ISSN 2545-4366
www.mja.mk

MJA

Macedonian Journal of Anaesthesia

A Journal on Anaesthesiology, Resuscitation, Analgesia and Critical Care

Vol. 10 No 2, June 2026

Journal of the Macedonian Society of Anaesthesiologists
and Macedonian Society of Critical Care Medicine

Publisher:
Department of Anaesthesia and Reanimation Faculty of Medicine,
"Ss. Cyril and Methodius" University, Skopje, R. N. Macedonia

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I.V. Paracetamol

БЕЗБЕДНА АНАЛГЕЗИЈА

менаџирање на болка кога сте загрижени за безбедноста

I.V. paracetamol за прв пат во Европа е применет во 2001 година, а денес поради неговата докажана безбедност и ефикасност е прв од избор **аналгетик и антипиретик.**

Предоперативна и Интраоперативна Аналгезија:
Предоперативна анелгезија е дефинирана како третман кој што започнува пред оперативниот зафат се со цел да се превенира воспоставувањето на централна сензибилизација на болка.
i.v. paracetamol е безбеден, добро толериран лек со докажана ефикасност како **предоперативна и интраоперативна анелгезија** за умерена до средна болка при оперативни зафати.
Голем број на клинички студии ја докажуваат ефикасноста на **i.v. paracetamol** како **преодоперативна и интраоперативна анелгезија**.

КЛИНИЧКА СТУДИЈА:
Ефект од **предоперативен i.v. paracetamol** за постоперативни аналгетски потреби кај пациенти кои се подлежни на оперативни зафати. A Sreenivasulu , R Prabhavathi, 2015
Цел: Да се утврди ефикасноста на **предоперативната употреба на 1000mg i.v. paracetamol** кај постоперативните болки и анелгетски потреби кај пациенти подлежни на хируршки зафати.
Метод: 60 пациенти беа поделени во две рандомизирани групи од по 30 пациенти.
На I. Група им беше администриран**о ампула од 1000mg i.v. paracetamol разредена 0,9%NaCl** р-ор 30 минути пред индукција **(ГРУПА П)**,
На II. Група им беше администрирано **i.v. 0,9% NaCl р-ор 100мл** 30 минути пред индукција **(ГРУПА НС)**
Сите пациенти беа индуцирани со i.v. thiopentone 5mg/kg, i.v. fentanyl 2µg/kg, i.v. vecuronium 0.1mg/kg
Постоперативниот резултат на болка беше мерен со **Визуелна Аналогна Скала (ВАС) од "0-10"**. Исто така беше забележувана и **постоперативната употреба на tramadol** како спасувачки аналгетик. Инциденцата на **постоперативно гадење и повраќање (ПОГП)** и други компликации исто така беа забележувани во пост оперативниот период.
Резултатот на постоперативната болка беше забележуван во интервали 15 мин, 30 мин, 1 час, 2 часа, и 6 часа.

Резултат:

Табела 1: *Споредба на средниот резултат на болка (ВАС) помеѓу двете групи*

Интервали	I Група П	II Група НС	*P вредност*
15 мин	2.06 ± 0.63	2.61 ± 0.56	0.0006
30 мин	2.35 ± 1.17	3.84 ± 1.55	0.0001
1 час	2.42 ± 1.12	2.87 ± 0.99	0.0989
2 часа	2.13 ± 1.06	2.52 ± 0.89	0.1219
6 часа	2 ± 0.52	2.52 ± 0.89	0.0549

Табела 2: *Споредба за потребите од tramadol помеѓу двете групи*

Интервали	I Група П	II Група НС	*P вредност*
До 1 час	4 (12.90%)	15 (50%)	0.0002
1-2 часа	3 (9.68%)	2 (6.45%)	0.64
2-6 часа	1 (3.23%)	3 (9.68%)	0.301
Вкупно	**8 (25.81%)**	**20 (64.52%)**	**0.002**

Табела3: *Споредба на ПОПГ помеѓу двете групи*

ПОГП	
I Група П	II Група НС
0	4

Заклучок: Предоперативна администрација на **1000mg i.v. paracetamol** кај пациенти подлежни на оперативен зафат обезбедува **статистички задоволителна анелегизија**, и ја **намалува постоперативната употреба на tramadol**. Оттука **1000mg i.v. paracetamol** може безбедно да се администитрира како превенција при оперативни зафати.

i.v. Paracetamol + јак опоид	МНОГУ ЈАКА БОЛКА
i.v. Paracetamol + слаб опоид	ЈАКА БОЛКА
i.v. Paracetamol + NSAID i.v. Paracetamol + rescue medicine	УМЕРЕНА БОЛКА
i.v. Paracetamol + rescue medicine	СЛАБА БОЛКА

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Macedonian Journal of Anaesthesia

A Journal on Anaesthesiology, Resuscitation, Analgesia and Critical Care

Publisher: Department of Anaesthesia and Reanimation Faculty of Medicine
"Ss. Cyril and Methodius" University Skopje, R. N. Macedonia

Proofreading: Nikolina Stojanova, R. N. Macedonia

Editorial Designer: Gavrilo Angeloski, R. N. Macedonia
(Arbëria Design - Tetovo)

Printing: Arbëria Design - Tetovo, R. N. Macedonia

CONTENT

EDITORIAL *UDK: 616-089-053.2:004.8616-089-053.2:007.52*

www.doi.org/10.67214/fx2z2n26

ARTIFICIAL INTELLIGENCE AND ROBOTICS IN PEDIATRIC SURGERY: EMERGING CHALLENGES AND OPPORTUNITIES FOR PEDIATRIC ANESTHESIOLOGY

Risteski T.

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The integration of artificial intelligence (AI) and robotic technologies into modern healthcare represents a transformative shift in surgical and perioperative medicine. Over the past decade, these innovations have evolved from experimental concepts into clinically relevant tools, significantly influencing surgical precision, workflow optimization, and patient outcomes (1,2,4,5). In pediatric surgery, where anatomical limitations, physiological variability, and strict safety requirements are central to clinical practice, the adoption of these technologies is particularly significant. Importantly, this transformation extends beyond the surgeon's domain and has profound implications for anesthesiology, redefining perioperative management and the role of the pediatric anesthesiologist (4,5,12).

The contemporary pediatric operating room is no longer solely dependent on manual expertise and clinical intuition.

It is increasingly becoming a technologically advanced environment characterized by robotic platforms, intelligent monitoring systems, and data-driven decision-making tools (4,12). Within this evolving ecosystem, anesthesiologists must not only maintain physiological stability but also interpret complex data outputs and adapt to new intraoperative dynamics. This shift requires a redefinition of traditional roles and highlights the growing importance of interdisciplinary collaboration.

The Changing Surgical Environment

Robotic-assisted surgery has become an important component of minimally invasive pediatric procedures. Systems such as the da Vinci Surgical System offer enhanced dexterity, tremor elimination, and superior three-dimensional visualization, enabling surgeons to perform highly precise interventions in confined anatomical spaces (1,8,9). These advantages are particularly beneficial in pediatric patients, where surgical margins are narrow and tissue handling must be meticulous.

However, the use of robotic systems significantly alters the intraoperative setting. The presence of robotic arms can limit direct access to the patient, complicating airway management and vascular access. Fixed positioning required for robotic procedures may contribute to physiological stress, especially in neonates and infants. Furthermore, the effects of pneumoperitoneum, including increased intra-abdominal pressure and carbon dioxide absorption, can influence respiratory mechanics and cardiovascular stability (3,14).

From an anesthesiology perspective, these factors necessitate careful preoperative planning and continuous intraoperative vigilance. Securing the airway and ensuring reliable intravenous access prior to docking the robotic system are essential steps.

Additionally, anesthesiologists must be prepared to manage rapid physiological changes in an environment where immediate physical access to the patient may be restricted (3).

Artificial Intelligence in Perioperative Care

Artificial intelligence is rapidly emerging as a powerful tool in perioperative medicine. Machine learning algorithms can analyze large volumes of clinical data to identify patterns and generate predictive models, offering new opportunities for risk assessment, decision support, and real-time monitoring (2,4,5).

In pediatric anesthesia, where patient responses to anesthesia can vary significantly, AI-driven systems hold particular promise. These technologies may assist in predicting difficult airway scenarios, optimizing anesthetic dosing, and identifying early signs of perioperative complications (7,15). The ability to anticipate and prevent adverse events represents a major advancement in patient safety.

Moreover, advanced monitoring systems integrated with artificial intelligence can enhance intraoperative management. Continuous analysis of physiological parameters may allow earlier detection of subtle changes in hemodynamic or respiratory status, enabling timely intervention (4,5,15). In the context of pediatric robotic surgery, where physical access to the patient is limited, such predictive capabilities are especially valuable.

The pediatric operating room is progressively evolving into a data-rich, interconnected ecosystem in which surgeons, anesthesiologists, and intelligent technologies function synergistically rather than independently (4,5,12). The integration of AI-driven analytics into perioperative workflows has the potential to improve patient safety, optimize resource utilization, and enhance clinical decision-making. Nevertheless, implementing AI in pediatric care poses challenges.

The limited availability of pediatric-specific datasets raises concerns regarding the accuracy and reliability of predictive models (2,15). Ensuring the transparency, validation, and clinical applicability of these systems remains essential before widespread adoption.

Synergy Between Robotics and Artificial Intelligence

The convergence of robotics and artificial intelligence represents the next stage in the evolution of surgical and anesthetic practice. Future systems are expected to incorporate real-time feedback mechanisms, allowing adaptive surgical performance and improved procedural safety (10,14).

For anesthesiologists, this integration may enable synchronized perioperative management. Communication between robotic systems and anesthetic monitoring devices could facilitate dynamic adjustments in ventilation, fluid therapy, and pharmacologic interventions. Closed-loop anesthesia systems, guided by AI, are already being explored and have demonstrated potential for maintaining stable anesthetic depth through continuous feedback (11).

In pediatric anesthesia, where precision and stability are critical, artificial intelligence may become an essential component of perioperative care. Artificial intelligence may evolve from a supportive technology into a fundamental element of individualized perioperative management, particularly in high-risk patients and complex surgical procedures (4,5,11).

Ethical and Practical Considerations

Despite their potential, AI and robotic technologies introduce important ethical and practical considerations. Data privacy and security are fundamental concerns, particularly in pediatric populations. Ensuring responsible data management and compliance with ethical standards is essential.

Algorithmic bias is another critical issue. AI systems trained on incomplete or unrepresentative datasets may generate inaccurate predictions, potentially affecting patient safety. This concern is particularly relevant in pediatrics, where data availability is limited (13). Furthermore, the increasing use of semi-autonomous technologies raises questions regarding accountability, transparency, and clinical oversight (13,14).

Additionally, the high cost of robotic systems and AI infrastructure may restrict accessibility, contributing to disparities in healthcare delivery. Training requirements also pose a significant challenge, as anesthesiologists must acquire new competencies in technology use, data interpretation, and interdisciplinary collaboration.

The Role of the Pediatric Anesthesiologist

The role of the pediatric anesthesiologist is evolving in response to these technological advancements. In addition to traditional responsibilities, anesthesiologists are increasingly involved in data-driven perioperative planning, intraoperative management in complex technological environments, and postoperative care supported by predictive analytics (4,5,12).

Collaboration with surgeons, engineers, and data scientists is becoming essential. At the same time, anesthesiologists must maintain their role as patient advocates, ensuring that technological innovations are applied safely and ethically. In pediatric anesthesia, where physiological reserve is limited and dosing precision is critical, artificial intelligence may be not merely supportive, but essential (4,5,15).

Future Directions

The future of pediatric surgery and anesthesiology lies in the integration of human expertise with technological innovation.

Further research is required to validate AI models in pediatric populations and to assess the long-term safety and efficacy of robotic-assisted procedures (2,9,15).

The challenge ahead is not whether artificial intelligence and robotics will be incorporated into pediatric perioperative care, but whether clinicians will guide their implementation responsibly,

ethically, and collaboratively (5,13,14). Education and training programs must adapt to prepare clinicians for this evolving landscape.

Conclusion

Artificial intelligence and robotics are redefining pediatric surgical care, offering new opportunities for precision and improved outcomes. For anesthesiology, these advancements present both challenges and opportunities. By embracing innovation while maintaining a strong commitment to patient safety and clinical judgment, pediatric anesthesiologists can play a central role in shaping the future of perioperative medicine.

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ORIGINAL ARTICLE *UDK: 615.273.53:616.12-089]:616.61-008.64*

www.doi.org/ 10.67214/g94vzw89

EFFECTS OF TWO TRANEXAMIC ACID DOSES ON CARDIAC SURGERY-ASSOCIATED ACUTE KIDNEY INJURY IN NON-ANAEMIC PATIENTS UNDERGOING ON-PUMP CARDIAC SURGERY

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Abstract

Objective: Cardiac surgery-associated acute kidney injury is a frequent and clinically significant complication, while the potential impact of tranexamic acid dosing on postoperative renal function remains uncertain. The study aims to compare the incidence of Cardiac surgery-associated acute kidney injury (CSA-AKI) and the stages of AKI between two different doses of Tranexamic acid (TXA) in non-anemic patients undergoing on-pump cardiac surgery; to determine whether the TXA dose is independently associated with CSA-AKI; and to identify predictors of postoperative renal function change and to compare short term renal outcomes in patients with and without CSA-AKI.

Materials and Methods: Prospective, randomized study that evaluated the renal safety of low-dose (20 mg/kg) and high-dose (50 mg/kg) TXA in 120 non-anemic patients undergoing on-pump cardiac surgery. Monitored variables were baseline serum creatinine, peak serum creatinine, discharge serum creatinine, creatinine ratio, 24-hour bleeding, and the incidence of transfusion.

Results: CSA-AKI occurred in 25% of patients in the low-dose TXA group, and 20% in the high-dose TXA group. Among patients who developed CSA-AKI, AKI stage 1 was the most common severity stage, 66.7% and 75% respectively. The TXA dose was not independently associated with CSA-AKI (OR 1.666, 95% CI 0.599–4.634, p=0.328). Transfusion was an independent predictor associated with higher peak-to-baseline serum creatinine ratio ($\beta = 0.191$, 95% CI 0.061–0.322, p=0.004). Patients who developed CSA-AKI had lower estimated glomerular filtration rate (eGFR) at discharge compared to patients without CSA-AKI (48 (40–59) vs 83 (68.5–107.5) mL/min/1.73 m^2; Mann–Whitney U test, $Z = -5.97$, $p < 0.001$).

Conclusion: Within the studied dosing range, the tranexamic acid dose was not independently associated with renal outcomes, suggesting that dosing decisions may prioritize bleeding and transfusion risk rather than renal safety concerns.

Keywords: *Acute kidney injury; Cardiac surgery; Cardiac surgery-associated acute kidney injury; Tranexamic acid.*

Introduction

Acute kidney injury (AKI) after cardiac surgery is ubiquitous. It occurs in a substantial proportion of patients depending on the differences in definitions and patient populations, where the incidence ranges from approximately 5% to over 40% (1), based on standardized criteria such as the Kidney Disease: Improving Global Outcomes (KDIGO) classification. It is a major factor for postoperative morbidity and mortality. Cardiac surgery-associated acute kidney injury (CSA-AKI) is defined as AKI occurs in the perioperative period after cardiac surgery, usually 48 to 72 hours after cardiac surgery, and it can be transient. The more severe forms of AKI according to the KDIGO classification (2) that may require renal replacement therapy (RRT) are less common, ranging from 1% to 4%; however they do carry a particularly high risk of postoperative morbidity and mortality. The development of CSA-AKI has profound implications for patient outcomes. AKI is independently associated with prolonged intensive care and hospital stay, increased incidence of RRT and higher short and long-term mortality in comparison with patients without AKI. Severe AKI substantially increases the perioperative mortality rates that can range from 20% to 60%, and indicates poorer long-term survival, worsening the preoperative kidney function, which may progress to chronic kidney disease (3).

The pathophysiology of CSA-AKI is multifactorial because of the unique conditions that arise during the perioperative cardiac surgery period, including surgical stress and cardiopulmonary bypass (CPB), which is associated with the hemodynamic and inflammatory response of the patient. Central mechanisms are renal hypoperfusion, ischemia and reperfusion exacerbated by inflammatory response, hemolysis, oxidative stress, endothelial disfunction and micro embolic events (4). At baseline, these insults compromise normal glomerular function and tubular integrity, resulting in declines in renal function and in fluid and electrolyte homeostasis. Tranexamic acid, a synthetic lysine analogue, is widely used in cardiac surgery to reduce perioperative bleeding and transfusion requirements by inhibiting fibrinolysis through blockade of plasminogen activation and suppression of plasmin activity. By stabilizing fibrin clot formation, TXA effectively reduces blood loss and allogeneic blood transfusion. Although higher doses may provide greater antifibrinolytic efficacy, they could also theoretically compromise renal safety. Excessive inhibition of fibrinolysis may promote a hypercoagulable state within the renal microcirculation, impairing fibrin degradation, leading to capillary thrombosis and microvascular obstruction. In addition to its role in fibrinolysis, plasmin participates in key inflammatory pathways and contributes to the maintenance of endothelial homeostasis. Its suppression may therefore alter the balance of inflammatory mediators and exacerbate acute kidney injury (5). Whether the enhanced hemostatic benefits of higher-dose TXA can be achieved without increasing the risk of postoperative acute kidney injury remains an important clinical question. The aim of the study was to compare the incidence of CSA-AKI and the stages of AKI between the studied doses of TXA in non-anemic patients undergoing on-pump cardiac surgery; to determine whether the TXA dose is independently associated with the incidence of CSA-AKI; to identify independent predictors of postoperative renal function change and to compare short term renal outcomes in the patients with and without CSA-AKI.

