (engl.



Slika 3. Dopplerski spektar hepatalne vene s dominacijom D vala nad S valom (VExUS gradus 2)

Sodium-Glucose Cotransporter 2) odgođeno je zbog prisutnosti urinarne infekcije. Tri mjeseca nakon prve hospitalizacije bolesnica je ponovno zbrinuta u Hitnoj medicinskoj službi zbog urinarne infekcije, a potom je nakon tri dana ponovno primljena na bolničko liječenje zbog progresivne dispneje i hipoksije. Unatoč poduzetim mjerama liječenja, bolesnica je preminula.

Rasprava

Prikazani slučaj potvrđuje kliničku vrijednost VExUS protokola u kliničkom razlikovanju kongestivnih stanja. Kod starijih bolesnika s višestrukim pridruženim bolestima i smanjenom pokretljivošću, navedeni ultrazvučni protokol pruža značajnu korist za neposrednu i vizualnu procjenu venskog opterećenja. Standardizirani protokoli obrade trebali bi uključivati snimanje elektrokardiograma (EKG), laboratorijsku obradu, radiografiju srca i pluća, te u slučajevima sumnje na plućnu emboliju MSCT-plućnu angiografiju. Preporučuje se određivanje NT-proBNP kao biološkog pokazatelja srčanog zatajenja, jetrenih enzima (AST, ALT, GGT, bilirubin) zbog potencijalne venske kongestije, te funkcije bubrega (kreatinin, urea, Na, K), D-dimera i troponina. Potencijalno se preporučuje i određivanje tiroidno stimulirajućeg hormona (TSH) radi isključivanja tireoidnih uzroka srčanog zastoja, kao i analiza urinskih bioloških pokazatelja, primjerice omjera albumin/kreatinin. Sovetova i sur. pokazali su da bolesnici s VExUS ocjenom 3 imaju značajno povećan rizik od akutnog oštećenja bubrega (AOB), otpornost na diuretike, potrebu za primjenom inotropnih lijekova te povišenu bolničku smrtnost (1). Ako se bolesnici ranije uspiju svrstati u niži VExUS stupanj, povećava se vjerojatnost preživljenja, dok analiza renalnog indeksa te S i D vala omogućuje uvid u postojeće oštećenje i sprječavanje budućih oštećenja. Landi i sur. ističu prednosti uvođenja standardiziranog VExUS protokola u hitnu medicinsku službu putem strukturiranog ultrazvučnog obrasca unutar radiološkog informacijskog sustava (RIS), uz kratku edukaciju osoblja i integraciju u algoritam zbrinjavanja akutnog zatajivanja srca, čime se poboljšava procjena venske kongestije i rano prepoznavanje bolesnika s visokim rizikom bubrežnog zatajenja (2). Trenutno u Hrvatskoj postoje strukturirani obrasci u obliku dodatnog softvera, prvenstveno namijenjeni probiru za rak pluća i dojke. Ako bi se standardizirani VExUS protokol implementirao, potrebno je razmotriti može li postojeći softver podržati takvu integraciju u RIS, ili je potrebna izrada posebnog programa namijenjenog specifično za praćenje ovih bolesnika i rad u hitnoj medicinskoj službi.

Assavapokee i sur. pružaju praktični vodič za izvođenje VExUS protokola unutar POCUS-a (engl. *point-of-care ultrasound*), jasno definirajući tehniku, interpretaciju Doppler nalaza i kriterije za klasifikaciju venske kongestije. Takav pristup omogućuje standardiziranu i reproducibilnu procjenu bolesnika s kongestivnim zatajenjem srca (4). Longino i sur. potvrđuju visoku pouzdanost i suglasnost između ocjenjivača VExUS protokola, čime se dodatno opravdava njegova primjena u kliničkoj evaluaciji bolesnika

s hemodinamskom nestabilnošću i rizikom od akutnog oštećenja bubrega (AOB) (5).

VExUS protokol je u ovom slučaju primijenjen pri prvom zbrinjavanju bolesnice u hitnoj medicinskoj službi, što je omogućilo preciznu procjenu venske kongestije i usmjerilo početno liječenje.

Terapija vođena nalazom VExUS-a omogućava ciljano i precizno propisivanje diuretika u svrhu postizanja pravovremene kliničke stabilizacije.

Time je postignuta stabilnost kliničkog stanja, te je bolesnica otpuštena na kućno liječenje. Tijekom sljedeće hospitalizacije i dvaju naknadnih pregleda u hitnoj medicinskoj službi protokol se nije koristio, no postavlja se pitanje bi li njegova ponovljena primjena mogla značajnije optimizirati terapijski pristup. Ovo ukazuje na potrebu za sustavnijim uključivanjem VExUS protokola u praćenje visokorizičnih bolesnika sa srčanim popuštanjem, budući da je rezultat VExUS protokola primjenjiv u bolesnika s multiorganskom venskom kongestijom.

Početno učinjena MSCT plućna angiografija (PA) pokazala je upalne infiltrate i radiomorfološke uzorke karakteristične za "mliječno staklo" (engl. *ground glass opacification,* GGO), te uzorak "stabla s pupovima" (engl. *tree in bud*). Međutim, kongestija desnog srca može biti podcijenjena ako se oslanjamo isključivo na laboratorijske ili kliničke znakove. U ovom slučaju posebno je uočena dilatacija donje šuplje vene i hepatalnih vena, što je dežurnog internistu u multidisciplinarnom pristupu i komunikaciji s radiologom potaknulo da se izvrši analiza prema VExUS protokolu. Liječenje desnog srčanog zatajenja zahtijeva pažljivo upravljanje cirkulirajućim volumenom, kontraktilnom funkcijom desnog ventrikla i tlačnim opterećenjem (engl. *afterload*). U hemodinamski nestabilnih bolesnika osnovne terapijske mjere čine diuretici i inotropni lijekovi (dobutamin, milrinon), što omogućuje privremenu hemodinamsku stabilizaciju dok se istovremeno rješava uzrok opterećenja desnog srca (6). Prepoznavanje etiologije zatajivanja desnog srca važno je za određivanje terapijskog pristupa, osobito u bolesnika s plućnom embolijom, infarktom desne klijetke ili valvularnim bolestima, gdje ciljano liječenje uzroka može značajno utjecati na tijek bolesti. Etiološki usmjereno liječenje u kombinaciji s hemodinamskom potporom često omogućuje oporavak bez potrebe za invazivnim zahvatima (7). U bolesnika s plućnom hipertenzijom i zatajivanjem desne klijetke indicirana je primjena specifične plućne vazodilatacijske terapije, uključujući endotelin-antagoniste, prostanoide i inhibitore fosfodiesteraze tip 5 (PDE-5) uz standardnu hemodinamsku potporu. Ova terapija može smanjiti opterećenje desne klijetke, poboljšati njegovu kontraktilnu funkciju i odgoditi potrebu za transplantacijom srca ili pluća, posebno u mlađih bolesnika. U bolesnika sa srčanim zatajenjem i desnostranim kongestivnim znakovima, kombinacija plućne vazodilatacijske terapije, optimizacije volumskog opterećenja (engl. *preload*) i primjene inotropnih lijekova predstavlja temelj liječenja, uz kontinuirani individualni hemodinamski nadzor.

Pristup liječenju treba biti individualiziran i prilagođen stupnju zatajivanja, mogućnosti reverzibilnosti i sistemskim posljedicama. U slučajevima refraktornog zatajivanja desne klijetke, osobito kod razvoja kardiogenog šoka, potrebno je razmotriti privremenu mehaničku potporu desnog ventrikla (uređaj za potporu desne klijetke, engl. Right Ventricular Assist Device, RVAD, te ekstrakorporalnu membransku oksigenaciju, engl. Extracorporeal Membrane Oxygenation, ECMO), osobito ako postoji mogućnost oporavka ili planirana transplantacija. Odluka o uvođenju takve potpore zahtijeva multidisciplinarni pristup i jasno definirane kriterije za izbor bolesnika. Primjenom VExUS skora u hitnoj medicinskoj službi ili tijekom hospitalizacije moguće je identificirati bolesnike s visokim rizikom za nepovoljne ishode, osobito one sa srčanim popuštanjem

Sustavna i opetovana upotreba VExUS protokola može pomoći u ranijem prepoznavanju visokorizičnih bolesnika sa srčanim popuštanjem, optimizaciji strategija liječenja i smanjenju učestalosti neželjenih ishoda.

Zaključak

VExUS protokol predstavlja jednostavan, lako dostupan i klinički vrijedan alat koji može poduprijeti donošenje terapijskih odluka u bolesnika s brojnim pridruženim bolestima i kardiorenometaboličkim poremećajima, kao što je bio slučaj ove bolesnice. U ovom specifičnom slučaju, prvom dokumentiranom u Kliničkoj bolnici Merkur, protokol je poslužio kao vodič kroz složenu kliničku situaciju, omogućivši bolje razumijevanje mehanizama srčanog popuštanja i primjenu individualno prilagođene terapije u skladu sa smjernicama.

SUKOB INTERESA

Autori ne prijavljuju sukob interesa.

ETIČKA IZJAVA

Obitelj bolesnice dala je informirani pristanak za objavu anonimnih kliničkih podataka i slika u skladu s Helsinškom deklaracijom.

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PRIKAZ SLUČAJA / CASE REPORT

URETERIC RUPTURE FOLLOWING INADVERTENT FOLEY'S CATHETER BALLOON INFLATION: A CASE REPORT

RUPTURA URETERA POSLJEDIČNO NENAMJERNOM NAPUHIVANJU FOLEYEVOG KATETERA: PRIKAZ SLUČAJA

Ashraf Butt[1], *Ahad Nawaz[1], Nida Fatima[1]

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Abstract

Background: Ureteric rupture is one of the rarest but serious complication of Foley`s catheterization. We present a case of ureteric rupture along with retroperitoneal haematoma following attempted Foley`s catheterization

Case presentation: A general physician attempted Foley`s catheterization on a male patient in his 70's in community because of recurrent urinary incontinence and deranged renal function tests, during the procedure inadvertent intra-ureteric balloon inflation occurred. Following the procedure, patient presented to emergency department with severe lower abdominal pain and sepsis, imaging studies revealed left ureter rupture and retroperitoneal haematoma. Patient was referred to a tertiary referral urology centre and surgical intervention was performed. Patient recovered post operatively without any further complication.

Conclusion: Ureteric rupture following Foley`s catheter balloon inflation is although rare but should be considered in cases of post procedural abdominal pain and sepsis. Timely diagnosis and management is important for a better outcome.

Keywords: balloon inflation; Foley`s catheter; ureteric rupture; urinary tract injury

Sažetak

Uvod: Ruptura uretera je rijetka, ali ozbiljna komplikacija postavljanja Foleyevog katetera. Predstavljamo slučaj rupture uretera s retroperitonealnim hematomom kao posljedica pokušaja postavljanja Foleyevog katetera.

Prikaz slučaja: Liječnik opće medicine je pokušao postaviti Foleyev kateter muškom bolesniku u 70-im godinama života zbog mokraćne inkontinencije i pogoršanja bubrežne funkcije. Tijekom zahvata se dogodilo nenamjerno napuhivanje balona intraureteralno. Nakon zahvata, bolesnik je zaprimljen u hitni bolnički prijam s jakom boli u donjem hemiabdomenu i sepsom, a radiološke su pretrage pokazale rupturu lijevog uretera s retroperitonealnim hematomom. Bolesnik je premješten na Odjel za urologiju te je učinjen operacijski zahvat. Nakon operacije bolesnik se oporavio bez daljnjih komplikacija.

Zaključak: Ruptura uretera uslijed napuhivanja balona Foleyevog katetera rijetka je komplikacija, no treba je uzeti u obzir kod bolova u trbuhu i sepse nakon postupka. Pravovremena dijagnoza i odgovarajuće zbrinjavanje ključni su za povoljniji ishod.

Ključne riječi: Foleyev kateter; napuhivanje balona; ozljeda mokraćnih puteva; ruptura uretera.

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Introduction

Foley`s catheterization is one of the common and usually safe procedures done in hospital and in community as well. However it also carries risk of some common complications like infection, urethral trauma, bleeding, bladder spasm, leakage, irritation or pain at urethral meatus but also carries risk of some very rare and serious complications like rupture of ureter (1). We report a similar case of ureteric rupture following Foley`s catheter balloon inflation in community by general physician and patient was initially managed at emergency department and then referred to a urology tertiary referral centre.

Ureteric rupture is a rare but serious complication of Foley's catheterization that can occur due to inadvertent intra-ureteric balloon inflation and should be suspected in patients presenting with acute abdominal pain and sepsis after the procedure.

Case report

In June 2023, a male in his 70's was referred from general physician to our emergency department with severe lower abdominal pain following attempt of Foley`s catheterization.

General physician attempted Foley`s catheterization with a 16 Fr Foley`s catheter due to recurrent urinary incontinence and deranged renal functions of the patient but unfortunately patient developed sudden severe lower abdominal pain with a pain score of 10/10. The general physician stopped and repositioned the catheter, which lead to frank haematuria. After that general physician attempted with 14Fr size Foley`s catheter but it started bypassing when he tried to flush it. Therefore he removed the catheter. The patient was then referred to our Emergency department.

On arrival to Emergency department, patient was complaining of severe lower abdominal pain. On examination, he was apyrexial, tachycardiac 109 per minute and tachypnoeic 24 per minute. His lower abdomen was tender on palpation. His lactate was 3.99 mol/L, white blood cells count of 17.3 and C reactive protein of 31. A bed side urinary bladder ultrasound scan revealed 10 ml volume. He was commenced on sepsis six bundle. His case was discussed with Urology department in a tertiary referral centre. They advised to do a CT Urogram with query of bladder perforation. CT Urogram with contrast revealed left ureter rupture with contrast extravasation and retroperitoneal haematoma (figure 1).

Early imaging with CT urogram enables prompt diagnosis of ureteric rupture allowing timely referral and definitive intervention.

The patient was urgently transferred to urology team for further management. The Patient was admitted in ICU in the tertiary referral centre and had continuous bladder irrigation commenced. It was planned for Interventional radiology insertion of a left percutaneous nephrostomy but it was delayed because patient was administered edoxaban 1 day previously. The following day, the Interventional Radiology team successfully performed a left percutaneous nephrostomy and also placed an anterograde stent. Patient's nephrostomy was removed by interventional radiology after 7 days while the anterograde stent was left in place. Patient was discharged from the hospital with a follow up plan as an outpatient in 10 weeks. Patient total length of stay in hospital was 2 weeks. After 4 months, cystoscopy was done along with

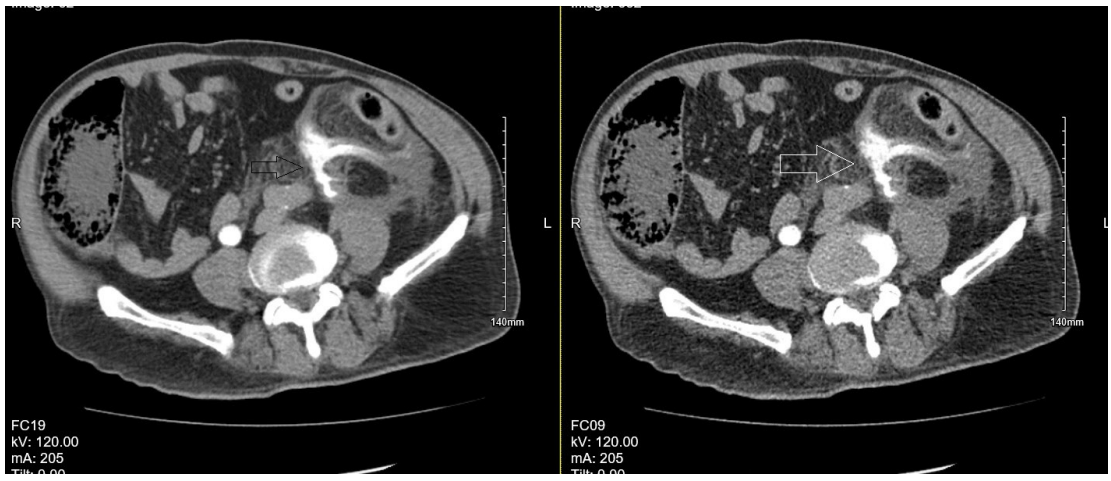

Figure 1. Contrast-enhanced CT demonstrating rupture of the left ureter with active contrast extravasation and associated retroperitoneal haematoma.

JJ stent removal as a day case and patient was discharged on same day with no further urology follow up plan.

Informed consent for publication of this case was obtained.

Discussion

Ureteric rupture following Foley`s catheterization is rare and 8 cases have been reported in the literature in the past. This complication happens when the catheter accidently goes into the ureter and then the balloon is inflated inside the ureter, which might lead to rupture or tearing of ureter. The key warning sign is severe abdominal pain which starts after inflation of catheter balloon, especially if there is little or no urine draining through the catheter.

A literature review (2) published in 2024 identified 48 patients across 39 published case reports of inadvertent ureteric catheterization. Among these the most frequent complications of inadvertent ureteric catheterisation were acute pyelonephritis (35%), acute kidney injury (27%), urosepsis (21%) and ureteric rupture (17%). In our case, the patient developed both ureteric rupture and urosepsis, which are among the more severe reported outcomes. The most important way to prevent it is to confirm urine flow before inflating the balloon.

Prevention of ureteric injury relies on confirming free urine flow before balloon inflation and immediate cessation of the procedure if severe pain occurs, followed by urgent urological assessment and imaging.

If the patient experiences sudden, severe abdominal pain during balloon insertion or inflation, the balloon should be deflated immediately, the catheter removed, and further assessment should include prompt imaging and consultation with the urology team.

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REVIEW ARTICLE / PREGLEDNI ČLANAK

PERICAPSULAR NERVE GROUP BLOCK – A NARRATIVE REVIEW

BLOK PERIKAPSULARNE SKUPINE ŽIVACA – NARATIVNI PREGLED

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Abstract

This narrative review of the Pericapsular Nerve Group (PENG) Block of the hip describes the indications, technique and performance of the ultrasound-guided peripheral nerve block. Possible complications and their avoidance are discussed, as are the technical details of block performance.

Keywords: emergency ultrasound; nerve block; PENG block; regional anesthesia

Sažetak

Ovaj pregledni rad o bloku perikapsularne skupine živaca (PENG) kuka opisuje indikacije, tehniku i izvođenje ultrazvukom navođenog perifernog bloka živaca. Moguće komplikacije i izbjegavanje istih se opisuju, kao i tehničke pojedinosti pojedinosti same izvedbe bloka.

Ključne riječi: blok živaca; hitni ultrazvuk; PENG blok; regionalna anestezija

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Introduction

The treatment of pain is a fundamental aspect of emergency medical care. Administration of analgesia by oral, intra-muscular and intravenous routes is so common as to barely merit comment, while infiltration of local anesthetics is similarly a daily part of patient care. While regional anesthesia has been a part of the emergency medicine specialist's practice for decades, the introduction of ultrasound has expanded the scope and precision of regional anesthesia in the emergency department (1). Regional anesthesia is the unsung hero of emergency department analgesia: it allows powerful reduction of pain while sparing use of opioid analgesics that can complicate patient care in those at risk of respiratory and hemodynamic impairment, as well as those at risk of delirium (2).

Ultrasound guided nerve block of the hip can be successfully performed by emergency physicians.

One place where regional anesthesia has been consistently shown to improve patient pain and reduce the complications of opioid use is in the patient with an acute fractured hip. (4). Regional anesthesia for hip fracture (referring here to both femoral neck and intertrochanteric femur fractures) began as femoral nerve blocks and landmark-based fascia iliaca nerve blocks to the ultrasound guided supra-inguinal fascia iliaca nerve block and, more recently, the pericapsular nerve group (PENG) block. This paper will review the PENG block, detailing its indications and correct performance, as well as complications that can arise while performing the block and how to successfully avoid them.

Methods

We began this narrative review with a literature search in PubMed and Google Scholar, using keywords 'PENG Block,' 'pericapsular nerve group block,' 'regional anesthesia of the hip,' 'nerve block of the hip' and related terms to identify relevant studies. The search was not intended to be exhaustive, but rather to identify the most current ideas on the performance of the PENG block, with the focus upon

how the block is performed, its common complications and how to avoid these complications, and its efficacy.

Origins of the PENG Block

The pericapsular nerve group (PENG) block was first described in 2018 by Drs. Girón-Arango, Peng, Chin and their team. The technique was developed to reduce pain after total hip arthoplasties while minimizing nerve blockade to motor nerves to allow for early rehabilitation (3).

The PENG block is a novel method of providing anesthesia to the hip that is efficacious and easy to perform.

Indications

The PENG block provides anesthesia to anteromedial aspect of joint capsule of the hip. Because most sensory nerves for the hip run in the anterior aspect of the joint capsule, it will effectively capture these nerves (5). There is also some spread of anesthesia beyond the anteromedial joint capsule, which allows blockade of nerves innervating surrounding soft tissues (iliopsoas muscle, etc) (3, 6-7). Practitioners should be aware that administration of high volumes of anesthetic can result in femoral nerve blockade, potentially causing quadriceps weakness (8).

The PENG block provides excellent anesthesia for acetabular fractures and femoral neck fractures. It can provide anesthesia for intertrochanteric or subtrochanteric fractures, but the effect is not always as consistent. In such cases, consideration should be given to performing a suprainguinal fascia iliaca block, either as the primary regional anesthesia technique or as an adjunct if the PENG block fails to achieve adequate pain control.

How to Perform the PENG Block

1) Obtain consent and gather materials. You will need:

Required equipment includes topical local anesthetic (1% lidocaine), a long-acting local anesthetic such as ropivacaine or bupivacaine, sterile saline for flushing, a 10-mL syringe for local injections, and a 60-mL syringe for the plane block. Additional supplies include IV extension tubing approximately 10 cm in length, an 18-gauge needle for drawing up anesthetic agents, a 25-gauge needle for skin anesthesia, and a 21-gauge nerve block needle (or a non-cutting spinal needle) for block performance. When possible, an 80-mm needle should be selected to ensure adequate length, particularly in patients with a larger body habitus. Ultrasound equipment should be available, including an ultrasound machine and a sterile ultrasound probe cover. Skin preparation should be performed using chlorhexidine, and sterile gloves should be worn throughout the procedure.

2) Place the patient on a cardiac monitor to ensure the team will be altered to the accidental intravascular administration of high dose local anesthetic.

3) Orient the ultrasound and patient to facilitate performance of the block (figure 1).

4) Complete patient skin cleaning and preparation with chlorhexidine (preferred) and/or provodone/iodine.

5) Using either a linear or curved transducer, place the ultrasound probe over the anterior superior iliac spine, then move the probe medially to find the anterior inferior iliac spine and psoas muscle. For larger patients, the curvilinear probe often affords better visualization.

6) Administer skin anesthetic. Take care to avoid the lateral femoral cutaneous nerve. Attach the 60ml syringe to the extension tubing and the extension tubing to the needle to be used for performance of the nerve block. This allows the

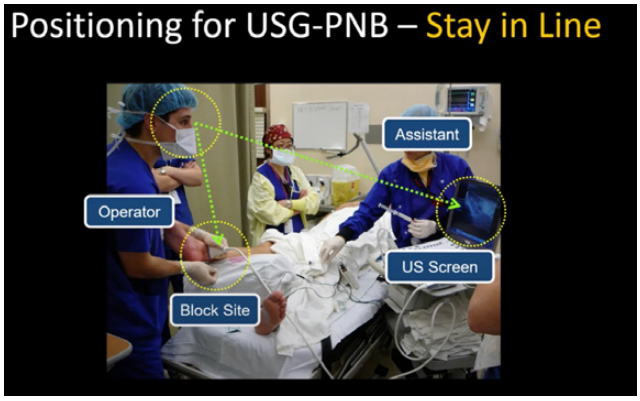

Figure 1. Correct operator orientation relative to ultrasound and patient. The operator should take a position that allows visualization of the patient, block site and ultrasound without turning of the body or head.

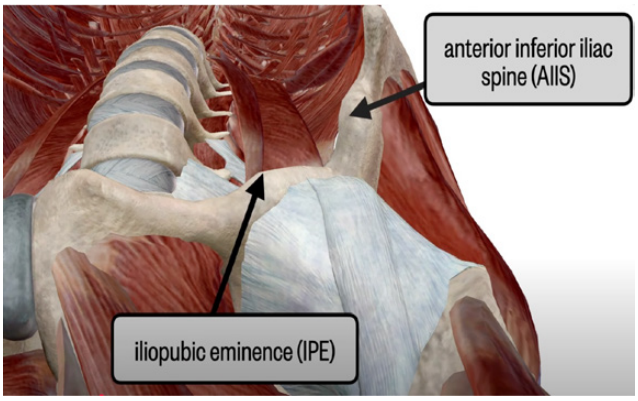

Figure 2. Relevant bony anatomy for PENG block.

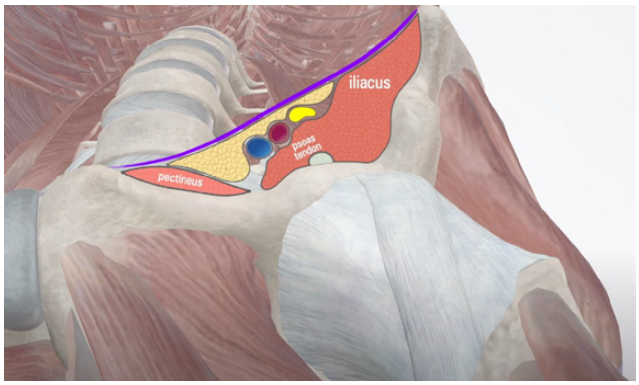

Figure 3. Illustration of the relevant anatomy for the PENG block. The femoral vein, artery and nerve are indicated by the blue, red and yellow circles, respectively.

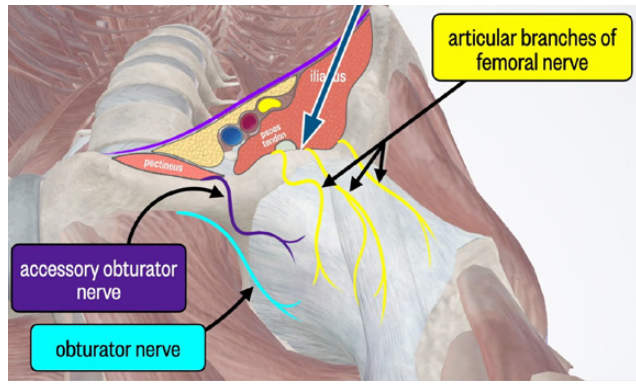

Figure 4. The blue arrow represents the correct needle path, aiming to place the needle under the psoas tendon, towards the iliopubic eminence

operator to keep the needle in position while an assistant delivers the anesthetic with the 60ml syringe.

7) Advance the needle under direct visualization to the psoas muscle. Use an in-plane approach, moving from lateral to medial until contact with the ilium is made under the psoas tendon (figures 3,4,5).

8) Once on the fascia investing the bone beneath the psoas tendon, spin the needle to help ensure the needle cuts below fascia.

9) Administer a test saline injection of 0.5ml normal saline to ensure the needle is not in muscle or tendon.

10) Now administer 15-20 ml of dilute local anesthetic. Highly concentrated anesthetic is not needed for the PENG block because the nerves are small. No more than 20ml is required for successful block (larger volumes of anesthetic increases the spread of anesthetic and the consequent risk of lumbar plexus blockade). Correct administration of anesthetic will cause a lift of the iliopsoas tendon (figures 5,6,7).

Complications and How to Avoid Them.

When performed with care and under direct ultrasound guidance, the risk of complications with the PENG block is low. There are, however, several complications the astute operator will look out for (9).

Complication number one: Accidental blockade of the femoral nerve with resulting quad weakness. As noted above, femoral nerve blockade is usually a consequence of overzealous administration of local anesthetic during the block (i.e. the operator administers too much volume). This will cause quad and hip weakness, which is not a problem in the emergency department, but can lead to difficulty with rehabilitation after surgical repair if the block is performed immediately prior to surgery.

The most important complication to avoid is femoral nerve blockade, which occurs when excessive local anesthetic is administered.

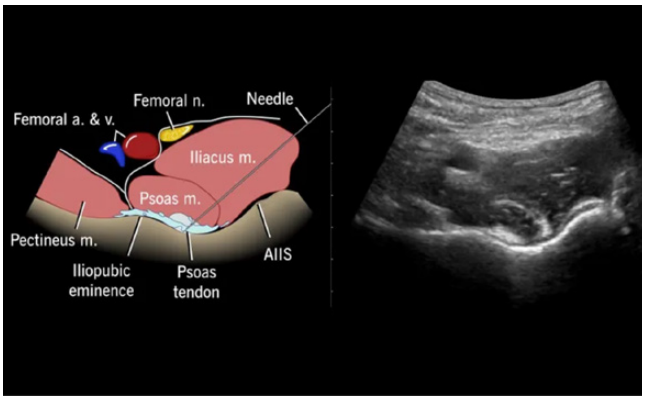

Figure 5. Schema of correct needle placement, with needle tip under the psoas tendon demonstrating lift of the tendon with anesthetic administration (left). Ultrasound image with curved probe demonstrating the AIIS, psoas tendon and iliopubic eminence (right). AIIS, anterior inferior iliac spine.

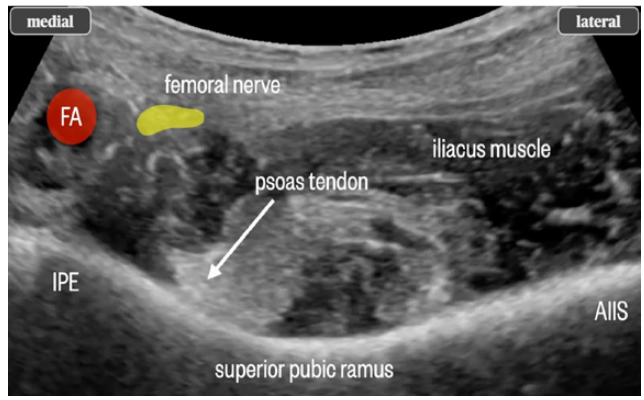

Figure 6. Close-up ultrasound image of anatomy relevant to PENG block. AIIS, anterior inferior iliac spine; IPE, iliopubic eminence; FA, femoral artery.

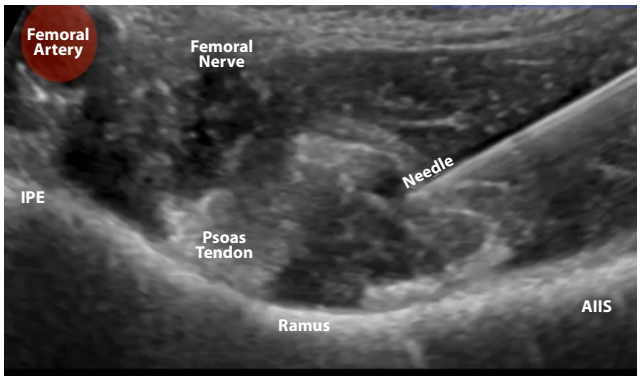

Figure 7. Ultrasound image demonstrating needle approach. Note how the needle is seen in-plane, approaching the psoas tendon. The femoral artery and femoral nerves are clearly seen and avoided.

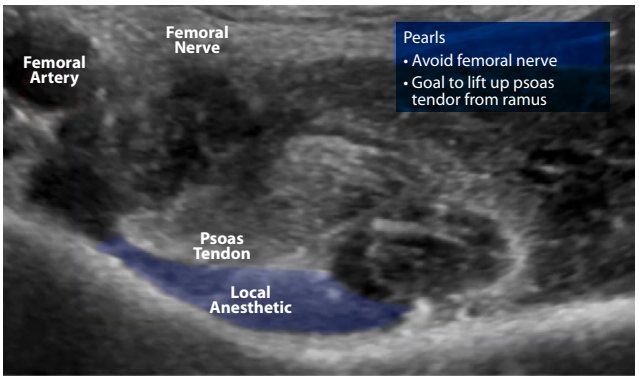

Figure 8. Ultrasound image demonstrating anesthetic lifting the psoas tendon from the pubic ramus, indicating successful anesthetic deposition. The femoral nerve and artery have been avoided.

Complication number two: Inadvertent intravascular injection and local anesthetic toxicity. When the block is performed correctly under ultrasound guidance, the femoral vasculature is distant from the block site and the consequent risk of this complication is low. It is important to note that the toxicity is higher with bupivacaine than with lidocaine.

Complication number three: Inability to injection anesthetic due to high resistance. While not a true complication, high resistance to injection can render the PENG block difficult to execute. This occurs when the needle is not in the right location or the fascia has not been penetrated. There should be some resistance to injection, but if resistance is very high, ask yourself: are you in the right place?

Complication number four: After administration of the block, the anesthetic moves out of place. This complication is more common with other nerve blocks (for example, the fascia iliaca nerve block), it can occur if the anesthetic is administered in the wrong location, or if too much anesthetic is administered.

Complication number five: Allergic reaction to local anesthetic. Allergic reactions to local anesthetics are known to occur, and the mindful operator should watch for their occurrence, even if they are uncommon.

Discussion

The PENG block is a useful tool for emergency medicine specialists trying to treat the pain after hip fracture. We believe it is straightforward to learn, and straightforward to perform. While perhaps not the less effective for some hip fractures (intertrochanteric fractures), it has the has the benefit of analgesia with less motor nerve paralysis, allowing for more accurate assessment by orthopedic surgery prior to surgical repair.

Acknowledgements

This author acknowledges his deep debt to the work of Dr. Ki Jinn Chin of the University of Toronto, for his pioneering work in regional anesthesia. He is a peerless educator whose brilliance and generosity cannot be overstated.

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PRIKAZ SLUČAJA / CASE REPORT

KAMELEON MEĐU MOŽDANIM UDARIMA: INFARKT ARTERIJE PERCHERON KAO DIJAGNOSTIČKI IZAZOV U HITNOJ MEDICINI

THE CHAMELEON AMONG STROKES: PERCHERON ARTERY INFARCTION AS A DIAGNOSTIC CHALLENGE IN THE EMERGENCY MEDICINE

***Ivanka Jurica[1], Domagoj Kihas[1], Boris Bezak[1], Martina Pavletić[1,2]**

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Sažetak

Uvod: Irigacija talamusa i mezencefalona podložna je brojnim anatomskim varijacijama, među kojima se izdvaja arterija Percheron kao rijedak ogranak stražnje cerebralne arterije s heterogenom irigacijom. Zbog niske učestalosti i šarolike kliničke slike, infarkt u njezinu slivu predstavlja dijagnostički izazov, osobito u hitnoj medicini.

Prikaz slučaja: Prikazujemo 80-godišnju bolesnicu koja se prezentirala kratkotrajnim gubitkom svijesti i početnom prolaznom desnostranom slabošću, nakon čega je došlo do progresije poremećaja stanja svijesti. Standardna neuroradiološka i laboratorijska obrada nije otkrila jasnu etiologiju poremećaja svijesti. Daljnjim pogoršanjem kliničkog stanja uz obostranu miozu zjenica postavljena je sumnja na leziju moždanog debla, zbog čega je učinjena magnetska rezonanca mozga u hitnoj medicinskoj službi kojom se dokaže infarkt u opskrbnom području arterije Percheron.

Zaključak: Ovaj prikaz naglašava važnost temeljite anamneze i ponavljanja neurološkog pregleda kod neobjašnjivog poremećaja stanja svijesti uz uredan CT nalaz, kako bi se rijetki, ali klinički značajni entiteti poput infarkta arterije Percheron prepoznali dovoljno rano.

Ključne riječi: cerebrovaskularni inzult stražnje moždane arterije; mezencefalon; talamus

Abstract

Background: The irrigation of the thalamus and midbrain is subject to numerous anatomical variations, among which the artery of Percheron stands out as a rare branch of the posterior cerebral artery. Due to its low incidence, infarction in its territory represents a diagnostic challenge, particularly in emergency medicine.

Case report: We present an 80-year-old female patient who initially presented with a brief loss of consciousness and transient right-sided weakness, followed by progressive deterioration of consciousness. Standard neuroradiological and laboratory workup did not reveal a clear etiology of the altered mental status. With further clinical deterioration accompanied by bilateral pupillary miosis, a brainstem lesion was suspected, leading to urgent brain magnetic resonance imaging, which demonstrated an infarction in the artery of Percheron vascular territory.

Conclusion: This case highlights the importance of thorough history taking and repeated neurological examination in patients with unexplained altered consciousness and normal CT findings, in order to recognize rare but clinically significant entities such as artery of Percheron infarction in a timely manner.

Keywords: midbrain; posterior cerebral artery cerebrovascular insult; thalamus

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Uvod

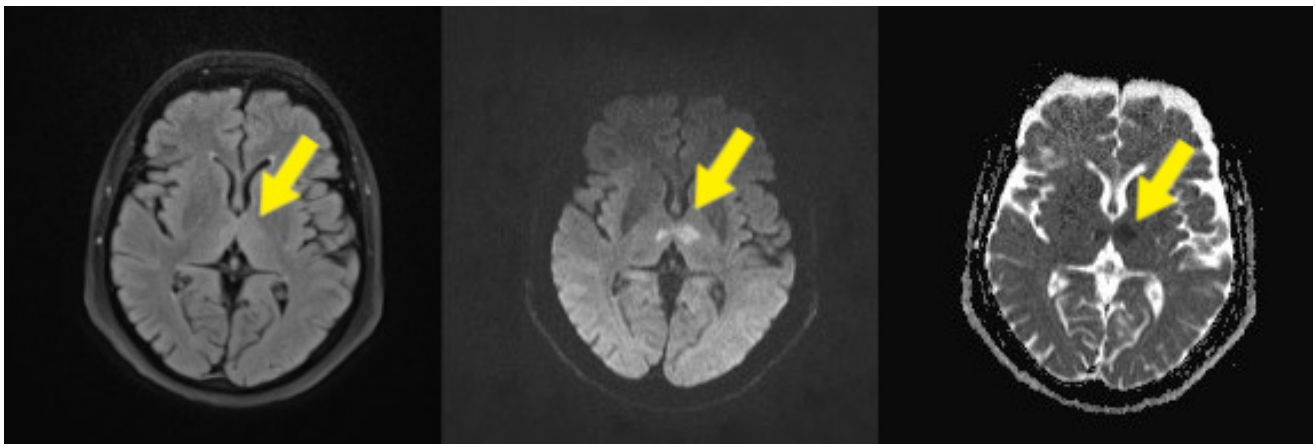
Irigacija talamusa i mezencefalona izrazito je složena te podložna brojnim značajnim anatomskim varijacijama. Od njih jedna je i arterija Percheron, koja obostrano opskrbljuje paramedijalni talamus, a varijabilno i anteriorni talamus te rostralni mezencefalon (1-4). Budući da je riječ o rijetkoj anatomskoj varijaciji, slučajevi lezija njenog opskrbnog područja čine mali dio (do 2 %) svih ishemijskih inzulta (4,5) zbog čega nisu dio svakodnevne kliničke prezentacije. Upravo zahvaljujući značajnoj anatomskoj varijabilnosti klinička prezentacija infarkta u opskrbnom području arterije Percheron vrlo je složena i heterogena (4), što predstavlja diferencijalno dijagnostički izazov u hitnim bolničkim prijamima. Cilj ovog prikaza slučaja jest upoznavanje s navedenim kliničkim entitetom u svrhu ranog prepoznavanja i pravovremene reperfuzije zahvaćenog dijela moždanog parenhima.

Prikaz slučaja

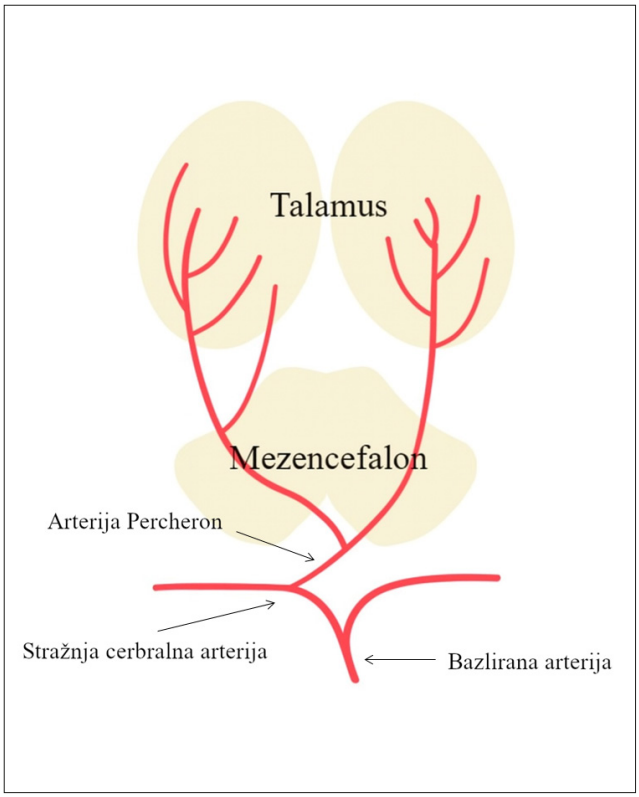
Bolesnica u dobi od 80-godina dovezena je u sjedećem položaju u Objedinjeni hitni bolnički prijam (OHBP) zbog kratkotrajnog gubitka svijesti. Po oporavku svijesti u neurološkom statusu zamijećena je prostorna i vremenska dezorijentiranost. Tijekom transporta bolesnica je postala somnolentna uz razvoj desnostrane slabosti po centralnom tipu.

Po prijamu u OHBP bolesnica je disala spontano, suficijentno, bila je izrazito hipertenzivna (vrijednosti krvnoga tlaka 230/110 mmHg) uz uredan elektrokardiografski (EKG) zapis, uredne vrijednosti glukoze i tjelesne temperature te uredan somatski status. U neurološkom statusu bila je prisutna somnolencija bez odgovarajućeg verbalnog odgovora, uz otvaranje oči na poziv. Zjenice su bile uže, izokorične, simetrične i fotoreaktivne uz urednu bulbomotoriku i negativne meningealne znakove. Asimetriju lica nije imala, ali je perzistirala desnostrana slabost po centralnom tipu. Radi kliničke slike cerebrovaskularnog inzulta bio je pokrenut protokol za neurointervenciju. Rezultati učinjenih pretraga, kompjuterizirane tomografije (engl. *computed tomography*, CT) mozga, CT angiografije karotidnih, vertebralnih i intrakranijskih krvnih žila nisu pokazali znakova svježe hemoragije i ishemije, kao ni vidljivog ispada perfuzije. U tijeku radiološke obrade u bolesnice je došlo do normalizacije krvnog tlaka i regresije desnostrane slabosti, ali bez potpunog oporavka stanja svijesti i uspostave verbalnog kontakta. Po prispijeću urednih nalaza učinjene neuroradiološke obrade, a u nedostatku fokalnog neurološkog ispada proširila se obrada u svrhu pronalaska druge etiologije poremećaja stanja svijesti. Proširena laboratorijska obrada pristigla je uredna, izuzev pozitivnog nalaza benzodiazepina u urinu koje je bolesnica imala u kroničnoj terapiji. Primjena flumazenila intravenski bila je bez kliničkog odgovora. U daljnjem tijeku zbog razvoja izrazite mioze zjenica obostrano bez oporavka budnosti postavljena je sumnja na leziju moždanog debla, što je bio ključan trenutak kliničke prezentacije. Indicirana je hitna magnetska rezonancija (MR) mozga u dogovoru s dežurnom radiološkom službom kojom se dokazala akutna ishemijska lezija u irigacijskom području arterije Percheron (obostrano talamično i rostralno mezencefalično) (slika 1).

Zbog daljnje progresije poremećaja stanja svijesti uz epizode apneje bolesnica je endotrahealno intubirana uz indukciju u brzome slijedu, strojno ventilirana uz analgosedaciju te zaprimljena na daljnje liječenje u Jedinicu intenzivnog liječenja Klinike za neruologiju. Konzervativnim liječenjem kroz nekoliko dana došlo je do postepenog, djelomičnog oporavka deficita. Nakon produžene hospitalizacije bolesnica je otpuštena na fizikalnu rehabilitaciju uz zaostalu vremensku i prostornu dezorijentiranost te blagu desnostranu slabost po centralnom tipu.



Slika 1. Radiološke snimke bolesnice. Na lijevoj slici prikazana je FLAIR sekvenca (engl. *Fluid-Attenuated Inversion Recovery*), na kojoj se uočava diskretna zona povišenog signala. Na istom mjestu, na DWI/ADC sekvencama (engl. *Diffusion Weighted Imaging / Apparent Diffusion Coefficient*), prikazanim na srednjoj i desnoj slici, vidi se restrikcija difuzije.



Slika 2. Irigacijsko područje arterije Pecheron

Rasprava

Talamus i mezencefalon opskrbljeni su krvlju od strane perforirajućih grana stražnje cerebralne i komunikantnih arterija (1,4). Paramedijani dijelovi talamusa i varijabilno mezencefalon najčešće su irigirani od strane parnih paramedijanih arterija koje su ogranci lijeve i desne stražnje cerebralne arterije (1,5). Međutim, u manjem broju ljudi (4-12 %) (4,5) navedeno područje opskrbljuje samo jedna arterija, arterija Percheron koja unilateralno polazi iz P1 segmenta stražnje cerebralne arterije. (1,2,4,5) (Slika 2).

Klinička slika infarkta opskrbnog područja arterije Percheron najčešće uključuje trijadu simptoma: vertikalnu parezu pogleda, poremećaje pamćenja i poremećaje stanja svijesti sve do kome (4-7), što odgovara bilateralnom zahvaćanju paramedijanih područja talamusa. Ovisno o daljnjoj anatomskoj varijabilnosti irigacija arterije Percheron može obuhvaćati i anteriorne dijelove talamusa te rostralne dijelove mezencefalona; čime se klinička prezentacija dodatno komplicira (2,4,5,8). Ukoliko su zahvaćeni anterirorni dijelovi talamusa, poremećaji pamćenja značajno su teži (5); dok tzv. „mezencefalotalamični" sindrom karakteriziraju još i hemiplegija, ataksija, poremećaji kretanja te drugi okulomotorni poremećaji – primjerice horizontalna pareza pogleda i mioza (4-6). U našem slučaju prisutna su bila dva od tri „klasična" simptoma, uz dodatne znakove zahvaćenosti mezencefalona.

Atipična „kameleonska" klinička prezentacija infarkta arterije Percheron pokazuje kako se rijetki neurovaskularni entiteti mogu previdjeti ako se oslanjamo isključivo na početni CT nalaz.

Diferencijalno dijagnostički u obzir dolaze brojna nevaskularna, kao i nekoliko vaskularnih stanja. Nevaskularni uzroci uključuju trovanja (npr. ugljikov monoksid, cijanid, metanol), sistemne bolesti (npr. bolesti jetre, poremećaje glikemije, hipoksiju, Wilsonovu bolest, Wernickeovu encefalopatiju i drugo), neurodegenrativne bolesti (npr. Huntingtonovu bolest, Creutzfeldt-Jakobovu bolest); kao i infektivne uzroke i neoplazme (8,9). Pažljivim uzimanjem anamneze i pregledom, kao i laboratorijskom i radiološkom obradom navedena se stanja mogu brzo isključiti s velikom sigurnošću. Od vaskularnih uzroka bitalamičkih lezija uz okluziju arterije Percheron u obzir dolaze okluzija bazilarne arterije, kao i tromboza venskih sinusa. Međutim, oba entiteta zahvaćaju značajno veći dio moždanog parenhima, zbog čega se obično i klinički i radiološki prezentiraju drugačije od infarkta u području arterije Percheron (8,10).

Važno je napomenuti da je kod okluzije arterije Percheron nativni CT mozga u većini slučajeva početno uredan te da CT angiografijom u velikoj većini slučajeva nije moguće izravno prikazati arteriju, (4, 5, 8) što zahtjeva snimanje MR-a mozga i u hitnoj medicinskoj službi. Navedeno, uz nisku učestalost i heterogenost kliničke prezentacije, značajno komplicira postavljanje ispravne dijagnoze u hitnim prijamima.

Sustavan pristup, koji uključuje detaljnu anamnezu, opetovane neurološke preglede te pravodobno učinjenu MR mozga, ključan je za točnu i pravodobnu dijagnozu u hitnoj službi.

Zaključak

Infarkt u opskrbnom području arterije Percheron je rijedak, ali značajan entitet koji se očituje varijabilnom, složenom i povremeno nespecifičnom kliničkom slikom. Upravo zbog heterogenosti prezentacije te često urednog početnog nalaza CT mozga, njegovo prepoznavanje predstavlja dijagnostički izazov. U prikazanom slučaju su temeljita anamneza i ponovna procjena neurološkog statusa doveli do visoke razine kliničke sumnje, što je omogućilo pravovremenu indikaciju hitne MR pretrage i posljedično postavljanje ispravne dijagnoze. Ovaj prikaz ističe važnost serijskih kliničkih pregleda i podsjeća da kod neobjašnjivog

poremećaja stanja svijesti, osobito uz znakove zahvaćanja moždanog debla, uvijek treba razmotriti i rijetke vaskularne uzroke poput infarkta arterije Percheron, s obzirom da pravovremena dijagnostika i liječenje mogu značajno utjecati na ishod bolesnika.

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REVIEW ARTICLE / PREGLEDNI ČLANAK

DIJAGNOSTIČKO – TERAPIJSKI POSTUPCI U ZBRINJAVANJU EPILEPTIČKOG NAPADAJA I EPILEPTIČKOG STATUSA U HITNOJ MEDICINI

DIAGNOSTIC AND THERAPEUTIC PROCEDURES IN THE MANAGEMENT OF EPILEPTIC SEIZURE AND EPILEPTIC STATUS IN THE EMERGENCY MEDICINE

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Sažetak

Epilepsija je kronična neurološka bolest obilježena trajnom predispozicijom mozga za nastanak epileptičkih napadaja. Radi se o ponavljanim, neprovociranim epileptičkim napadajima koji su posljedica poremećene sinkronizacije i prijenosa električnih impulsa među neuronima u mozgu. Klinička prezentacija epileptičkih napadaja izrazito je heterogena, od kratkotrajnih poremećaja svijesti do izraženih generaliziranih konvulzija, što dodatno naglašava složenost dijagnostike i liječenja. Poseban klinički i terapijski izazov predstavlja epileptički status, jedno od najhitnijih stanja u neurologiji, definiran kao produljeni epileptički napadaj ili niz napadaja bez potpunog oporavka svijesti između epizoda. Prekasno započeto liječenje ili neliječeni epileptički status povezan je s visokim rizikom trajnog oštećenja mozga, sistemskih komplikacija i smrtnog ishoda. Liječenje epileptičkog napadaja i epileptičkog statusa mora započeti što ranije, idealno već u izvanbolničkim uvjetima, uz paralelnu stabilizaciju vitalnih funkcija. Terapija se provodi u jasno definiranim fazama: benzodiazepini kao prva linija liječenja, ne-benzodiazepinski antiepileptici kao druga linija u slučaju trajanja epileptičkog statusa te nadalje opći anestetici kod refraktornog epileptičkog statusa. Brzo i pravilno zbrinjavanje napadaja, pravodobna primjena lijekova te kontinuirano praćenje bolesnika ključni su za smanjenje komplikacija, prevenciju recidiva i poboljšanje ishoda liječenja. Ovaj rad prikazuje pregled spoznaja o vrstama epileptičkih napadaja, dijagnostičkom pristupu u u hitnoj medicini te načelima akutnog zbrinjavanja i liječenja, s posebnim naglaskom na terapijske algoritme kod epileptičkog statusa.

Ključne riječi: epileptički napadaj; epileptički status; hitna medicina; liječenje

Abstract

Epilepsy is a chronic neurological disease. It is characterized by a permanent predisposition of the brain to epileptic seizures. These seizures are repeated and unprovoked, resulting from impaired synchronization and transmission of electrical impulses between neurons. The clinical presentation of seizures is extremely heterogeneous, ranging from short-term disturbances of consciousness to pronounced generalized convulsions. This variation emphasizes the complexity of diagnosis and treatment. Status epilepticus presents a special clinical and therapeutic challenge. It is one of the most urgent conditions in neurology and is defined as a prolonged seizure or a series of seizures without recovery of consciousness between episodes. Treatment that is delayed or not started can lead to a high risk of permanent brain damage, systemic complications, and death. Management must begin as early as possible, ideally in outpatient settings, along with stabilization of vital functions. Therapy follows

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clearly defined phases: benzodiazepines as first-line treatment, non-benzodiazepine antiepileptics as second line if status epilepticus persists, and general anesthetics in refractory cases. Rapid and proper management, timely medication, and continuous monitoring are key to reducing complications, preventing relapse, and improving outcomes.

This article reviews current knowledge on seizure types, emergency diagnostic methods, acute management principles, and treatment, with emphasis on therapeutic algorithms for status epilepticus.

Keywords: emergency medicine; seizure; status epilepticus; treatment

Epilepsija i epileptički napadaji

Definicija

Epilepsija je kronična neurološka bolest i poremećaj funkcije središnjeg živčanog sustava (SŽS), obilježena trajnom predispozicijom mozga za stvaranje epileptičkih napadaja te neurobiološkim, kognitivnim, psihološkim i socijalnim posljedicama ovog stanja (1,2,3). Spontana, nepredvidiva i prekomjerna električna pražnjenja neurona klinički se očituju epileptičkim napadajima (EN), čiji simptomi i klinička slika ovise o anatomskoj lokalizaciji i širenju epileptiformne aktivnosti (1,2). Epilepsija nije jedinstvena bolest, već heterogena skupina poremećaja različite etiologije i kliničke prezentacije, čija je zajednička osobina trajna sklonost pojavljivanju EN-a, odnosno naglih i prolaznih epizoda moždane disfunkcije (1,3,4,5).

Epilepsija je kronična neurološka bolest s trajnom sklonošću epileptičkim napadajima, s mogućim kognitivnim, psihološkim i socijalnim posljedicama; pogađa oko 50 milijuna ljudi u svijetu te 40 000–45 000 osoba u Hrvatskoj.

Prevalencija i incidencija

Procjenjuje se da oko 50 milijuna ljudi u svijetu boluje od epilepsije, što je čini jednom od najčešćih kroničnih neuroloških bolesti (2).

Prevalencija, odnosno udio oboljelih od epilepsije s aktivnom bolesti iznosi približno 1 % u općoj populaciji, dok se incidencija novodijagnosticiranih slučajeva u razvijenim državama kreće od 50 do 80/100 000 stanovnika godišnje, a u slabije razvijenim državama doseže oko 190/100 000 stanovnika (1). Procjenjuje se da u Republici Hrvatskoj od epilepsije boluje približno 40000–45000 osoba (1-3,6), uz prevalenciju od 4,8–5,5/1000 stanovnika (7).

Tijekom života oko 10 % opće populacije doživi barem jedan EN; međutim, pojava jednog neprovociranog napadaja sama po sebi nije dovoljna za postavljanje dijagnoze epilepsije. Prema suvremenim kriterijima, epilepsija se obično dijagnosticira nakon najmanje dva neprovocirana (ili refleksna) EN-a u razmaku ≥24 sata, ili nakon jednog neprovociranog EN-a uz dokazan visoki rizik recidiva, usporediv s tim da bi osoba imala dva EN-a (2).

Etiologija

EN-i se dijele na neprovocirane i provocirane, ovisno o tome postoji li jasan provocirajući čimbenik. Neprovocirani EN-i posljedica su trajnih patoloških promjena u mozga koje dovode do epileptogene sklonosti. Provocirani (akutni simptomatski) EN-i javljaju se u sklopu akutnog poremećaja ili oštećenja SŽS-a i/ili sistemskog stanja, koji dovode do privremenog snižavanja praga podražljivosti neurona (tzv. konvulzivni prag). Takva stanja uključuju akutni moždani udar, traumatsku ozljedu mozga, infekcije SŽS-a, intoksikacije i apstinencijske sindrome, metaboličke i elektrolitske poremećaje te povišenu tjelesnu temperaturu. Provocirani EN-i sami po sebi ne znače da osoba boluje od epilepsije te se ne liječe antiepileptičkim lijekovima, već uklanjanjem provocirajućeg čimbenika (1,3,8).