Materials and Methods

Type of study: This was a prospective, randomized, controlled study conducted at the department of Cardiac Surgery at Acibadem Sistina Hospital Skopje, between May 2024 and May 2025.

The study protocol was approved by the institutional ethics committee and written informed consent was obtained from all of the participants before their enrollment.

Study Population: Adult non-anemic patients scheduled for elective or urgent isolated Aorto-coronary bypass surgery (CABG), aortic valve surgery and combined CABG, and aortic valve surgery requiring cardiopulmonary bypass (CPB) were eligible for inclusion. Anemia was defined according to the World Health Organization (WHO) criteria (6) as Hemoglobin concentration <130g/L in men and < 120g/L in women.

Exclusion criteria: Patients aged less than 18 years; known hypersensitivity or allergy to tranexamic acid; pregnancy; preoperative anemia; chronic kidney disease stage 4 and 5; planned surgery involving the Aorta or Mitral valve; Re-Do cardiac surgical procedures; off-pump cardiac surgery; treatment with vitamin K antagonists within 5 days before surgery or an International normalized ratio (INR) >1,5; treatment with direct oral anticoagulants 2 days before surgery; treatment with oral P2Y12 inhibitors without the recommended discontinuation period before surgery (Ticagrelor ≤2 days, Clopidogrel ≤4 days or Prasugrel ≤6 days); history of seizure disorder or current anticonvulsant therapy.

Randomization and Study Intervention: On the day of hospital admission, patients were randomly assigned in a 1:1 ratio to one of the two study groups using a computer-generated sequence of random numbers. Allocation concealment was ensured using sealed, opaque envelopes. Patients were assigned to receive either:

- Low-dose Tranexamic acid group (n=60): 20 mg/kg intravenous tranexamic acid or
- High-dose Tranexamic acid group (n=60): 50 mg/kg intravenous tranexamic acid.
- Tranexamic acid was administered as a single prophylactic intravenous dose 45 minutes before skin incision.

No additional doses were administered intraoperatively or during the first 24 postoperative hours. The selected dosing regimens were based on the recommendations of the International Society for Minimally Invasive Cardiothoracic Surgery (7), the Enhanced Recovery After Surgery Society (ERAS) perioperative guidelines for cardiac surgery (8), and published meta-analytic data regarding optimal tranexamic acid dosing in cardiac surgery by Zufferey et al. (9).

Perioperative Management: All patients underwent standardized perioperative care in line with institutional protocols, including anesthesia, cardiopulmonary bypass management, surgical techniques, and postoperative intensive care. Management was delivered by a multidisciplinary heart team.

Data Collection and Outcome Definitions: The following variables were collected for all participants: baseline serum creatinine, peak postoperative serum creatinine, serum creatinine level at hospital discharge, creatinine ratio (defined as peak serum creatinine divided by baseline serum creatinine), estimated Glomerular filtration rate (eGFR), incidence and stage of CSA-AKI, 24-hour bleeding (defined as thoracic drain output for 24 hours after surgery) and incidence of transfusion during hospitalization. CSA-AKI was defined according to the KDIGO criteria as an increase in serum creatinine to at least 1.5 times the baseline value or an absolute increase of ≥26.5 μmol/L during the postoperative period (2). The severity of CSA-AKI was classified according to KDIGO staging criteria (2). Stage 1: increase in serum creatinine to 1.5–1.9 times baseline or an absolute increase of ≥26.5 μmol/L; Stage 2: increase in serum creatinine to 2.0–2.9

times baseline; Stage 3: increase in serum creatinine to ≥3.0 times baseline, an absolute serum creatinine concentration ≥353.6 μmol/L or initiation of renal replacement therapy. Creatinine clearance was calculated using the Cockcroft–Gault equation and was used to estimate preoperative peak and eGFR discharge. Calculations were performed using the MDCalc online calculator (10). Short-term renal outcomes were assessed by comparing baseline eGFR and hospital discharge eGFR between patients with and without CSA-AKI.

Statistical Analysis: Continuous variables are presented as mean ± standard deviation (SD) for normally distributed data and as median (interquartile range (IQR)) for non-normally distributed data. Categorical variables are expressed as absolute counts and percentages. Baseline characteristics between the two randomized groups were compared using one-way analysis of variance (ANOVA) for normally distributed continuous variables and the Mann–Whitney U test for non-normally distributed variables. Categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate. The primary outcome, the incidence of CSA-AKI, is presented as the number and percentage of affected patients in each study group. The association between tranexamic acid dose and the occurrence of CSA-AKI was evaluated using multivariable logistic regression analysis and is reported as odds ratios (ORs) with 95% confidence intervals (CIs).

To identify independent predictors of postoperative renal function, postoperative creatinine change was analyzed using a generalized linear model with gamma distribution and log-link function. The dependent variable was the creatinine ratio, defined as peak postoperative serum creatinine divided by baseline serum creatinine. All statistical analyses were performed using IBM SPSS Statistics version 26. A p value <0.05 was considered statistically significant.

Results

In this study 120 non-anemic patients undergoing on-pump cardiac surgery were enrolled and randomized in two TXA groups. The anthropometric measurements and medical history are shown in Table 1.

Table 1. Preoperative data, low-dose TXA (20mg/kg) and high-dose TXA (50mg/kg)

	low-dose TXA (n=60)	**high-dose TXA (n=60)**	**p value**
Gender (male)	32 (53,3%)	39 (65%)	0.194
Weight (kg)	80,54±16,18	82,59±16,85	0.498
Height (m)	1,66±0,98	1,69±0,87	0.118
Age (year)	66 (62-73)	66,5 (62,2-73,7)	0.735
Hypertension	57 (95%)	60 (100%)	0.244
Diabetes Mellitus	21 (35%)	23 (38,3%)	0.705
Peripheral artery disease	10 (16,7%)	13 (21,7%)	0.487
ASA			0.810

	low-dose TXA (n=60)	high-dose TXA (n=60)	p value
2	10 (16,7%)	11 (18,3%)	
3	49 (81,7%)	47 (79,5%)	
4	1 (1,6%)	2 (2,2%)	
STS risk score	1,11 (0,73-1,72)	1,06 (0,54-2)	0.562
Hemoglobin (g/L)	140 (133-149)	141 (133-154)	0.544
Serum Creatinine (μmol/l)	75 (66-97)	83 (69-94,75)	0.337
eGFR ml/min/1,73²	69 (52,25-88,5)	72,5 (58,25-93)	0.553
ACE inhibitors	45 (75%)	45 (75%)	1
Diuretics	23 (38,3%)	27 (45%)	0.459

There were no statistical differences between the randomized groups. In both groups, the male gender was predominant with 53,3% vs 65%. The studied patients were at similar age and with similar comorbidities. The preoperative hemoglobin level was similar between the groups, p=0.544 for comparison. The high-dose TXA group had higher preoperative serum creatinine and preoperative eGFR levels, though statistically insignificant, in comparison to the low-dose TXA group, p=0.337 and p=0.553. There was no significant statistical difference in the preoperative therapy in the two study groups.

Elective surgical procedures predominated in both study groups (88,3% vs 93,3%, p=0.529). Coronary bypass surgery was the most common procedure in both study groups, 61,7% in the low-dose and 51,6% in the high-dose TXA group. In the low-dose TXA group, the aortic cross-clamp time was insignificantly shorter, 46 min, than in the high-dose TXA group, 50 minutes, p=0.226.

There was no statistical difference in the catecholamine support across the studied groups, 71,7% and 75% respectively. There were no significant statistical differences in the postoperative data across the studied groups. The volume of 24-hour bleeding between the groups was 355ml and 340ml, low- and high-dose groups respectively (p=0.944). There was borderline significance in the incidence of transfusion across the low-dose and high-dose TXA groups (p=0.060), as shown in Table 2.

Table 2. Intra and postoperative data, low-dose TXA (20mg/kg) and high-dose TXA (50mg/kg)

	low-dose TXA (n=60)	high-dose TXA (n=60)	p value
Status of procedure			0.529
Elective	53 (88,3%)	56 (93,3%)	
Urgent	7 (11,7%)	4 (6,7%)	
Procedure type			0.269

	low-dose TXA (n=60)	high-dose TXA (n=60)	p value
Aortocoronary bypass	37 (61,7%)	31 (51,6%)	
Open chamber surgery	23 (38,3%)	29 (48,4%)	
Aortic cross-clamp time (min)	46 (31-60,75)	50 (39,25-64,75)	0.226
Catecholamine support	43 (71,7%)	45 (75%)	0.679
Peak Serum Creatinine (μmol/l)	81 (59,75-112,5)	79 (67-103,5)	0.753
Acute Kidney Injury	15 (25%)	12 (20%)	0.512
24-hour bleeding (ml)	355 (292,5-447,5)	340 (270-475)	0.944
Transfusion	42 (70%)	32 (53%)	0.060
Discharge Serum Creatinine (μmol/l)	75 (57-97,75)	76 (65,25-95,25)	0.378
Discharge eGFR ml/min/1,73²	72,5 (53,25-98,5)	76 (58,25-99,5)	0.444

There was similar renal safety for both dosing groups of TXA. No significant statistical difference between the incidence of CSA-AKI was observed between the studied groups, (p=0.512), although the incidence was higher in the low-dose than the high dose TXA group, (25% vs 20%), as shown in Figure 1.

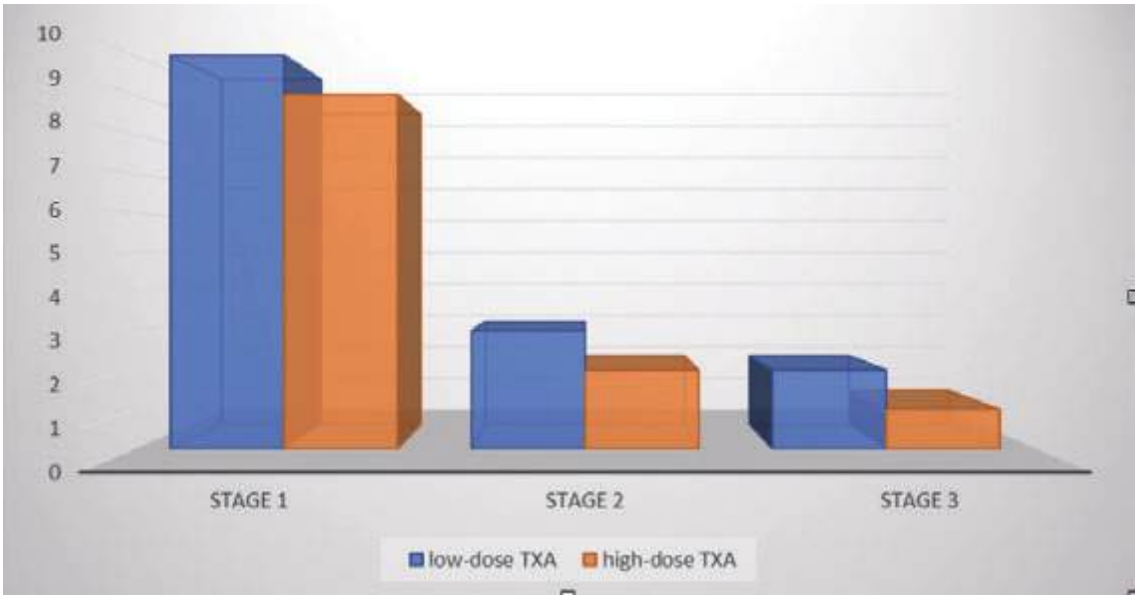

Figure 1. Graphical presentation of the incidence of CSA-AKI across the studied groups

As shown in Figure 2, Acute Kidney Injury Stage 1 was the most frequently observed category of CSA-AKI in both study groups, occurring in 10 patients in the low-dose group and in 9 patients in the high-dose Tranexamic acid group. There was no statistically significant difference in the distribution of CSA-AKI stages between the two groups (p = 0.877). Renal replacement therapy was required in only one patient in the low-dose tranexamic acid group.

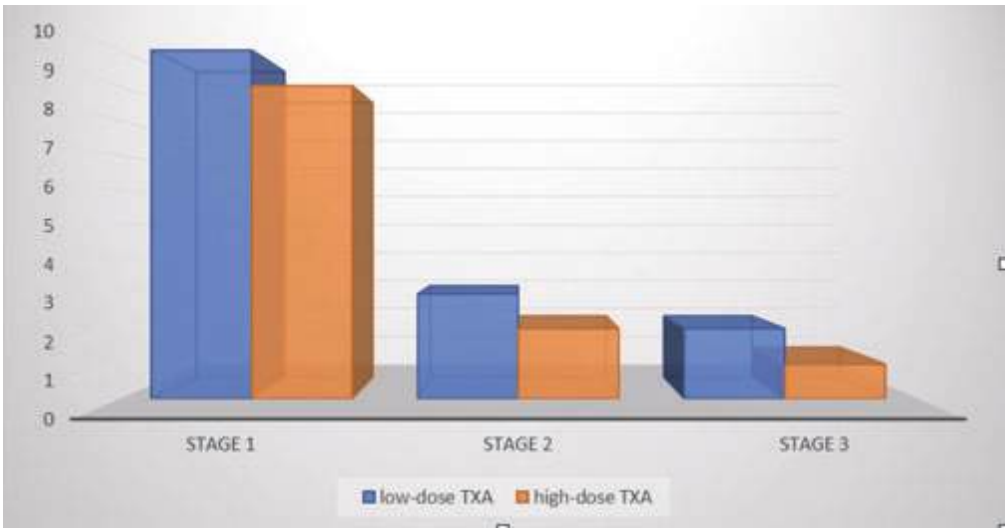

Figure 2. Graphical presentation of stages of CSA-AKI across the studied groups

In a multivariate logistic regression analysis, after adjustment for age, baseline serum creatinine, type of cardiac surgery, aortic cross-clamp time and transfusion incidence there was no independent association between the dose of TXA and the incidence of CSA-AKI (OR 1.666, 95% CI 0.599–4.634, p=0.328). Also, a Gamma log-link generalized linear model was used with creatinine ratio (peak creatinine divided by baseline creatinine) as a dependent variable to estimate the subtle changes of the two doses of TXA on postoperative serum creatinine change. After adjusting for BMI, type of surgical procedure, aortic cross-clamp time and incidence of transfusion, the studied doses of TXA were not independently associated with postoperative creatinine change (β = -0.015, 95% CI 0.137-0.108, p = 0.813). However, the incidence of transfusion was an independent predictor associated with increased postoperative serum creatinine change (β = 0.191, 95% CI 0.061–0.322, p =0.004). Patients with CSA-AKI had a significantly lower eGFR at discharge compared to the patients without CSA-AKI (48 (40-59) vs 83 (68,5-107,5) ml/min/1,73^2; Mann-Whitney U test, Z=-5,97, p<0,001), with a large effect size (r=0,55), shown in Figure 3.

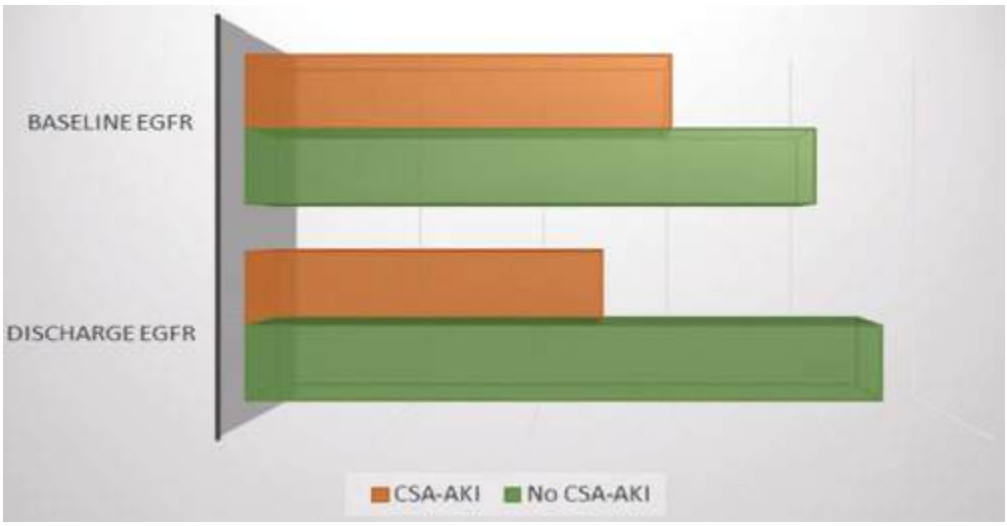

Figure 3. Graphical presentation of baseline eGFR and discharge eGFR across the patients with CSA-AKI and without CSA-AKI

Discussion

This randomized prospective study evaluated the effects of different prophylactic doses of TXA on the incidence and severity of CSA-AKI in non-anemic patients undergoing on-pump cardiac surgery and identified predictors of postoperative renal function changes and short-term renal outcomes.