Ranije se epilepsija etiološki dijelila u tri kategorije: idiopatske, simptomatske i kriptogene epilepsije. Budući da je takva podjela bila neprecizna i preopćenita, od 2017. godine, prema klasifikaciji Međunarodne lige protiv epilepsije (engl. *International League Against Epilepsy*, ILAE), epilepsije se etiološki svrstavaju u šest kategorija:

1. Strukturna etiologija obuhvaća epilepsije povezane s jasno definiranim abnormalnostima i oštećenjima mozga, vidljivima neuroslikovnim metodama, ponajprije kompjuteriziranom tomografijom (CT) ili magnetskom rezonancijom (MR), koja su u skladu s kliničkom slikom i elektroencefalografskim (EEG) nalazom bolesnika. Strukturne promjene mogu biti stečene (npr. posljedica moždanog udara, tumora, traumatske ozljede mozga) ili prirođene (npr. kortikalne malformacije) (1,8).

Uzroci epilepsije ovise o dobi, pri čemu u djece prevladavaju genski i razvojni uzroci, a u starijih osoba cerebrovaskularne bolesti i tumori mozga.

2. Genska etiologija podrazumijeva epilepsije u kojih je EN glavni klinički simptom izravno povezan s genskom mutacijom. U velikom broju slučajeva točan genski uzrok još uvijek nije poznat. Genska etiologija ne znači nužno da je epilepsija nasljedna, budući da se često radi o mutacijama *de novo*. U određenih bolesnika epilepsija može biti posljedica složenih interakcija više genskih čimbenika i utjecaja okoliša, pri čemu specifična mutacija ostaje neidentificirana (1,8).

3. Infektivna etiologija odnosi se na epilepsije koje se razvijaju u osoba s preboljelom infekcijom SŽS-a. EN-i koji se javljaju tijekom akutne faze infekcije smatraju se provociranima i ne dijagnosticiraju se kao epilepsija. Nasuprot tome, kasni neprovocirani EN-i koji se pojavljuju mjesecima ili godinama nakon infekcije predstavljaju oblik stečene epilepsije. Na globalnoj razini infekcije SŽS-a jedan su od najčešćih uzroka epilepsije, osobito u zemljama niskog i srednjeg dohotka (1,9).

4. Metabolička etiologija označava epilepsiju koja nastaje kao izravna posljedicu kroničnog ili ponavljajućeg metaboličkog poremećaja, pri čemu EN-i čine jednu od glavnih kliničkih manifestacija bolesti.. Može se pojaviti u bilo kojoj životnoj dobi, a u podlozi može imati gensku ili stečenu osnovu. EN-i uzrokovani akutnim metaboličkim disbalansom (npr. hipoglikemija, hiponatremija) ne ubrajaju se u metaboličke epilepsije, već se klasificiraju kao akutni simptomatski (provocirani) napadaji (1,8,9).

5. Imunosno-posredovana etiologija podrazumijeva epilepsiju kao izravnu posljedicu poremećaja imunosnog sustava, pri čemu EN-i predstavljaju glavni ili jedan od vodećih simptoma. U patogenezi sudjeluju prirođeni i stečeni imunosni mehanizmi. EN-i mogu se javiti u sklopu autoimunih encefalitisa, ali i u okviru sistemskih autoimunih bolesti, poput sistemskog eritemskog lupusa.

6. Nepoznata etiologija označava epilepsiju kod koje uzrok nastanka, unatoč provedenoj standardnoj dijagnostičkoj obradi, nije moguće utvrditi (1,8).

Prisutnost pridruženih bolesti nužno je razmotriti u svakog bolesnika, jer oni mogu utjecati na kliničku prezentaciju, izbor terapije i dugoročni ishod bolesti. Pravodobno prepoznavanje i liječenje pratećih stanja jednako je važno kao i liječenje same epilepsije (8,9).

Najčešći uzroci epilepsije prikazani su u Tablici 1 (10).

Najčešći uzroci EN-a razlikuju se ovisno o dobi pojave:

- Prije 2. godine života: povišena tjelesna temperatura, razvojne ili prirođene malformacije, porođajne ozljede i metabolički poremećaji.
- Od 2. do 14. godine života: genske epilepsije i epilepsije nepoznatog etiologije.
- U odrasloj dobi: traumatska ozljeda mozga, ustezanje od alkohola, tumori mozga, moždani udari te epilepsije nepoznatog uzroka (u približno 50 % slučajeva).
- U starijoj životnoj dobi: tumori mozga i cerebrovaskularne bolesti (11).

Tablica 1. Najčešći uzroci epileptičkih napadaja prema etiologiji i kliničkom kontekstu

Skupina uzroka	Primjeri	Tip napadaja (najčešće)
Primarni neurološki poremećaji	Benigne febrilne konvulzije u djetinjstvu	Provocirani
	Malformacije kortikalnog razvoja, hipokampalna skleroza	Neprovocirani
	Traumatska ozljeda mozga	Akutni simptomatski / kasna epilepsija
	Moždani udar, vaskularne malformacije	Akutni ili neprovocirani
	Tumori, apscesi mozga	Neprovocirani
	Infekcije središnjeg živčanog sustava	Akutni simptomatski
	Genske epilepsije	Neprovocirani
Sistemski poremećaji	Hipoglikemija, hiponatremija, hipokalcemija	Akutni simptomatski
	Hiperosmolarna stanja	Akutni simptomatski
	Uremija, hepatička encefalopatija	Akutni simptomatski
	Porfirija	Akutni simptomatski (ponavljajući)
	Toksičnost lijekova	Akutni simptomatski
	Nagli prestanak lijekova ili alkohola	Akutni simptomatski
	Intoksikacija alkoholom ili drogama	Akutni simptomatski
	Globalna cerebralna ishemija	Akutni simptomatski
	Hipertenzivna encefalopatija	Akutni simptomatski
	Hipertermija	Akutni simptomatski
	Eklampsija	Akutni simptomatski

Legenda: ILAE - Međunarodna liga protiv epilepsije (engl. *International League Against Epilepsy*)
prilagođeno prema ref. 10.

Klasifikacija epileptičkih napadaja

Klasifikacija EN-a temelj je suvremenog dijagnostičkog i terapijskog pristupa epilepsiji. ILAE klasifikacija iz 2017. godine uvela je modernu, operativnu i klinički primjenjivu terminologiju, koja je 2025. dodatno revidirana s ciljem još jasnijeg opisivanja semiologije napadaja i bolje primjenjivosti u svakodnevnoj kliničkoj praksi (Tablica 2) (3,4,7,10). Središnja koncepcija klasifikacije ostala je nepromijenjena. EN-i se klasificiraju prema vrsti početka, dominantnim kliničkim obilježjima i utjecaju na svijest, uz mogućnost naknadnog preciziranja kako se dostupni klinički i dijagnostički podaci proširuju (3).

Prema aktualnoj reviziji, EN-i se dijele u četiri temeljne skupine:

- žarišni (fokalni) napadaji,
- generalizirani napadaji,
- napadaji nepoznate vrste,
- neklasificirani napadaji (4,9,12).

Žarišni EN-i započinju u ograničenom području jedne moždane hemisfere. Njihova klinička prezentacija ovisi o zahvaćenoj moždanoj regiji i širenju epileptiformne aktivnosti. Prema razini svijesti dijele se na: žarišne napadaje s očuvanom sviješću i žarišne napadaje s poremećenom sviješću. Dodatno se klasificiraju prema dominantnim početnim manifestacijama na motoričke ili nemotoričke (npr. žarišni motorički napadaj s toničkom aktivnošću, žarišni nemotorički napadaj s osjetnim simptomima) (4,9,12). Razina svijesti ne koristi se za klasifikaciju generaliziranih napadaja, jer većina (iako ne svi) generaliziranih napadaja dovode do poremećaja svijesti.

Kod žarišnih EN-a dodatno se opisuje klinička slika (motorički, osjetni, autonomni, kognitivni, emocionalni i dr.), dok se kod generaliziranih napadaja zadržavaju tradicionalni, dobro poznati nazivi (npr. generalizirani toničko-klonički, apsansi, miokloni, atonički). Dogovorno se smatra da je za pouzdano određivanje vrste početka potrebna najmanje 80 % vjerojatnost da napadaj započinje na opisani način. Ako taj kriterij nije ispunjen, napadaj se klasificira kao napadaj nepoznatog vrste (1,3,4,9,12).

Napadaji nepoznate vrste su oni kod kojih nije moguće pouzdano odrediti početni tijek epileptičke aktivnosti, često zbog nedostatka svjedoka, neodgovarajućih kliničkih podataka ili izostanka dijagnostičkih zapisa. Oni mogu biti klinički motorički (npr. toničko–klonički, epileptički spazmi) ili nemotorički (npr. prekid radnje). Ako se ni nakon dodatne kliničke i dijagnostičke obrade napadaj ne može svrstati u neku od definiranih kategorija, označava se kao neklasificirani napadaj (1,3,4,9,12).

Aura predstavlja subjektivni, nagli i kratkotrajni fenomen koji može prethoditi vidljivoj manifestaciji EN-a. Iako se u svakodnevnom govoru opisuje kao „predosjećaj“ ili „upozorenje“, u modernoj klasifikaciji aura se smatra žarišnim EN-om s očuvanom sviješću. Najčešće uključuje osjetne, kognitivne, emocionalnim ili autonomne simptome. Može se javiti kao izolirani žarišni napadaj ili progredirati u napadaj s poremećenom sviješću i/ili bilateralnim motoričkim širenjem (1,3,4,9,12).

Klasifikacija epilepsija

Klasifikacija epilepsija obuhvaća širi i složeniji koncept od same klasifikacije EN-a, jer polazi od činjenice da jedan bolesnik može imati više različitih vrsta napadaja. Za

Tablica 2. Klasifikacija glavnih vrsta epileptičkih napadaja prema ILAE reviziji iz 2025. godine

Vrsta napadaja	Opis / kriteriji	Primjeri napadaja
Žarišni (fokalni)	Napadaj koji započinje u ograničenom području jedne moždane hemisfere.	Žarišni napadaj s očuvanom sviješću Žarišni napadaj s poremećenom sviješću Žarišni napadaj s prelaskom u bilateralni toničko-klonički napadaj
Generalizirani	Napadaj koji zahvaća obje moždane hemisfere od samog početka.	Apsans Generalizirani toničko-klonički napadaj Ostali generalizirani napadaji (npr. miokloni, atonički, negativni mioklonus)
Nepoznate vrste	Početak napadaja nije moguće pouzdano odrediti na temelju dostupnih kliničkih i dijagnostičkih podataka.	Bilateralni toničko-klonički napadaj Napadaj nepoznate vrste, s ili bez drugih vidljivih kliničkih manifestacija
Neklasificirani	Nedovoljno podataka za pouzdanu klasifikaciju.	–

prilagođeno prema ref. 9

razliku od klasifikacije pojedinačnih napadaja, klasifikacija epilepsije integrira cjelokupni klinički kontekst, uključujući dob početka bolesti, semiologiju svih zabilježenih napadaja, elektroencefalografske i neuroradiološke nalaze, moguće genske čimbenike, očekivanu prognozu te prisutnost pridruženih bolesti. Početak u klasifikaciji epilepsije jest precizna klasifikacija svih vrsta napadaja koje bolesnik ima, nakon čega se, na temelju dodatnih kliničkih i dijagnostičkih podataka, određuje tip epilepsije. Ovakav hijerarhijski pristup omogućuje jasnije razumijevanje bolesti, racionalniji terapijski odabir i realniju procjenu ishoda (4,5,12).

Prema ILAE klasifikaciji epilepsija iz 2017. godine, epilepsije se razvrstavaju u jednu od četiri temeljne kategorije (4,5,8):

1. Žarišna epilepsija
2. Generalizirana epilepsija
3. Kombinirana generalizirana i žarišna epilepsija
4. Epilepsija nepoznatog tipa (4,8).

Dijagnostika

EN-i čest su razlog dolaska u hitnu službu, a procjenjuje se da će ih tijekom života doživjeti oko 8–10% opće populacije. U inicijalnoj procjeni bolesnika od presudne je važnosti razlikovati akutni simptomatski (provocirani) EN od neprovociranog EN-a, budući da se njihovo daljnje zbrinjavanje, liječenje i prognoza značajno razlikuju.

Akutni simptomatski napadaji čine približno 25–30 % prvih prezentacija EN-a. Ovim se pojmom označavaju napadaji koji se javljaju u neposrednoj vremenskoj povezanosti sa sistemskim poremećajem ili akutnim oštećenjem mozga. To uključuje napadaje koji se pojavljuju unutar tjedan dana od moždanog udara, traumatske ozljede mozga, anoksične encefalopatije ili intrakranijalne operacije, pri prvoj prezentaciji subduralnog hematoma, tijekom aktivne faze infekcije SŽS-a ili unutar 24 sata od nastanka teškog metaboličkog poremećaja (3,12).

Neprovocirani epileptički napadaji javljaju se bez jasnog akutnog precipitacijskog čimbenika te mogu biti izraz neprepoznate etiologije, posljedica ranije postojeće strukturne lezije mozga ili dio progresivnog neurološkog poremećaja. Upravo ponavljani neprovocirani napadaji čine osnovu za postavljanje dijagnoze epilepsije.

Dijagnostička obrada započinje detaljnim uzimanjem anamnestičkih i heteroanamnestičkih podataka, uz neurološki i opći fizikalni pregled. Kod prve manifestacije EN-a važno je prikupiti podatke o trudnoći i porodu, ranom psihomotornom razvoju, obrazovanju, febrilnim konvulzijama u djetinjstvu, ranijim traumama glave te preboljelim infekcijama SŽS-a (5,12).

Pravodobno prepoznavanje vrste epileptičkog napadaja i etiologije ključno je za uspješno liječenje, kontrolu bolesti i poboljšanje kvalitete života oboljelih.

U dijela bolesnika mogu se identificirati precipitirajući čimbenici ili „okidači“ napadaja, poput snažnih emocionalnih podražaja, intenzivnog fizičkog napora, glasne glazbe ili blještavih svjetala (fotosenzitivnost), koje bolesnici često navode neposredno prije napadaja. Fiziološka stanja poput povišene tjelesne temperature, deprivacije spavanja, stresa i perimenstrualnog razdoblja također mogu sniziti konvulzivni prag i precipitiraju epileptičke napadaje (3,11,12,13).

Neurološki status u većine bolesnika nakon napadaja je uredan, no osobitu pozornost treba posvetiti prisutnosti žarišnih neuroloških ispada, koji mogu upućivati na strukturnu leziju mozga (12,13,14,15).

Bolesnici s novonastalim EN-om najčešće se obrađuju u hitnom prijamu. Nakon temeljite kliničke procjene, dio bolesnika može se sigurno otpustiti uz daljnje ambulantno praćenje. Tijekom početne obrade nužno je kontinuirano pratiti vitalne znakove te provesti laboratorijsku, neuroradiološku i, kada je dostupno, elektroencefalografsku obradu, uz dodatne pretrage prema kliničkoj indikaciji (6).

Osnovna laboratorijska procjena uključuje određivanje glukoze u serumu, kompletnu krvnu sliku, osnovne biokemijske ppkazatelje (jetreni enzimi, urea, kreatinin), elektrolite (natrij, kalij, klor, ukupni i ionizirani kalcij, magnezij). U hitnoj neuroradiološkoj obradi najčešće se indicira MSCT (*engl. multi-slice computed tomography)* mozga, dok se elektroencefalografija (EEG) preporučuje učiniti što je prije moguće, kada je dostupan. Dodatne pretrage indicirane su u prisutnosti simptoma ili znakova potencijalno lječivog poremećaja, poput traume, infekcije ili metaboličkog disbalansa (9,12).

Kod sumnje na infekciju SŽS-a (povišena tjelesna temperatura, promjena mentalnog statusa, glavobolja, pozitivni meningealni znakovi) potrebno je učiniti lumbalnu punkciju s analizom cerebrospinalnog likvora. Toksikološki probir usmjeren je na tvari koje često uzrokuju EN-e (kokain, simpatomimetici, etanol, kanabionidi). Ovisno o kliničkoj slici mogu se učiniti i proširene laboratorijske pretrage (amonijak u serumu, parametri koagulacije, plinska analiza arterijske krvi, serijsko određivanje troponina). U svih bolesnika preporučuje se učiniti EKG (*Elektrokardiogram*) radi isključenja aritmija kao uzroka epizode gubitka ili poremećaja svijesti (npr. sindrom produljenog QT- intervala) (12,13,14,15).

Cilj dijagnostičke obrade je utvrditi radi li se doista o EN-u ili o drugom poremećaju svijesti, poput psihogenih neepileptičkih napadaja ili sinkope, a zatim identificirati vjerojatni uzrok i moguće precipitirajuće čimbenike (15). U bolesnika s već poznatom epilepsijom, urednim ili nepromijenjenim neurološkim statusom i tipičnom kliničkom prezentacijom, opsežna dodatna obrada često nije potrebna, osim po potrebi određivanja koncentracija antiepileptičkih lijekova (6).

Epilepsija se u pravilu dijagnosticira nakon dva ili više neprovociranih EN-a koji su se pojavili u razmaku duljem

od 24 sata. U određenim okolnostima dijagnoza može postaviti i nakon prvog neprovociranog napadaja, ako postoji visok rizik recidiva, primjerice kod jasno definirane strukturne lezije mozga ili prepoznatog epileptičkog sindroma. Dijagnoza se temelji na kliničkoj slici, detaljnoj anamnezi, neurološkom pregledu i EEG nalazu. uz istodobno isključivanje drugih mogućih uzroka epilepsije (12,15).

EEG je ključna metoda u dijagnostici EN-a, jer može potvrdi epileptičku prirodu događaja te pomoći u određivanju vrste napadaja i tipa epilepsije (6). Može pokazati epileptiformne abnormalnosti, poput šiljaka, zašiljenih valova, kompleksa šiljak–val, polišiljaka i sporih valova, koje su najčešće bilateralne, simetrične i sinkrone u bolesnika s generaliziranim napadajima, odnosno lokalizirane u bolesnika sa žarišnim napadajima (6). Ipak, važno je naglasiti da uredan EEG nalaz ne isključuje epilepsiju, kao što ni prisutnost epileptiformnih promjena sama po sebi nije dovoljna za postavljanje dijagnoze. Nalaz je uvijek potrebno tumačiti u kontekstu kliničke slike (14,15).

Neuroslikovna obrada, najčešće MSCT mozga u akutnoj fazi, provodi se radi isključenja intrakranijalnog krvarenja, tumora ili drugih hitnih strukturnih uzroka. U djece s tipičnim febrilnim konvulzijama, urednim neurološkim statusom i brzim oporavkom, MSCT se može odgoditi ili izbjeći. MR (engl. *magnetic resonance*) mozga preporučuje se kada je MSCT uredan ili nedovoljno informativan, jer omogućuje detaljniju detekciju tumora, apscesa, kortikalnih malformacija, tromboze venskih sinusa i encefalitisa. Protokol za epilepsiju kod MR mozga koristi T1 i T2 sekvence visoke razlučivosti kojima se mogu otkriti hipokampalna hipotrofija ili skleroza, malformacije kortikalnog razvoja u djece, meziotemporalna skleroza, traumatska glioza i mali tumori u odraslih (16).

Diferencijalna dijagnoza

U diferencijalnoj dijagnostici bolesnika nakon prvog EN-a nužno je razmotriti i isključiti niz stanja koja mogu oponašati EN-e. Najvažnija među njima uključuju psihogene neepileptičke napadaje (PNEN), konvulzivnu sinkopu, tranzitornu ishemičku ataku (osobito u starijoj životnoj dobi), migrenu, panične atake, tranzitornu globalnu amneziju, narkolepsiju s katapleksijom te paroksizmalne poremećaje pokreta (12,15,16). Precizna diferencijacija ključna je kako bi se izbjegla pogrešna dijagnoza epilepsije i nepotrebno dugotrajno liječenje antiepileptičkim lijekovima.

PNEN-i paroksizmalni su događaji koji klinički mogu nalikovati EN-ima, ali nisu praćeni abnormalnom, sinkronom neuronskom aktivnošću karakterističnom za epilepsiju. Predstavljaju somatsku manifestaciju psihičkog poremećaja te se mogu javiti i u osoba bez epilepsije, ali i u bolesnika s istodobno prisutnom epilepsijom (17). U usporedbi s EN-ima, obično su duljeg trajanja, gotovo se uvijek događaju u prisutnosti drugih osoba, a tijekom epizode obično nema stvarnog poremećaja svijesti. Bolesnici mogu djelomično ili potpuno kontrolirati tijek napadaja, ponekad ih spontano započeti ili prekinuti, te tijekom epizode mogu odgovarati na pitanja ili reagirati na podražaje (17). Klinička obilježja koja upućuju na psihogenu prirodu uključuju trzaje glave lijevo–desno, čvrsto zatvorene oči uz otpor pri pokušaju otvaranja vjeđa, izraženo izvijanje trupa i podizanje zdjelice, rotaciju tijela te pokrete ekstremiteta velikog opsega s nesinkroniziranim, nepravilnim trzajima koji se ne uklapaju u prepoznatljive semiološke obrasce EN-ova (9). Epizode su često praćene plakanjem ili vokalizacijama poput jaukanja, vikanja ili vriskanja. Ugriz jezika je rijedak, a ako je prisutan, češće zahvaća vrh jezika, za razliku od tipičnog lateralnog ugriza kod generaliziranog toničko-kloničkog EN-a (GTKN). Postiktalna smetenost obično izostaje; bolesnik se brzo razbistri, urednog je kontakta i orijentacije te se najčešće sjeća događaja (17).

Konvulzivna sinkopa je kratkotrajni reverzibilni gubitak svijesti uzrokovan globalnom hipoperfuzijom mozga, praćen kratkotrajnim mioklonim trzajima ekstremiteta. Za razliku od epileptičkog napadaja, konvulzivnoj sinkopi često prethode premonitorni vegetativni simptomi (mučnina, znojenje, bljedilo, osjećaj slabosti), epizoda je kratkog trajanja (obično do 30 sekundi), a oporavak stanja svijesti je brz i potpun. Koristan praktični pokazatelj je tzv. pravilo 10/20: u konvulzivnoj sinkopi obično se javlja manje od 10 trzaja, dok GTKN najčešće uključuje više od 20 trzaja ekstremiteta (5,11,18).

Epileptički status

Definicija

Definicija epileptičkog statusa (ES) mijenjala se kroz vrijeme u skladu s novim spoznajama o njegovoj etiologiji i patofiziologiji, što je omogućilo ranije prepoznavanje, precizniju dijagnostičku obradu i pravodobno liječenje. ES predstavlja jedno od najhitnijih stanja u neurologiji, jer neliječen ili kasno liječen može dovesti do ireverzibilnog oštećenja mozga i smrti (19,20).

Epileptički status je neurološko hitno stanje koje zahtijeva trenutno liječenje uz stabilizaciju bolesnika i utvrđivanje uzroka.

Prema terminologiji ILAE, ES je stanje koje nastaje zbog neuspjeha mehanizama odgovornih za spontani prekid napadaja ili zbog aktivacije patofizioloških mehanizama koji dovode do abnormalno produljene epileptičke aktivnosti (20-24). Riječ je o kontinuiranoj ili brzo ponavljajućoj epileptičkoj aktivnosti koja, ovisno o trajanju i vrsti napadaja, može rezultirati neuronalnom smrću, strukturnim oštećenjem neurona i trajnim promjenama

u neuronskim mrežama, s dugoročnim neurološkim posljedicama (22-24).

Epidemiologija

ES najčešće se javlja u osoba bez ranije poznate epilepsije, osobito u djece i bolesnika sa strukturnom patologijom mozga, najčešće frontalnog režnja (23-27).

Godišnja incidencija ES-a procjenjuje se na približno 36,1/100 000 osoba. Od toga se oko 24,0/100 000 odnosi na ES s motoričkim (konvulzivnim) simptomima, dok na nekonvulzivni ES otpada oko 12,1/100 000 osoba godišnje (22-27). Među prvim epizodama ES-a, približno 7,2/100 000 klasificira se kao refraktorni ES, dok se oko 1,2/ 100 000 svrstava u superrefraktorni epileptički status (24-28). Nekonvulzivni ES nešto je češći u žena, a ukupna incidencija ES-a značajno raste u osoba starijih od 50 godina. Procjenjuje se da će najmanje 5% odraslih bolesnika s epilepsijom tijekom života doživjeti barem jednu epizodu ES-a, dok je taj udio u dječjoj populaciji znatno veći i kreće se između 10% i 25% (28). Smrtnost povezana s ES-om varira između 5% i 39%, a u razvijenim zemljama iznosi oko 15,9%, pri čemu uvelike ovisi o etiologiji i brzini započinjanja liječenja (17,28). Kod refraktornog i superrefraktornog ES-a stopa smrtnosti približno je tri puta viša nego kod nerefraktornog epileptičkog statusa (28).

Etiologija

Etiologija ES-a jedan je od najvažnijih prognostičkih čimbenika te u velikoj mjeri određuje ishod bolesnika. Unatoč tomu, uzrok ES-a često je teško precizno utvrditi već u hitnoj službi, osobito u ranoj fazi zbrinjavanja, kada je terapijski prioritet brzo prekidanje epileptičke aktivnosti (27,28).

U odrasloj populaciji ES najčešće nastaje kao posljedica akutnih patoloških stanja. Među najčešćim uzrocima su infekcije SŽS-a, traumatska ozljeda mozga (s ili bez intrakranijalnog krvarenja), akutni metabolički poremećaji poput hipoglikemije, hiponatremije i hipokalcemije, hepatička encefalopatija te poremećaji acidobazne ravnoteže. Dodatno, ES može biti izazvan intoksikacijama ili predoziranjem lijekovima, uključujući psihoaktivne tvari i lijekove s prokonvulzivnim učinkom (20,21,28,29). U dječjoj dobi etiološki spektar razlikuje se od odraslih. Najčešći uzroci ES-a u djece uključuju febrilna stanja, infekcije SŽS-a te urođene metaboličke bolesti, koje se često manifestiraju već u ranom djetinjstvu (20,21,28,29)

Osim akutnih uzroka, u podlozi ES-a mogu biti i kronični predisponirajući čimbenici. Oni uključuju epilepsiju s učestalim napadajima ili neodgovarajućim pridržavanjem antiepileptičke terapije, naglo ukidanje antiepileptika ili alkohola, kao i prisutnost tumora mozga. U ovih bolesnika epileptički status često predstavlja dekompenzaciju ranije postojeće bolesti (20,21,29).

Podjela epileptičkog statusa

ES može se klasificirati prema više kriterija, uključujući vrstu EN-a, etiologiju, EEG nalaz, dob bolesnika i odgovor na liječenje. U kliničkoj praksi najčešće se primjenjuje operativna klasifikacija i definicija ILAE iz 2015. godine, koja razlikuje konvulzivni ili toničko-klonički ES (s izraženim motoričkim simptomima) od nekonvulzivnog ES (bez izraženih motoričkih simptoma), pri čemu svaki od ovih oblika može progredirati refraktorni ES (20-22,30).

Konvulzivni (toničko-klonički) ES definira se prisutnošću barem jednog od sljedećih kriterija:

- kontinuirana toničko-klonička epileptička aktivnost u trajanju > 5 minuta,
- ≥ 2 toničko-klonička napadaja između kojih ne dolazi do potpunog oporavka svijesti.

Ranije korištena definicija, s pragom trajanja napadaja duljim od 30 minuta, napuštena je kako bi se potaknulo ranije prepoznavanje i pravodobno liječenje, budući da neliječeni konvulzivni ES koji traje ≥30 minuta nosi visok rizik trajnog oštećenja mozga i lošeg ishoda.

U cilju pravodobnog prepoznavanja, strukturiranog liječenja i sprječavanja progresije ES-a, u kliničkoj se praksi ES dijeli u uzastopne faze prema trajanju epileptičke aktivnosti i odgovoru na terapiju, koje obuhvaćaju rani (premonitorni/prehospitalni), uspostavljeni (razvijeni), refraktorni i superrefraktorni epileptički status.

Nekonvulzivni ES obuhvaća žarišni ES i apsans ES. Klinički se često prezentira kao produljena epizoda promijenjenog mentalnog statusa, uključujući smetenost, stupor ili neobjašnjeno pogoršanje svijesti, uz minimalne ili odsutne motoričke manifestacije. Zbog nespecifične kliničke slike, dijagnoza nekonvulzivnog ES-a u pravilu zahtijeva EEG potvrdu (21,27-30).