The findings suggest that there was no statistically significant difference in the incidence of CSA-AKI and the severity of AKI between the low-dose and high-dose TXA groups. The incidence of CSA-AKI was slightly higher in the low-dose than in the high-dose TXA group, (25% vs 20%). Although the incidence was statistically insignificant, it does suggest that the studied higher dose of TXA does not produce additional nephrotoxic burden in the perioperative cardiac surgical setting. Multivariate logistic regression analysis further confirmed the absence of independent association between the TXA dose and the incidence of CSA-AKI (OR 1.666, 95% CI 0.599–4.634, p=0.328), indicating the renal safety of TXA and a possibility that other perioperative factors have a more substantial role in the development of CSA-AKI. These findings align with the findings from the ATACAS trail (11) where TXA significantly reduced perioperative bleeding without increasing the risk of AKI in comparison to placebo in a large randomized trial of patients undergoing coronary bypass surgery. Meta-analyses by Henry et al. (12) and Zhang et al. (13) evaluating antifibrinolytic use in cardiac surgery have also shown no consistent increase in renal complication that can be attributed to TXA. The results of our study simply extend these observations by specifically comparing different doses of TXA and suggest that dose escalation within clinically acceptable ranges does not produce higher renal risk. The lack of dose-response relationship in our study is a strong point against clinically relevant renal burden in the studied dosing range.

Stage 1 AKI was the most common severity category, occurring in 10 patients in the low-dose TXA group and 9 patients in the high-dose TXA group. Stage 2 AKI was observed in 3 and 2 patients, respectively, while Stage 3 AKI occurred in 2 and 1 patients, respectively. Only 1 patient required renal replacement therapy in the low-dose TXA group. This distribution is consistent with the studies from Hobson et al. (14) and Rosner et al. (15), where mild AKI severity cases dominate, while more severe AKI cases occur less frequently but have substantial risk of morbidity and mortality. These findings further imply that higher TXA dosing group does not influence the CSA-AKI incidence, but also does not influence the clinical progression of AKI severity.

To assess whether TXA dosing exerted an independent effect on subtle postoperative renal dysfunction not captured by KDIGO-defined AKI (2), renal function was analyzed using a gamma log-link generalized linear model, with creatinine ratio (peak serum creatinine divided by baseline serum creatinine) being the dependent variable. There was no statistically significant association between the TXA dosing group and the creatinine ratio (β =-0.015, 95% CI 0.137-0.108, p=0.813), supporting the renal safety of the investigated TXA doses.

These results are consistent with the findings of Myles et al. (11) that demonstrate no excess risk of renal injury related to the administration of tranexamic acid in cardiac surgery patients. High-dose TXA was associated with a non-significant 1.5% reduction in the creatinine ratio, suggesting a potential but unproven renal protective effect. In contrast, perioperative blood transfusion emerged as an independent predictor of increased creatinine ratio (β=0.191, 95% CI 0.061–0.322, p=0.004), corresponding to an approximately 21% higher peak-to-baseline creati-

nine ratio in transfused patients compared with non-transfused patients. This finding is consistent with prior evidence by Rosner et al. (15) linking red blood cell transfusion to an increased risk of postoperative acute kidney injury and adverse renal outcomes in cardiac surgery.

Importantly, the patients who developed CSA-AKI had significantly lower discharge eGFR compared with patients without AKI, (Mann-Whitney U test, Z=-5,97, p<0,001).

This finding highlights the clinical relevance that even predominantly mild CSA-AKI has impact on renal recovery and long-term renal function, supporting evidence that postoperative AKI is associated with persistent renal dysfunction, increased risk of chronic kidney disease and adverse long-term outcomes (16). Thus, while TXA dosing appears not to influence renal risk, prevention of CSA-AKI remains a critical perioperative objective.

Several limitations should be considered. The sample size may limit detection of rare outcomes such as severe CSA-AKI and RRT. Renal function was assessed using serum creatinine measurements, which may not fully capture early and subclinical kidney injury. The findings apply to the studied dosing groups of TXA and cannot be generalized to the extremely high dosing regimens.

Conclusion

Tranexamic acid is widely used to reduce bleeding and transfusion requirements, and clinicians often balance hemostatic efficacy against potential adverse effects, including renal complications. Our results suggest that within the studied dosing range, TXA dose selection may be guided primarily by bleeding and transfusion risk factors rather than concerns about differential renal toxicity. Furthermore, the strong association between CSA-AKI and reduced discharge renal function emphasizes the need for continued focus on established renal protective strategies.

The absence of TXA dose–related renal burden supports its continued use as part of a comprehensive blood conservation protocol in cardiac surgery.

Declarations

Ethics approval and consent to participate: The study was approved by the institutional ethics committee of Acibadem Sistina Hospital, prior to patient enrollment, Approval reference: 02-15663/02, Date of approval: 04/12/2023, Chair of the Ethical Committee: Prof. Andrej Petrov, MD, PhD. All participants received detailed information regarding the study objectives and procedures, and provided written informed consent prior to inclusion.

Informed consent: Written informed consent was obtained from all participants included in the study.

*1*The authors declare no conflict of interest.

Funding: This research received no external funding.

Availability of data and materials: Data are available from the corresponding author upon reasonable request.

Author's contributions: Conceptualization R.A.; methodology, R.A. and S.M.; investigation, R.A., K.J.B., N.A., S.J., S.D.; data curation, R.A. and K.J.B.; writing – original draft, R.A. and S.M.; writing – review and editing, S.M. and K.J.B.; project administration N.A. All authors have read and agreed to the published version of the manuscript.

Acknowledgements: The authors would like to thank all employees at the Department of Cardiac Surgery who participated in this study.

Artificial Intelligence (AI) statement: No AI tools were used in the preparation of this manuscript.

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ORIGINAL ARTICLE *UDK: 616.711-089.168-009.7-085.212*

www.doi.org/10.67214/y2vqzw55

PERIOPERATIVE ANALGESIC EFFICACY OF THE ERECTOR SPINAE PLANE BLOCK WITHIN A MULTIMODAL ANESTHESIA PROTOCOL FOR OPEN THORACOLUMBAR SPINAL FIXATION SURGERY

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Abstract

Objective: Open thoracolumbar spinal fixation is associated with severe intraoperative and postoperative pain. Opioids are frequently used for perioperative analgesia in these procedures, but their use is associated with adverse effects, such as postoperative nausea and vomiting, sedation, pruritus, urinary retention, respiratory depression, and delayed recovery. Ultrasound-guided regional techniques, incorporated within a multimodal analgesic strategy, may improve perioperative pain control and reduce opioid requirements.

Materials and Methods: This randomized prospective interventional clinical study evaluated the perioperative analgesic effect of bilateral erector spinae plane block (ESPB) as part of multimodal anesthesia compared with opioid-based analgesia in patients undergoing open fixation for thoracic or lumbar vertebral fractures. Seventy patients were randomized into two groups: an opioid group (OG; n=35) and an ESPB with multimodal analgesia group (ESPB+MMA; n=35). Outcomes included intraoperative fentanyl consumption, postoperative tramadol requirements, postoperative Numerical Rating Scale (NRS) pain scores, postoperative nausea and vomiting (PONV), and neurological or psychotomimetic adverse effects.

Results: Patients in the ESPB+MMA group required only induction-dose fentanyl, whereas patients in the OG required 500-1200 mcg of fentanyl intraoperatively. Postoperative tramadol was required in only 4 patients (11.4%) in the ESPB+MMA group, compared with all patients in the OG, where total postoperative tramadol consumption ranged from 100 to 1500 mg. Postoperative pain scores were consistently lower in the ESPB+MMA group during the first 48 hours after surgery. PONV occurred in 14.3% of patients in the ESPB+MMA group and 31.4% of patients in the OG. No ESPB-related complications were recorded.

Conclusion: The combination of ESPB and multimodal analgesia provided effective perioperative analgesia, markedly reduced opioid consumption, lowered the incidence of PONV, and appeared safe in patients undergoing open thoracolumbar spinal fixation.

Keywords: *erector spinae plane block; multimodal analgesia; spine surgery; thoracolumbar fixation; postoperative pain.*

Introduction

Complex spinal procedures, including open spinal fixation, are associated with severe intraoperative and postoperative pain (1,2). Inadequately controlled postoperative pain may delay mobilization, increase the risk of venous thromboembolism, contribute to respiratory and cardiovascular complications, prolong recovery and hospital stay, and reduce patient satisfaction (2,3).

Insufficient treatment of acute postoperative pain is also an important risk factor for the development of chronic postoperative pain, which represents a major long-term burden for patients and healthcare systems (4,5). Opioids remain widely used for pain management in complex spine surgery; however, they are associated with numerous adverse effects, including somnolence, dizziness, postoperative nausea and vomiting, pruritus, urinary retention, respiratory depression, impaired wound healing, wound dehiscence, and short-term central muscle rigidity (4,6). Opioid-related adverse effects may impede enhanced postoperative recovery and prolong hospital stay (7,8).

Potent opioids may also lead to acute tolerance and opioid-induced hyperalgesia, which can paradoxically increase postoperative pain. Hyperalgesia is characterized by an exaggerated response to painful stimuli following opioid exposure and reflects nociceptive hypersensitization (9,10).

Multimodal analgesia combines drugs that act through different mechanisms within the nociceptive system, producing synergistic analgesic effects while reducing the required dose of each individual medication. Agents used in multimodal analgesia include ketamine, paracetamol, lidocaine, magnesium sulfate, dexamethasone and metamizole (11-14). Regional anesthetic techniques, including peripheral nerve and fascial plane blocks, are an important component of multimodal analgesia. Multiple randomized trials, systematic reviews and meta-analyses have shown that ESPB in spine surgery can reduce intraoperative and postoperative opioid consumption, lower postoperative pain scores, decrease PONV and improve patient satisfaction (15-18).

Objectives

The primary objective of this study was to evaluate the effect of ESPB as part of multimodal analgesia, compared with opioid-based anesthesia, on intraoperative and postoperative analgesia in patients undergoing open thoracolumbar spinal fixation.

Secondary objectives were to compare total intraoperative and postoperative opioid consumption, assess postoperative adverse effects including dizziness, diplopia, nystagmus, hallucinations and nightmares, and determine the incidence of PONV in both groups.

Materials and Methods

This was a randomized, prospective, interventional clinical study that included 70 patients scheduled for open thoracic or lumbar spinal fixation. Patients were randomized into two par-

allel groups of 35 patients each.

Eligibility Criteria

Inclusion criteria included hospitalization for open fixation of the thoracic or lumbar spine at two, three or four levels; age between18 and 65; and American Society of Anesthesiologists (ASA) physical status I-III.

Exclusion criteria were based on ASA physical status IV-V; allergy to fentanyl, tramadol, lidocaine, bupivacaine, magnesium sulfate, ketamine, paracetamol or metamizole; chronic use of benzodiazepines or opioids; pregnancy or breastfeeding; chronic pain; cardiac, renal or hepatic insufficiency; and psychiatric disease.

Randomization and Perioperative Protocol

During the preoperative visit, all patients were instructed on the use of the Numerical Rating Scale (NRS) for pain, where 0 indicates no pain and 10 indicates unbearable pain. Randomization was performed using a computer-generated allocation sequence. All patients received standard perioperative monitoring, treatment and care.

General anesthesia was induced according to a standardized protocol using midazolam 0.04 mg/kg for premedication, fentanyl 0.002 mg/kg, propofol 1-2 mg/kg and rocuronium 0.6 mg/kg. Anesthesia was maintained with balanced anesthesia using sevoflurane at approximately 1 MAC, aiming to keep mean arterial pressure within +/-20% of baseline.

Erector Spinae Plane Block

The erector spinae block (ESB) is a relatively simple and safe regional anesthetic technique widely used for perioperative analgesia in various surgical procedures.

Usually, a parasagittal approach is used for the Erector Spine Block, in which the ultrasound probe is placed parallel to the spine, 4-5 centimeters from the spinous processes of the vertebrae. At the lumbar level, a curved probe is typically used, whereas at the thoracic level, either a linear or curved probe may be used.

It is necessary to visualize the tips of the transfer processes. The ultrasound probe may also be positioned transversely over the spinous processes. After identifying the spinal processes, the probe is moved laterally by approximately 3-5 cm, in which the lamina and transverse processes are visualized.

After appropriate ultrasound-guided visualization of the transfer processes, most often in a cranio-caudal direction, or vice versa, a 10-centimeter hyperechoic needle is placed with the aim of touching the tip of the process. Then the needle is withdrawn a few millimeters, after which, following negative aspiration, the local anesthetic is injected and its craniocaudal spread is observed. (27)

Based on clinical studies performed on cadavers, as well as radiological examinations, the mech-1anism of the block's action has been assessed. The effect of the block is made possible through the spread of the local anesthetic, and its diffusion to the ventral and dorsal branches of the spinal nerves. The spinal nerves are in the anatomical space between the sheath of the erector

spinae muscle and the surrounding tissue compartments (27-28).

Study Groups

Patients in the opioid group (OG; n=35) received intermittent fentanyl for intraoperative analgesia.

Patients in the ESPB with multimodal analgesia group (ESPB+MMA; n=35) received bilateral ultrasound-guided ESPB after prone positioning and radiographic marking. The block was performed with 10 ml lidocaine 1% and 20 ml bupivacaine 0.25% on each side. Before induction, patients received dexamethasone 0.1 mg/kg and paracetamol 1 g. Immediately after intubation, ketamine 0.5 mg/kg was administered intravenously, followed by continuous intravenous magnesium sulfate 1.5 g. If blood pressure or heart rate increased by more than 30% from baseline during surgery in the absence of bleeding, fentanyl 50 mcg was administered.

Postoperative Management and Follow-up

Patients in the OG received metamizole 2 g every 12 hours and paracetamol 1 g every 8 hours for postoperative analgesia. Patients in the ESPB+MMA group received ketamine 0.1 mg/kg/hour as a continuous intravenous infusion for 48 hours, metamizole 2 g every 12 hours, paracetamol 1 g every 8 hours, and dexamethasone 8 mg daily for 3 days, followed by 4 mg daily for an additional 3 days. Postoperative pain was assessed using the NRS at 1, 4, 8, 12, 24, 36 and 48 hours after surgery. Tramadol 100 mg was administered as rescue analgesia when the NRS score exceeded 7. The following outcomes were monitored by the nurses from the Post Anesthesia Care Unit and the Traumatology Department, who did not know which patient belongs to which group. The following parameters were measured and recorded: pain at rest using NRS, total intraoperative and postoperative opioid consumption, PONV, and the postoperative occurrence of nystagmus, dizziness, diplopia, illusions and hallucinations.

Results

The study included 70 patients with thoracic or lumbar vertebral fractures scheduled for open spinal fixation. Patients were divided into the OG (n=35) and ESPB+MMA group (n=35). In the ESPB+MMA group, 23 patients (65.7%) were men and 12 (34.3%) were women; mean age was 51.2+/-11.7 years, and mean BMI was 28.4+/-2.8 kg/m2.

In the OG, 25 patients (71.4%) were men and 10 (28.6%) were women; mean age was 44.6+/-10.5 years, and mean BMI was 27.0+/-2.0 kg/m2. Mean duration of surgery was 182.6+/-23.8 minutes in the ESPB+MMA group and 192.9+/-42.6 minutes in the OG; the difference was not statistically significant ($p>0.05$).

Intraoperative Fentanyl Consumption

All patients in the ESPB+MMA group received only the induction dose of fentanyl and required no additional intraoperative fentanyl. In the OG, total intraoperative fentanyl consumption ranged from 500 to 1200 mcg (Table 1).

Table 1. Total intraoperative fentanyl consumption in the opioid group

Fentanyl dose (mcg)	Number of patients	%
500	1	2.9
700	2	5.7
800	7	20.0
900	9	25.7
1000	12	34.3
1100	2	5.7
1200	2	5.7

Level of Fixation

The most frequent level of fixation was L1 in both groups, followed by L2 and Th12 (Table 2)

Table 2. Level of fixation by study group

Level of fixation	ESPB+MMA n	ESPB+MMA %	OG n	OG %
L1	16	45.7	12	34.3
Th11	3	8.6	1	2.8
L2	8	22.9	11	31.4
Th12	7	20.0	5	14.3
L4	1	2.8	4	11.4
Th8	0	0.0	1	2.8

Postoperative Tramadol Consumption

In the ESPB+MMA group, postoperative tramadol was administered to 4 patients (11.4%): 3 patients received 100 mg and 1 patient received 200 mg. In the OG, all patients required postoperative tramadol, with total doses ranging from 100 to 1500 mg. The most common postoperative tramadol doses in the OG were 400 mg and 500 mg, each administered to 8 patients (22.9%) (Table 3).