Rani ES, koji se u literaturi opisuje i kao *premonitorni*, *prijeteći ili prijebolnički* ES, označava kontinuirani epileptički napadaj ili niz ponavljanih napadaja u trajanju 5 do 10 minuta, bez potpunog oporavka svijesti između epizoda.

Uspostavljeni (razvijeni) ES označava fazu ES-a koja traje od 10 do 30 minuta od početka napadaja, unatoč pravodobnoj i adekvatnoj primjeni benzodiazepina.

Refraktorni ES definira se kao kontinuirana ili ponavljana epileptička aktivnost (konvulzivna ili nekonvulzivna) koja traje dulje od 30-60 minuta unatoč odgovarajućoj primjeni najmanje dva antiepileptika u odgovarajućim dozama, uključujući početnu terapiju benzodiazepinima (18-24,30).

Superrefraktorni ES označava ES koji traje ili se ponovno javlja unatoč liječenju općom anestezijom dulje od 24 sata (21).

Produljeni superrefraktorni ES traje dulje od 7 dana i zahtijeva kontinuiranu primjenu anestetika i/ili ponavljane pokušaje ukidanja anestezije (21).

Tablica 3. Vremenske točke za početak liječenja (t_1) i nastanak trajnih posljedica (t_2) u različitim vrstama epileptičkog statusa (prema ILAE)

Vrsta epileptičkog statusa	t_1 – vrijeme za započinjanje liječenja	t_2 – vrijeme povećanog rizika trajnih posljedica
Toničko-klonički epileptički status	5 minuta	≥ 30 minuta
Žarišni epileptički status s poremećajem svijesti	10 minuta	30–60 minuta
Apsans epileptički status	10–15 minuta	Nedefinirano / nepoznato

Legenda: ILAE - Međunarodna liga protiv epilepsije (engl. *International League Against Epilepsy*) prilagođeno prema ref. 18-24,30,31.

U operativnoj definiciji ES-a ILAE uvodi dvije ključne vremenske točke: t_1 (operativno vrijeme nakon kojeg EN treba smatrati ES i započeti aktivno liječenje, najčešće primjenom benzodiazepina) i t_2 („kritično“ vrijeme nakon kojeg se značajno povećava rizik neuronalne smrti, oštećenja sinapsi i trajnih funkcionalnih posljedica (18-24,30). Vremenske točke t_1 i t_2 ovise o vrsti ES-a te su prikazane u Tablici 3.

EN-e prije dosezanja vremenske točke t_1 nije uvijek nužno zbrinjavati kao hitno stanje. Međutim, nakon što se dosegne t_1, napadaj se mora smatrati ES-om i liječiti kao hitno stanje, s ciljem postizanja potpune kontrole epileptičke aktivnosti najkasnije do vremenske točke t_2, kako bi se smanjio rizik trajnog oštećenja mozga i nepovoljnog ishoda (1).

Dijagnostička obrada epileptičkog statusa

Dijagnostički pristup ES-u razlikuje se ovisno o kliničkoj prezentaciji.

Konvulzivni epileptički status dijagnosticira se prvenstveno na temelju kliničkih znakova, dok se nekonvulzivni epileptički status u pravilu potvrđuje EEG nalazom. Neovisno o kliničkom obliku, nužna je hitna laboratorijska i neuroradiološka obrada radi razjašnjenja etiologije i planiranja daljnjeg liječenja (21,22,28,30).

U svakog bolesnika s ES-om potrebno je u najkraćem mogućem roku isključiti sljedeće uzroke ili pridružena stanja:

1. strukturnu abnormalnost mozga, uključujući intrakranijsko krvarenje, cerebralnu ishemiju ili traumatsku ozljedu mozga,
2. infekciju SŽS-a,
3. metaboličke poremećaje osobito poremećaje elektrolita (natrij, kalij, magnezij, kalcij), poremećaje glikemije, acidobazne ravnoteže i hiperamonijemiju,
4. intoksikacije te, u bolesnika s poznatom epilepsijom, neodgovarajuće koncentracije antiepileptičkih lijekova,
5. poremećaje srčanog ritma (21,30,31).

Odmah po prijemu u hitni bolnički prijam potrebno je učiniti osnovne laboratorijske pretrage krvi i urina. Unutar prvih 5 minuta obavezno je odrediti koncentraciju glukoze u kapilarnoj krvi (uzorak iz prsta), a u žena generativne dobi i test na trudnoću (19,28). Neuroradiološku obradu treba provesti što je ranije moguće, najčešće nativnim MSCT-om mozga, a prema potrebi i MR-om. EEG ima ključnu ulogu u potvrdi nekonvulzivnog ES, klasifikaciji vrste epileptičkog statusa te procjeni prognoze i terapijskog odgovora (19,21,28,30,31).

U bolesnika s ranije poznatom, dobro kontroliranom epilepsijom, bez znakova akutnog neurološkog događaja, neuroradiološka obrada ponekad nije nužna. U takvim slučajevima često je dostatno odrediti koncentracije antiepileptičkih lijekova te, prema kliničkoj procjeni, učiniti toksikološku analizu (28,30,32).

Ako se na temelju anamneze, inicijalnih laboratorijskih nalaza i neuroradiološke obrade ne utvrdi uzrok ES-a, osobito u imunokompromitiranih bolesnika, bolesnika s febrilitetom ili drugim znakovima infekcije, kao i u osoba s otežanom komunikacijom, indicirano je učiniti lumbalnu punkciju radi isključenja infekcije SŽS-a (22,28–31).

Preporučeni dijagnostički koraci u ES (provoditi što ranije, usporedno s terapijskim mjerama):

1. Mjerenje glikemije iz kapilarne krvi prsta pomoću glukometra.
2. Kontinuirano praćenje vitalnih znakova, uključujući EKG-monitoriranje.
3. Laboratorijske pretrage krvi, koje obuhvaćaju glukozu, kompletnu krvnu sliku, osnovni metabolički panel, ukupni i ionizirani kalcij, magnezij, jetrene enzime, ureju i kreatinin.
4. Nativni CT mozga radi isključenja akutne strukturne patologije.
5. Pokretanje kontinuiranog EEG-monitoriranja unutar 60 minuta, kada god je tehnički i organizacijski dostupno (22,28,30,31).

Dodatna dijagnostička obrada (ovisno o kliničkoj slici) uključuje:

1. MR mozga, osobito ako je CT nalaz uredan ili nedovoljno informativan.
2. Lumbalnu punkciju, kod sumnje na infekciju SŽS-a ili maligne bolesti.
3. Toksikološki probir i, prema potrebi, prošireni toksikološki panel, s posebnim naglaskom na tvari koje često mogu izazvati ES, uključujući tricikličke antidepresive, teofilin, kokain, simpatomimetike, etanol, organofosfate, izoniazid i ciklosporin.

4. Dodatne laboratorijske pretrage, prema kliničkoj procjeni, poput određivanja koncentracija antiepileptičkih lijekova u serumu, parametara koagulacije, plinske analize arterijske krvi te serijskog određivanja troponina (22,28,30,31).

Diferencijalna dijagnoza epileptičkog statusa

Diferencijalna dijagnoza ES-a široka je i obuhvaća niz stanja koja mogu uzrokovati produljene poremećaje svijesti i/ili motoričku aktivnost nalik EN-ima. Pravodobno razlikovanje ovih stanja ključno je za pravilno liječenje i izbjegavanje nepotrebne ili potencijalno štetne terapije. U prvom redu potrebno je razmotriti akutne intoksikacije, uključujući predoziranja lijekovima i izloženost psihoaktivnim tvarima. Nadalje, u diferencijalnoj dijagnozi treba uzeti u obzir ranu tešku hipoksiju mozga, kao i toksične i metaboličke encefalopatije, primjerice one uzrokovane teškim poremećajima elektrolita, glikemije ili zatajenjem jetre i bubrega. Važno je isključiti i akutni ishemijski ili hemoragijski moždani udar, osobito u starijih bolesnika ili onih s vaskularnim rizičnim čimbenicima, kao i posttraumatske konvulzivne epizode nakon traumatske ozljede glave. Posebnu dijagnostičku pozornost zahtijevaju PNEN-i, koji mogu klinički nalikovati ES-u, osobito u produljenim ili atipičnim prezentacijama (18-21,30).

Liječenje epileptičkog napadaja i epileptičkog statusa u hitnoj medicini

Liječenje EN-a i ES-a u hitnoj službi temelji se na usporednoj stabilizaciji bolesnika i brzom uvođenju specifične terapije, s ciljem što ranijeg prekida kliničke i električne epileptičke aktivnosti, uz istodobnu dijagnostičke obradu i identifikaciju mogućeg uzroka napadaja (19,31).

Zbrinjavanje započinje općim mjerama: sprječavanjem ozljeda, procjenom kardiorespiratornog statusa prema ABCD pristupu [engl. *A-airway (dišni put), B-breathing (disanje), C-circulation (cirkulacija), D-disability (neurološka procjena)*] , osiguravanjem prohodnosti dišnog puta, korekcijom hipo-/hipertermije te uspostavom venskog pristupa. U održavanju dišnog puta prednost se daje nazofaringealnom tubusu u odnosu na orofaringealni, uz ciljnu saturaciju kisikom >92%. U slučaju respiratorne insuficijencije, depresije respiracijskog centra ili razvoja refraktornog ES-a indicirana je endotrahealna intubacija i mehanička ventilacija (31,32).

Specifično farmakološko liječenje provodi se prema fazama progresije ES-a i obuhvaća tri linije medikamentozne terapije: benzodiazepine, ne-benzodiazepinske antiepileptike i opće anestetike. Prva linija (u prvih ≈5 minuta) uključuje intravensku primjenu benzidiazepina, najčešće lorazepama ili diazepama. Ako se epileptička aktivnost ne prekine nakon dviju adekvatnih doza, prelazi se na drugu terapijsku liniju. Druga linija liječenja, koja se primjenjuje unutar prvih 30 minuta od početka napadaja, uključuje intravensku primjenu ne-benzodiazepinskih antiepileptika, poput levetiracetama, valproata, fosfenitoina/fenitoina, lakozamida ili brivaracetama, s ciljem sprječavanja ponovne pojave ili perzistiranja epileptičke aktivnosti (21,22,30-32). U slučaju izostanka kontrole ES-a nakon primjene najmanje dvaju antiepileptika različitih mehanizama djelovanja, indicirana je treća linija liječenja, unutar 30–60 minuta od početka ES-a. Ona uključuje primjenu općih anestetika (najčešće midazolama, propofola ili tiopentala), uz obveznu endotrahealnu intubaciju, mehaničku ventilaciju i liječenje u jedinici intenzivnog liječenja, što odgovara zbrinjavanju refraktornog epileptičkog statusa (33-42).

Liječenje epileptičkog statusa u hitnoj medicini provodi se kroz tri terapijske linije, benzodiazepine, ne-benzodiazepinske antiepileptike i opće anestetike s ciljem brzog prekida epileptičke aktivnosti i sprječavanja progresije u refraktorni oblik.

U kliničkoj praksi mjere stabilizacije bolesnika i terapijski koraci provode se istodobno, a preporučeni algoritam liječenja može se jasno prikazati shematski ili tablično, s vremenski definiranim fazama, kako je prikazano u Tablici 4 (21, 30-44).

Prognoza nakon epileptičkog statusa

Unatoč napretku u dijagnostici i liječenju, smrtnost povezana s ES-om i dalje je značajna. Na ishod bolesti presudno utječu trajanje ES-a i brzina započinjanja specifične terapije jer se s produljenjem nekontrolirane epileptičke aktivnosti progresivno povećava rizik ireverzibilnog oštećenja mozga, trajnog neurološkog deficita i smrtnog ishoda (19,29,45).

Uz trajanje ES-a, na morbiditet i mortalitet značajno utječu i etiologija, dob bolesnika, vrsta ES-a (konvulzivni nasuprot nekonvulzivnom), kao i razvoj refraktornog ili superrefraktornog ES-a. Bolesnici kod kojih je potrebno liječenje općom anestezijom imaju lošiju prognozu u odnosu na bolesnike s brzim terapijskim odgovorom (45).

Za procjenu ishoda i donošenje odluka o intenzitetu i agresivnosti liječenja u kliničkoj se praksi koriste prognostičke ljestvice. Među njima se bodovna ljestvica težine statusa epilepticusa (engl. *status epilepticus severity score,* STESS) ističe kao jedna od najjednostavnijih i najpouzdanijih za primjenu u hitnim i bolničkim uvjetima. STESS se temelji na procjeni dobi bolesnika, kliničke prezentacije napadaja, podatka o prethodno poznatoj epilepsiji te početne razine svijesti, kako je prikazano u Tablici 5 (46).

Tablica 4. Algoritam zbrinjavanja i liječenja epileptičkog statusa u hitnoj službi

Vrijeme	Faza ES-a	Lijek / postupak	Doza i put primjene	Kliničke napomene
0–5 min	Sumnja na ES	Stabilizacija (ABCD) Neurološki pregled Vitalni pokazatelji O_2, venski put, EKG, GUK, laboratorij		Usporedno s terapijom
		Glukoza (ako je GUK ako je GUK <3 mmol/L)	10–20 g iv.	Prije drugih lijekova
5–10 min	Rani (premonitorni, prijebolnički) ES	Lorazepam	0,05–0,1 mg/kg iv. (obično 4 mg bolus tijekom 2 min); ponoviti 1× nakon 4 min (maks: 8 mg)	Lijek prvog izbora ako je dostupan
		Diazepam	5–10 mg iv. bolus tijekom 1 min; ponavljati nakon 5-10 min do ukupno 30 mg ili 10 mg rektalno; ponoviti jednom nakon 10 min	Kratko djelovanje, kod rektalne primjene smanjiti dozu na 5mg u starijih osoba ili osoba s TT <50 kg
		Midazolam	10 mg im. ponoviti 1x nakon 10 min ili bukalno / intranazalno 10 mg	Prednost bez iv pristupa, smanjiti dozu na 5mg u starijih osoba ili osoba s TT <50 kg
		Fenobarbital	10 do 20 mg/kg iv. bolus jednokratno	U većini smjernica se navodi kao kasna druga linija
10–30 min	Uspostavljeni (razvijeni) ES	Levetiracetam	30–60 mg/kg iv. kroz 10 min u inf, brzina 3-6 mg/kg/min (maks. 4500 mg)	Prilagodba kod bubrežnog zatajenja
		Valproat	15–40 mg/kg iv. kroz 10 min u inf, brzina 3-6 mg/kg/min (maks. 3000 mg)	✗trudnoća, zatajenje jetre, hiperamonemija, trombocitopenija
		Lakozamid	8 mg/kg, obično 400 mg iv. kroz 3-5 min u inf, (maks. 600 mg)	EKG nadzor ✗Child-Pugh C stadij zatajenja jetre, AV blokovi i druge značajne aritmije
		Brivaracetam	100–200 mg iv. kroz 15 min u inf (maks. 200 mg)	Brz početak djelovanja
		Fenitoin / fosfenitoin	fenitoin 20 mg/kg iv. (max 1500 mg) brzinom do 20 mg/min; fosfenitoin 20 mg PE/kg brzinom do 150 mg PE/min	✗aritmije, bradikardija, hipotenzija, trudnoća, zatajenje jetre, sumnja na toksičnu etiologiju
≥30 min	Refraktorni ES	Midazolam	0,1–0,3 mg/kg iv. udarna doza mak brzine 2-4 mg/min → inf. 0,05–0,4 mg/kg/h (maks. 0,4 mg/kg)	Cilj: EEG supresija
		Propofol	1–2 mg/kg iv. udarna doza, po potrebi ponoviti → inf. 2–10 mg/kg/h (titracija 3-5 mg/kg/h)	Cilj: EEG supresija Oprez: PRIS
		Tiopental	5–7 mg/kg iv. obično 100-250 mg iv. udarna doza kroz 20 sekundi, nastaviti s bolusima od 50 mg iv. svakih 2-3 minute do kontrole napadaja → inf. 3–5 mg/kg/h	Cilj: EEG supresija Oprez: kardiovaskularne komplikacije, imunosupresija i infekcije ✗trudnoća, ciroza jetre
		Ketamin	0,5-3 mg/kg iv. bolus (obično 1-2 mg/kg) → inf. 0,3–4 mg/kg/h (obično 0,6 mg/kg/h)	NMDA antagonizam
>24 h	Superrefraktorni ES	Dugotrajna anestezija	Individualno	Razmotriti imunoterapiju, ketogenu dijetu, VNS i dr.

Prilagođeno prema ref. 21,30-44.

Legenda: ES - epileptički status; ABCD - A-airway (dišni put), B-breathing (disanje), C-circulation (cirkulacija), D-disability (neurološka procjena); EKG - elektrokardiograf; EEG -elektroencefalogram; GUK – glukoza u krvi; IV - intravenski; IM - intramuskularno; inf.-infuzija; TT – tjelesna masa; PE - fenitoin ekvivalent (engl.phenytoin equivalents); PRIS-propofol infuzijski sindrom; NMDA - N-metil-D-aspartat; VNS - vagusna stimulacija

Tablica 5. STESS ljestvica (engl. *status epilepticus severity score*) – pokazatelji i bodovanje

Pokazatelji	Kategorija	Bodovi
Dob bolesnika	< 65 godina	0
	≥ 65 godina	2
Klinička prezentacija epileptičkog statusa	Žarišni ES (s ili bez poremećaja svijesti) ili apsans ES	0
	Generalizirani konvulzivni ES	1
	Nekonvulzivni ES s komom	2
Prethodno poznata epilepsija	Da	0
	Ne	1
Razina svijesti pri prijemu	Budan ili somnolentan	0
	Stupor ili koma	1

Legenda: ES - epileptički status, STES -bodovna ljestvica težine statusa epilepticusa (engl. *status epilepticus severity score*)
prilagođeno prema ref. 46
Tumačenje ukupnog STESS rezultata
Ukupni zbroj bodova: 0 – 6
STESS 0–2: povezan s povoljnijom prognozom i nižim rizikom smrtnosti
STESS ≥3 (osobito ≥4): povezan s povećanim rizikom smrtnosti i lošijim ishodom liječenja

Zaključak

EN-i i ES predstavljaju značajan klinički, organizacijski i javnozdravstveni izazov zbog svoje učestalosti, nepredvidivosti i potencijalno teških posljedica. Iako se većina EN-a može uspješno kontrolirati odgovarajućom dugoročnom terapijom, ES i dalje ostaje jedno od najkritičnijih neuroloških hitnih stanja, povezano sa značajnim morbiditetom i mortalitetom.

Ishod bolesnika s ES-om u najvećoj mjeri ovisi o etiologiji, trajanju nekontrolirane epileptičke aktivnosti te brzini i adekvatnosti terapijske intervencije. Stoga je ključno da liječnici u hitnoj službi raspolažu jasnim, praktičnim i vremenski orijentiranim algoritmima liječenja, uz istodobnu svijest o potrebi rane dijagnostičke obrade i ciljanog etiološkog liječenja.

Moderni terapijski pristupi, temeljeni na ILAE smjernicama i aktualnim kliničkim dokazima, omogućuju učinkovitije zbrinjavanje ES-a nego u ranijim razdobljima. Unatoč tome, pravodobno prepoznavanje ES-a i odlučno, strukturirano djelovanje ostaju presudni čimbenici u sprječavanju trajnog neurološkog oštećenja i u poboljšanju dugoročnih ishoda bolesnika.

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REVIEW ARTICLE / PREGLEDNI ČLANAK

TREBAMO LI KORISTITI „NEČISTI“ ADRENALIN?

SHOULD WE USE „DIRTY“ ADRENALINE?

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Sažetak

Adrenalin je neizostavan lijek u liječenju životno ugroženih bolesnika, osnova je moderne hitne medicinske službe. Njegova primjena, u smislu doze i načina primjene, jasno je definirana smjernicama. Sporadično se susrećemo s pojmom „nečistog“ adrenalina koji označava brzo pripremljenu razrijeđenu infuziju adrenalina (najčešće 1 mg adrenalina u 1 L 0,9 % NaCl) koja se primjenjuje putem perifernog venskog puta uz krevet bolesnika kao privremeni vazopresor kod bolesnika u šoku. Naziv „nečisti“ ne odnosi se na nečistoću pripravka, već na improvizirani, niskoprecizan način miješanja lijeka na licu mjesta. Koristi se u situacijama kada se bolesnik nalazi u udaljenim ruralnim krajevima, ambulantama koje vode samo medicinske sestre, bez standardne opreme i odgovarajućeg tima za zbrinjavanje. Svrha ovako priređenog pripravka adrenalina je terapijsko premoštenje kako bi se održao krvni tlak i tkivna perfuzija dok se ne osigura definitivno zbrinjavanje bolesnika. Podaci o ovakvoj primjeni adrenalina su i dalje vrlo oskudni i nedostupni u standardnoj literaturi. Cilj ovog rada je upoznati se s primjenom razrijeđenog ‘nečistog’ adrenalina u liječenju šoka u izvanbolničkim uvjetima, prikazati dostupne dokaze o njegovoj sigurnosti i učinkovitosti te kritički procijeniti ima li mjesta za njegovu primjenu u kontekstu smjernica i sve bolje dostupnosti perifernih vazopresora, osobito noradrenalina.

Ključne riječi: adrenalin; medicinske sestre; noradrenalin; septički šok; vazokonstriktori

Abstract

Adrenaline is an indispensable drug in the treatment of critically ill patients and represents a cornerstone of modern emergency medicine. Its administration, in terms of dosage and route, is clearly defined by current guidelines. The term “dirty” adrenalin is occasionally encountered and denotes a rapidly prepared diluted adrenaline infusion (most commonly 1 mg of adrenaline in 1 L of 0.9% NaCl) that is administered via a peripheral venous line at the patient’s bedside as a temporary vasopressor in patients in shock. The term ‘dirty’ does not refer to contamination of the solution, but to the improvised, low-precision method of mixing the drug on the spot. It is used in situations where patients are located in remote rural areas or in nurse-led clinics that lack standard equipment and an adequate resuscitation team. The purpose of this type of adrenaline preparation is therapeutic bridging to maintain blood pressure and tissue perfusion until definitive patient management can be arranged. Data on this mode of adrenaline administration remain very limited and are not readily available in standard literature. The aim of this paper is to review the use of diluted ‘dirty’ adrenaline in the treatment of shock in out-of-hospital settings, to present the available evidence on its safety and efficacy, and to critically assess whether there is a role for its use in the context of contemporary guidelines and the increasing availability of peripheral vasopressors, especially noradrenaline.

Keywords: epinephrine; norepinephrine; nurses; septic shock; vasoconstrictors

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Uvod

Moderna hitna medicinska služba se ne može zamisliti bez primjene adrenalina. Adrenalin je i dalje najvažniji katekolaminski vazopresor sa širokom primjenom u hitnoj medicinskoj službi i nezamjenjiv je u algoritmima za napredno održavanje života (1, 2). To je endogeni α1 i neselektivni β adrenergički agonist koji povećava sistemski vaskularni otpor, frekvenciju srca, srčani minutni volumen i krvni tlak te je indiciran u liječenju anafilaktičkog šoka, kardiopulmonalnoj reanimaciji, simptomatske bradikardije i određenim oblicima refraktorne hipotenzije nakon neuspjele volumne resuscitacije (1–3). Smjernice Europskog reanimatološkog vijeća iz 2025. godine naglašavaju njegovu ulogu u naprednim mjerama održavanja života u odraslih i djece, osobito kod nešokabilnih ritmova, te potvrđuju da rano davanje adrenalina poboljšava vjerojatnost povratka spontane cirkulacije, iako je i dalje upitan pozitivan učinak na dugoročno preživljavanje i neurološki ishod (2). Adrenalin se mora primjenjivati u odgovarajućim dozama, uz praćenje hemodinamskog odgovora i svijest o proaritmijskom djelovanju te riziku lokalne ishemije pri perifernoj infuziji (1-3).

Primjena adrenalina u izvanbolničkim uvjetima trenutno je jasno definirana u protokolima naprednih mjera održavanja života, liječenja anafilaktičkih reakcija i refraktornih bradikardija (1–4). Problemi nastaju kada se u izvanbolničkom okruženju treba zbrinuti bolesnik u šoku, gdje je liječenje otežano ograničenim resursima, ponajprije promjenjivom razinom educiranosti timova i često dugim vremenom transporta do bolnice (2,5,6). U ruralnim i udaljenim sredinama hitne medicinske službe nerijetko nemaju pristup drugim vazopresorima, infuzijskim pumpama, centralnim venskim kateterima ni kontinuiranom invazivnom monitoringu, pa se odluke o primjeni vazopresora moraju donositi u okolnostima smanjenih mogućnosti precizne titracije i kontrole neželjenih događaja (2, 6, 7). Istodobno, noviji podaci pokazuju da rana primjena vazopresora, uključujući i periferno započeta terapija noradrenalinom u sepsi, može poboljšati ishode, što dodatno naglašava potrebu za razvojem protokola za sigurnu i praktički izvedivu primjenu vazopresora u izvanbolničkom okruženju (5,8).

Kao jedno od mogućih rješenja liječenja šoka u oskudnim izvanbolničkim uvjetima navodi se i primjena tzv. „nečistog“ adrenalina (eng. *dirty adrenaline)* (6,7,9-11). Pod tim se pojmom, podrazumijeva brzo pripremljena razrijeđena infuzija adrenalina, najčešće 1 mg adrenalina u 1 L 0,9% NaCl (koncentracija≈1 µg/mL), namijenjena za perifernu intravensku primjenu kao privremeni vazopresor kod bolesnika u šoku koji prije toga nisu imali dobar odgovor na volumnu nadoknadu (6,7,9-13). Ključni dosad objavljeni podaci o takvoj primjeni potječu iz retrospektivne studije serije slučajeva Brahama i sur., koja je obuhvatila 57 bolesnika liječenih periferno primijenjenom razrijeđenom infuzijom adrenalina u udaljenim, sestrinski vođenim ambulantama u središnjoj Australiji prije aeromedicinskog transporta (6). U toj je kohorti, u kojoj je najčešća indikacija bio septički šok refraktoran na volumnu nadoknadu, zabilježen porast sistoličkog arterijskog tlaka i preživljenje do otpusta iz bolnice od 86 %, bez dokumentiranih značajnih neželjenih učinaka izravno povezanih s primjenom „nečistog“ adrenalina (6). Stoga se nameće pitanje bi li „nečisti“ adrenalin mogao postati terapija izbora za liječenje šoka u oskudnim izvanbolničkim uvjetima. Na žalost i dalje su podaci o ovakvoj primjeni adrenalina oskudni, većinom se oslanjajući na neformalne izvore poput podkasta i medicinskih blogova.

„Nečisti“ adrenalin predstavlja razrijeđenu perifernu infuziju adrenalina koja se može koristiti kao privremeni vazopresor u teškom, na tekućinu refraktornom šoku u okruženjima s ograničenim terapijskim mogućnostima.

Cilj ovog rada je upoznati se s primjenom razrijeđenog „nečistog“ adrenalina u liječenju šoka u izvanbolničkim uvjetima, prikazati dostupne dokaze o njegovoj sigurnosti i učinkovitosti te kritički procijeniti ima li mjesta za njegovu primjenu u kontekstu suvremenih smjernica i sve bolje dostupnosti perifernih vazopresora, osobito noradrenalina.

Standardna primjena adrenalina u hitnim stanjima

Anafilaktički šok

Adrenalin je lijek prvog izbora u liječenju anafilaktičkog šoka, a rana intramuskularna primjena ključna je za preživljenje i smanjenje rizika pojave bifazičnih reakcija (14,15). Kod odraslih smjernice preporučuju IM dozu 0,5 mg u anterolateralni dio natkoljenice u odraslih, s ponavljanjem nakon 5 minuta ako nema kliničkog poboljšanja, pri čemu se većina ozbiljnih nuspojava povezuje s pogrešnom intravenskom primjenom ili pogrešnom koncentracijom lijeka (2,3,14,15). U bolesnika kod kojih unatoč dvjema intramuskularnim dozama adrenalina i odgovarajućoj volumnoj resusitaciji i dalje ne dolazi do poboljšanja simptoma anafilaktičkog šoka, preporučuje se kontinuirana intravenska infuzija razrijeđenog adrenalina (2,3,14,15). U nacionalnim kliničkim smjernicama razrjeđenje se provodi tako da se 1 mg adrenalina (1 mL koncentracije 1 mg/mL) razrijedi u 100 mL 0,9% NaCl, pri čemu se terapija započinje s brzinom 0,5–1,0 mL/kg/h, ovisno o težini reakcije, uz titraciju do najniže učinkovite brzine i uz stalno praćenje kliničkog odgovora i monitoring bolenika (14) .

Kardiopulmonalna reanimacija

U naprednim mjerama održavanja života odraslih adrenalin ostaje standardni lijek u liječenju srčanog zastoja, osobito kod nešokabilnih ritmova (PEA/asistolija) (2,3). Preporučuje se davanje 1 mg adrenalina IV/IO svakih 3–5 minuta tijekom reanimacije, pri čemu novije analize pokazuju da rana primjena povećava vjerojatnost povratka spontane cirkulacije, iako učinak na dugoročni neurološki ishod ostaje i dalje predmet rasprave (2,3).

Simptomatske bradikardije

Kod simptomatskih bradikardija koje ne odgovaraju na atropin, kao i bradikardija kod kojih atropin nije prvi lijek izbora, adrenalin se primjenjuje kao kontinuirana intravenska infuzija u dozi 2–10 µg/min, titrirano prema kliničkom odgovoru, u skladu s algoritmima napredne kardiovaskularne reanimacije i napredne potpore života (engl. *Advanced Cardiovascular Life/ Advanced Life Support,* ACLS/ALS) (2,3). Primjena zahtijeva stalno praćenje srčane frekvencije, ritma i krvnog tlaka, uz prilagodbu brzine infuzije najmanjoj dozi koja održava adekvatnu perfuziju (2,3).

Refraktorna hipotenzija

U pojedinim situacijama kada nakon odgovarajuće volumne resuscitacije imamo bolesnika s refraktornom hipotenzijom, osobito kada je potrebna i inotropna i vazopresorska potpora, adrenalin se može koristiti kao kratkoročni 'most' dok se ne uspostavi standardna vazopresorska terapija (najčešće noradrenalin) (1,3). U takvim se slučajevima preporučuje započeti kontinuiranu IV infuziju adreanlina u rasponu 0,05–0,5 µg/kg/min (otprilike 3–30 µg/min u odraslih), uz postupnu titraciju prema ciljanom srednjem arterijskom tlaku uz hemodinamski nadzor, te preporuku za što raniji prijelaz na primarno preporučene vazopresore (1,3).

Noradrenalin *versus* adrenalin

Noradrenalin je primarno indiciran i lijek je izbora u distribucijskom šoku sa sniženim sistemskim vaskularnim otporom, ponajprije septičkom šoku, ali i u drugim distribucijskim šokovima i vazodilatacijskim stanjima poput neurogenog šoka i poslijeanestezijske vazoplegije (8, 16, 17) . U kardiogenom šoku najčešće se kombinira s inotropima poput dobutamina (1, 4, 18). Noradrenalin je endogeni katekolamin koji dominantno stimulira α1 adrenergičke receptore, uz slabiji β1 učinak i minimalan β2 učinak, što rezultira izraženom perifernom vazokonstrikcijom i umjerenim pozitivnim inotropnim učinkom (1,4). Glavni farmakološki učinak je porast sistemskog vaskularnog otpora i srednjeg arterijskog tlaka uz relativno manji porast frekvencije srca nego kod adrenalina, čime se poboljšava perfuzija vitalnih organa uz manji rizik od tahiaritmija (4,19).

Internacionalne smjernice *Surviving Sepsis Campaign 2021* preporučuju noradrenalin kao prvi izbor vazopresora u odraslih sa septičkim šokom, ispred dopamina, adrenalina, vazopresina i drugih vazopresora (5,8). Noradrenalin se primjenjuje kao kontinuirana intravenska infuzija, najčešće u rasponu 0,02–1,0 µg/kg/min, uz mogućnost titracije i na više doze (npr. do 1–1,5 µg/kg/min) u refraktornom šoku, uz cilj održavanja srednjeg arterijskog tlaka ≥ 65 mmHg (1, 4,5,16). Uobičajeni neželjeni učinci primjene uključuju perifernu i visceralnu ishemiju (osobito pri visokim dozama i neodgovarajućoj volumnoj resuscitaciji), hladne ekstremitete i rijetko aritmije. Potreban je poseban oprez kod periferne primjene zbog rizika od ekstravazacije (4). Kao način primjene, smjernice preporučuju centralni venski put kad god je to moguće. Međutim, noviji radovi i smjernice prihvaćaju i perifernu primjenu noradrenalina u resursno ograničenim ili izvanbolničkim uvjetima, uz nadzor mjesta primjene. Periferna primjena ne bi smela biti duža od 72 sata (4,5,16,20).

U odnosu na adrenalin, noradrenalin ima α dominantni vazopresorski profil, pa pouzdano podiže arterijski tlak uz manje izraženu tahikardiju i niži rizik aritmija. Meta analize i pregledi pokazuju da je noradrenalin u septičkom šoku povezan s manjom učestalošću aritmija i boljom hemodinamskom stabilnošću od drugih vazopresora, dok adrenalin često uzrokuje tahikardiju, porast laktata i potencijalnu splanhničku vazokonstrikciju, otežavajući interpretaciju laktata i povećavajući metaboličko opterećenje (1,4,19). Smjernice ga stoga svrstavaju kao prvi izbor vazopresora, a adrenalin preporučuju tek kao dodatni ili alternativni lijek u refraktornom šoku ili kada noradrenalin nije dostupan (5).

Što je „nečisti" adrenalin?

„Nečisti" adrenalin označava brzo pripremljenu razrijeđenu infuziju adrenalina (najčešće 1 mg adrenalina u 1 L 0,9 % NaCl) koja se primjenjuje putem perifernog venskog puta uz krevet bolesnika kao privremeni vazopresor u bolesnika u šoku. Naziv „nečisti" ne odnosi se na nečistoću pripravka, već na improvizirani, niskoprecizan način miješanja uz krevet bolesnika, za razliku od standardiziranih, točno titriranih infuzijskih pripravaka koji se precizno doziraju putem infuzijske pumpe ili perfuzora (9,10). Koristi se u situacijama kada standardna vazopresorska infuzija i infuzijska pumpa ili perfuzori nisu odmah dostupni. Svrha mu je terapijsko premoštenje kako bi se održao krvni tlak i tkivna perfuzija dok se ne osigura definitivno zbrinjavanje bolsnika (centralni venski put, infuzijska pumpa/perfuzor, transport u višu ustanovu). Podaci o ovakvoj primjeni adrenalina su i dalje vrlo oskudni i nedostupni u standardnoj literaturi (6,7,9–13).

Indikacije za primjenu „nečistog" adrenalina

Indikacije za primjenu „nečistog" adrenalina su uznapredovali, na tekućinu refraktan šok, ponajprije septički i druge vrste distribucijskog šoka, ali i drugi oblici šoka (kardiogeni, hemoragijski, anafilaktički,

postreanimacijska hipotenzija) u uvjetima bez infuzijske pumpe i bez mogućnosti standardne primjene noradrenalina (6,10). Najčešće se primjenjuje u udaljenim ruralnim, resursno ograničenim ambulantama i klinikama u kojima liječnici nisu odmah dostupni, gdje je dostupno minimalno osoblja i opreme, a transport do intenzivne skrbi traje satima (6,7).

Način pripravljanja i primjene

Infuzijska otopina „nečistog" adrenalina pripravlja se dodavanjem 1 mg adrenalina u 1 L kristaloida (najčešće 0,9 % NaCl), pri čemu se dobije koncentracija od 1 µg/mL (6, 9-11). Pripremljena otopina primjenjuje se kroz periferni venski put brzim 'slobodnim' protokom, pri čemu stvarna doza adrenalina ovisi o promjeru intravenske kanile, gravitaciji i visini vrećice. Brzina protoka se može orijentacijski odrediti na osnovu tvornički određene brzine protoka intravenske kanile ovisno o njezinom promjeru. Idealno bi bilo koristiti barem brojač kapi ili infuzijsku pumpu. Terapiju započeti sa dozom od 1 µg/kg/sat, uz titraciju doze do zadovoljavajućeg kliničkog odgovora. Odgovor na primijenjenu terapiju se prati intenzivnim kliničkim praćenjem i nadzorom bolesnika, bilo invazivno ili neinvazivno ovisno o dostupnim sredstvima (7, 9-11).

Pozitivni učinci i neželjeni učinci

Pozitivan učinak je porast arterijskog tlaka i poboljšanje perfuzije kod bolesnika u teškom šoku kada su druge opcije nedostupne (6,7). U dostupnim podacima bilježi se kliničko poboljšanje bolesnika u peri-arrest stanju te njihova stabilizacija do dolaska tima višeg nivoa skrbi (6,11). Najčešće sustavni neželjenu učinci i komplikacije uključuju tahikardiju, povećan rizik od aritmija, prolaznu hipertenziju i povećanje laktata (6,9) . Od lokalnih neželjenih učinaka najčešće su opisani hladni prsti, ekstravazacija ili curenje iz kanile, iako ozbiljne trajne komplikacije nisu zabilježene (6). Najveći problem predstavlja nepreciznost doziranja, koja ovisi o gravitaciji, visini infuzijske vrećice i kalibru kanile. Stoga se radi o krajnjoj terapijskoj opciji, a ne o standardnoj zdravstvenoj skrbi (9-13) .

Dostupne studije o primjeni „nečistog" adrenalina

Braham i sur. proveli su retrospektivnu deskriptivnu studiju slučajeva o izvanbolničkoj primjeni „nečistog" adrenalina u središnjoj Australiji, u udaljenim klinikama koje vode medicinske sestre, prije aeromedicinskog transporta. U studiju je uključeno 57 bolesnika svih dobnih skupina (medijan dobi je bio 50 godina, raspon 2–96 godina) kod kojih je u ambulanti, prije dolaska liječnika, započeta primjena infuzije razrijeđenog adrenalina putem perifernog venskog puta. Primarni kriterij za uključenje u studiju bila je dokumentirana primjena periferne infuzije razrijeđenog adrenalina zbog šoka refrakternog na volumnu nadoknadu. Septički šok bio je najčešća indikacija (40/57 slučajeva), a adrenalinska infuzija pripremana je u standardnoj koncentraciji 1 mg adrenalina u 1 L 0,9 % NaCl i davana periferno (IV ili IO) kroz različite veličine kanila (6) .

Dostupni dokazi o sigurnosti i učinkovitosti „nečistog" adrenalina vrlo su ograničeni i temelje se uglavnom na jednoj retrospektivnoj seriji slučajeva iz udaljenih ruralnih sredina.

Način primjene i ishodi

Medijan trajanja infuzije bio je 155 minuta, a medijan sistoličkog tlaka porastao je s 75,5 mmHg pri početku infuzije na 91 mmHg pri dolasku tima za definitivno zbrinjavanje, što ukazuje na klinički značajnu hemodinamsku stabilizaciju. Preživljavanje do otpusta iz bolnice iznosilo je 86% (49/57 bolesnika), uz napomenu da se radi o visoko selekcioniranoj skupini u specifičnom geografskom i organizacijskom kontekstu, bez kontrolne skupine i bez formalne statističke analize zbog malog uzorka (6) .

Komplikacije i neželjeni učinci u studiji

Nisu zabilježeni značajni ozbiljni neželjeni događaji izravno pripisani infuziji „nečistog" adrenalina. Opisani su pojedinačni slučajevi hladnih prstiju u ekstremitetu na kojem se primjenjivala infuzija te prolazne tahikardije i hipertenzivne reakcije koje su se povukle nakon smanjenja ili prekida infuzije. Zabilježena su dva slučaja preopterećenja tekućinom kod bolesnika s kroničnom bubrežnom bolesti, koji su primili ≥ 250 mL kristaloida putem ove infuzije i ukupno 750–1280 mL tekućine u izvanbolničkim uvjetima. Autori napominju da bi, bez ranog uvođenja adrenalina, ukupna primljena količina tekućine vjerojatno bila još veća. (6,8). Zaključak autora jest da primjena „nečistog" adrenalina u tom specifičnom okruženju predstavlja izvediv i relativno siguran način zbrinjavanja teškog, na tekućinu refrakternog šoka, uz evidentan porast tlaka i visoku stopu preživljenja, ali da se, zbog opisnog dizajna, malog uzorka i niza mogućih pristrasnosti, ne može smatrati dokazom za široko uvođenje ove prakse izvan udaljenih i resursno ograničenih uvjeta (6).

Rasprava

Podaci o „nečistom" adrenalinu i dalje su relativno oskudni, uglavnom ograničeni na neformalne izvore, iskustvene prikaze te jednu noviju deskriptivnu studiju Brahama i suradnika, koja ipak pokazuje pozitivne ishode u smislu hemodinamske stabilizacije i preživljenja (6, 7, 9-11). Premda u toj seriji slučajeva nije zabilježen veći broj ozbiljnih komplikacija izravno pripisanih infuziji razrijeđenog adrenalina, riječ je o malom uzorku, bez kontrolne skupine i s mogućnošću brojnih pristrasnosti, pa razina dokaza ostaje ograničena. Na temelju dostupnih podataka „nečisti" adrenalin ima smisla razmatrati samo u jasno definiranom kontekstu: kod teškog, na tekućinu refrakternog šoka, u udaljenim ruralnim područjima, malim

ambulantama i izvanbolničkim timovima s ograničenim ljudstvom i opremom, gdje standardna vazopresorska infuzija noradrenalina i infuzijska pumpa nisu dostupni, a transport do više razine skrbi traje satima (6,7,9-13) .

Unatoč mogućoj ulozi u iznimnim okolnostima, noradrenalin ostaje vazopresor izbora prema smjernicama, dok se „nečisti" adrenalin treba smatrati isključivo privremenim terapijskim premoštenjem, a ne standardom skrbi.

U svim ostalim okolnostima, osobito u bolničkim uvjetima i organiziranim hitnim službama, noradrenalin ostaje neprikosnoven, standardni vazopresor za liječenje šoka, u skladu sa smjernicama. 'Nečisti' adrenalin treba promatrati isključivo kao privremenu, krajnju terapijsku opciju u udaljenim područjima s ograničenim resursima, uz jasne protokole, edukaciju i svjesnost o riziku nepreciznog doziranja. Takve situacije nisu iznimka ni u Hrvatskoj, gdje u udaljenim područjima od nedavno samostalno djeluju i medicinske sestre/tehničari, specijalisti hitne medicine u timovima T2 (dvije medicinske sestre/tehničara sačinjavaju tim hitne medicinske pomoći), uz liječnika koji je dostupan po pozivu. Budući da ove sestre/tehničari već imaju ovlasti za primjenu adrenalina u standardnim indikacijama, poznavanje koncepta razrijeđene infuzije adrenalina kao terapije premoštenja u krajnje ograničenim uvjetima moglo bi biti od praktične koristi, naravno uz jasne protokole, edukaciju i naglašavanje da to nije zamjena za noradrenalin ni standardnu intenzivističku skrb (21).

Zaključak

Adrenalin je dugi niz desetljeća ostao temeljni lijek hitne medicinske službe i standard u zbrinjavanju brojnih životno ugrožavajućih stanja, s jasno definiranim dozama i načinima primjene (npr. anafilaksija, reanimacija). Noradrenalin je, sukladno smjernicama, primarni vazopresor za liječenje šoka, posebno septičkog i drugih vrsta distribucijskog šoka. U ekstremnim okolnostima, poput velikih udaljenosti ruralnih područja, izrazito ograničenih resursa, odsutnosti infuzijskih pumpi i nemogućnosti brzog uspostavljanja standardne noradrenalinske infuzije, „nečisti" adrenalin može imati privremenu, strogo ograničenu ulogu kao terapijsko rješenje za održavanje perfuzije do dolaska tima višeg nivoa skrbi. Potrebne su dodatne studije, a sukladno njihovim rezultatima i preporukama stručnih društava, kako bi se ovakva primjena adrenalina mogla uvesti u svakodnevnu kliničku praksu.

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ORIGINAL ARTICLE / IZVORNI ZNANSTVENI ČLANAK

WHAT CAN BODY COMPOSITION ANALYSIS REVEAL ABOUT INSPIRATORY AND PERIPHERAL MUSCLE STRENGTH?

ŠTO MOŽE OTKRITI ANALIZA SASTAVA TIJELA O SNAZI INSPIRACIJSKIH I PERIFERNIH MIŠIĆA?

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Abstract

Introduction: Body composition analysis measured with bioelectrical impedance analysis (BIA) is a method which has been frequently used in body composition assessment. The goal of this research is to determine the correlation of the derived measurements with the help of BIA with the strength of peripheral and inspiratory muscles as well as with the diaphragm's function and thickness in healthy population.

Participants and methods: Participants in this research were healthy individuals. They were tested on body composition with the help of bioelectrical impedance on Tanita *MC-780MA* device, maximal inspiratory pressure (MIP) with the POWERbreathe device, dynamometry of forearm muscle flexor and tibia extensor with the help of a dynamometer as well as ultrasound evaluation of diaphragm's function.

Results: The study sample consisted of a total of 50 participants, including 31 females (62%) and 19 males (38%) with a mean age of 41 years. The results have proved that the strength of peripheral and inspiratory muscles together with the diaphragm's thickness and mobility are in strong correlation with muscle mass, sarcopenic index and phase angle measured by BIA.

Conclusion: Bioelectrical impedance analysis is a reliable and practical method for assessing body composition and detecting early signs of muscle dysfunction. The established associations with muscle strength and diaphragmatic function highlight its potential as a simple screening tool for maintaining muscular health in clinical and preventive settings.

Keywords: adult; bioelectric impedance analysis; diaphragm; muscle strength; respiratory muscles

Sažetak

Uvod: Analiza sastava tijela mjerena bioelektričnom impedancijom (engl. *Bioelectric Impedance Analysis,* BIA) metoda je koja se sve učestalije koristi u procjeni sastava tijela. Cilj rada je utvrditi korelaciju dobivenih mjerenja pomoću BIA-e sa snagom perifernih i inspiracijskih mišića te debljine i funkcije ošita u zdravoj populaciji.

Ispitanici i metode: Ispitanici u ovom istraživanju bili su zdravi pojedinci. Na ispitanicima je provedena analiza sastava tijela na Tanita *MC-780MA* uređaju, testiranje maksimalne inspiracijske snage (MIP) pomoću uređaja *POWERbreathe*, dinamometrija mišića fleksora podlaktice i ekstenzora potkoljenice pomoću dinamometra te ultrazvučna procjena funkcije ošita.

Rezultati: Uzorak na kojem je provedeno istraživanje sastojao se od 50 ispitanika od čega je 31 (62%) osoba ženskog spola i 19 (38%) osoba muškog spola, prosječne dobi

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od 41 godine. Rezultati ukazuju na snažnu korelaciju snage perifernih i inspiracijskih mišića i funkcije ošita s mišićnom masom, sarkopenijskim indeksom i faznim kutom mjerenim BIA-om.

Zaključak: Bioelektrična impedancija predstavlja pouzdanu i praktičnu metodu za procjenu sastava tijela i otkrivanje ranih znakova mišićne disfunkcije. Utvrđene povezanosti sa snagom mišića i funkcijom ošita ističu njezin potencijal kao jednostavni alat za rano otkrivanje i očuvanje mišićnog zdravlja u kliničkom i preventivnom kontekstu.

Ključne riječi: bioelektična impedancija; mišićna snaga; odrasli; ošit; respiracijski mišići

Introduction

Preserving muscle mass and functional ability is a cornerstone of healthy aging and maintaining quality of life. Muscle strength, including respiratory muscles is crucial for mobility, autonomy, and resilience against illness (1). Age-related loss of muscle mass and function, known as sarcopenia, and the related phenotype of sarcopenic obesity are increasingly common in today's population, particularly among older adults (2).

Phase angle and sarcopenic index may help in early identification of muscle dysfunction.

These conditions frequently go undetected until marked functional decline, increased fall risk, chronic disease, disability and even elevated mortality have occurred (3). The consequences of sarcopenic obesity have a multifaceted impact on quality of life. Reduced muscle mass and strength, combined with increased adipose tissue, result in decreased mobility, a higher risk of falls, greater incidence of chronic diseases, and reduced independence in performing activities of daily living. In more advanced stages, sarcopenic obesity may lead to disability and significantly increase both morbidity and mortality among older adults (4). In this context, assessment of body composition and muscle function is not only essential for diagnosing sarcopenia or malnutrition, but is also fundamental for early prevention and rehabilitation strategies (6). Techniques such as bioelectrical impedance analysis (BIA) provide a simple, non-invasive and practical method to estimate body composition parameters (e.g., fat-free mass, skeletal muscle mass, appendicular skeletal muscle mass) and cellular health (e.g., phase angle) using measures like impedance and phase angle, together with anthropometric data. Bioelectrical impedance analysis (BIA) assesses the electrical characteristics of the body, specifically impedance (Z) and phase angle (PhA). Using these variables, along with anthropometric measures such as age, height, and body weight, predictive equations can estimate key body composition parameters, including fat-free mass (FFM), skeletal muscle mass (SM), and appendicular skeletal mass (ASM) (5).

Coupling these composition data with functional assessments—such as maximal inspiratory pressure (MIP), handgrip dynamometry, diaphragm thickness and excursion—facilitates a comprehensive evaluation of both peripheral and respiratory muscle function (7,8). Respiratory muscle strength, diaphragm thickness, and respiratory function are known to be reduced in older adults with sarcopenia or frailty. Deniz et al. (9) found that individuals with sarcopenia had reduced diaphragm thickness and lower peak expiratory flow compared with non-sarcopenic individuals.

Diaphragm thickness and mobility associate positively with muscle mass and phase angle.

Additionally, Ohara et al. (10) compared 383 individuals with sarcopenia with healthy participants and reported reduced respiratory muscle strength and handgrip strength in the sarcopenic group. Within the clinical context, the use of straightforward and reliable indicators of nutritional condition and muscular performance can assist in distinguishing various nutritional phenotypes among elderly individuals—whether they live independently or are affected by acute and chronic diseases (4). Evaluating nutritional status and physical fitness is fundamental for performing a comprehensive, multidisciplinary assessment, as well as for preventing conditions such as malnutrition and sarcopenia in older adults. Moreover, these evaluations represent a vital component of both rehabilitation strategies and the overall nutrition care process (11).

By conducting this study in a healthy population, we aim to explore the associations between BIA-derived parameters and functional measures of muscle strength (both peripheral and respiratory) in healthy individuals. Establishing these associations in healthy adults can provide reference data and underscore the utility of BIA as a simple screening tool for early muscle functional impairment. These reference data may serve as a

benchmark for comparison with patient populations, in whom preservation of muscle mass and respiratory muscle function is critically linked to outcomes and quality of life.

Methods

The study was conducted at the Special Hospital for Lung Diseases in Zagreb between June 1, 2024, and August 31, 2024. Participants were healthy hospital employees aged 30 to 65. Individuals were considered healthy if they had no self-reported history or clinical signs of respiratory or neuromuscular diseases. A convenience sample of 50 participants was included for the purpose of this pilot study. Exclusion criteria comprised professional athletes and individuals diagnosed with respiratory or neuromuscular disorders.

Before participation, eligible individuals received written and verbal information explaining the purpose of the study. Those who agreed to participate signed an informed consent form in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines. Participation was voluntary. Ethical approval for the study was obtained from the Ethics Committee of the Special Hospital for Lung Diseases in Zagreb.

Body height and weight were measured following a standardized protocol, with participants barefoot and wearing light clothing. Height was measured using a stadiometer, and weight was assessed with a digital medical scale (SECA 799). BMI was calculated as weight divided by height squared (kg/m^2). Body composition was evaluated using a multi-frequency, eight-electrode bioelectrical impedance analyzer (TANITA MC-780MA P, Tanita Corp., Tokyo, Japan), providing segmental analysis of fat-free mass (FFM), muscle mass, bone mass, skeletal muscle mass, fat and muscle percentages, skeletal muscle mass index (SMMI), visceral fat, intracellular and extracellular fluid, total body water, and phase angle. The device has been validated for clinical use (12). All BIA measurements were performed in the morning, in a fasted state after a 12-hour fast to ensure reliability.

Maximal inspiratory pressure (MIP) was assessed using a PowerBreathe device (Powerbreathe International Ltd., Southam, UK) connected to a computer. This non-invasive method measures the highest negative pressure generated during a maximal inspiratory effort and reflects diaphragm and accessory inspiratory muscle strength. Participants were thoroughly instructed and familiarized with the procedure. Measurements were performed in a seated position, with the nose clipped, and the highest value from five attempts was recorded (13). Predicted MIP values were calculated based on age and sex: males, MIP_predicted = 120 − (0.41 × age); females, MIP_predicted = 108 − (0.61 × age). Measured values were compared to predicted normative data.

Isometric strength of upper and lower limb muscles on the dominant side was assessed using a digital hand dynamometer (Pelican 1150, Lafayette Instrument Company, Lafayette, USA). Maximal voluntary force of elbow flexors (m. biceps brachii) and knee extensors (m. quadriceps femoris) was measured in a seated position. Three attempts were recorded, with a one-minute rest between trials, and the mean value was used for analysis (14, 15)

Diaphragm thickness was measured using ultrasonography (Mindray DC-8, Mindray Medical International, Shenzhen, China) with a 7.5–10 MHz linear probe in the supine position. The probe was positioned at the zone of apposition of the right diaphragm, between the 8th and 9th intercostal space. Thickness was assessed at end-expiration (functional residual capacity) and end-inspiration, with each measurement repeated at least three times and averaged (16, 17,18). All ultrasonography was performed by the same experienced operator to reduce inter-operator variability (19). Measured parameters were compared with literature reference values for age- and sex-matched populations (17).

Categorical variables are presented as counts and percentages. Continuous variables are summarized as mean ± standard deviation for normally distributed data or as median (interquartile range) for non-normal data. Group differences were assessed using the chi-square or Fisher's exact test for categorical variables, and the Mann-Whitney U or Kruskal-Wallis test for continuous variables, as appropriate. Correlations were performed when required. All tests were two-sided, with a significance level of $\alpha = 0.05$. Statistical analyses were conducted using IBM SPSS Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY, USA; 2019).

Results

The sociodemographic characteristics of the study participants, including sex distribution and age-related variables such as mean, minimum, and maximum age values, are presented in Table 1.

Table 1. Sociodemographic characteristics of participants

Participants	Male	Female	Total
Number	19	31	50
Percentage (%)	38	62	100
Mean age (years)	37,63	43,35	41,18
Youngest age (years)	30	30	30
Oldest age (years)	62	63	63

The median values of the parameters obtained using bioelectrical impedance analysis are shown in Table 2, providing an overview of body composition characteristics relevant to the assessment of muscle health in the study population.

Table 2. Median results of body composition analysis Parameters

Parameter	Median
Height (cm)	170,00
Weight (kg)	72,80
Body mass index (kg/m²)	26,05
Lean mass (kg)	52,25
Muscle mass (kg)	49,60
Skeletal muscle mass (kg)	27,35
Sarcopenic index (kg/m²)	7,68
Phase angle (°)	6,00

Median values of upper and lower limb muscle strength and diaphragm function parameters in the study population are showed in Table 3.

Table 3. Median values of measured parameters

Parameter	Median
Biceps brachii muscle strength (N)	194.64
Quadriceps femoris muscle strength (N)	247.55
Maximal Inspiratory Pressure (MIP – measured value) (cmH_2O)	94.95
Diaphragm excursion during deep breathing (mm)	71.90
Diaphragm excursion during quiet breathing (mm)	25.45
Diaphragm thickness at end-expiration (mm)	1.50
Diaphragm thickness at end-inspiration (mm)	3.05
Diaphragm thickness ratio (Tmax/Tmin)	2.00

To further examine the relationships between the observed variables, Spearman's correlation coefficient was calculated. The correlation coefficients for the analyzed parameters are presented in Table 4, allowing for a clearer interpretation of their interdependence.

Discussion

Sarcopenia, characterized by the age-related loss of skeletal muscle mass and function, is a major contributor to decreased functional capacity and respiratory performance in both healthy and clinical populations (20, 4). Shin et al. (21) investigated the relationship between skeletal muscle mass assessed by bioelectrical impedance analysis and maximal inspiratory and expiratory pressures in 65 healthy individuals. They demonstrated that both MIP and MEP were positively associated with skeletal muscle mass. Similarly, our findings showed a strong association between skeletal muscle mass and MIP values.