Table 3. Total postoperative tramadol consumption

Tramadol dose (mg)	ESPB+MMA n	ESPB+MMA %	OG n	OG %
100	3	75.0	3	8.6
200	1	25.0	0	0.0
300	0	0.0	4	11.4
400	0	0.0	8	22.9
500	0	0.0	8	22.9

Tramadol dose (mg)	ESPB+MMA n	ESPB+MMA %	OG n	OG %
600	0	0.0	1	2.9
700	0	0.0	3	8.6
900	0	0.0	2	5.7
1000	0	0.0	1	2.9
1100	0	0.0	1	2.9
1200	0	0.0	2	5.7
1300	0	0.0	1	2.9
1500	0	0.0	1	2.9

Postoperative Pain Scores

Postoperative pain at rest was assessed using the NRS at 1, 4, 8, 12, 24, 36 and 48 hours after surgery. In the ESPB+MMA group, NRS scores ranged from 0 to 8, with an NRS score of 8 recorded in only one patient at 12 hours. An NRS score of 7 was recorded in four patients: one at 1 hour, two at 8 hours and one at 12 hours. In the OG, NRS scores ranged from 3 to 9. NRS 7 was recorded in 45.7% of patients at 1 hour, 57.1% at 4 hours, 60.0% at 8 hours, 22.9% at 12 hours and 14.3% at 24 hours. NRS 8 was recorded in 17.1% at 1 hour, 34.3% at 4 hours, 28.6% at 8 hours and 11.4% at 12 hours (Tables 4a and 4b).

Table 4a. Postoperative NRS pain scores in the ESPB+MMA group

NRS score	1 h n (%)	4 h n (%)	8 h n (%)	12 h n (%)	24 h n (%)	36 h n (%)	48 h n (%)
0	6 (17.1)	1 (2.9)	2 (5.7)	1 (2.9)	1 (2.9)		
1	1 (2.9)	4 (11.4)	1 (2.9)	1 (2.9)	3 (8.6)	6 (17.1)	8 (22.9)
2	4 (11.4)	4 (11.4)	3 (8.6)	3 (8.6)	10 (28.6)	10 (28.6)	7 (20.0)
3	8 (22.9)	11 (31.4)	12 (34.3)	16 (45.7)	12 (34.3)	12 (34.3)	14 (40.0)
4	8 (22.9)	14 (40.0)	11 (31.4)	8 (22.9)	9 (25.7)	6 (17.1)	4 (11.4)
5	5 (14.3)	3 (8.6)	5 (14.3)	2 (5.7)	1 (2.9)	1 (2.9)	
6	3 (8.6)	1 (2.9)	1 (2.9)				
7	1 (2.9)		2 (5.7)	1 (2.9)			
8				1 (2.9)			

Table 4b. Postoperative NRS pain scores in the opioid group

NRS score	1 h n (%)	4 h n (%)	8 h n (%)	12 h n (%)	24 h n (%)	36 h n (%)	48 h n (%)
3							5 (14.3)
4	1 (2.9)				4 (11.4)	13 (37.1)	17 (48.6)
5	1 (2.9)	2 (5.7)	6 (17.1)	15 (42.9)	16 (45.7)	11 (31.4)	

NRS score	1 h n (%)	4 h n (%)	8 h n (%)	12 h n (%)	24 h n (%)	36 h n (%)	48 h n (%)
6	11 (31.4)	3 (8.6)	1 (2.9)	17 (48.6)	11 (31.4)	6 (17.1)	2 (5.7)
7	16 (45.7)	20 (57.1)	21 (60.0)	8 (22.9)	5 (14.3)		
8	6 (17.1)	12 (34.3)	10 (28.6)	4 (11.4)			
9			1 (2.9)				

Postoperative Adverse Effects

PONV was observed in 5 patients (14.3%) in the ESPB+MMA group and in 11 patients (31.4%) in the OG (difference test, p=0.0884). Nystagmus or vertigo occurred in 3 patients (8.6%) in the ESPB+MMA group and was transient. No cases of nystagmus or vertigo were recorded in the OG (Table 5). No complications related to ESPB were recorded.

Table 5. Postoperative nausea and vomiting, and nystagmus/vertigo

Adverse effect	ESPB+MMA no n (%)	ESPB+MMA yes n (%)	OG no n (%)	OG yes n (%)
PONV	30 (85.7)	5 (14.3)	24 (68.6)	11 (31.4)
Nystagmus/ vertigo	32 (91.4)	3 (8.6)	35 (100.0)	0 (0.0)

Discussion

This randomized prospective interventional study evaluated the perioperative analgesic effect of bilateral ESPB as part of multimodal anesthesia in patients undergoing open thoracolumbar spinal fixation. The main finding is that the ESPB+MMA strategy reduced the need for intraoperative and postoperative opioids and was associated with lower postoperative pain scores during the first 48 hours after surgery compared with opioid-based analgesia.

In the ESPB+MMA group, patients required only the initial induction dose of fentanyl, and none required additional intraoperative fentanyl. By contrast, patients in the OG required total intraoperative fentanyl doses between 500 and 1200 mcg. The difference in postoperative opioid requirement was also pronounced: only 4 patients in the ESPB+MMA group required rescue tramadol, whereas all patients in the OG required tramadol postoperatively, with doses up to 1500 mg. These findings support the opioid-sparing effect of ESPB when integrated into a structured multimodal analgesic regimen.

The postoperative NRS findings further support the analgesic benefit of the combined ESPB+MMA approach.

In the ESPB+MMA group, severe pain scores were uncommon and transient, with only one patient reaching an NRS score of 8 and four reaching an NRS score of 7 during the observation period. In the OG, severe pain scores were frequent during the early postoperative period, particularly at 1, 4 and 8 hours after surgery. The lower pain intensity in the ESPB+MMA group likely reflects the combined effect of the fascial plane block and systemic multimodal analgesic

agents acting at different levels of nociceptive transmission.

An important methodological point should be emphasized. In the present study, the analgesic effect of ESPB was not evaluated as an isolated intervention because the block was administered as one component of a predefined multimodal analgesic protocol. Therefore, the observed reduction in pain scores and opioid consumption should be interpreted as the effect of the combined ESPB+MMA strategy rather than the independent pharmacodynamic effect of the fascial plane block alone. Nevertheless, the marked difference between groups supports the clinical value of incorporating ESPB into multimodal analgesia for open thoracolumbar fixation.

Although the independent analgesic effect of ESPB could not be isolated in our protocol, several studies in spinal surgery have directly evaluated ESPB as an analgesic intervention. In these studies, ESPB was associated with lower postoperative pain scores, reduced time-dependent opioid consumption, delayed need for rescue analgesia, and lower rates of opioid-related adverse effects. The meta-analysis by Liu et al., which included 19 randomized clinical trials, concluded that ultrasound-guided ESPB provides effective short-term postoperative analgesia in lumbar spine surgery (15). Fu et al. also demonstrated that ESPB is effective and safe for perioperative pain management in lumbar spinal surgery and reduces opioid consumption and opioid-related adverse effects (16).

Similarly, Duan et al. reported that patients receiving ESPB for spinal surgery had lower intraoperative opioid requirements and a lower incidence of PONV (17). Liang et al., in a systematic review and meta-analysis of 12 randomized trials including 696 patients, found that ESPB significantly reduced intraoperative and postoperative opioid consumption, postoperative pain scores, need for additional analgesia, and PONV (18). These findings provide external support for the analgesic contribution of ESPB within the combined protocol used in our study.

In the present study, the incidence of PONV was lower in the ESPB+MMA group than in the OG (14.3% versus 31.4%). Although the difference did not reach conventional statistical significance ($p=0.0884$), the direction of the effect is clinically relevant and consistent with opioid reduction. Lower opioid exposure is a plausible mechanism for reduced PONV, improved patient comfort, and potentially faster postoperative recovery.

Safety is an important consideration when applying regional anesthesia in patients undergoing spine surgery. In this study, no complications related to ESPB were observed. This is consistent with the retrospective analysis by Oezel et al., which included 342 consecutive patients undergoing lumbar spine surgery with ultrasound-guided ESPB and found no procedure-specific ESPB-related complications (19). ESPB is anatomically distant from the neuraxis and major vascular structures, which may contribute to its favorable safety profile when performed under ultrasound guidance by trained practitioners.

The multimodal regimen used in this study included ketamine, paracetamol, lidocaine, magnesium sulfate, dexamethasone and metamizole. Low-dose ketamine is particularly relevant in spine surgery because of its N-methyl-D-aspartate receptor antagonism and its potential to reduce central sensitization, opioid tolerance and opioid-induced hyperalgesia. Jouguelet-Lacoste et al. concluded that low-dose ketamine, administered as a bolus or continuous infusion, reduces opioid requirements and provides effective postoperative analgesia without major complications when used for up to 48 hours postoperatively (20). Zhou et al., in a meta-analysis of 30 randomized trials including 1865 patients undergoing spine surgery, found that perioperative

low-dose ketamine reduced postoperative opioid consumption and pain scores at 24 and 48 hours without increasing adverse effects (21).

Dexamethasone and magnesium sulfate were also relevant components of the multimodal protocol used in our study. Dexamethasone may contribute to postoperative analgesia through anti-inflammatory effects, reduction of tissue edema and inhibition of prostaglandin-mediated nociceptive sensitization, while also reducing PONV. In lumbar spine surgery, Sharma et al. reported that a single preoperative intravenous dose of dexamethasone improved intraoperative and early postoperative analgesia (22). In addition, the meta-analysis by De Oliveira et al. showed that systemic single-dose dexamethasone, particularly at doses above 0.1 mg/kg, reduced postoperative pain and opioid consumption and supported its role as an adjunct within multimodal analgesic strategies (23). In the context of our protocol, dexamethasone may have contributed to opioid sparing and to the lower incidence of PONV observed in the ESPB+MMA group.

Magnesium sulfate acts primarily as an N-methyl-D-aspartate receptor antagonist and calcium-channel modulator. By attenuating central sensitization and reducing excitatory neurotransmission, magnesium may enhance analgesia and reduce opioid requirements when used perioperatively. In an umbrella review, and updated meta-analysis of randomized controlled trials, Choi et al. found that perioperative magnesium generally improved postoperative pain-related outcomes, although the overall certainty of evidence varied and heterogeneity was substantial (24). More specifically for spinal surgery, the systematic review and meta-analysis by Jin and Zhao, including 10 randomized controlled trials with 641 patients, showed that intravenous magnesium sulfate reduced 24-hour postoperative pain scores and opioid consumption without significant hemodynamic differences between groups (25). These data support the use of magnesium sulfate as a rational adjunct in opioid-sparing multimodal analgesia for spine surgery.

Metamizole also contributed to the multimodal analgesic strategy. Korkmaz Dilmen et al. found that intravenous metamizole reduced postoperative pain intensity and morphine consumption after lumbar disc surgery (26). Its analgesic and spasmolytic effects make it a useful component of multimodal analgesia in spinal surgery, particularly when the goal is to reduce opioid exposure.

This study has several limitations. The sample size was relatively small and included patients undergoing fixation for thoracic or lumbar vertebral fractures, which may limit generalizability to other types of elective spine surgery. Another important limitation is that the isolated analgesic effect of ESPB could not be measured separately, because ESPB was combined with several systemic analgesic adjuncts within a multimodal protocol. Therefore, the study demonstrates the clinical effectiveness of the ESPB+MMA strategy rather than the independent effect size of ESPB alone. Long-term follow-up was not performed; therefore, the effect of ESPB+MMA on chronic postoperative pain could not be evaluated. Future studies with larger samples, factorial designs or separate comparator arms are needed to distinguish the individual contribution of ESPB from the effects of ketamine, dexamethasone, magnesium sulfate and other multimodal agents, and to define the optimal components of multimodal analgesic protocols for open spinal fixation.

Conclusion

Bilateral erector spinae plane block combined with multimodal analgesia provided effective intraoperative and postoperative analgesia in patients undergoing open thoracolumbar spinal fixation. Compared with opioid-based analgesia, this strategy reduced intraoperative fentanyl use, lowered

postoperative tramadol requirements, improved postoperative pain scores and was associated with a lower incidence of PONV. No block-related complications were observed. ESPB appears to be a safe and useful component of multimodal anesthesia for open thoracolumbar spinal fixation.

Declarations

Ethics approval and consent to participate: The study was approved by the relevant institutional ethics committee. Approval number and date: 03-2031/9 / 16.04.2024

Informed consent: Written informed consent was obtained from all participants included in the study.

Availability of data and materials: The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Conflict of interest: The author declares no conflict of interest.

Funding: This research received no external funding.

Author contributions: Co-autors contributed to study design, data collection, data analysis, interpretation of results and manuscript preparation.

Acknowledgements: The author thanks the mentors, colleagues and participants involved in the study.

Artificial intelligence statement: ChatGPT (OpenAI) was used exclusively for language translation and linguistic editing of the manuscript. The author reviewed and edited the output and takes full responsibility for the content of the manuscript.

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ORIGINAL ARTICLE *UDK: 616-001-083.98-036.88*

www.doi.org/10.67214/3kpwbk66

EVALUATION OF RAPID TRAUMA SCORING SYSTEMS FOR PREDICTING IN-HOSPITAL MORTALITY IN POLYTRAUMA PATIENTS ADMITTED TO AN EMERGENCY CENTER

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Abstract

Objective: Polytrauma remains a major cause of mortality and disability worldwide and requires rapid risk stratification during the early phase of emergency care. Simple physiological trauma scoring systems, such as the New Trauma Score (NTS), Glasgow Coma Scale, Age and Systolic Blood Pressure score (GAP), and Mechanism, Glasgow Coma Scale, Age and Arterial Pressure score (MGAP), may support early triage and prediction of adverse outcomes.

This study aimed to evaluate and compare the predictive accuracy of NTS, GAP, and MGAP scores for in-hospital mortality in polytrauma patients admitted to the Emergency Center.

Materials and Methods: A single-center retrospective-prospective observational cohort study was conducted at the University Emergency Surgical Center in Skopje from January 2024 to November 2025. A total of 65 polytrauma patients who met the inclusion criteria were analyzed. Demographic characteristics, mechanism of injury, Glasgow Coma Scale (GCS), systolic blood pressure, peripheral oxygen saturation, and in-hospital outcome were recorded at admission. NTS, GAP, and MGAP scores were calculated and compared for their ability to predict in-hospital mortality using receiver operating characteristic (ROC) curve analysis.

Results: Among 65 patients, 57 were male and 8 were female. Forty-nine patients survived, while 16 patients died during hospitalization. Mortality was higher among patients aged ≥60 years and among those with lower initial GCS scores.

All three scoring systems demonstrated excellent diagnostic accuracy for predicting in-hospital mortality, with area under the curve (AUC) values above 0.90. MGAP showed the highest predictive accuracy (AUC = 0.94), followed by GAP (AUC = 0.93) and NTS (AUC = 0.91).

Conclusion: NTS, GAP, and MGAP are simple and rapidly applicable scoring systems with excellent predictive accuracy for in-hospital mortality in polytrauma patients. MGAP showed the highest AUC value in this cohort, likely due to the additional inclusion of injury mechanism. However, because the performance of all three scores was excellent and closely comparable, they may all be considered useful tools for early risk stratification and triage in emergency center settings.

Keywords: *emergency center; GAP score; in-hospital mortality; polytrauma; trauma scoring systems.*

Introduction

Polytrauma, defined as significant injury involving two or more body regions or organ systems, represents a major challenge in emergency medicine and remains a leading cause of mortality and disability, particularly among younger patients (1). Globally, injuries account for a substantial proportion of preventable deaths, with road traffic accidents, falls, occupational injuries, and violence-related trauma representing important mechanisms of severe injury (2).

The initial period after trauma, often referred to as the "golden hour," is critical for patient outcome. During this period, rapid assessment, early recognition of life-threatening injuries, appropriate triage, and timely initiation of treatment may significantly reduce morbidity and mortality (3). In emergency settings, clinicians therefore need simple, rapid, and reliable tools that can identify patients at high risk of deterioration or death during the first minutes after admission.

Several trauma scoring systems have been developed to quantify injury severity and predict outcome. Anatomical and combined scoring systems, such as the Injury Severity Score (ISS), Trauma and Injury Severity Score (TRISS), and Revised Trauma Score (RTS), have shown prognostic value, but some require detailed anatomical diagnosis or additional information that may not be immediately available during the primary survey (3,4). This limits their practical use for early triage, particularly in busy emergency departments or lower-resource settings where rapid decision-making is essential (5,6).