The diaphragm, as the primary muscle of inspiration, plays a critical role in maintaining adequate pulmonary function. Ultrasonographic assessment of diaphragm thickness and excursion provides a non-invasive measure of respiratory muscle function, and has been shown to correlate with both peripheral muscle strength and sarcopenic indices (22,16).

Bioelectrical impedance analysis measurements correlate with peripheral and inspiratory muscle strength.

In addition, our research found that skeletal muscle mass correlated positively with diaphragm thickness measured at end-inspiration and end-expiration. These correlations were also confirmed in the study by Smargiassi et al. (23), conducted in patients with chronic obstructive pulmonary disease, which reported significant correlations between muscle mass and diaphragm thickness. Lee et al. (22) investigated 45 healthy individuals and reported significant positive correlations between diaphragm thickness and handgrip strength ($r = 0.759$, $p < 0.01$), calf circumference ($r = 0.499$, $p < 0.01$), and muscle mass/body mass index ratio ($r = 0.609$, $p < 0.01$). They also demonstrated significant positive associations between MIP and handgrip

Table 4. Spearman's correlation coefficients between examined variables

	Body Mass Index (kg/m²)	Muscle Mass (kg)	Skeletal Muscle Mass (kg)	Sarcopenic Index (kg/m²)	Phase Angle (°)
M. biceps brachii strength	0,173	0,703**	0,704**	0,575**	0,596**
M. quadriceps femoris strength	0,065	0,536**	0,565**	0,414**	0,465**
Maximal inspiratory pressure	0,118	0,663**	0,682**	0,551**	0,469**
Diaphragm thickness at end-inspiration	0,295*	0,424**	0,432**	0,464**	0,309*
Diaphragm thickness at end-expiration	0,571**	0,565**	0,523**	0,665**	0,371**
Diaphragmatic excursion during quiet breathing	0,212	0,337*	0,311*	0,291*	0,024
Diaphragmatic excursion during deep breathing	0,317	0,584**	0,497**	0,450**	0,096

Note: * indicates statistically significant correlation at $p < 0.05$;
** indicates statistically significant correlation at $p < 0.01$.

strength ($r = 0.437$, $p < 0.01$), calf circumference ($r = 0.408$, $p < 0.01$), and diaphragm thickness ($r = 0.652$, $p < 0.01$). Additionally, inspiratory muscle strength, typically assessed via maximal inspiratory pressure (MIP), reflects the functional capacity of the diaphragm and accessory respiratory muscles and serves as an important clinical marker in various populations (11,13). Phase angle, measured by bioelectrical impedance analysis (BIA), has emerged as a reliable indicator of cellular health and nutritional status. Lower phase angle values have been linked to adverse clinical outcomes, including prolonged hospitalization and reduced survival, while higher values indicate better muscle quality and functional reserve (24, 25). This metric, together with direct measures of muscle mass and strength, provides a comprehensive evaluation of sarcopenia and its impact on respiratory function.

Despite growing evidence supporting the importance of skeletal muscle and diaphragm assessment in clinical practice, data integrating these measures in healthy populations remain limited. Therefore, the present study aimed to investigate the relationships between skeletal muscle mass, diaphragm thickness and mobility, inspiratory muscle strength, peripheral muscle strength, and phase angle in a cohort of healthy adults. Understanding these associations may provide insights into early markers of sarcopenia and guide interventions to preserve respiratory and muscular function.

Conclusion

Bioelectrical impedance analysis is a reliable method for assessing body composition, and its measurement outcomes can be utilized as indicators of health, for the early identification of dysfunctions and alterations in body composition that may lead to the development of disease. These results highlight the interdependence of peripheral and respiratory muscle health and support the use of combined assessments, including bioelectrical impedance analysis, ultrasonography, and hand-held dynamometry, for early detection of sarcopenia. Monitoring these parameters in clinical and healthy populations may provide valuable insights for preventive strategies aimed at maintaining muscular and respiratory function. BIA may have significant value in clinical practice; therefore, close attention should be given to specific body composition components that may indicate potential muscular dysfunctions, particularly in patients with chronic diseases.

Future studies with larger and more diverse populations are warranted to validate these findings and to explore potential interventions that preserve both skeletal and respiratory muscle function, thereby improving overall physical performance and quality of life.

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REVIEW ARTICLE / PREGLEDNI ČLANAK

UNDERSTANDING ACCIDENTAL HYPOTHERMIA IN EMERGENCY MEDICINE: FROM PATHOPHYSIOLOGY TO DIAGNOSIS AND MANAGEMENT

RAZUMIJEVANJE SLUČAJNOG PODHLAĐIVANJA U HITNOJ MEDICINI: OD PATOFIZIOLOGIJE DO DIJAGNOZE I ZBRINJAVANJA

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Abstract

Introduction: Accidental hypothermia or unintentional lowering of core temperature below 35°C is a critical, multi-organ emergency affecting diverse populations year-round. It arises from trauma, old age, homelessness, environmental exposure, or immersion in cold water.

Objective: This review summarizes current evidence on classifying hypothermia by temperature, its pathophysiology, diagnostic features, and tailored management. The aim is to provide emergency clinicians a clear approach for recognizing, triaging, and treating hypothermic patients.

Methods: A narrative review was conducted, sourcing data from peer-reviewed articles, surveys, observational studies, and guidelines via PubMed, covering definitions, physiology, epidemiology, and treatment.

Results: Hypothermia is classified as mild (32–35°C), moderate (28–32°C), or severe (<28°C). Severe hypothermia leads to reduced brain blood flow, lower cardiac output and pressure, and a higher risk of dangerous arrhythmias. Electrolyte imbalances especially hyperkalemia along with acidosis and coagulopathy are linked to worse outcomes. Treatment ranges from passive rewarming in mild cases to active internal methods and extracorporeal Life Support, Extracorporeal Membrane Oxygenation (ECLS/ECMO) in severe cases. In specialized centres, ECLS has led to nearly 100% survival for select patients with hypothermic cardiac arrest.

Conclusions: Effective management relies on accurate staging, preventing further heat loss, focused diagnostics and timely active or extracorporeal rewarming for unstable patients. Clear protocols and ECLS referral criteria enhance outcomes. Future research should focus on comparing rewarming techniques, developing standardized triage approaches, and evaluating system-wide strategies.

Keywords: body temperature; cardiac arrest; emergency medicine; hypothermia; rewarming.

Sažetak

Uvod: Slučajno podhlađivanje (hipotermija) ili nehotično snižavanje tjelesne temperature ispod 35°C predstavlja hitno stanje koje zahvaća više organskih sustava i može pogoditi različite skupine ljudi tijekom cijele godine. Nastaje uslijed traume, starije životne dobi, beskućništva, izloženosti okolišnim uvjetima ili uranjanja u hladnu vodu

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Cilj: Ovaj pregledni rad sažima postojeće dokaze o klasifikaciji pothlađenosti prema temperaturi, njezinoj patofiziologiji, dijagnostičkim obilježjima i prilagođenom liječenju. Cilj je pružiti liječnicima hitne medicine jasan pristup za prepoznavanje, trijažiranje i liječenje bolesnika s hipotermijom.

Metode: Proveden je pregled literature, koristeći podatke iz recenziranih članaka, anketa, opservacijskih studija i smjernica putem PubMed-a, obuhvaćajući definicije, fiziologiju, epidemiologiju i liječenje.

Rezultati: Podhlađenost se klasificira kao blaga (32–35°C), umjerena (28–32°C), ili teška (<28°C). Teška hipotermija dovodi do smanjenog protoka krvi kroz mozak, sniženog srčanog minutnog volumena i tlaka te povišenog rizika nastanka aritmija. Elektrolitni disbalansi osobito hiperkalemija zajedno s acidozom i koagulopatijom povezani su s lošijim ishodima. Liječenje se sastoji od pasivnog zagrijavanja u blagim slučajevima do aktivnih metoda unutarnjeg zagrijavanja i izvantjelesne potpore/izvantjelesne membranske oksigenacije (engl. *Extracorporeal Life Support/Extracorporeal Membrane Oxygenation,* ECLS/ECMO) kod teških slučajeva. U specijaliziranim centrima, ECLS je doveo preživljenje probranih bolesnika s hipotermnim srčanim arestom do blizu 100%.

Zaključci: Učinkovito zbrinjavanje podhlađivanja oslanja se na točno određivanje stupnja podhlađivanja, sprječavanje daljnjeg gubitka topline, ciljanu dijagnostiku i pravovremeno aktivno ili izvantjelesno ponovno zagrijavanje kod nestabilnih bolesnika. Jasni protokoli i kriteriji za upućivanje bolesnika na ECLS poboljšavaju ishode. Buduća istraživanja trebala bi se usmjeriti na usporedbu metoda ponovnog zagrijavanja, razvoj standardiziranih trijažnih pristupa te evaluaciju strategija na razini sustava.

Ključne riječi: hipotermija; hitna medicina; srčani zastoj; tjelesna temperatura; zagrijavanje

Introduction

Cold-induced collapse and successful resuscitation have long been reported, leading to hypothermia's recognition as a unique scenario in advanced life support guidelines by the late 20th century (1). Key statements established that even seemingly lifeless hypothermic patients may survive with persistent resuscitation and controlled rewarming—principles now standard in modern protocols (1,2). Research in the 1980s and 1990s further detailed the physiological progression of hypothermia and shaped current rewarming and extracorporeal referral recommendations (1,3). Accidental hypothermia is defined as an unintentional drop in core temperature below 35°C. It is categorised into three stages (Table 1), each indicating increasing physiological compromise. These categories are used in clinical protocols and guidelines to guide rewarming and adapt resuscitation approaches, corresponding to specific physiological changes in emergency care (1,2).

Table 1. Clinical classification based on core temperature

Severity Level	Core Temperature Range
Mild Hypothermia	32–35°C
Moderate Hypothermia	28–32°C
Severe Hypothermia	< 28°C

Rates of accidental hypothermia and related deaths vary: Europe reports 2–5 deaths per 100,000, while around 1,300 annual deaths were recorded in the U.S. from 1999–2011. Data are likely underestimated due to underreporting and inconsistent coding, highlighting the need for better registries and regional coordination (6-9).

> **Patients with severe accidental hypothermia, even those presenting without detectable vital signs, may achieve full recovery if subjected to sustained resuscitation and controlled rewarming.**

Accidental hypothermia affects all climates yearround and impacts urban and rural populations. Atrisk groups include the homeless, older adults, those with substance use disorders, outdoor enthusiasts, trauma victims, and individuals submerged in cold water. Its global epidemiology is shaped by environmental and socioeconomic factors (1,2). Hypothermia commonly presents in emergency settings and, especially in trauma, is part of the "lethal triad" (with coagulopathy and acidosis), predicting higher mortality and requiring prompt recognition and prevention of further heat loss (1,10). Severe hypothermia suppresses cardiac and cerebral function, raising the risk of

Table 2. Global Patterns in Accidental Hypothermia

Region / Setting	Examples	Key Epidemiologic Features	Primary Risk Factors / HighRisk Groups
Northern & Arctic regions	Canada, Scandinavia, Russia	Highest documented rates; long, severe winters; remote geography; delayed access to care	Indigenous and rural communities; outdoor workers; individuals with alcoholrelated exposure; submersion victims
Temperate regions	Western Europe, United States, Japan	Significant morbidity and mortality despite milder climates; substantial urban hypothermia burden	Elderly adults; homeless individuals; trauma patients; people with substance use disorders
Mountainous & highaltitude regions	Alps, Himalayas, Andes	High proportion of severe cases; rescue delays; limited onscene resources	Climbers, trekkers, mountaineers, rescue personnel
Maritime & coastal environments	North Atlantic, Baltic Sea, Pacific Northwest	Coldwater immersion as major cause of severe hypothermia and cardiac arrest	Commercial fishers, sailors, recreational boaters
Low and middleincome countries (LMICs)	Global LMIC regions	Underrecognized due to limited surveillance; high exposure among outdoor laborers; neonatal hypothermia prevalent	Outdoor workers; socioeconomically vulnerable populations; neonates (separate epidemiologic category)

dangerous arrhythmias and arrest, so emergency protocols must include early internal or extracorporeal rewarming for unstable patients (1,2). Advances in extracorporeal methods have notably improved outcomes and are now central to hypothermia management (2).

Objectives of this review seek to outline current consensus definitions and temperaturebased staging systems that inform clinical decisionmaking, provide an integrated overview of the pathophysiologic changes affecting multiple organ systems, with particular attention to their relevance in emergency care, present severitybased diagnostic and management pathways, including criteria for initiating ECLS or cardiopulmonary bypass, summarize characteristic laboratory abnormalities and ECG findings that influence prognosis and therapeutic choices, discuss considerations for highrisk or special populations, including paediatric, geriatric, and trauma patients and finally evaluate existing evidencebased guidelines and highlight key gaps requiring further research. A narrative review was conducted, sourcing data from peer-reviewed articles, surveys, observational studies, and guidelines via PubMed, covering definitions, physiology, epidemiology, and treatment.

Pathophysiology

Thermoregulation and Compensatory Mechanisms

Core temperature is maintained by balancing heat production (metabolism, shivering) with heat loss, regulated by hypothalamic control and autonomic responses such as vasoconstriction and sympathetic activation. When heat loss exceeds production, core temperature drops. Early compensatory mechanisms include shivering, vasoconstriction, increased metabolic rate, and sympathetic drive. With further cooling, these responses fail—shivering stops, metabolism slows, mental status declines, and cardiovascular depression develops.

Mechanisms of Heat Loss

Heat is lost through four pathways (table 3.)

Table 3. Heat loss pathways

Conduction: Direct transfer to colder surfaces; dominant in cold-water immersion.
Convection: Loss to moving air or water.
Radiation: Infrared heat loss to the environment.
Evaporation: Loss via skin moisture and respiration.

Rapid cooling occurs with icy-water immersion (<5°C), wet clothing, and wind exposure. Exact realworld contributions of each mechanism remain poorly quantified.

Cardiovascular Changes by Temperature Stage

With a drop in body temperature, the cardiovascular system undergoes changes ranging from barely noticeable to profound, with fatal consequences if hypothermia is not controlled.

These changes form the basis for modified ACLS recommendations in hypothermia.

Respiratory Effects

Cold exposure initially increases respiratory rate, followed by slow, shallow breathing as cooling progresses. Severe hypothermia causes hypoventilation, hypoxemia, and hypercapnia. Reduced metabolic rate lowers oxygen demand, but hypothermia combined with hypoxia (e.g., drowning) worsens outcomes.

Table 4. Cardiovascular changes in hypothermia

Hypothermia Stage	Core Temperature	Key Physiologic Changes	Arrhythmia Risk	Hemodynamic Effects
Mild	32–35°C	• Sympatheticdriven tachycardia • Peripheral vasoconstriction	Low	• Cardiac output generally preserved • Increased systemic vascular resistance
Moderate	28–32°C	• Bradycardia and slowed conduction • Declining myocardial contractility	• Atrial fibrillation • Supraventricular arrhythmias	• Reduced cardiac output • Risk of hypotension
Severe	<28°C	• Marked reduction in cerebral perfusion and oxygen use • Myocardial depression	• Ventricular tachycardia/ fibrillation • Asystole	• Very low cardiac output and arterial pressure • Heart often unresponsive to drugs and defibrillation until rewarmed

Neurological Manifestations

Cooling progressively reduces cerebral metabolism and blood flow:

- Mild: Confusion, slowed cognition
- Moderate: Stupor, diminished reflexes
- Severe: Coma with minimal signs of life

Profound hypothermia may mimic death, supporting the principle of continuing resuscitation until rewarmed unless clear signs of irreversible death exist.

Metabolic Alterations

Hypothermia causes:

- Reduced metabolic rate
- Impaired insulin release and altered glucose handling
- Metabolic acidosis
- Slowed drug metabolism
- Electrolyte shifts, especially potassium abnormalities

Electrolyte Abnormalities

- Hyperkalaemia: Common during rewarming; very high levels predict poor prognosis.
- Hypokalaemia: May result from cold diuresis.
- Additional disturbances in sodium, calcium, and magnesium may occur. Hyperkalemia is sometimes used to guide decisions about aggressive rewarming or ECLS candidacy.

Renal and Endocrine Effects

- Reduced renal blood flow and vasoconstriction impair kidney function.
- Cold diuresis from central volume shifts and reduced ADH contributes to hypovolemia and electrolyte loss.
- Early catecholamine and cortisol release may diminish in severe hypothermia.
- Preexisting thyroid or adrenal insufficiency may worsen.

Coagulation Abnormalities

Hypothermia impairs haemostasis through platelet dysfunction, slowed enzymatic activity, prolonged clotting times, and increased bleeding risk. These issues are critical in trauma and during ECMO, where anticoagulation is required.

Afterdrop Phenomenon

Afterdrop is a continued fall in core temperature during early rewarming due to cold peripheral blood returning centrally. It is minimized by controlled rewarming and avoiding rapid peripheral vasodilation. Close monitoring during transport and early rewarming is essential.

Implications for Emergency Management

Physiologic stage guides rewarming strategy:

- Mild: Passive or active external warming
- Moderate: Active external ± internal warming
- Severe or unstable: Active internal rewarming and consideration of extracorporeal life support/ cardiopulmonary bypass (ECLS/CPB)

Extracorporeal techniques provide circulatory support and controlled rewarming, improving survival in severe hypothermic arrest. Impaired drug metabolism at low temperatures requires ACLS medication adjustments when core temperature is <30°C.

In severe or unstable hypothermia, timely internal rewarming potentially with extracorporeal support is critical to restore circulation and improve survival.

Clinical presentation and diagnosis

Clinical Signs by Severity

Clinical changes vary according to the level of hypothermia, ranging from shivering and vasoconstriction to the development of coma and pronounced bradycardia.

Electrocardiographic Findings

ECG monitoring is essential. Key features:

- Osborn (J) waves: Classic in moderate–severe hypothermia; correlate with lower temperature and higher arrhythmia risk.
- Other changes: Bradyarrhythmias, prolonged PR/QRS/QT, atrial fibrillation, ventricular arrhythmias (<28°C).
- Refractory myocardium: Limited response to drugs and defibrillation until rewarmed.

Core Temperature Measurement

Preferred methods: Esophageal (during resuscitation), rectal, bladder, lowtemperature tympanic probes. Avoid: Oral, axillary, standard tympanic, skin readings. Note: Do not delay transport or rewarming; obtain core temperature early in the emergency department.

Laboratory Abnormalities

Laboratory abnormalities in hypothermia are shown in the table below.

Prompt action following the hypothermia diagnostic algorithm on patient arrival in the emergency department is crucial to prevent complicatons. (see Figure 1. below)

Differential diagnosis

Accidental hypothermia may result from direct environmental exposure—such as prolonged cold exposure, homelessness, outdoor activity, or coldwater immersion (1,12)—but can also reflect underlying medical conditions. Endocrine disorders, sepsis, neurologic injury, toxicologic impairment, metabolic derangements, and dermatologic disease may all contribute to or mimic hypothermia (1,4,16). Iatrogenic factors, including perioperative cooling, unwarmed transfusions, and therapeutic hypothermia protocols, are additional considerations (1,17). Evaluation must account for both primary and secondary causes, and in infants, hypothermia should prompt assessment for serious bacterial infection (18).

Risk factors and etiology

Accidental hypothermia is mainly caused by environmental exposure—prolonged cold, poor shelter, wilderness or work exposure, and cold-water immersion, which rapidly lowers body temperature (1,12). Submersion combines hypothermia with hypoxia; rapid cooling may sometimes protect the brain during arrest (1,6). Annually, about 1,300 deaths occur in the U.S., and 2–5 per 100,000 in Europe, though true rates are likely underestimated due to coding

Table 5. Clinical sings of hypothermia by severity

Severity	Core Temp	Key Features
Mild	32–35°C	Shivering, tachycardia, vasoconstriction, normal or mildly altered mental status, increased respirations
Moderate	28–32°C	Confusion, bradycardia, atrial arrhythmias, hypotension, reduced respiratory drive, shivering stops, poor coordination
Severe	<28°C	Stupor/coma, marked bradycardia or VT/VF/asystole, severe hypotension, minimal respirations, depressed reflexes, may appear clinically dead

Legend: VT/VF - ventricular tachycardia / ventricular fibrillation

Table 6. Laboratory abnormalities in hypothermia

Parameter	Findings	Notes
Electrolytes	Hyperkalaemia (poor prognosis if very high)	Possible hypo/hypernatraemia, calcium/magnesium abnormalities
Acid–base	Metabolic acidosis	Elevated lactate in severe hypoperfusion
Coagulation	Prolonged PT/INR/aPTT, platelet dysfunction	Standard labs underestimate coagulopathy (tested at 37°C)
CBC	Elevated haematocrit (haemoconcentration), variable WBC	
Renal	Elevated creatinine/BUN	High CK if rhabdomyolysis
Glucose	Hypo- or hyperglycaemia	Due to impaired insulin regulation

Legend: PT – prothrombin time;
INR – international normalized ratio; aPTT –activated partial thromboplastin time; WBC - white blood cells; BUN - blood urea nitrogen; CK – creatine kinase

Patient with suspected hypothermia
↓
IMMEDIATE ACTIONS:
• Measure core temperature (esophageal/rectal/bladder)
• Continuous cardiac monitoring
• Pulse oximetry
• Remove wet clothing, prevent further heat loss
• Handle gently (minimize movement to reduce VF risk)
↓
OBTAIN:
• 12-lead ECG (look for Osborn waves, arrhythmias, conduction delays)
• Serum electrolytes (especially potassium)
• Arterial blood gas
• Lactate
• Coagulation studies
• Complete blood count
• Renal function
• Blood glucose
• Toxicology screen if indicated
↓
CLASSIFY SEVERITY:
• Mild (32-35°C)
• Moderate (28-32°C)
• Severe (<28°C)
↓
ASSESS STABILITY:
• Perfusing rhythm vs. cardiac arrest
• Hemodynamic stability
• Presence of arrhythmias
↓
INITIATE APPROPRIATE REWARMING STRATEGY
(See Section 5: Management Protocols)

Figure 1. Emergency Department Diagnostic Approach to Hypothermia

issues (6-8). Medical conditions increasing risk include hypothyroidism, adrenal insufficiency, hypopituitarism (5,16), stroke, spinal injury, Parkinson's, dementia (16), heart failure, vascular disease (11), sepsis (especially elderly), and infections in infants (18). Malnutrition and vitamin deficiencies also lower resistance (5).Trauma-related hypothermia results from exposure, shock, unwarmed IV fluids, and poor thermoregulation, forming the "lethal triad" with coagulopathy and acidosis, which raises mortality (1,10). It leads to worse outcomes, more transfusions, and longer ICU stays, so early prevention and correction are needed (10). Certain drugs (alcohol, sedatives, opioids, antipsychotics, anesthetics) and toxins (CO, ethanol, sympatholytics) impair thermoregulation and shivering, increasing risk (5,16). Management must address both toxicity and temperature (16). Demographics matter: older adults have impaired thermoregulation, comorbidities, polypharmacy, and social isolation, making them more vulnerable (2,19). Neonates/infants are at risk due to high surface area, immature regulation, and dependence on caregivers; hypothermia may indicate infection (18). Homeless, mentally ill, and substance users face higher exposure and risk (1,14). Iatrogenic hypothermia occurs perioperatively (anaesthesia, cold operating rooms, long procedures) and with unwarmed transfusions (1,10). Therapeutic hypothermia after cardiac arrest can cause overcooling if not monitored, requiring similar management to accidental hypothermia (2,17).

Management protocols in the emergency medicine

Prehospital Care and Transport

Immediate priorities in the prehospital setting include environmental extraction, removal of wet clothing, patient insulation with blankets or vapor barriers, wind protection, and movement minimization (1). Rough handling and extremity massage must be avoided to reduce ventricular fibrillation risk (1). Temperature management strategies include passive rewarming through insulation, administration of warmed humidified oxygen when available, and warmed intravenous fluids when protocols permit (1). Core temperature measurement should not delay transport (1). Destination selection is critical for optimal outcomes. Patients presenting with severe hypothermia (core temperature <28°C), hemodynamic instability, ventricular arrhythmias, or cardiac arrest require triage to extracorporeal life support (ECLS)-capable centers when feasible (1,2). Continuous cardiopulmonary resuscitation (CPR), potentially utilizing mechanical CPR devices for prolonged transport, should be maintained in cardiac arrest cases, with pre-notification of receiving facilities to mobilize ECLS teams (1,2).

Emergency Department Initial Assessment

The primary survey follows standard airway, breathing, and circulation (ABC) protocols with hypothermia-specific modifications (1). Airway patency assessment and intubation for unconsciousness or inadequate ventilation, supplemental oxygen provision (preferably heated and humidified), and circulation assessment requiring prolonged pulse checks (30-45 seconds) are essential (1). Vascular access establishment and cardiac monitoring initiation complete the primary survey (1). Immediate interventions include continuous cardiac monitoring for arrhythmia detection (particularly ventricular fibrillation/

ventricular tachycardia), core temperature measurement via oesophageal, rectal, or bladder probe, 12-lead electrocardiography to document rhythm and identify Osborn waves, prevention of further heat loss through removal of wet clothing and application of warm blankets, gentle handling to minimize movement, and establishment of intravenous access (preferably central for warmed fluid administration) (1,4).

Essential laboratory studies comprise serum electrolytes (with particular attention to potassium), arterial blood gas analysis, lactate, complete blood count, coagulation studies (prothrombin time/international normalized ratio, activated partial thromboplastin time), renal function assessment (creatinine, blood urea nitrogen), creatine kinase if rhabdomyolysis is suspected, blood glucose, and toxicology screening when indicated (1,4). Prognostic markers include serum potassium, with markedly elevated nonhemolyzed values (>10-12 mmol/L) associated with poor outcomes and used as a triage consideration in some protocols (1,2). Elevated lactate correlates with severity and mortality, while severe acidosis predicts worse outcomes (1,2).

Rewarming Strategies Overview

Rewarming strategies are selected based on hypothermia severity and hemodynamic stability. Passive external rewarming, appropriate for mild hypothermia (32-35°C) with stable vital signs, achieves rewarming rates of 0.5-2°C per hour through insulation, warm environment, and wet clothing removal (1). Active external rewarming, indicated for moderate hypothermia or inadequate passive rewarming response, utilizes forced-air warming systems, heating blankets, radiant heaters, and warm packs applied to the trunk, achieving rates of 1-2.5°C per hour (4). Active internal rewarming (non-ECMO), employed for moderate to severe hypothermia without ECLS indications, incorporates warmed intravenous fluids (42-44°C), heated humidified oxygen (42-46°C), gastric/bladder lavage, peritoneal lavage, pleural lavage, and intravascular warming catheters, with rewarming rates of 1-3°C per hour (1,4,20). Extracorporeal rewarming (ECLS/ECMO), recommended for cardiac arrest, severe hypothermia (<28°C) with unstable circulation, or refractory ventricular arrhythmias, achieves the most rapid rewarming (3-10°C per hour) and demonstrates marked survival improvements in case series (2,14).

Passive Rewarming

Passive rewarming serves as the initial step for all hypothermic patients and may suffice as sole therapy for mild cases (32-35°C) with stable hemodynamics (1,4). Techniques include removal of all wet clothing, insulation with dry blankets or sleeping bags, ambient room temperature elevation (25-28°C), head covering to prevent scalp heat loss, and vapor barrier application to reduce evaporative losses (1). Monitoring includes serial core temperature measurements every 15-30 minutes, continuous cardiac monitoring, vital signs assessment, and mental status evaluation (4). Limitations include slow rewarming rates (0.5-2°C per hour) and insufficiency for severe hypothermia (1).

Active External Rewarming

Active external rewarming is indicated for moderate hypothermia (28-32°C), mild hypothermia inadequately responding to passive methods, or as an adjunct to active internal rewarming in severe cases (4). Forced-air warming systems (e.g., Bair Hugger, Warm Touch), the most common method in modern emergency departments, apply warming blankets preferentially to the trunk at temperatures of 40-43°C (4). Conductive heating blankets utilizing circulating warm water, radiant overhead warming lights, and warm packs applied to trunk areas (axillae, groin, neck) provide additional options (1,4). Precautions include afterdrop monitoring, wherein peripheral vasodilation returns cold blood to the core causing transient temperature decrease, thermal injury surveillance for burns particularly in patients with altered sensation, and rewarming shock management with intravenous fluid preparation for vasodilation-induced hypotension (1,4).

Active Core Rewarming: Warmed Intravenous Fluids

Warmed intravenous fluid administration is indicated for moderate to severe hypothermia, all patients requiring intravenous resuscitation, and as an adjunct to other rewarming methods (1). Isotonic crystalloids (normal saline or lactated Ringer's solution) warmed to 42-44°C are delivered via fluid warmers, with central venous administration preferred in severe cases at rates typically of 150-200 mL per hour, adjusted based on hemodynamics and volume status (1). Precautions include volume overload monitoring for pulmonary oedema, electrolyte shift surveillance (particularly potassium), and avoidance of peripheral intravenous access in severe cases due to poor extremity perfusion (1,4).

Active Core Rewarming: Heated Humidified Oxygen

Heated humidified oxygen (42-46°C) is indicated for all intubated hypothermic patients and spontaneously breathing patients with severe hypothermia when equipment is available (1). Delivery occurs via ventilator circuit or high-flow nasal cannula systems with essential humidification to prevent airway desiccation (1). Benefits include airway and core warming, respiratory heat loss prevention, oxygenation support, relative non-invasiveness, and compatibility with all other rewarming methods (1).

Active Core Rewarming: Body Cavity Lavage

Gastric and bladder lavage, involving warmed saline (40-42°C) instillation via nasogastric tube or urinary catheter, provides limited contribution to core rewarming due to

restricted surface area and serves only an adjunctive role (1). Peritoneal lavage (peritoneal dialysis) is indicated for severe hypothermia when ECLS is unavailable (1,4). Technique involves peritoneal dialysis catheter insertion, instillation of warmed (approximately 43°C) potassium-free dialysis fluid in 2-liter volumes with 20-30 minute dwell times, followed by drainage and repetition (1,4). The large surface area for heat exchange and feasibility in most hospitals constitute advantages, while invasiveness, perforation risk, infection risk, and slower rewarming compared to ECMO represent disadvantages (1). Pleural/thoracic lavage is indicated for severe hypothermia, especially with cardiac arrest, when ECLS is unavailable (1,21). Bilateral chest tube placement (typically 36-40 French), warmed normal saline (40-42°C) instillation into one hemithorax with drainage from the contralateral chest tube in volumes of 300-500 mL per exchange characterize the technique (1,21). Greater effectiveness than peritoneal lavage due to cardiac and great vessel proximity represents an advantage, while high invasiveness, chest tube placement requirements, and risks of pneumothorax, haemothorax, and infection constitute disadvantages (1,21). Case reports and small series demonstrate feasibility and success (21).

Active Core Rewarming: Intravascular Warming Devices

Endovascular warming catheters placed in central veins (femoral, internal jugular) circulate warm saline through balloon or coil structures to achieve direct blood warming (20). Indications include severe hypothermia and situations requiring an intermediate option between external methods and ECMO when ECMO is not immediately available (20). Advantages encompass less invasiveness than ECMO, controlled rewarming rates (1-3°C per hour), emergency department or intensive care unit placement capability, and elimination of perfusionist or cardiac surgery team requirements (20). Disadvantages include central venous access and expertise requirements, slower rewarming than ECMO, absence of hemodynamic support, and limited center availability (20). A growing body of literature supports efficacy, though comparative outcome data versus ECMO remain limited (20).

Extracorporeal Life Support and Cardiopulmonary Bypass

Strong indications for ECLS include hypothermic cardiac arrest (ventricular fibrillation, ventricular tachycardia, pulseless electrical activity, or asystole), severe hypothermia (<28°C) with hemodynamic instability, refractory ventricular arrhythmias, or hypotension unresponsive to fluids and vasopressors, and moderate hypothermia (28-32°C) with cardiac arrest or severe cardiovascular instability (1,2,14). Relative contraindications include very high nonhemolyzed serum potassium (>10-12 mmol/L in some protocols), lethal injuries incompatible with survival, known terminal illness, prolonged warm cardiac arrest prior to cooling, and evidence of tissue necrosis suggesting prolonged exposure with irreversible damage, though clinical judgment is required as some patients with elevated potassium have survived with ECLS (1,2).

Resuscitation Modifications in Hypothermia

For core temperatures <30°C, repeated resuscitation drug boluses are generally withheld due to altered metabolism and risk of toxicity upon rewarming (1). At 30–35°C, if drugs are used, dosing intervals should be doubled (applies to epinephrine, amiodarone, lidocaine, atropine) (1). Defibrillation: Up to three shocks for ventricular fibrillation/tachycardia; further attempts deferred until core temperature >30°C (some protocols use 32°C) (1). Continue CPR during rewarming; prolonged resuscitation is justified due to neuroprotective effects ("no one is dead until they are warm and dead") (1,2). Pulse checks may require 30–45 seconds due to bradycardia; consider mechanical CPR for extended resuscitation or transport (1,2). Termination criteria are not well-defined: consider exposure duration, serum potassium (>10–12 mmol/L), lethal injuries, frozen body cavities, and clear signs of death. Resuscitation should continue until rewarming to at least 32–35°C unless irreversible death is evident (1,2). Criteria for resuscitation termination are not well-defined but should consider exposure duration, serum potassium (>10-12 mmol/L), evidence of lethal injuries, frozen body cavities, and obvious signs of death (rigor mortis, dependent lividity), with the general principle of continuing resuscitation until rewarming to at least 32-35°C unless clear evidence of irreversible death exists (1,2).

Severe hypothermia with hemodynamic instability or cardiac arrest requires rapid active internal rewarming, preferably with extracorporeal life support (ECLS/ECMO), to restore circulation and improve survival.

Airway Management

Intubation is indicated for unconsciousness (Glasgow Coma Scale ≤8), inadequate ventilation, inability to protect airway, cardiac arrest, and severe hypoxemia (1). Technique considerations include gentle laryngoscopy to avoid excessive stimulation potentially precipitating ventricular fibrillation, preoxygenation with warmed humidified oxygen when available, rapid sequence intubation modifications considering hemodynamic effects of induction agents, and post-intubation provision of heated humidified oxygen via ventilator circuit (1).

Fluid Resuscitation

All intravenous fluids should be warmed (42-44°C) using fluid warmers or rapid infusion systems, with central venous access preferred in severe hypothermia (1). Initial resuscitation is guided by hemodynamics, with anticipation of shifts during rewarming as vasodilation causes relative hypovolemia (1). Careful monitoring is required to avoid both under-resuscitation and pulmonary edema, while excessive crystalloid administration may worsen hypothermia-induced coagulopathy (1,10). Blood products, indicated for trauma, ongoing bleeding, or severe anemia, must be warmed, with anticipation of worsened coagulation necessitating early use of plasma, platelets, and tranexamic acid in trauma (10).

Special populations

Pediatric Hypothermia

Neonates and infants (≤90 days) demonstrate unique vulnerabilities including high surface area-to-volume ratio causing rapid heat loss, immature thermoregulation, limited shivering ability, dependence on brown fat thermogenesis, and thin subcutaneous fat layers (18). Hypothermia in young infants may indicate serious bacterial or viral infection, with emergency department practice showing high variability and substantially greater rates of invasive testing in infants ≤30 days, including blood cultures, urine cultures, lumbar puncture for cerebrospinal fluid analysis, and empirical antibiotics (18). Older children demonstrate better thermoregulation than infants but remain vulnerable, with behavioral factors (inadequate clothing, water play) and submersion incidents representing common causes (1). Management follows adult principles scaled to size with lower threshold for ECLS consideration in paediatric centers and essential family-centered care (1).

Neonates and young infants are highly vulnerable to hypothermia due to immature thermoregulation, high surface area-to-volume ratio, and limited shivering, and hypothermia in this age group may indicate serious infection.

Trauma-Associated Hypothermia

Hypothermia is part of the trauma "lethal triad" (hypothermia → coagulopathy → acidosis), with each factor worsening the others (10). Causes include prolonged scene time, clothing removal, haemorrhagic shock, cold environment, room-temperature IV fluids, open wounds, and cold operating rooms (10). Each 1°C drop below 35°C increases mortality, transfusion needs, coagulation times, acidosis, platelet dysfunction, and length of hospital/ICU stay (1,10). Prevention: minimize scene time, remove wet clothing, use blankets/insulation, warm ambulance, and give warmed IV fluids when possible (10). Emergency department: warm resuscitation bay, remove clothing only as needed, cover exposed areas, use forced-air warming, give warmed fluids/blood, provide heated humidified oxygen, and limit unnecessary exposure (10). Operating room: increase ambient temperature, use forced-air warming, warmed irrigation fluids, warmed IV fluids/blood, and minimize surgical time (damage control principles) (10).

Submersion and Cold-Water Immersion

Water conducts heat 25 times faster than air, with immersion in icy water (<5°C) causing profound hypothermia within minutes and core temperature dropping 1-2°C within the first few minutes (1,6). The cold-water immersion sequence progresses through cold shock response (0-3 minutes) with gasping, hyperventilation, and tachycardia; cold incapacitation (3-30 minutes) with loss of muscle function and inability to swim; hypothermia (>30 minutes) with progressive cooling and altered consciousness; and circum-rescue collapse with cardiac arrest during or immediately after rescue (1). Rapid cooling may reduce cerebral metabolic rate before severe hypoxia, potentially explaining rare cases of good neurological recovery after prolonged submersion, with maximal protection in very cold water (<5°C) with rapid submersion (1,22).

Outcomes and prognosis

Cardiac Arrest Outcomes

Pre-ECLS era survival from hypothermic cardiac arrest typically remained below 50%, limited by conventional rewarming methods' inability to provide circulatory support (2). Contemporary ECLS era outcomes demonstrate survival approaching 100% in highly selected patients (young, previously healthy, witnessed arrest, rapid CPR initiation, rapid ECLS access, no prolonged warm cardiac arrest) (2,22), while real-world multicentre data reveal more variable outcomes with survival rates of 30-70% depending on patient selection and system factors, better outcomes in specialized centres with established protocols, and selection bias in published series where sicker patients may not be offered ECLS (14,20)

Prognostic Factors and Predictors of Mortality

Strong predictors of poor outcome include markedly elevated nonhemolyzed serum potassium (>10-12 mmol/L), which strongly associates with mortality, serves as a triage consideration in some ECLS protocols, reflects prolonged tissue hypoxia and cell death, though survivors with potassium exceeding 10 mmol/L have been reported, precluding absolute contraindication (1,2). Lower core temperature associates with higher mortality, with each degree below 28°C increasing risk and temperatures

below 24°C historically associated with very poor outcomes, though survivors have been reported (2,4). Factors associated with better outcomes include younger age, previously healthy status, witnessed arrest or rapid discovery, rapid CPR initiation, short transport time to ECLS centers, icy water submersion versus environmental exposure, and ventricular fibrillation as presenting rhythm (1,2,22).

Neurological Outcomes

Hypothermia's neuroprotective effects result from reduced cerebral metabolic rate, decreased oxygen consumption, potential neurological function preservation during prolonged arrest, and form the basis for therapeutic hypothermia post-cardiac arrest (1,22). Full neurological recovery remains possible even after prolonged cardiac arrest (>60 minutes in cold water), profound hypothermia (<24°C), and prolonged resuscitation, with case reports documenting complete recovery with return to baseline function (22).

Even in profound hypothermic cardiac arrest, patients can achieve full survival and neurological recovery due to hypothermia's neuroprotective effects, particularly when rapid CPR and timely ECLS are provided.

Current evidence and guidelines

Major Guideline Recommendations

American Heart Association (AHA)/Advanced Cardiovascular Life Support (ACLS) key recommendations include gentle handling to prevent ventricular fibrillation, prevention of further heat loss, staged rewarming approach (passive → active external → active internal → extracorporeal), modified resuscitation algorithms limiting defibrillation attempts (up to three shocks) with deferral of repeated shocks until core temperature exceeds 30°C, withholding or spacing resuscitation drugs when temperature remains below 30°C, continuing cardiopulmonary resuscitation during rewarming, administering warmed humidified oxygen, providing warmed intravenous fluids (central administration preferred), considering extracorporeal rewarming for cardiac arrest or hemodynamic instability, and continuing resuscitation until rewarmed consistent with the principle "no one is dead until they are warm and dead" (1). European Resuscitation Council (ERC) recommendations align with AHA guidance with variations including emphasis on early ECLS triage for severe cases, structured regional protocols for hypothermia management, consideration of mechanical CPR for prolonged transport, and specific temperature thresholds for treatment modifications (2). Wilderness Medical Society provides specific guidance for remote settings including field rewarming techniques when evacuation is delayed, decision algorithms for field versus evacuation, and practical considerations for resource-limited environments (23). International Commission for Mountain Emergency Medicine (ICAR MEDCOM) endorsed recommendations include temperature-based staging and triage, ECLS as preferred method for severe hypothermia with arrest, regional coordination for mountain rescue and hypothermia care, and specific protocols for avalanche victims (2). It is also of importance to mention Croatian national recommendations for diagnosis and treatment of accidental hypothermia in emergency medicine which present contribution to successful management of accidental hypothermia (24).

Accidental hypothermia, caused by environmental exposure, medical conditions, trauma, or drugs, is life-threatening and requires early recognition and careful management, especially in vulnerable populations.

Conclusion

Accidental hypothermia is most often caused by environmental exposure, but medical conditions, trauma, drugs, and social factors also increase risk. Submersion in cold water can rapidly induce hypothermia, sometimes with brain-protective effects. Mortality rates are significant but likely underreported. Medical conditions such as endocrine disorders, cardiovascular disease, and infections, especially in infants and the elderly, heighten vulnerability. Trauma-related hypothermia worsens outcomes due to its role in the "lethal triad." Certain drugs and toxins further impair the body's ability to regulate temperature. Older adults, infants, the homeless, and those with mental illness or substance use are particularly at risk. Iatrogenic hypothermia can occur during surgery or with unwarmed transfusions, and therapeutic hypothermia requires careful monitoring. Early recognition, prevention, and tailored management are essential to improve outcomes in hypothermic patients.

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REVIEW ARTICLE / PREGLEDNI ČLANAK

NOSNA KANILA VISOKOG PROTOKA U AKUTNOJ HIPOKSEMIJI U HITNOM BOLNIČKOM PRIJAMU: UTJECAJ NA ANESTEZIOLOŠKU PRAKSU

HIGH-FLOW NASAL CANNULA IN ACUTE HYPOXEMIA IN THE EMERGENCY DEPARTMENT: IMPLICATIONS FOR ANESTHESIA PRACTICE

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Sažetak

Akutna hipoksemija čest je i potencijalno životno ugrožavajući razlog dolaska bolesnika u hitni bolnički prijam te često predstavlja rani znak akutnog respiracijskog zatajenja. U bolesnika s izraženim respiracijskim radom i povećanim inspiracijskim zahtjevima standardna oksigenoterapija može biti nedostatna. Posljednjih godina nosne kanile visokog protoka sve se češće primjenjuju u akutnoj skrbi jer omogućuju primjenu zagrijanog i ovlaženog zraka pri visokim protocima uz preciznu kontrolu udjela kisika u udahnutom zraku**.** Njihovi fiziološki učinci uključuju poboljšanje oksigenacije, smanjenje anatomskog mrtvog prostora i smanjenje respiracijskog napora.

Ovaj pregledni rad prikazuje saznanja o primjeni nosnih kanila visokog protoka u hitnom bolničkom prijamu, s posebnim naglaskom na utjecaj na anesteziološku praksu. Razmatra se njihova uloga u oksigenaciji u periintubacijskom razdoblju, zbrinjavanju dišnog puta u nepredvidivim uvjetima te tijekom sedacije pri zahvatima. Posebna pozornost posvećena je sigurnosti primjene, praćenju bolesnika i kriterijima neuspjeha terapije. Nosne kanile visokog protoka predstavljaju značajnu terapijsku opciju u zbrinjavanju akutne hipoksemije u hitnoj službi, uz uvjet pažljivog odabira bolesnika i stalne kliničke procjene.

Ključne riječi: anesteziologija; hipoksemija; hitna bolnička služba; terapija inhalacijom kisika; zbrinjavanje dišnog puta

Abstract

Acute hypoxemia is a frequent and potentially life-threatening condition encountered in the emergency department and often represents an early manifestation of acute respiratory failure. In patients with increased respiratory effort and high inspiratory demand, conventional oxygen therapy may be insufficient. In recent years, high-flow nasal cannula has become increasingly used in acute care, as it delivers heated and humidified gas at high flow rates with precise control of the inspired oxygen fraction. Its physiological effects include improved oxygenation, reduced anatomical dead space, and decreased work of breathing.

This narrative review summarizes the current evidence on the use of high-flow nasal cannula in the emergency department, with a particular focus on implications for anesthesiology practice. Its role in periintubation oxygenation, airway management in unpredictable conditions and during procedural sedation is discussed. Special attention is given to safety aspects, patient monitoring, and criteria for treatment failure.

High-flow nasal cannula represents a valuable option in the management of acute hypoxemia in the emergency setting, provided that appropriate patient selection and continuous clinical assessment are ensured.

Keywords: airway management; anesthesiology; emergency department; hypoxemia; oxygen therapy;

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Uvod

Akutna hipoksemija jedan je od najčešćih i najzahtjevnijih kliničkih problema s kojima se susreću zdravstveni timovi u hitnoj medicinskoj službi (1). Pojavljuje se u širokom spektru stanja, od pneumonije (2) i sepse do akutnog kardiogenog plućnog edema (3), te često predstavlja prvi znak ozbiljnog respiracijskog zatajenja. U takvim okolnostima ključno je pravodobno prepoznati težinu poremećaja oksigenacije i odabrati odgovarajuću strategiju respiracijske potpore, pritom uspostavljajući ravnotežu između potrebe za stabilizacijom bolesnika i rizika od preuranjene ili odgođene invazivne ventilacije.

Standardna terapija kisikom niskim protokom, iako široko dostupna, u bolesnika s izraženim respiracijskim radom i povećanim potrebama tijekom udaha često ne osigurava stabilnu i dostatnu oksigenaciju (4). Posljednjih godina terapija nosnim kanilama visokog protoka (engl. *high-flow nasal cannula,* HFNC) zauzima sve značajnije mjesto u akutnoj skrbi jer omogućuje isporuku visokih protoka zagrijanog i ovlaženog zraka uz preciznu kontrolu udjela kisika u udahnutom zraku (FiO2). Takav način primjene kisika utječe na više fizioloških mehanizama istodobno, uključujući smanjenje anatomskog mrtvog prostora, poboljšanje alveolarne ventilacije i smanjenje respiracijskog napora, što je od posebne važnosti u ranim fazama akutne hipoksemije (1,5).

Posebna je pažnja posvećena studijama koje su analizirale kliničke ishode, sigurnost primjene i kriterije za prijelaz na višu razinu respiracijske potpore, osobito u situacijama u kojima je anesteziološka procjena dišnog puta i odabir ventilacijske strategije imao ključnu ulogu.

Hitna služba je kliničko okruženje u kojem se isprepliću principi hitne medicinske službe, intenzivne skrbi i anesteziologije, posebno kada je riječ o procjeni i zbrinjavanju dišnog puta. Anesteziološki pristup u takvim okolnostima ne svodi se samo na tehničko provođenje oksigenacije i ventilacije, nego uključuje cjelovitu procjenu tijeka bolesti, pravodobno prepoznavanje potrebe za prijelaz na višu razinu liječenja (eskalacija oksigenoterapije), te osiguravanje sigurnosti bolesnika tijekom dijagnostičkih i terapijskih postupaka. U tom smislu, HFNC može predstavljati prijelazni oblik respiracijske potpore između standardne oksigenoterapije i invazivne ventilacije, pod uvjetom da se primjenjuje uz jasno definirane kriterije praćenja i pravodobnog prepoznavanja neuspjeha terapije (6).

Cilj ovog rada je prikazati ulogu HFNC-a u zbrinjavanju akutne hipoksemije u hitnom bolničkom prijamu, s posebnim naglaskom na utjecaj na anesteziološku praksu, uključujući zbrinjavanje dišnog puta, oksigenaciju u periintubacijskom razdoblju, te sigurnu primjenu tijekom sedacije pri zahvatima.

Metodologija

Rad predstavlja pregled znanstvene i stručne literature s ciljem sustavnog prikaza i sinteze dosadašnjih spoznaja o primjeni nosne kanile visokog protoka u liječenju akutne hipoksemije u hitnoj medicinskoj službi. Takav pristup odabran je kako bi se omogućilo povezivanje heterogenih kliničkih studija, preglednih radova i smjernica iz područja anesteziologije, intenzivne i hitne medicine, koje se u ovom kontekstu prirodno preklapaju.

Pretraživanje literature provedeno je u bazama *PubMed, Scopus* i *Web of Science*. U obzir su uzeti radovi objavljeni od 2015. godine nadalje, s posebnim naglaskom na novije publikacije koje odražavaju modernu kliničku praksu i sadašnje preporuke. Uključeni su radovi koji su se bavili odraslom populacijom bolesnika zbrinutih u hitnom bolničkom prijamu ili drugim oblicima akutne skrbi, a koji su analizirali primjenu HFNC-a u okolnostima akutne hipoksemije ili akutnog respiracijskog zatajenja.

Posebna je pažnja posvećena studijama koje su analizirale kliničke ishode, sigurnost primjene i kriterije za prijelaz na višu razinu respiracijske potpore, osobito u situacijama u kojima je anesteziološka procjena dišnog puta i odabir ventilacijske strategije imao ključnu ulogu. U pregled su uključeni originalni znanstveni radovi, sustavni i pregledni članci te važeće kliničke smjernice.

Iz pregleda su isključeni radovi koji su se odnosili isključivo na pedijatrijsku populaciju, studije usmjerene na kroničnu kućnu primjenu HFNC-a, kao i radovi bez jasno definiranih kliničkih ishoda ili bez neposredne primjenjivosti u akutnom kliničkom okruženju. Na taj je način osigurano da pregled obuhvati literaturu koja je važna za kliničku praksu u hitnoj medicinskoj službi i anesteziološko donošenje odluka u akutnim stanjima. Ovaj rad predstavlja pregled znanstvene literature te ne uključuje izravna istraživanja na ljudima niti obradu osobnih podataka, zbog čega nije bilo potrebno ishoditi odobrenje etičkog povjerenstva.

Rasprava

Fiziološki mehanizmi djelovanja oksigenoterapije visokim protokom

HFNC djeluje kroz međusobno povezane fiziološke mehanizme koji zajedno doprinose poboljšanju oksigenacije i smanjenju respiracijskog opterećenja u bolesnika s akutnom hipoksemijom (7–9). Za razliku od standardnih sustava za primjenu kisika, omogućuje isporuku visokih protoka zagrijanog i ovlaženog zraka koji mogu zadovoljiti ili nadmašiti inspiracijske zahtjeve bolesnika (5,8). Time se smanjuje nekontrolirano miješanje s okolnim zrakom i postiže stabilniji udio kisika

u udahnutom zraku, što je osobito važno u bolesnika s tahipnejom i povećanim respiracijskim radom.

Kontinuirani visoki protok plina doprinosi i ispiranju anatomskog mrtvog prostora gornjih dišnih putova. Uklanjanjem izdahnutog ugljikova dioksida iz nazofarinksa smanjuje se ponovno udisanje izdahnutog zraka te se povećava učinkovitost ventilacije (8). Taj učinak može rezultirati smanjenjem ventilacijskih potreba za održavanje odgovarajuće izmjene plinova, što ima izravan utjecaj na smanjenje respiracijskog napora i subjektivnog osjećaja dispneje.

Primjena HFNC-a povezana je i s nastankom blagog pozitivnog ekspiracijskog tlaka, čiji se intenzitet povećava s porastom protoka. Iako se ne radi o razinama tlaka usporedivima s neinvazivnom ventilacijom, taj učinak može doprinijeti povećanju plućnog volumena na kraju izdisaja, poboljšanju alveolarne regrutacije i ujednačenijoj raspodjeli ventilacije. Posljedično se postiže poboljšanje oksigenacije, osobito u ranim fazama akutne respiracijske insuficijencije (10).

HFNC predstavlja vrijedan alat koji može proširiti mogućnosti periintubacijskog zbrinjavanja, osobito u fazi preoksigenacije.

Zajednički učinak navedenih mehanizama očituje se u smanjenju respiracijskog rada i poboljšanju ugode bolesnika. Optimalno ovlaživanje i zagrijavanje plina smanjuju nadražaj sluznice dišnih putova, olakšavaju mukocilijarni klirens i povećavaju toleranciju terapije (8,9). U području djelovanja hitne medicinske službe, gdje su bolesnici često izloženi stresu, anksioznosti i hemodinamskoj nestabilnosti, takvi učinci imaju dodatnu kliničku vrijednost jer omogućuju stabilizaciju bolesnika bez dodatnog pogoršanja subjektivnog doživljaja disanja.

Indikacije primjene HFNC u hitnoj službi

Primjena HFNC-a u hitnoj medicinskoj službi najčešće dolazi u obzir u bolesnika s akutnim hipoksemičnim zatajenjem disanja kod kojih standardna oksigenoterapija ne osigurava zadovoljavajuću oksigenaciju, a neposredna potreba za invazivnom ventilacijom još nije jasno izražena (1,2). U toj skupini osobito se ističu bolesnici s upalom pluća i sepsom, kod kojih je hipoksemija često praćena povećanim respiracijskim radom i hemodinamskom nestabilnošću. U ranim fazama zbrinjavanja, HFNC može omogućiti stabilizaciju respiracijskih pokazatelja, olakšati daljnju dijagnostičku obradu i pružiti vremenski prostor za procjenu tijeka bolesti i odgovora na terapiju (11,12). Slično tome, u bolesnika koji se u hitnoj medicinskoj službi prezentiraju nejasnom dispnejom, primjena takvog oblika oksigenoterapije može imati ulogu privremene potpore tijekom početne kliničke procjene, uz pažljivo praćenje bolesnika i jasno definiranu strategiju prijelaza na višu razinu respiracijske potpore (13,14).

U akutnom kardiogenom plućnom edemu, gdje dominira kombinacija hipoksemije i povećanog rada disanja, standardni pristup često uključuje ranu primjenu neinvazivne ventilacije. Iako terapija nosnim kanilama visokog protoka ne može zamijeniti učinke neinvazivne ventilacije koja primjenjuje stalni pozitivni tlak ili dvije različite razine pozitivnog tlaka tijekom udisaja i izdisaja, u blažim i umjerenim oblicima respiracijske insuficijencije može pridonijeti poboljšanju oksigenacije i smanjenju dispneje (15). U takvim okolnostima, HFNC može se razmotriti kao početna mjera respiracijske potpore, osobito u bolesnika koji slabije toleriraju neinvazivnu ventilaciju ili kod kojih je potrebna kratkotrajna stabilizacija prije donošenja odluke o daljnjem liječenju.

Posebnu skupinu čine imunokompromitirani bolesnici, kod kojih je invazivna strojna ventilacija povezana s visokim rizikom komplikacija i nepovoljnim ishodima. U takvih bolesnika strategije koje omogućuju odgodu ili izbjegavanje intubacije imaju osobitu kliničku važnost (16). HFNC se u takvim okolnostima nameće kao prijelazna strategija respiracijske potpore, omogućujući poboljšanje oksigenacije uz očuvanje spontanog disanja. Međutim, upravo u navedenoj populaciji nužno je jasno definirati granice primjene i kriterije neuspjeha, kako bi se izbjegao odgođen prijelaz na višu razinu liječenja u slučaju progresije respiracijskog zatajenja.

Nosna kanila visokog protoka i anesteziološka praksa u hitnoj službi

Uloga anesteziologa u hitnoj službi često je usmjerena na procjenu i osiguranje dišnog puta u okolnostima koje su obilježene vremenskim pritiskom, ograničenim informacijama i kliničkom nepredvidivošću. Stoga HFNC predstavlja vrijedan alat koji može proširiti mogućnosti periintubacijskog zbrinjavanja, osobito u fazi preoksigenacije. Omogućujući kontinuiranu isporuku visokog protoka kisika uz očuvano spontano disanje, spomenuti sustav može produljiti sigurno apneično vrijeme i smanjiti rizik brze desaturacije tijekom pripreme i izvođenja intubacije (17). Takav učinak ima posebnu važnost u bolesnika s ograničenom respiracijskom rezervom, pretilošću ili očekivano otežanim dišnim putem.