Simplified physiological trauma scores have become increasingly important in the initial assessment of trauma patients. These scores are based on parameters that are readily available at admission, including the Glasgow Coma Scale (GCS), systolic blood pressure, age, oxygen saturation, and mechanism of injury. Recent comparative studies have assessed the Glasgow Coma Scale, Age and Systolic Blood Pressure score (GAP), the Mechanism, Glasgow Coma Scale, Age and Arterial Pressure score (MGAP), and other rapid trauma scores for predicting mortality in trauma patients (7).

The New Trauma Score (NTS), a modification of the Revised Trauma Score, incorporates peripheral oxygen saturation instead of respiratory rate and has demonstrated good predictive performance for trauma mortality (8). Subsequent studies have also evaluated the accuracy of GAP, MGAP, and NTS in trauma populations, supporting their use as simple tools for early risk stratification (9). Although these scoring systems are simple and clinically applicable, their predictive performance may vary across different trauma populations and healthcare settings. Therefore, local validation is important before their routine implementation in a specific emergency center setting.

The aim of this study was to evaluate and compare the predictive accuracy of NTS, GAP, and MGAP scores for predicting in-hospital mortality in polytrauma patients admitted to the Emergency Center. In addition, the study assessed the association of age, mechanism of injury, and initial neurological status, evaluated by GCS, with treatment outcome. By comparing the diagnostic performance of these scores using receiver operating characteristic curve analysis,

this study aimed to identify a simple and reliable tool for early risk stratification of high-risk polytrauma patients in our clinical setting.

Materials and Methods

Study design and setting

This was a single-center observational cohort study conducted at the University Emergency Surgical Center in Skopje, North Macedonia, between January 2024 and November 2025. The study included patients admitted to the Emergency Center after severe trauma or polytrauma requiring urgent evaluation and treatment.

All patients were assessed immediately after admission according to standard trauma protocols, including primary survey, clinical examination, available medical history, and non-invasive monitoring. Initial management was performed according to the ABCDE approach.

Study population

A total of 65 patients with polytrauma who met the inclusion criteria were included in the analysis. Polytrauma was defined as severe injury involving two or more body regions or organ systems, associated with potential or actual life-threatening physiological impairment.

Patients were included if they were older than 15 years and admitted to the Emergency Center with severe trauma or polytrauma requiring urgent assessment and treatment. Both blunt and penetrating mechanisms of injury were included, such as road traffic accidents, pedestrian injuries, workplace injuries, falls from height, crush or blast injuries, stab wounds, gunshot injuries, and other severe traumatic mechanisms.

Patients were excluded if they had no signs of life on arrival, had insufficient data required for calculation of the trauma scores, were younger than 15 years, were pregnant, had drowning-related injury, or had been initially treated in another institution before referral to the tertiary center. Patients who left the Emergency Center before completion of emergency evaluation were also excluded.

Initial assessment and data collection

Upon admission, all patients were managed according to the standard ABCDE trauma approach. Airway, breathing, circulation, neurological status, and exposure were assessed during the primary survey. Non-invasive monitoring, including systolic blood pressure, heart rate, electrocardiographic monitoring, and peripheral oxygen saturation, was established immediately after admission.

Data were collected from trauma score sheets, emergency medical records, the institutional electronic health record system, and medical documentation. The following variables were recorded at admission: age, sex, mechanism of injury, Glasgow Coma Scale (GCS), systolic blood pressure, peripheral oxygen saturation, and in-hospital outcome.

In patients with impaired consciousness or inability to provide history, information regarding the mechanism and circumstances of injury was obtained from emergency medical personnel,

witnesses, family members, or available medical documentation.

The primary outcome was in-hospital mortality, defined as death during hospital stay. Patients were followed until hospital discharge or death.

Trauma scoring systems

The New Trauma Score (NTS), Glasgow Coma Scale, Age and Systolic Blood Pressure score (GAP), and Mechanism, Glasgow Coma Scale, Age and Arterial Pressure score (MGAP) were calculated at admission using the initial physiological parameters recorded during emergency assessment.

The GCS was used to assess the initial level of consciousness, with values ranging from 3 to 15. Patients were classified as having severe impairment of consciousness when GCS was 3–8, moderate impairment when GCS was 9–12, and mild or no impairment when GCS was 13–15.

NTS, GAP, and MGAP were calculated at admission according to their published definitions. Patients were categorized into risk groups according to previously published cut-off values for each scoring system, as shown in Table 1.

Table 1. Components and risk categories of the trauma scoring systems

Scoring system	*Components*	*Risk categories used in the study*
NTS	GCS, systolic blood pressure, peripheral oxygen saturation	Low risk: 18–23; intermediate risk: 12–17; high risk: 6–11; very high risk: 3–5
GAP	GCS, age, systolic blood pressure	Low risk: 19–24; moderate risk: 11–18; high risk: <11
MGAP	Mechanism of injury, GCS, age, systolic blood pressure	Low risk: 23–29; moderate risk: 18–22; high risk: <18

*NTS: New Trauma Score; GAP: Glasgow Coma Scale, Age and Systolic Blood Pressure score; MGAP: Mechanism, Glasgow Coma Scale, Age and Arterial Pressure score; GCS: Glasgow Coma Scale.

Ethical considerations

Patient data were analyzed anonymously and used exclusively for the purposes of this study. The study was approved by the Institutional Review Board of the Faculty of Medicine, University "Ss. Cyril and Methodius", Skopje, Republic of North Macedonia.

Written informed consent was obtained from patients when possible. In patients with impaired consciousness or inability to provide consent, consent was obtained from a close family member or legally authorized representative according to institutional practice.

Statistical analysis

Statistical analysis was performed using SPSS version 27.0 (IBM Corp., Armonk, NY, USA). The normality of data distribution was assessed using the Shapiro–Wilk test. Categorical variables were presented as frequencies and percentages. Comparisons between survivors and non-survi-

vors were performed using the χ^2 test or Fisher's exact test, as appropriate.

Spearman's correlation was used to evaluate associations between trauma scoring systems. Receiver operating characteristic (ROC) curve analysis was performed to assess the diagnostic accuracy of NTS, GAP, and MGAP for predicting in-hospital mortality. The area under the curve (AUC) with 95% confidence intervals was calculated for each scoring system. A p-value <0.05 was considered statistically significant.

Results

Patient characteristics and clinical outcome

A total of 65 polytrauma patients who met the inclusion criteria were included in the study. Of these, 57 patients were male (87.7%) and 8 were female (12.3%). Forty-five patients (69.2%) were aged 15–59 years, while 20 patients (30.8%) were aged 60 years or older.

Blunt trauma was the predominant mechanism of injury and was present in 58 patients (89.2%), while penetrating trauma was recorded in 7 patients (10.8%).

According to in-hospital outcome, 49 patients survived (75.4%), while 16 patients died during hospitalization (24.6%). Mortality was higher among patients aged ≥60 years compared with younger patients: 8 of 20 patients aged ≥60 years died (40.0%), compared with 8 of 45 patients aged 15–59 years (17.8%).

Initial level of consciousness, assessed using the Glasgow Coma Scale (GCS), was strongly associated with in-hospital mortality. Among patients with severe impairment of consciousness (GCS 3–8), 9 of 12 patients died (75.0%). Among patients with moderate impairment of consciousness (GCS 9–12), 6 of 12 patients died (50.0%). In contrast, only 1 of 41 patients with GCS 13–15 died (2.4%) ($p < 0.001$).

Table 2. Baseline characteristics and in-hospital outcome of polytrauma patients

Variable	Total n (%)	Survivors n (%)	Non-survivors n (%)	p-value
Total	65 (100)	49 (75.4)	16 (24.6)	—
Sex				0.668
Male	57 (87.7)	42 (73.7)	15 (26.3)	
Female	8 (12.3)	7 (87.5)	1 (12.5)	
Age group				0.068
15–59 years	45 (69.2)	37 (82.2)	8 (17.8)	
≥60 years	20 (30.8)	12 (60.0)	8 (40.0)	
Mechanism of injury				0.671
Blunt trauma	58 (89.2)	43 (74.1)	15 (25.9)	
Penetrating trauma	7 (10.8)	6 (85.7)	1 (14.3)	

Variable	Total n (%)	Survivors n (%)	Non-survivors n (%)	p-value
GCS category				<0.001
GCS 3–8	12 (18.5)	3 (25.0)	9 (75.0)	
GCS 9–12	12 (18.5)	6 (50.0)	6 (50.0)	
GCS 13–15	41 (63.1)	40 (97.6)	1 (2.4)	

Note: Percentages for survivors and non-survivors are calculated within each category.

*GCS: Glasgow Coma Scale.

Mortality according to trauma scoring systems

The initial NTS, GAP, and MGAP risk categories differed significantly between survivors and non-survivors.

According to the NTS classification, 43 patients were categorized as low risk, of whom 1 patient died (2.3%). Fourteen patients were categorized as intermediate risk, of whom 9 died (64.3%). Six patients were categorized as high risk, of whom 4 died (66.7%), while both patients in the very high-risk group died (100%) ($p < 0.001$).

According to the GAP score, none of the 39 patients in the low-risk group died. Among 19 patients in the moderate-risk group, 10 died (52.6%), while among 7 patients in the high-risk group, 6 died (85.7%) ($p < 0.001$).

According to the MGAP score, none of the 39 patients in the low-risk group died. Among 17 patients in the moderate-risk group, 8 died (47.1%), while among 9 patients in the high-risk group, 8 died (88.9%) ($p < 0.001$).

Table 3. Mortality according to NTS, GAP, and MGAP risk categories

Scoring system / risk category	Total n	Survivors n (%)	Non-survivors n (%)	p-value
NTS				<0.001
Low risk	43	42 (97.7)	1 (2.3)	
Intermediate risk	14	5 (35.7)	9 (64.3)	
High risk	6	2 (33.3)	4 (66.7)	
Very high risk	2	0 (0.0)	2 (100.0)	
GAP				<0.001
Low risk	39	39 (100.0)	0 (0.0)	
Moderate risk	19	9 (47.4)	10 (52.6)	
High risk	7	1 (14.3)	6 (85.7)	
MGAP				<0.001
Low risk	39	39 (100.0)	0 (0.0)	

Scoring system / risk category	Total n	Survivors n (%)	Non-survivors n (%)	p-value
Moderate risk	17	9 (52.9)	8 (47.1)	
High risk	9	1 (11.1)	8 (88.9)	

Note: Percentages are calculated within each risk category. NTS: New Trauma Score; GAP: Glasgow Coma Scale, Age and Systolic Blood Pressure score; MGAP: Mechanism, Glasgow Coma Scale, Age and Arterial Pressure score.

Correlation between trauma scoring systems

Spearman correlation analysis demonstrated strong associations between the evaluated trauma scoring systems. NTS showed a strong positive correlation with GAP (rho = 0.796, $p < 0.001$) and MGAP (rho = 0.758, $p < 0.001$), while GAP and MGAP demonstrated a very strong positive correlation (rho = 0.944, $p < 0.001$).

The categorized GCS variable showed a negative correlation with NTS, GAP, and MGAP because higher GCS category codes represented more severe impairment of consciousness. This confirms that worsening neurological status was associated with lower trauma score values and higher mortality risk.

Table 4. Spearman correlation between GCS category and trauma scoring systems

Variable	GCS category*	NTS	GAP	MGAP
GCS category*	1.000	-0.945**	-0.746**	-0.710**
NTS	-0.945**	1.000	0.796**	0.758**
GAP	-0.746**	0.796**	1.000	0.944**
MGAP	-0.710**	0.758**	0.944**	1.000

Note: **$p < 0.001$. GCS category was coded according to severity of consciousness impairment, with higher category values indicating more severe neurological impairment. GCS: Glasgow Coma Scale; NTS: New Trauma Score; GAP: Glasgow Coma Scale, Age and Systolic Blood Pressure score; MGAP: Mechanism, Glasgow Coma Scale, Age and Arterial Pressure score.

Diagnostic accuracy for prediction of in-hospital mortality

The diagnostic performance of NTS, GAP, and MGAP for predicting in-hospital mortality was evaluated using receiver operating characteristic (ROC) curve analysis (Figure 1).

All three scoring systems demonstrated excellent diagnostic accuracy, with area under the curve (AUC) values above 0.90. The highest predictive accuracy was observed for MGAP, with an AUC of 0.94 (95% CI: 0.82–0.99). GAP showed a similar predictive performance, with an AUC of 0.93 (95% CI: 0.86–0.99), while NTS also demonstrated excellent accuracy, with an AUC of 0.91 (95% CI: 0.88–0.99).

These findings indicate that all three scoring systems were highly effective in discriminating between survivors and non-survivors, with MGAP showing the strongest overall performance.

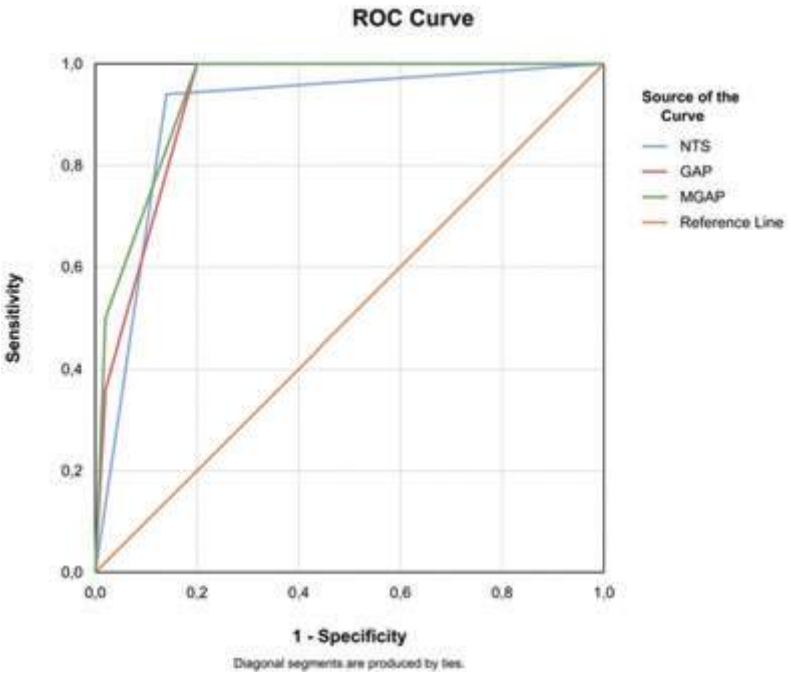

Figure 1. Receiver operating characteristic curves of NTS, GAP, and MGAP for predicting in-hospital mortality.

Table 5. Diagnostic accuracy of NTS, GAP, and MGAP for predicting in-hospital mortality

Scoring system	AUC	95% CI	Diagnostic performance
MGAP	0.94	0.82–0.99	Excellent
GAP	0.93	0.86–0.99	Excellent
NTS	0.91	0.88–0.99	Excellent

Note: AUC: area under the receiver operating characteristic curve; CI: confidence interval; NTS: New Trauma Score; GAP: Glasgow Coma Scale, Age and Systolic Blood Pressure score; MGAP: Mechanism, Glasgow Coma Scale, Age and Arterial Pressure score.

Discussion

The present study evaluated the predictive accuracy of three rapid physiological trauma scoring systems — NTS, GAP, and MGAP — for in-hospital mortality in polytrauma patients admitted to a single Emergency Center. The main finding was that all three scoring systems demonstrated excellent discriminatory ability, with AUC values above 0.90. MGAP showed the numerically highest AUC value, followed closely by GAP and NTS. These findings are consistent with previous comparative studies showing that simple physiological trauma scores can accurately predict mortality in trauma patients (1,3,7,9). However, because the differences between AUC values in our study were small and no formal statistical comparison between ROC curves was performed, the observed advantage of MGAP should be interpreted with caution.

In this cohort, in-hospital mortality was 24.6%, reflecting the severity of the included trauma population. This rate may be explained by the fact that the study included patients with severe

trauma or polytrauma admitted to an emergency surgical center.

Previous studies have shown that the performance of trauma scoring systems depends on patient selection, injury severity, prehospital care, transport time, and healthcare system organization (3,5). Therefore, local validation of trauma scores is important before their routine implementation in a specific emergency center setting.

Initial neurological status was strongly associated with in-hospital mortality in our study. Mortality was highest among patients with severe impairment of consciousness: 75.0% of patients with GCS 3–8 died, compared with 50.0% of patients with GCS 9–12 and only 2.4% of patients with GCS 13–15. This finding confirms the central prognostic role of GCS in trauma patients. Since GCS is included in NTS, GAP, and MGAP, its strong association with mortality partly explains the excellent performance of all three scores. Previous studies on GAP and MGAP also emphasize GCS as one of the key components for early trauma mortality prediction (10,11).

Older patients showed higher mortality in our cohort, although the difference did not reach statistical significance.

Mortality among patients aged ≥60 years was 40.0%, compared with 17.8% among younger patients. This trend is clinically relevant and is consistent with previous trauma literature showing that advanced age contributes to poorer outcomes because of reduced physiological reserve, comorbidities, and lower tolerance to hemorrhage, hypoxia, traumatic brain injury, and shock. The inclusion of age in both GAP and MGAP supports its prognostic value in early trauma assessment (10,11).

The MGAP score demonstrated the numerically highest predictive accuracy in our study, with an AUC of 0.94. This finding is consistent with the original study by Sartorius et al., who introduced MGAP as a simple prehospital triage score for predicting mortality in trauma patients (10).

The potential advantage of MGAP may be related to the inclusion of injury mechanism in addition to GCS, age, and systolic blood pressure. In polytrauma patients, mechanism of injury provides important contextual information regarding the expected severity and pattern of injuries. Similar findings have been reported in studies comparing MGAP with other trauma scoring systems, where MGAP demonstrated strong predictive performance for mortality (1,3,7,11).

The GAP score also demonstrated excellent performance, with an AUC of 0.93. This finding is in line with the study by Kondo et al., who developed the GAP score as a simplified scoring system for predicting in-hospital mortality in emergency department trauma patients (12). The main strength of GAP is its simplicity, as it includes only three variables: GCS, age, and systolic blood pressure. These parameters are available immediately at admission, making the score suitable for early triage. In our study, GAP and MGAP showed a very strong positive correlation, indicating that both scores classify patients in a similar prognostic direction. Previous multicenter and comparative studies have also shown that GAP and MGAP have closely related performance in trauma mortality prediction (3,7,13).

The NTS score also showed excellent discriminatory ability, with an AUC of 0.91. Although this value was slightly lower than those of MGAP and GAP, its performance remained clinically strong. NTS is a modification of the Revised Trauma Score and replaces respiratory rate with peripheral oxygen saturation, which may be more objective and easier to obtain during emergency

assessment. Jeong et al. proposed the NTS and demonstrated that the use of oxygen saturation may improve trauma mortality prediction compared with traditional physiological scoring systems (8). Wang et al. also reported that NTS may be useful for predicting mortality in multiple trauma patients (14).

In our cohort, NTS successfully differentiated low-risk from higher-risk patients, with mortality increasing across NTS risk categories.

A clinically important finding of this study is that all three scoring systems identified low-risk patients with very low or no mortality. No deaths were recorded in the low-risk groups of GAP and MGAP, while only one death occurred in the NTS low-risk group. This has practical implications for triage and resource allocation. Previous studies have similarly suggested that low-risk categories of GAP and MGAP are associated with very low mortality and may help clinicians rapidly identify patients who are less likely to require immediate life-saving interventions (10,12,13).

From a practical perspective, our findings support the use of rapid physiological trauma scores in the Emergency Center setting. Anatomical scores such as ISS and combined models such as TRISS have established prognostic value, but they often require complete diagnostic evaluation and are not always available during the primary survey (4). In contrast, NTS, GAP, and MGAP can be calculated within minutes of admission using simple clinical and physiological parameters. This makes them particularly useful in busy emergency departments and in resource-limited settings where rapid decision-making is essential (3,5).

The findings of the present study are also relevant because trauma score performance may vary between populations and healthcare systems. Feldhaus et al. emphasized that the feasibility and applicability of trauma scoring systems in low- and middle-income countries depend on data availability, workflow, and system organization (5). Similarly, studies conducted in low-resource settings have shown that simplified trauma scoring systems such as GAP and MGAP may be more practical than complex anatomical or combined models (3). Therefore, our results provide useful local evidence supporting the applicability of these scores in our emergency center.

This study has several limitations. First, it was conducted at a single center and included a relatively small sample of 65 patients, which may limit the generalizability of the findings. Second, the number of deaths was limited, which may affect the precision of AUC estimates and subgroup comparisons. Third, although MGAP showed the numerically highest AUC, formal statistical comparison between ROC curves was not performed; therefore, definitive superiority of one score over another cannot be concluded. Fourth, the study evaluated in-hospital mortality but did not include long-term outcomes, functional recovery, or neurological outcome after discharge. Fifth, although the scores were calculated from admission data, some variables may have been influenced by prehospital care, transport time, or early resuscitation before hospital arrival. Finally, this study did not compare rapid physiological scores with anatomical scores such as ISS or combined models such as TRISS, which could provide additional insight into their relative performance.

Despite these limitations, the study provides useful local evidence on the performance of rapid trauma scoring systems in polytrauma patients treated in an Emergency Center. The findings suggest that NTS, GAP, and MGAP are simple, rapidly applicable, and accurate tools for early mortality risk assessment. MGAP showed the numerically highest AUC value, while GAP and

NTS demonstrated closely comparable excellent performance. Further larger, multicenter studies are needed to validate these findings and to determine whether routine implementation of these scores can improve triage decisions, resource allocation, and patient outcomes.

Conclusion

In this single-center cohort of polytrauma patients, NTS, GAP, and MGAP demonstrated excellent predictive accuracy for in-hospital mortality. MGAP showed the highest AUC value, followed closely by GAP and NTS, suggesting that all three scoring systems may be useful for early mortality risk assessment in the Emergency Center.

The findings confirm the importance of initial neurological status, age, systolic blood pressure, oxygen saturation, and mechanism of injury in early trauma prognosis. Because these variables are rapidly available at admission, NTS, GAP, and MGAP can support timely triage, early identification of high-risk patients, and more efficient allocation of emergency and intensive care resources.

Among the evaluated scores, MGAP showed the numerically strongest overall performance, likely due to the inclusion of injury mechanism. However, GAP and NTS also demonstrated excellent and closely comparable accuracy and may be valuable alternatives depending on data availability and clinical workflow.

Declarations

Ethics approval and consent to participate: This study was approved by the Institutional Review Board of the Faculty of Medicine, University "Ss Cyril and Methodius", Skopje, Republic of North Macedonia (at the 9th regular session (Decision No.03-2987/8)

Informed consent: Written informed consent was obtained from patients when possible. In patients with impaired consciousness or inability to provide consent, consent was obtained from a close family member or legally authorized representative according to institutional practice.

Conflict of interest: The authors report no financial or personal conflicts of interest.

Funding: This research received no external funding.

Availability of data and materials: The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Author Contributions: Conceptualisation, J.S. and A.G.B.; methodology, N.M. and N.B.; investigation, J.S., A.G., N.B. and O.L.; data curation, J.S. and N.M.; writing – original draft preparation, J.S. and N.B.; writing – review and editing, J.S. and A.G.B..; supervision, A.G.B.; project administration, O.L.. All authors have read and agreed to the published version of the manuscript.

Acknowledgments: None

Use of Artificial Intelligence (AI) tools: The authors declare that no artificial intelligence tools were used in the preparation of this manuscript.

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ORIGINAL ARTICLE *UDK: 616.24-007.63-073.756.8:004*

www.doi.org/10.67214/mk4e4641

CT-BASED ANALYSIS OF PULMONARY NEOPLASTIC LESIONS IN PATIENTS WITH EMPHYSEMA: PREVALENCE AND IMAGING CORRELATES — A RETROSPECTIVE STUDY

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Abstract

Objective: Computed tomography (CT) plays a central role in the early detection and characterization of lung neoplasms and allows simultaneous assessment of structural lung diseases such as emphysema. The aim is to determine the prevalence of emphysema in patients with CT-detected pulmonary neoplastic lesions and to evaluate its association with tumor size, morphology, and anatomical distribution.

Materials and Methods: This retrospective observational study was conducted at the University Clinic of Pulmonology and Allergology. A total of 1045 thoracic CT examinations performed between August 2025 and January 2026 using a PHILIPS Incisive CT scanner protocol optimized for thoracic imaging were reviewed. One hundred patients with CT-detected lung neoplasms were included.

Demographic characteristics, emphysema subtype, tumor features, and associated CT findings were analyzed. Emphysema was assessed visually and classified by subtype. Statistical analysis included chi-square testing, t-tests, Mann–Whitney U tests, ANOVA, and multivariable logistic regression.

Results: Lung neoplasms were identified in 9.6% of CT examinations. Emphysema was detected in 48% of patients, predominantly of the centrilobular type. The mean tumor size was 52.4 ± 22.1 mm, with a predominance of the upper lobe and central segment. No statistically significant associations were observed between emphysema and tumor size, morphology, lobar distribution, or segmental localization. Male sex was associated with increased odds of emphysema (OR ≈ 2.4), although the association did not reach statistical significance. The regression model showed limited explanatory power (Pseudo $R^2 = 0.066$).

Conclusion: Emphysema frequently coexists with lung neoplasms in tertiary clinical practice. However, within the limitations of this retrospective imaging-based study, emphysema was not associated with measurable differences in CT tumor phenotype. Emphysema should be regarded primarily as a background risk substrate rather than a determinant of tumor imaging characteristics.

Keywords: *CT; emphysema; prevalence; neoplastic lesions; lungs.*

Introduction

Lung cancer remains the leading cause of cancer-related mortality worldwide, largely due to late diagnosis and advanced disease at presentation. Computed tomography (CT) plays a central role in early detection, characterization, and staging of lung neoplasms and has demonstrated a significant impact on mortality reduction in high-risk populations through screening programs such as the National Lung Screening Trial and the NELSON trial.

Emphysema, a smoking-related structural lung disease, has been independently associated with increased lung cancer risk even after adjustment for smoking exposure.

Chronic inflammation, altered extracellular matrix, and regional hypoxia in emphysematous lungs may theoretically influence tumor development and growth patterns. However, whether emphysema modifies the radiologic phenotype of established tumors remains uncertain (1-3). This study was designed to evaluate this relationship in a real-world tertiary-care population.

In addition to tumor detection, CT provides a detailed evaluation of structural lung abnormalities, including emphysema. Emphysema represents a chronic smoking-related parenchymal disorder characterized by permanent enlargement of airspaces and destruction of alveolar walls. Several studies have demonstrated that CT-detected emphysema is independently associated with increased risk of lung cancer development, even after adjustment for smoking exposure and airflow limitation (4–6). This association has led to growing interest in understanding whether emphysema merely reflects shared risk factors or influences tumor behavior and radiologic phenotype.

Previous studies have suggested potential relationships between emphysema and tumor location, morphology, and aggressiveness; however, results remain inconsistent, and data derived from real-world clinical populations remain limited. Furthermore, the influence of different emphysema subtypes on tumor characteristics has not been fully clarified.

Given the increasing role of CT as an integrated diagnostic tool that simultaneously evaluates malignant lesions and structural lung disease, further investigation of the relationship between emphysema and lung carcinoma imaging characteristics is warranted.

Objective of the Study

To determine the prevalence of emphysema in patients with CT-detected pulmonary neoplastic lesions and to evaluate whether emphysema is associated with tumor size, morphology, or anatomical distribution.

Specific objectives were:

- To determine the prevalence of emphysema among patients with CT-detected pulmonary neoplastic lesions.
- To analyze the distribution of emphysema subtypes.
- To evaluate tumor anatomical distribution according to lobar and segmental localization.

- To compare tumor morphology and dimensions between patients with and without emphysema.
- To assess associations between emphysema and additional CT findings, including nodules, lymph nodes, pleural effusion, and distant metastasis.
- To identify independent predictors of emphysema using multivariable statistical analysis.

Materials and Methods

Study Design and Population

This retrospective observational study included 100 patients with CT-detected pulmonary neoplastic lesions identified among 1045 thoracic CT examinations performed over a six-month period (August 2025 to January 2026) at the University Clinic of Pulmonology and Allergology in Skopje, N. Macedonia. Thoracic CT examinations were imaged on a PHILIPS INCISIVE CT Scanner with a 1 mm thin section protocol and a spatial reconstruction algorithm optimized for thoracic imaging.

Variables recorded included age, sex, presence and subtype of emphysema (centrilobular, paraseptal, combined), tumor size, morphology, lobar and segmental location, lymph node involvement, pleural effusion, and distant metastasis.

Emphysema was assessed visually according to established radiologic criteria. Quantitative densitometric analysis was not available due to constraints imposed by the retrospective design.

Smoking exposure data were not consistently available in medical records and could not therefore be included in regression modeling, representing an important limitation.

Statistical analysis included chi-square testing, t-tests, Mann–Whitney U tests, ANOVA, and multivariable logistic regression. Confidence intervals were calculated for odds ratios. No formal power calculation was performed. All examinations were performed using standard thoracic CT protocols. Images were evaluated by radiologists experienced in thoracic imaging.

Statistical Analysis

Statistical analysis was performed using standard comparative and multivariable methods. Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were presented as frequencies and percentages.

Comparisons between categorical variables were performed using the Chi-square test or Fisher's exact test as appropriate. Continuous variables were compared using the Welch t-test or the Mann–Whitney U test depending on data distribution. Comparisons among multiple emphysema subtypes were performed using one-way ANOVA or the Kruskal–Wallis test. Multivariable logistic regression analysis was conducted with emphysema presence as the dependent variable, including demographic and tumor-related imaging variables as predictors. A p-value less than 0.05 was considered statistically significant, and values between 0.05 and 0.10 were interpreted as borderline trends.

Results

During the six-month study period (August 2025–January 2026), a total of 1045 thoracic CT examinations were performed at the University Clinic of Pulmonology and Allergology. Among these, CT findings consistent with pulmonary neoplastic lesions were identified in100 patients, corresponding to a prevalence of 9.6%. The mean patient age was approximately 69 years, and the study population was predominately male (72% male, 28% female).

Table 1. Study Population and Demographics

Variable	Value
Total CT examinations	1045
Patients with pulmonary neoplastic lesions	100
Prevalence	9.6%
Mean age (years)	69
Male	72 (72%)
Female	28 (28%)

Emphysematous changes were identified in 48% of patients, whereas 52% had no CT evidence of emphysema. Subtype analysis revealed a predominance of centrilobular emphysema (25%), followed by combined emphysema patterns (14%) and paraseptal emphysema (9%). Male patients were more prevalent in the emphysema group (39 males and 9 females) than in the non-emphysema group (33 males and 19 females). Statistical analysis yielded an odds ratio of 2.49 for male sex, with $\chi^2 = 3.09$ ($p = 0.079$) and Fisher's exact $p = 0.074$, indicating a borderline association and suggesting a clinically relevant trend toward a higher prevalence of emphysema among male patients.

Table 2. Emphysema Prevalence and Subtypes

Emphysema status/subtype	n	%
No emphysema	52	52%
Any emphysema	48	48%
Centrilobular	25	25%
Combined (both)	14	14%
Paraseptal	9	9%

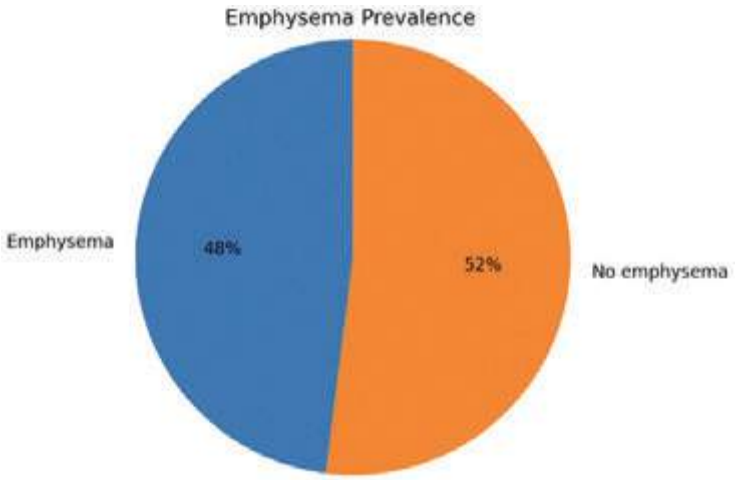

Figure 1.

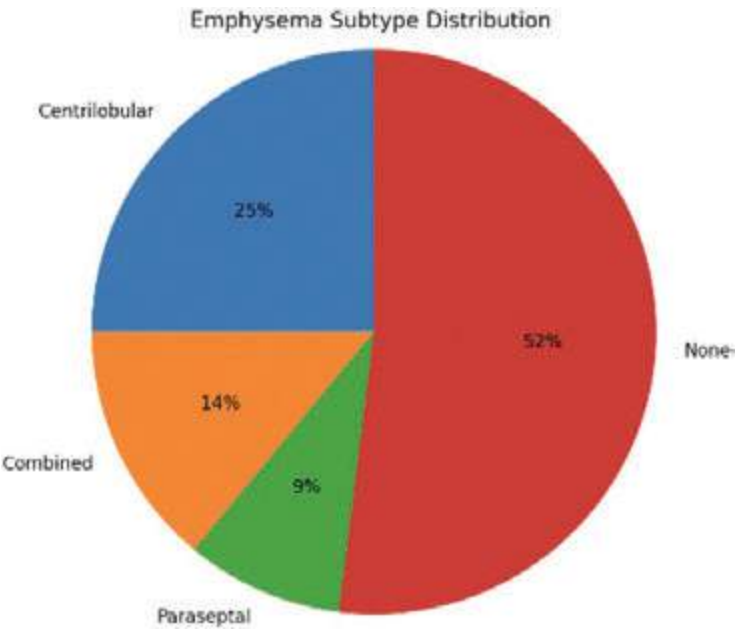

Figure 2.