Unatoč tim prednostima, primjena HFNC-a u periintubacijskom razdoblju ima svoja ograničenja. U bolesnika s teškom hipoksemijom, izraženim intrapulmonalnim šantom ili progresivnim respiracijskim zatajenjem, fiziološki učinci navedenog oblika terapije kisikom mogu biti nedostatni za sprječavanje značajne desaturacije (17,18). U takvim situacijama anesteziološka procjena mora biti usmjerena na pravodobno prepoznavanje neuspjeha i donošenje odluke o prijelaz na višu razinu respiracijske potpore, uključujući primjenu neinvazivne ventilacije ili hitnu intubaciju.

Hitna medicinska služba često predstavlja okruženje u kojem se zbrinjavanje dišnim putem odvija u nepovoljnim uvjetima, uz ograničen prostor i resurse, te uz istodobno zbrinjavanje drugih životno ugrožavajućih stanja. U tom okviru, HFNC može poslužiti kao potporna strategija koja omogućuje privremenu stabilizaciju bolesnika i dobivanje vremena za planiranje daljnjih koraka (6,12). Njezina primjena može olakšati suradnju između anesteziologa i liječnika hitne medicine, osobito u situacijama kada je potrebno zajednički procijeniti rizike, definirati strategiju zbrinjavanja dišnim putem i uskladiti trenutak prijelaza na višu razinu respiracijske potpore.

Osim u kontekstu intubacije, HFNC sve se češće razmatra i tijekom sedacije pri zahvatima u hitnoj medicinskoj službi. Sedativi, iako nužni za izvođenje dijagnostičkih i terapijskih postupaka, nose rizik depresije disanja i gubitka zaštitnih refleksa dišnog puta (19). U tom smislu, primjena HFNC-a može doprinijeti sprečavanju epizoda desaturacije, osobito tijekom duljih ili tehnički zahtjevnih zahvata (19). Opisana strategija može biti od posebne koristi u rizičnim skupinama bolesnika, poput starijih osoba, pretilih bolesnika ili onih s postojećom respiracijskim zatajenjem, kod kojih i kratkotrajni poremećaji ventilacije mogu dovesti do brzog pogoršanja kliničkog stanja.

Sigurnost, praćenje i kriteriji neuspjeha

Unatoč brojnim prednostima koje HFNC pruža u zbrinjavanju akutne hipoksemije, njezina primjena zahtijeva visoku razinu kliničke opreznosti. Jedan od ključnih izazova povezanih s navedenom terapijom je rizik od odgođene intubacije, osobito u bolesnika kod kojih se u početku postiže subjektivno poboljšanje disanja bez stvarne stabilizacije respiracijske funkcije (20,21). U okolnostima prividnog poboljšanja može se prikriti progresija respiracijskog zatajenja, što naposljetku može dovesti do intubacije u nepovoljnijem trenutku i uz veći rizik komplikacija.

Rana identifikacija neuspjeha terapije stoga ima presudnu važnost. Procjena odgovora na HFNC mora biti dinamična i temeljena na kombinaciji kliničkih i objektivnih pokazatelja. Respiracijska frekvencija jedan je od najosjetljivijih pokazatelja jer trajna tahipneja, unatoč primjeni visokog protoka kisika, upućuje na trajno povišen respiracijski napor i iscrpljivanje ventilacijskih rezervi (22). Jednako je važno sustavno procjenjivati rad disanja, uključujući korištenje pomoćnih respiracijskih mišića, neusklađenost torakalnog i abdominalnog disanja i subjektivni osjećaj dispneje (8).

U kliničkoj praksi sve veću ulogu ima i indeks omjera saturacije kisika i udjela kisika u udahnutom zraku u odnosu na frekvenciju disanja, ROX indeks (engl. *ratio of arterial oxygen saturation (SpO_2) to the fraction of inspired oxygen (FiO_2), divided by respiratory rate*). Taj pokazatelj omogućuje sustavnu procjenu odgovora na terapiju i može pomoći u ranoj identifikaciji bolesnika kod kojih je vjerojatnost neuspjeha povećana (23). Ipak, ROX indeks ne smije se promatrati izolirano, već kao dio kliničke slike koja uključuje i hemodinamski status, mentalno stanje bolesnika i dinamiku osnovne bolesti.

Sigurna primjena HFNC-a u hitnoj medicinskoj službi neodvojiva je od kontinuiranog monitoringa i učinkovite timske komunikacije. Pravodobno prepoznavanje pogoršanja zahtijeva jasno definirane odgovornosti unutar tima, redovitu ponovnu procjenu bolesnika i otvorenu razmjenu informacija između liječnika hitne medicine, anesteziologa i medicinskih sestara (18,24). Zbog svega navedenog, HFNC ne smije se promatrati kao sredstvo koje odgađa donošenje odluka, već kao terapijska opcija koja, uz pravilno praćenje, može olakšati pravodoban i siguran prijelaz na višu razinu liječenja kada je potreban..

Uloga medicinskih sestara anestezije i intenzivne medicine

Primjena HFNC-a u hitnoj medicinskoj službi ne predstavlja isključivo tehničku intervenciju, već proces koji zahtijeva kontinuirano kliničko promišljanje i timski pristup, u kojem medicinske sestre anestezije i intenzivne skrbi imaju središnju ulogu (24). Njihovo znanje o respiracijskoj fiziologiji, iskustvo u radu s akutno ugroženim bolesnicima i stalna prisutnost uz bolesnika čine ih ključnim nositeljima sigurnosti i učinkovitosti ove terapije.

Titracija protoka i udjela kisika u udahnutom zraku zahtijeva individualizirani pristup, prilagođen kliničkom stanju bolesnika i njegovom odgovoru na terapiju. Medicinske sestre anestezije i intenzivne skrbi aktivno sudjeluju u prilagodbi postavki uređaja, uzimajući u obzir oksigenaciju, respiracijsku frekvenciju i opći napor disanja (18,24). Takav pristup omogućuje postizanje terapijskog učinka uz istodobno smanjenje rizika nelagode ili intolerancije, što je osobito važno u stresnom okruženju hitne medicinske službe.

Procjena ugode i tolerancije terapije predstavlja važan, ali često podcijenjen aspekt skrbi. Neodgovarajuća tolerancija može dovesti do nemira, pogoršanja respiracijskog rada i prijevremenog prekida terapije. Medicinske sestre, kroz neposredan kontakt s bolesnikom, imaju jedinstvenu mogućnost prepoznati blage promjene u ponašanju, izrazu nelagode ili anksioznosti, te pravodobno intervenirati prilagodbom postavki ili komunikacijom s liječničkim timom (9,18).

Jednako je važna i uloga medicinskih sestara u ranom prepoznavanju pogoršanja kliničkog stanja. Promjene u respiracijskoj frekvenciji, pojava izraženijeg rada disanja, pad zasićenosti kisikom ili promjene u mentalnom statusu često se prvo uočavaju upravo tijekom kontinuirane sestrinske skrbi (24). Pravodobno prepoznavanje tih znakova i njihovo jasno komuniciranje liječnicima omogućuju brzu procjenu učinkovitosti terapije i donošenje odluke o prijelazu na višu razinu liječenja.

U okviru hitne medicinske službe, gdje su dinamika i opterećenje rada izraženi, medicinske sestre anestezije i intenzivne skrbi predstavljaju ključnu poveznicu između tehnologije i kliničke sigurnosti. Njihova uloga nadilazi tehničko upravljanje uređajem te uključuje aktivno sudjelovanje u kliničkom odlučivanju, praćenju bolesnika i osiguravanju kontinuiteta skrbi. Upravo kroz takav integrirani pristup moguće je maksimalno iskoristiti prednosti HFNC-a, uz istodobno smanjenje rizika i poboljšanje ishoda liječenja.

Zaključak

HFNC predstavlja učinkovitu opciju respiracijske potpore u zbrinjavanju akutne hipoksemije u hitnoj službi, osobito u bolesnika kod kojih standardna oksigenoterapija ne osigurava zadovoljavajuću oksigenaciju. Njezina primjena omogućuje stabilizaciju respiracijskih pokazatelja uz očuvanje spontanog disanja i dobru podnošljivost terapije.

Iz perspektive anesteziološke prakse, HFNC ima posebnu vrijednost u periintubacijskoj skrbi i zbrinjavanju dišnog puta, kao i tijekom sedacije pri zahvatima. Međutim, uspješnost ove terapije ovisi o pravilnom odabiru bolesnika, stalnom praćenju kliničkog odgovora i pravodobnom prijelazu na višu razinu liječenja u slučaju neuspjeha.

Daljnja istraživanja usmjerena specifično na hitnu medicinsku službu potrebna su kako bi se dodatno razjasnila optimalna uloga HFNC-a u akutnoj skrbi i unaprijedila sigurnost njezine primjene.

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REVIEW ARTICLE / PREGLEDNI ČLANAK

PSYCHOGENIC NON-EPILEPTIC SEIZURES IN THE EMERGENCY DEPARTMENT: A REVIEW

PSIHOGENI NE-EPILEPTIČKI NAPADAJI U HITNOM BOLNIČKOM PRIJAMU: PREGLEDNI RAD

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Abstract

Psychogenic non-epileptic seizures (PNES) present a significant diagnostic and management challenge in the emergency department (ED). Although PNES may closely resemble epileptic seizures, their origins are functional and psychological rather than electrical, often leading to misdiagnosis and unnecessary interventions. In emergency settings, this confusion can result in inappropriate antiepileptic medication use, intubation, and prolonged hospitalization. This review summarizes current evidence on the epidemiology, proposed pathophysiology, and characteristic clinical features of PNES, with emphasis on bedside indicators that can assist clinicians in distinguishing PNES from epileptic events during acute presentations. Key diagnostic considerations, including the role and limitations of history, physical examination, and video assessment are discussed, along with strategies for communicating the diagnosis sensitively and effectively to patients. The review further outlines principles of acute management focused on patient safety, avoidance of iatrogenic harm, and appropriate disposition planning, including when referral for definitive evaluation such as video-EEG monitoring is warranted. By increasing clinician awareness and confidence in recognizing PNES, emergency providers can improve patient outcomes, reduce unnecessary resource utilization, and facilitate timely engagement with mental health and neurological services.

Keywords: emergency sevices; epilepsy; psychogenic non-epileptic seizures

Sažetak

Psihogeni ne-epileptički napadaji (PNEN) predstavljaju značajan izazov za dijagnostiku i zbrinjavanje u hitnom prijamu (HP). Iako PNEN-i mogu izgledati slično epileptičkim napadajima, njihovo je izvorište funkcionalno i psihološko, a ne električno, a zbog navedene sličnosti često dolazi do pogrešne dijagnoze i nepotrebnih intervencija. U okružju hitnog prijama, ova zabluda može dovesti do neprimjerene upotrebe antiepileptičkih lijekova, intubacije i produljenog bolničkog liječenja. Ovaj pregledni rad prikazuje aktualne dokaze o epidemiologiji, patofiziologiji i kliničkim obilježjima PNEN-a, s posebnim naglaskom na kliničke pokazatelje za razlikovanje PNEN-a od epileptičkih napadaja u akutnom razdoblju. Ključna dijagnostička razmatranja , uključujući ulogu i ograničenja anamneze, pregleda i video procjene su navedena, zajedno sa strategijama učinkovitog i osjetljivog komuniciranja dijagnoze bolesnicima. Ovaj pregledni rad opisuje načela akutnog zbrinjavanja s naglaskom na sigurnost bolesnika, izbjegavanje jatrogenog oštećenja i pravilno planiranje daljnjeg liječenja, uključujući raspravu o situacijama u kojima je indicirano upućivanje na definitivnu dijagnostičku obradu, poput video-EEG monitoriranja. Povećavajući svijest o i sigurnost u prepoznavanje PNEN-a, liječnici hitne medicine mogu poboljšati ishode bolesnika, smanjiti nepotrebno korištenje resursa i olakšati pravovremeno upućivanje prema neurološkim i psihijatrijskim službama.

Ključne riječi: epilepsija; hitna služba; psihogeni ne-epileptički napadaji

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Introduction

Psychogenic non-epileptic seizures (PNES), also known as functional seizures, are episodic events that clinically resemble epileptic seizures but occur without ictal epileptiform activity (1). They fall within the spectrum of functional neurological disorders (FND) and are driven by psychological mechanisms rather than abnormal cortical discharges. PNES account for a substantial proportion of seizure-related ED visits and frequently lead to unnecessary pharmacologic interventions. Emergency clinicians are often the first providers to evaluate acute seizure-like presentations. Given time pressures and the potential for catastrophic consequences of missed convulsive status epilepticus, PNES is both easily overlooked and often over-treated (2,3). Recognition of PNES in the ED is critical for preventing iatrogenic complications and ensuring appropriate follow-up.

Epidemiology and pathophysiology

PNES are estimated to affect 2–33 per 100,000 individuals, though true prevalence may be higher due to under-recognition. Among all patients referred to epilepsy centers, 10–40% is ultimately diagnosed with PNES. In emergency settings, studies suggest that up to one-third of patients treated for status epilepticus may in fact be experiencing PNES episodes. PNES is more common in women (approximately 70% of cases) and frequently arises during adolescence or early adulthood (4). Risk factors include trauma, chronic psychological stress, psychiatric comorbidities (e.g., depression, anxiety, PTSD), and a history of chronic pain or somatization. The pathophysiology of PNES is conceptualized within modern frameworks of functional neurological disorders, where alterations in attention, emotion regulation, and sensorimotor processing create involuntary symptoms without structural neurological disease (5).

PNES are common seizure-like events in the ED, driven by psychological mechanisms, and early recognition is essential to prevent unnecessary interventions and iatrogenic harm.

Clinical presentation

PNES (psychogenic nonepileptic seizures) can mimic virtually any seizure semiology; however, several clinical characteristics increase suspicion for this diagnosis, particularly in the emergency department. Compared with typical epileptic generalized tonic-clonic seizures, PNES episodes are often of longer duration, usually exceeding 2–3 minutes, and are characterized by a gradual onset and offset rather than abrupt transitions (table 1). Motor manifestations commonly include asynchronous or side-to-side movements, pelvic thrusting, irregular thrashing, head rolling, and other non-stereotyped movement patterns that may vary between events. Eye closure during the episode is frequent and may be accompanied by resistance to passive eye opening. Protective reflexes are typically preserved, including avoidance of injury during falls. Ictal crying, verbalization, or prominent emotional expression may occur. After the event, post-ictal confusion is usually absent or very brief. Autonomic signs are generally minimal, with limited tachycardia, cyanosis, hypersalivation, or tongue biting.

In contrast, although no single feature is definitive, findings that are less consistent with PNES and raise concern for epileptic seizures include lateral tongue biting, highly stereotyped tonic-clonic activity, post-ictal confusion lasting longer than 5–10 minutes, documented medication non-adherence in patients with known epilepsy, and witnessed apnea or cyanosis (6).

Table 1. Clinical features suggestive of psychogenic nonepileptic seizures vs. epileptic seizures

Feature	Psychogenic nonepileptic seizures	Epileptic Seizure
Onset/offset	Gradual; waxing/waning	Sudden, abrupt
Duration	Typically prolonged (>2–3 min)	Usually <2 min (generalized tonic–clonic)
Movement pattern	Asynchronous, variable, side-to-side, pelvic thrusting, irregular thrashing	Stereotyped, rhythmic tonic–clonic activity
Eye status	Often closed tightly; resistance to passive opening	Typically open or non-resistant
Responsiveness	May retain partial responsiveness; may follow simple commands	Unresponsive during generalized seizures
Vocalization/crying	Common: weeping, shouting, speech during event	Rare during ictal phase
Tongue biting	Uncommon; if present, usually tip of tongue	More common; often lateral
Injury patterns	Rare, due to protective behaviors	More common: abrasions, bruises, fractures
Autonomic signs	Mild or inconsistent tachycardia, minimal cyanosis	Marked tachycardia, cyanosis, hypersalivation
Post-ictal phase	Often absent or very brief	Confusion, somnolence, headache common
Provoking factors	Emotional stress, interpersonal conflict	Sleep deprivation, missed ASM doses, metabolic triggers

PNES mimic epileptic seizures, but prolonged, non-stereotyped episodes with preserved reflexes and minimal post-ictal confusion suggest PNES.

Features less consistent with psychogenic nonepileptic seizures

In contrast, although no single feature is definitive, findings that are less consistent with PNES and raise concern for epileptic seizures include lateral tongue biting, highly stereotyped tonic-clonic activity, post-ictal confusion lasting longer than 5–10 minutes, documented medication non-adherence in patients with known epilepsy, and witnessed apnea or cyanosis. Ultimately, definitive differentiation between PNES and epileptic seizures often requires further evaluation, with video-EEG monitoring considered the diagnostic gold standard (7).

Diagnostic evaluation in the emergency department

Initial priorities

Emergency clinicians must prioritize stabilization, treating life-threatening conditions first. The guiding principle is: PNES can only be diagnosed after ruling out acute medical emergencies, including epileptic seizures, hypoglycemia, electrolyte derangements, toxicologic causes, and trauma (8).

Bedside assessment

Bedside assessment of a suspected PNES episode should include several key components. Vital signs should be measured, noting that PNES often lack pronounced autonomic changes. A focused neurologic examination should be performed both before and after the event. Bedside glucose testing is important to exclude metabolic causes of altered consciousness or seizure-like activity. Gathering a detailed history from witnesses is crucial, emphasizing the onset, duration, movement patterns, and the patient's state after the event. Finally, reviewing the patient's prior diagnoses, psychiatric history, and current medications helps provide context and may assist in differentiating PNES from epileptic seizures.

Key components of bedside assessment for suspected PNES include measurement of vital signs, noting that PNES often lack pronounced autonomic changes; performing a focused neurologic examination before and after the event; bedside glucose testing to exclude metabolic causes; obtaining a detailed history from witnesses, with emphasis on onset, duration, movement patterns, and the patient's post-event state; and reviewing prior diagnoses, psychiatric history, and current medications (2,8,9).

Laboratory and imaging testing

Routine laboratory evaluation may include electrolytes, pregnancy testing, and toxicology screens when clinically indicated. Neuroimaging is not mandatory unless trauma, focal deficits, or first-time seizure concerns are present.

Role of electroencephalography

Gold standard diagnosis requires event capture during video-EEG monitoring, which is rarely available in the ED. Short-term ED EEG may help exclude ongoing epileptic activity in suspected status epilepticus.Normal interictal EEG does not confirm PNES and should not be used diagnostically.

Table 2. Recommended emergency department workup for suspected psychogenic nonepileptic seizures

Domain	Evaluation Components	Rationale
Immediate stabilization	Airway, breathing, circulation; glucose; vital signs	Rule out life-threatening causes and metabolic emergencies
Focused history	Witness account, event duration, semiology, prior diagnosis, psychiatric history	Supports differentiation between PNES and epileptic seizure
Physical examination	Neurological exam pre- and post-event; injury assessment	Identifies focal deficits or trauma requiring further workup
Labs	Glucose, electrolytes; pregnancy test; tox screen if indicated	Identify reversible medical triggers
Imaging	Head CT only if trauma, first-time seizure, persistent deficits	Avoid unnecessary radiation and over-testing
EEG	Not routinely required; consider only in suspected status epilepticus or unclear diagnosis	Video-EEG is the gold standard but rarely available in ED
Disposition planning	Safe discharge, neurology referral, psychiatric evaluation as needed	Facilitates ongoing care and prevents repeat ED use

Bedside maneuvers

Gentle verbal reassurance and instructions (e.g., asking patient to open eyes or follow simple commands) may differentiate PNES from epileptic seizures in some cases. These must be used ethically and never confrontationally (10).

Management in the emergency department

Table 2 shows the recommended emergency department workup for suspected psychogenic nonepileptic seizures.

General principles

Once life-threatening conditions have been excluded and PNES is suspected, it is important to avoid escalating antiepileptic medications or sedatives, as these provide no benefit and may increase the risk of respiratory depression. Supportive monitoring should be maintained until the episode resolves. Additionally, any comorbid conditions, such as anxiety or metabolic abnormalities, should be identified and treated appropriately.

Communication with the patient

Clear, compassionate communication is essential when managing suspected PNES. Patients should be reassured that their symptoms are real and involuntary. Clinicians should avoid statements such as "nothing is wrong" or any implication that the events are intentional. It is helpful to briefly explain that the episodes may represent a functional neurological disorder, which requires outpatient evaluation. Patients should be encouraged to follow up with neurology or specialized Functional Neurological Disorder / Psychogenic Nonepileptic Seizures services for further management (FND/PNES) (11).

Avoiding iatrogenic harm in patients with suspected psychogenic nonepileptic seizures

In patients with suspected PNES, common unnecessary interventions include repeated boluses of benzodiazepines or antiseizure medications, intubation for non-epileptic "status epilepticus," and excessive imaging or laboratory testing. Studies have demonstrated that inappropriate intubation and ICU admission carry substantial risks, including complications related to sedation, mechanical ventilation, and prolonged hospitalization, without providing clinical benefit (table 3).

Management of suspected PNES in the ED focuses on avoiding unnecessary interventions, providing supportive care, clear patient communication, and ensuring safe disposition with appropriate outpatient follow-up.

Disposition Planning

After stabilization, appropriate disposition decisions for patients with suspected PNES include safe discharge with clear instructions and outpatient follow-up when events strongly suggest PNES and there is no medical instability. Neurology consultation should be obtained if the diagnosis remains uncertain. Psychiatric evaluation is indicated when there is acute behavioral risk, suicidality, or severe emotional distress (12,13).

Long-term management

Although long-term management generally falls outside the emergency department's scope, awareness of evidence-based interventions can help guide disposition and follow-up planning. Recommended interventions include cognitive behavioral therapy (CBT), trauma-focused therapies when post-traumatic stress disorder (PTSD) is present, and multidisciplinary programs for functional neurological disorders. Comorbid psychiatric conditions, such as anxiety or depression, should be addressed, and patients should receive education about seizure physiology and stress responses. Anti-seizure medications are not effective for PNES unless coexisting epilepsy is confirmed (14).

Table 3. Common emergency department pitfalls in managing psychogenic nonepileptic seizures and how to avoid them

Pitfall	Consequence	Recommended Strategy
Treating psychogenic nonepileptic seizures as epileptic status	Oversedation, intubation, ICU admission	Use structured psychogenic nonepileptic seizures recognition criteria; reassess frequently
Excessive benzodiazepines	Hypoventilation, hypotension	After excluding epileptic activity, avoid escalating sedatives
Negative or dismissive communication	Patient distress, worsened symptoms	Use clear, empathetic language; validate symptoms
Over-reliance on CT/MRI	Radiation exposure, increased costs	Reserve imaging for clear indications
Failure to arrange follow-up	Return emergency department visits, diagnostic delay	Provide neurology/ functional neurological disorder clinic referrals and written discharge plan

Special populations

Children and Adolescents

PNES may present differently in younger patients and often relate to school stress, bullying, family dysfunction, or trauma. In the ED, evaluation should include careful psychosocial assessment and parental guidance (15).

Older Adults

PNES is less common but may be misinterpreted as late-onset epilepsy or syncope. Comorbid cognitive decline can complicate diagnosis.

Coexisting Epilepsy

Up to 10–20% of patients with PNES also have epileptic seizures. Lack of clear differentiation in the ED necessitates caution; follow-up EEG monitoring is essential.

Implications for emergency medicine practice

Enhancing recognition of PNES in the emergency department can reduce unnecessary use of antiepileptic medications and decrease iatrogenic complications, including respiratory depression and ICU admission. Improved recognition may also shorten ED length of stay, optimize resource utilization, and enhance patient trust while facilitating appropriate referral pathways. Educational initiatives, such as simulation training, standardized care pathways, and recognition checklists, and adherence to diagnostic algorithms (fig 1), have been shown to improve clinician comfort and diagnostic accuracy (12).

Rapid recognition of PNES in the ED, coupled with avoidance of unnecessary interventions, empathetic communication, and structured referral pathways, reduces harm and improves patient outcomes.

Cluster of findings commonly seen in PNES:
Eye closure with resistance
Asynchronous limb movements
Side-to-side head rocking
Pelvic thrusting
Ictal crying or verbalization
Prolonged duration (>2–3 minutes)
Rapid recovery without post-ictal confusion

Figure 2. Clinical Signs Supporting PNES Diagnosis

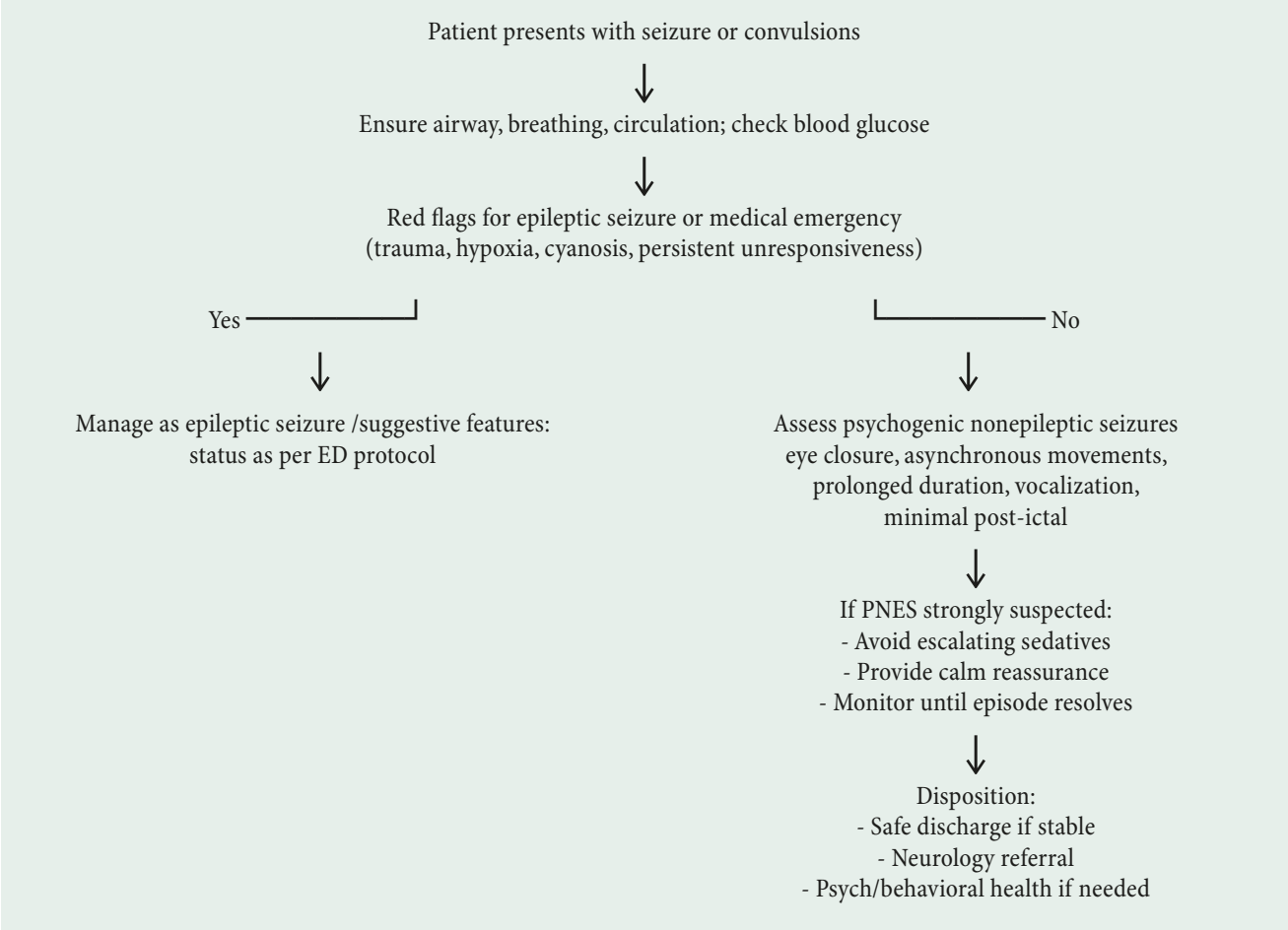

Figure 1. Practical emergency department algorithm for suspected psychogenic nonepileptic seizures

Conclusion

Psychogenic non-epileptic seizures are a frequent and challenging presentation in the emergency department. Effective ED management hinges on rapid identification of features suggestive of PNES, avoidance of unnecessary interventions, empathetic communication, and appropriate referral for definitive diagnosis and long-term care. Greater clinician awareness and structured management approaches can significantly reduce harm and improve outcomes for this vulnerable population.

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