Table 3. Sex Distribution According to the Presence of Emphysema

Sex	Emphysema	No emphysema
Male	39	33
Female	9	19

Statistics: OR = 2.49; $\chi^2 = 3.09$; p = 0.079; Fisher p = 0.074

The mean lesion dimension for the entire cohort was 52.4 ± 22.1 mm (median 48 mm; range 13–100 mm). When analyzed by morphology, polylobular lesions had larger mean dimensions (60.5 mm) than spiculated (40.1 mm) or irregular lesions (39.2 mm), indicating variability in growth characteristics across morphologic types.

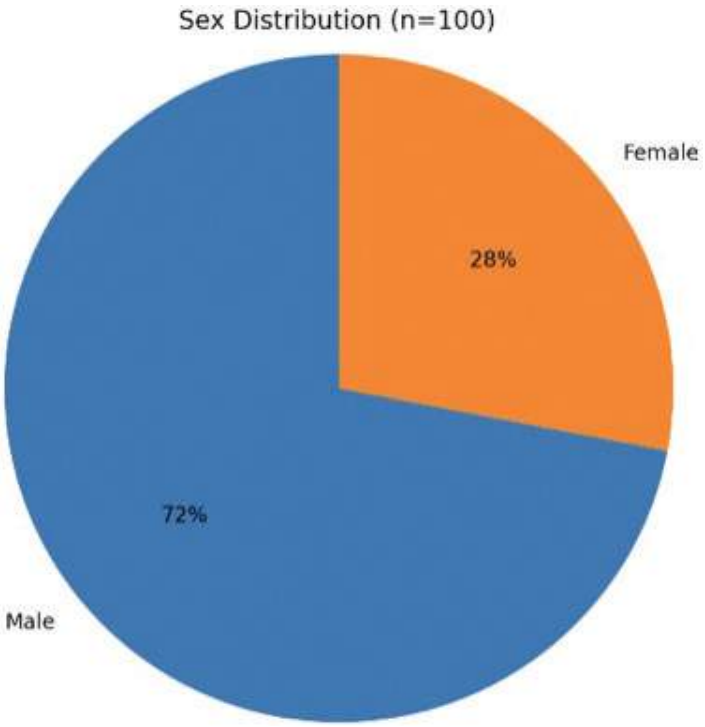

Figure 3.

Table 4. Lesion Size by Morphology

Morphology	Mean size (mm)
Polylobular	60.5
Spiculated	40.1
Irregular	39.2

An upper-lobe predominance was observed in the conducted anatomical distribution, with the right upper lobe representing the most frequently involved location (34%), followed by the right lower lobe (22%), left upper lobe (21%), left lower lobe (17%), and right middle lobe (6%). Segmental analysis showed the highest frequency in the hilar region (26%), followed by the superior segment (12%), the apicoanterior segment (9%), the posterobasal segment (7%), and the lateral segment (6%), reflecting a predominance of central and upper segment involvement.

Table 5. Lobar Distribution of Pulmonary Neoplastic Lesions

Lobe	n	%
Right upper lobe	34	34%
Right lower lobe	22	22%
Left upper lobe	21	21%
Left lower lobe	17	17%
Right middle lobe	6	6%

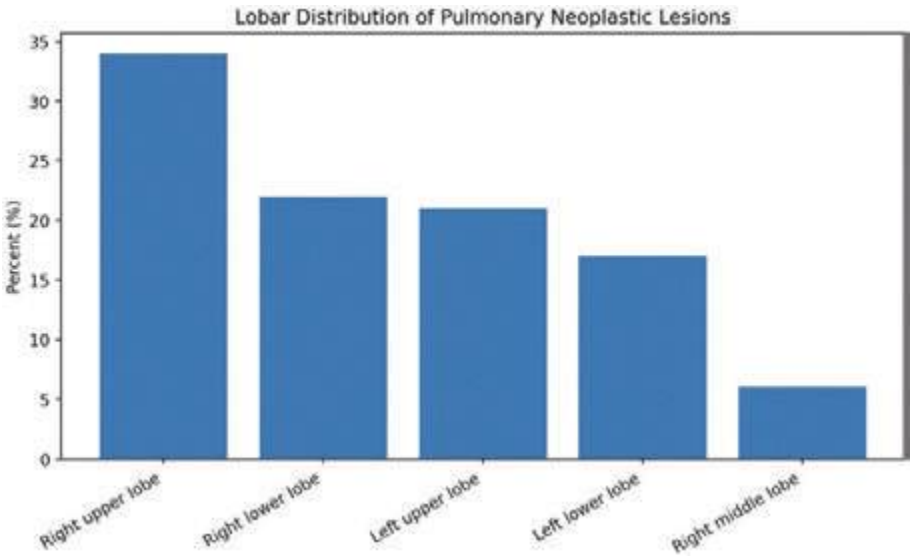

Figure 4.

Table 6. Segmental Distribution

Segment	n	%
Hilar	26	26%
Superior	12	12%
Apicoanterior	9	9%
Posterobasal	7	7%
Lateral	6	6%

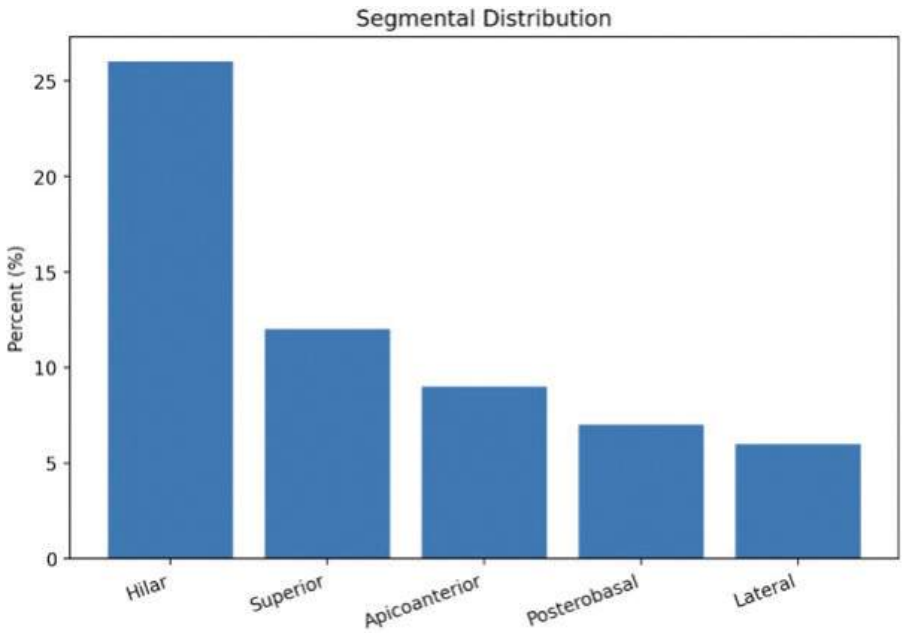

Figure 5.

A comparative analysis between patients with concomitant emphysema (n = 48) and those without emphysema (n = 52) showed no statistically significant difference in lesion size.

In the emphysema group, the mean lesion dimension was 53.7 ± 22.0 mm (median 50 mm) and 51.2 ± 22.4 mm (median 46 mm) in the non-emphysema group (Welch t-test p = 0.681; Mann–Whitney U p = 0.609), indicating no significant association to lesion size at the time of CT detection.

Table 7. Lesion Size: Emphysema vs No Emphysema

Group	Mean size (mm)	SD	Median
Emphysema	53.7	22.0	50
No emphysema	51.2	22.4	46

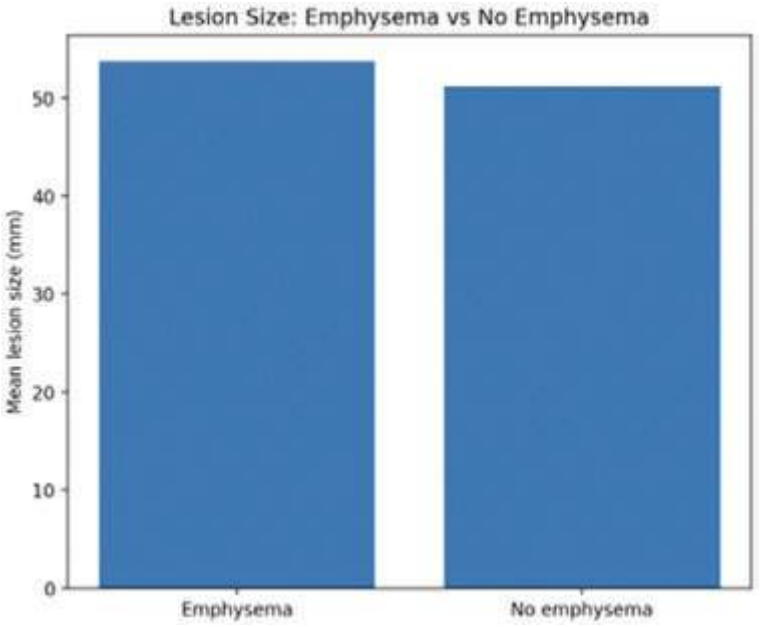

Figure 6.

Lesion morphology showed no statistically significant association with emphysema presence (χ^2 = 9.59, p = 0.088), although a borderline trend toward differing morphology distribution was observed. Similarly, no significant associations were identified between emphysema and lobar tumor distribution (χ^2 = 5.94, p = 0.312) or segmental localization (χ^2 = 1.65, p = 0.895), indicating that emphysema does not determine macroscopic or segmental anatomical localization.

Further analysis of lesion dimensions in relation to associated CT findings showed that lesions accompanied by nodules were larger (54.4 mm vs 46.5 mm), with borderline statistical significance (t-test, p = 0.084; Mann–Whitney, p = 0.077). An identical borderline trend was observed in lesions with lymph node involvement (54.4 mm vs 46.5 mm; p ≈ 0.08), reflecting substantial overlap between nodules and lymph node findings within the dataset. No significant differences in lesion size were observed according to the presence of pleural effusion (50.8 mm vs 49.5 mm; p = 0.760) or distant metastasis (50.0 mm vs 49.9 mm; p = 0.988).

Table 8. Lesion Size vs Associated CT Findings

Finding	Mean size YES (mm)	Mean size NO (mm)	p-value
Nodules	54.4	46.5	0.084
Lymph nodes	54.4	46.5	0.084
Pleural effusion	50.8	490.760	
Far metastasis	50.0	490.988	

Subtype-specific analysis of emphysema found no significant differences in lesion dimensions (ANOVA p = 0.209; Kruskal–Wallis p = 0.190), with mean lesion sizes of 55.0 mm in centrilobular emphysema, 45.3 mm in paraseptal emphysema, and 56.8 mm in combined patterns. The identical p-values reflect substantial overlap between patients presenting with pulmonary nodules and lymph node involvement within the study cohort.

Table 9. Lesion Size by Emphysema Subtype

Emphysema subtype	Mean size (mm)
Centrilobular	55.0
Paraseptal	45.3
Combined	56.8

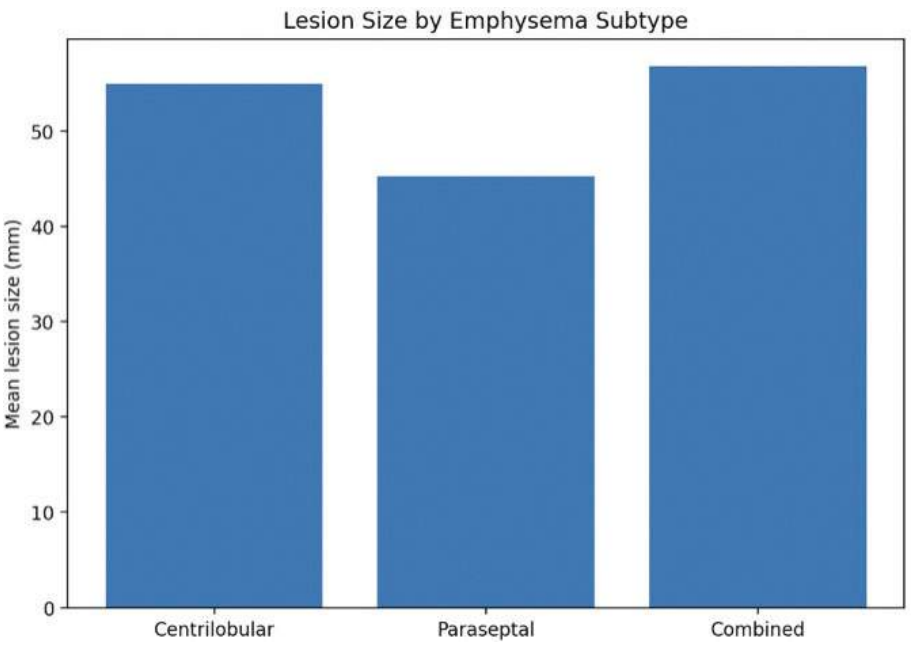

Figure 7.

Multivariable logistic regression analysis was performed to identify independent predictors of emphysema. Variables included sex, age, lesion size, upper-lobe location, and morphology. Male sex showed the strongest association with emphysema (OR ≈ 2.4), although the association did not reach statistical significance. Age, lesion size, morphology, and upper-lobe location were not

independently associated with emphysema presence. The model demonstrated modest explanatory power (Pseudo $R^2 = 0.066$), indicating that emphysema occurrence is likely influenced by factors beyond the analyzed imaging characteristics.

Table 10. Multivariable Logistic Regression (Predictors of Emphysema)

Variable	Association
Male sex	OR ≈ 2.4 (borderline)
Age	Not significant
Lesion size	Not significant
Morphology	Not significant
Upper-lobe location	Not significant
Model Pseudo R^2	0.066

Overall, across multiple comparative analyses, no statistically significant differences were identified in lesion size, morphology, or anatomical distribution between patients with and without emphysema. The only variable demonstrating a borderline association was male sex, suggesting that demographic characteristics may exert a greater influence on emphysema prevalence than imaging characteristics of pulmonary neoplastic lesions. The consistency of findings across independent statistical analyses supports the interpretation that emphysema primarily functions as a patient-level risk substrate and background risk condition, rather than a determinant or modifier of CT imaging phenotype.

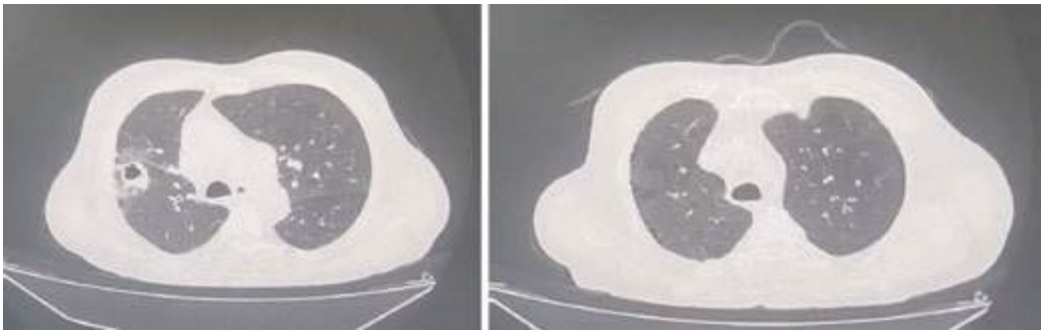

Image 1, Image 2. Axial HRCT image (lung window setting) showing a right side pulmonary neoplasm in the presence of mild paraseptal emphysema in a patient

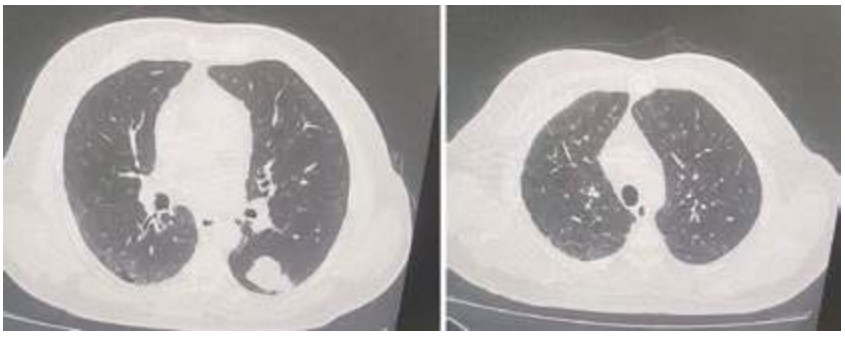

Image 3, Image 4. Axial HRCT image (lung window setting) showing a dense pulmonary neoplasm in the left lower lobe in the presence of mild centrilobular and paraseptal emphysematous changes.

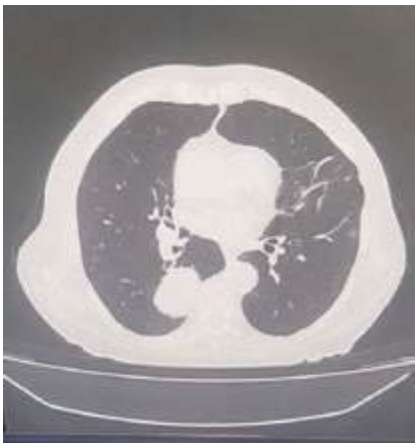

Image 5, Axial HRCT image (lung window setting) showing a pulmonary mass in a patient without radiological evidence of emphysema

Discussion

This study demonstrates a high coexistence of emphysema and lung neoplastic lesions, with emphysema identified in nearly half of patients undergoing CT evaluation for lung neoplasms. Although emphysema was highly prevalent, no statistically significant associations were observed between emphysema and tumor size, morphology, or anatomical distribution. These findings suggest that emphysema acts primarily as a background carcinogenic condition rather than a determinant of tumor phenotype.

The observed prevalence of emphysema among patients with lung carcinoma is consistent with findings from previous CT-based studies.

De Torres et al. reported that emphysema detected on low-dose CT was independently associated with an increased risk of lung, even after adjustment for smoking history (1). Similarly, Wilson et al. showed that radiographic emphysema is associated with increased incidence of lung cancer independent of airflow obstruction (2).

Large screening trials, such as the National Lung Screening Trial (NLST) and the NELSON study, confirmed the central role of CT in early detection of lung malignancies and highlighted structural lung abnormalities as important risk markers (3–5). Our findings extend these observations into a real-world tertiary pulmonology population, where prevalence rates are higher than those seen in screening cohorts. The relatively high prevalence observed in our tertiary institution may be attributed to several contributing factors, including the socioeconomic status of the population, insufficient health education, the absence of a structured lung cancer screening program, and the high smoking prevalence in Europe.

Centrilobular emphysema was the predominant subtype in our cohort, consistent with the CT-based emphysema classification proposed by the Fleischner Society (6). This subtype predominance likely reflects smoking-related small-airway destruction, which has been repeatedly associated with increased carcinogenic susceptibility.

Despite the strong coexistence of emphysema and cancer, subtype analysis demonstrated no significant differences in tumor size or distribution, including patients with combined (“both”)

emphysema patterns. This supports previous imaging studies suggesting that emphysema subtype may influence risk but not tumor characteristics (7).

Upper-lobe predominance observed in this cohort aligns with prior reports showing smoking-related tumors occurring more frequently in upper lung regions (8).

Regional differences in ventilation, perfusion, and carcinogen deposition have been proposed as possible explanations.

However, statistical analysis revealed no association between emphysema and lobar or segmental tumor location. This finding suggests that although emphysema and tumors frequently coexist in similar anatomical regions, emphysema itself does not determine where tumors develop.

The mean tumor size in our cohort (52.4 mm) reflects typical lesion size encountered in symptomatic clinical populations rather than screening cohorts. Polylobular lesions had larger mean dimensions than spiculated tumors, likely reflecting different growth stages.

Importantly, tumor dimensions did not differ between patients with and without emphysema, nor between emphysema subtypes. These findings are consistent with studies indicating that emphysema increases cancer risk but does not alter tumor growth kinetics or imaging phenotype (9).

One of the most important findings of this study is that patient factors were more strongly associated with emphysema than tumor-related characteristics. Male sex was associated with approximately 2.5-fold increased odds of emphysema, although the significance was borderline. Similar demographic patterns have been reported in epidemiologic studies of smoking-related lung disease (10).

Multivariable analysis confirmed that tumor morphology, size, and location were not independent predictors of emphysema. This supports the concept that emphysema primarily functions as a patient-level risk substrate.

Although statistically significant associations were not identified, the consistency of findings across multiple analyses suggests a stable biological pattern.

Rather than indicating absence of relevance, these results imply that emphysema contributes to carcinogenesis without modifying tumor behavior after malignant transformation.

This interpretation is increasingly supported by contemporary models of smoking-related lung injury, where chronic inflammation promotes cancer initiation but does not necessarily influence tumor phenotype (11-13).

From a radiologic perspective, emphysema should be regarded as an important contextual risk marker during CT interpretation. Radiologists should maintain increased vigilance in emphysematous lungs, yet apply identical morphologic criteria for malignancy evaluation regardless of emphysema subtype.

The high prevalence of emphysema observed in this cohort also has important implications for anesthesiologists involved in the perioperative management of patients undergoing thoracic surgery. Patients with emphysema are at increased risk of postoperative pulmonary complica-

tions, including respiratory failure, prolonged mechanical ventilation, persistent air leaks, and bronchopleural fistula formation following lung resection. Recognition of emphysema on preoperative CT, therefore, contributes not only to risk stratification but also to anesthetic planning. Protective intraoperative ventilation strategies, including lower tidal volumes, individualized positive end-expiratory pressure (PEEP), avoidance of dynamic hyperinflation and auto-PEEP, and careful monitoring for barotrauma, may be particularly important in this patient population. Consequently, CT assessment of emphysema provides clinically relevant information extending beyond oncologic characterization of pulmonary lesions.

Several limitations should be acknowledged: retrospective single-center design; moderate sample size; absence of quantitative smoking exposure data; segmental classification based on routine reporting terminology.

These factors may limit the detection of subtle associations.

This study confirms a high prevalence of emphysema among patients with lung neoplasms in a tertiary-care setting. However, emphysema was not associated with measurable differences in CT tumor phenotype.

The absence of smoking exposure data limits interpretation, as smoking represents the principal shared etiologic factor. Additionally, visual rather than quantitative assessment of emphysema may have reduced sensitivity for detecting subtle associations.

The study population consisted primarily of symptomatic patients with relatively large tumors, limiting generalizability to screening populations and early-stage disease. These findings suggest that while emphysema increases carcinogenic risk, it does not substantially modify established tumor morphology on CT within the constraints of this dataset. The consistency of findings across analyses supports a biologically coherent interpretation in which emphysema primarily acts as a background carcinogenic substrate rather than a modifier of tumor imaging phenotype (15).

Future prospective studies incorporating automated quantitative CT densitometry, including calculation of the percentage of lung volume below −950 HU, may provide a more precise assessment of emphysema burden and allow detection of subtle relationships between emphysema severity and tumor characteristics that could not be identified in the present study.

Conclusion

CT-based evaluation demonstrates a high prevalence of emphysema among patients with pulmonary neoplastic lesions, confirming the frequent coexistence of structural smoking-related lung disease and neoplastic imaging findings in routine clinical practice. Although emphysema was common, it was not associated with differences in lesion size, morphology, or anatomical distribution, indicating that underlying emphysematous change does not substantially modify CT imaging phenotype. These findings support the role of CT as an integrated diagnostic tool capable of simultaneously characterizing pulmonary lesions and background parenchymal abnormalities, emphasizing the importance of recognizing emphysema primarily as a patient-level risk context rather than an imaging determinant of lesion behavior.

Emphysema frequently coexists with pulmonary neoplastic lesions in routine clinical practice. Within the methodological limitations of this retrospective imaging-based study, no significant association was observed between emphysema and CT tumor phenotype. Future prospective studies incorporating quantitative CT analysis and detailed smoking exposure data are warranted.

Given the high prevalence of emphysema among patients with pulmonary neoplasms, recognition of emphysematous changes on preoperative CT may also provide valuable information for perioperative risk assessment and anesthetic management.

Declarations

Ethics approval and consent to participate: Protocol number – 01/2026

Informed consent: Written informed consent was obtained from all participants included in the study.

Conflict of Interest: The first author and all co-authors declare that they have no conflicts of interest related to this study.

Funding information: The author declares that no funding was received for this study.

Availability of data and materials: The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Author contributions statement: The First Author, K. D. contributed to study conception and design, data collection, image analysis, statistical analysis, interpretation of results and manuscript drafting. Co-author S. P. contributed to clinical data acquisition and manuscript analysis. Co-author D. K. contributed to the acquisition of clinical data and the analysis of the manuscript. Co-author I. A. contributed to the acquisition of clinical data and the analysis of the manuscript. Co-author S. M. contributed to clinical data acquisition and manuscript analysis.

Acknowledgments: None

Artificial Intelligence (AI) Statement AI tools - Artificial intelligence (AI) tools, were not used in the preparation of this manuscript.

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ORIGINAL ARTICLE *UDK: 616.711-089.168-009.7-085.212*

www.doi.org/10.67214/za07yq95

BILATERAL ERECTOR SPINAE PLANE BLOCK IN OPEN SPINAL FIXATION SURGERY: A COMPARATIVE STUDY OF SAFETY AND CLINICAL OUTCOMES

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Abstract

Objective: Open thoracic and lumbar spinal fixation surgery is associated with severe postoperative pain resulting from extensive tissue injury, muscle dissection, periosteal trauma, and instrumentation. Effective postoperative analgesia is essential for early mobilization and functional recovery. Regional anesthesia techniques have become increasingly important components of multimodal analgesic protocols aimed at reducing perioperative opioid exposure and opioid-related adverse effects. The primary objective of this study was to evaluate the safety profile of bilateral erector spinae plane block (ESPB) in patients undergoing open thoracic and lumbar spinal fixation surgery.

Secondary objectives included assessment of intraoperative and postoperative opioid requirements, postoperative pain intensity during the first 48 hours, length of hospital stay, postoperative nausea and vomiting.

Materials and Methods: We performed a comparative clinical study involving 100 patients scheduled for open thoracic or lumbar spinal fixation surgery. Patients were divided into two groups, each comprising 50 patients.

The opioid group (OG) received intermittent fentanyl-based analgesia, whereas the ESPB group (ESPBG) underwent bilateral ultrasound-guided erector spinae plane block with administration of 10 mL of 1% lidocaine and 20 mL of 0.25% bupivacaine on each side.

Postoperative pain intensity was assessed using the Numeric Rating Scale (NRS) at 1, 4, 8, 12, 24, 36, and 48 hours after surgery. Statistical analysis included Student's t-test, Mann–Whitney U test, Pearson chi-square analysis, Cramer's V coefficient, Friedman ANOVA, and Pearson correlation analysis.

Results: Compared with intermittent opioid analgesia, bilateral ESPB was associated with significantly lower fentanyl and tramadol consumption, lower postoperative pain scores, shorter

hospital stay, and reduced incidence of postoperative nausea and vomiting.

No major block-related complications were observed.

Conclusion: Bilateral erector spinae plane block demonstrated a favorable safety profile and significant opioid-sparing effects in patients undergoing spinal fixation surgery. These findings support the incorporation of ESPB into multimodal analgesic protocols and enhanced recovery pathways.

Keywords: *enhanced recovery after surgery; erector spinae plane block; fentanyl; multimodal analgesia; opioid consumption.*

Introduction

Open thoracic and lumbar spinal fixation surgery is associated with substantial postoperative pain due to extensive tissue injury, periosteal trauma, muscle dissection, instrumentation, and activation of inflammatory pathways (1,2). Inadequately controlled acute pain delays mobilization, impairs rehabilitation, prolongs hospital stay, and contributes to the development of persistent postsurgical pain (3,4).

Although opioids remain the cornerstone of perioperative analgesia, their use is limited by adverse effects such as postoperative nausea and vomiting, sedation, respiratory depression, ileus, urinary retention, opioid-induced hyperalgesia, and the risk of prolonged opioid exposure (2,5).

Consequently, contemporary perioperative pain management increasingly emphasizes multimodal analgesic strategies designed to minimize opioid consumption while maintaining adequate analgesia (6,7).

The erector spinae plane block (ESPB), first described by Forero et al. in 2016, represents a relatively novel ultrasound-guided interfascial plane block initially introduced for the treatment of thoracic neuropathic pain (8). Since its original description, the indications for ESPB have expanded considerably, including thoracic, breast, abdominal, cardiac, orthopedic, and spinal surgery (9-11).

The technique involves deposition of local anesthetic deep to the erector spinae muscle and superficial to the transverse process, resulting in cranio-caudal spread and multisegmental analgesia through effects on the dorsal and ventral rami of spinal nerves (12,13). Cadaveric and imaging studies have demonstrated extension of local anesthetic toward the paravertebral space and neural foramina, supporting the anatomical basis of the block (12).

Compared with epidural analgesia and paravertebral block, ESPB is technically simpler and potentially safer because the injection site is superficial and distant from the pleura, spinal cord, and major vascular structures (9,10,14). Therefore, ESPB has emerged as an attractive component of multimodal analgesic and Enhanced Recovery After Surgery (ERAS) protocols (6,7).

Several systematic reviews and meta-analyses have demonstrated that ESPB significantly reduces postoperative pain intensity and opioid consumption following lumbar spinal surgery (15-17). Similarly, randomized clinical studies have reported improved postoperative analgesia and decreased rescue opioid requirements after lumbar ESPB (18).

Nevertheless, despite growing evidence regarding the analgesic efficacy of ESPB, additional studies evaluating its safety profile and clinical outcomes in spinal fixation surgery remain necessary.

Therefore, the present study aimed to investigate the safety and clinical efficacy of bilateral erector spinae plane block in patients undergoing open thoracic and lumbar spinal fixation surgery.

Therefore, the present study aimed to investigate the safety and clinical efficacy of bilateral erector spinae plane block in patients undergoing open thoracic and lumbar spinal fixation surgery. The primary objective of the present study was to evaluate the safety profile of bilateral erector spinae plane block (ESPB) in patients undergoing open thoracic and lumbar spinal fixation surgery.

Secondary objectives included evaluation of: intraoperative fentanyl consumption; postoperative tramadol requirements; postoperative pain intensity during the first 48 hours; length of hospital stay; incidence of postoperative nausea and vomiting (PONV); occurrence of vertigo and nystagmus.

Materials and Methods

Study Design

The research is a randomized, prospective, interventional clinical study using parallel groups of randomly selected patients. A comparative clinical study involving 100 patients undergoing open thoracic or lumbar spinal fixation surgery was performed.

The randomization of patients was done using computer software that randomly allocated the study participants to one of the two groups (www.randomizer.org)

After induction of anesthesia, patients were divided into 2 groups:

- Group 1 (OG-opioid group): 50 patients who received intermittent opioid – fentanyl as analgesia
- Group 2 (ESPBG): 50 patients who received bilateral ESPB under ultrasound guidance after being placed in the prone position and marked with X-ray. The block was performed one level above the injury, using 10 ml Lidocaine 1% and 20 ml Bupivacaine 0.25% on each side.

Patients received Dexamethasone 0.1 mg/kg and 1 g. Paracetamol before induction of anesthesia (as preemptive analgesia). Immediately after intubation, an i.v. Ketamine 0.5 mg/kg and continuous intravenous (iv) infusion of Magnesium sulfate 1.5 g was given.

Fentanyl was added intermittently during surgery, if there was an increase in blood pressure (BP) and heart rate (HR) by over 20% of the initial (baseline) value without blood loss and sweating of the patient

Postoperative Analgesia

Patients from the opioid group (OG) for postoperative analgesia received amp. Metamizole 2 gr. every 12 hours and amp. Paracetamol 1 gr. every 8 hours.

Postoperatively, patients from group 2 (ESPBG) received a continuous intravenous 0.10 mg/kg/bw/hour Ketamine infusion for 48 hours, amp. Metamizole 2 g every 12 hours and amp Paracetamol 1 g every 8 hours. Amp. Dexamethasone 8 mg for 3 days, and another 3 days of 4 mg.

The NRS score at rest was monitored in each of the groups, and if the NRS score was above 7, Tramadol 100 mg was administered.

Patient Characteristics

Patients in both groups were classified according to the American Society of Anesthesiologists (ASA) physical status classification system.

The following demographic and perioperative variables were analyzed: age; sex; body mass index (BMI); fixation level; duration of surgery; postoperative pain intensity; opioid consumption; postoperative complications; duration of hospitalization.

Inclusion Criteria were: adult patients undergoing elective open thoracic or lumbar spinal fixation surgery; ASA physical status I–III; availability of complete perioperative and postoperative records.

Exclusion Criteria were: known allergy to local anesthetics; infection at the puncture site; coagulopathy or anticoagulant therapy contraindicating regional anesthesia; severe hepatic or renal dysfunction; incomplete clinical data.

Pain Assessment

Postoperative pain intensity was evaluated using the Numeric Rating Scale (NRS), where:

- 0 represented no pain;
- 10 represented the worst imaginable pain.

Measurements were obtained at: 1 hour; 4 hours; 8 hours; 12 hours; 24 hours; 36 hours; 48 hours after surgery.

Outcome Measures

Primary outcome were safety profile of bilateral ESPB. Secondary outcomes were: intraoperative fentanyl consumption; postoperative tramadol requirements; total tramadol dose; postoperative pain scores; length of hospital stay; postoperative nausea and vomiting; vertigo and nystagmus; chronic postoperative pain.

Statistical Analysis

Statistical analysis was performed using standard descriptive and inferential statistical methods. Continuous variables were expressed as mean ± standard deviation, minimum, and maximum values. Categorical variables were presented as absolute numbers and percentages. Comparisons between groups were performed using: Student's t-test; Mann–Whitney U test; Difference test; Pearson chi-square test; Cramer's V coefficient; Friedman analysis of variance (ANOVA); Pearson correlation analysis. A p value lower than 0.05 was considered statistically significant.

Results

Demographic and Operative Characteristics

A total of 100 patients were included in the study, with 50 patients in each group.

The groups were comparable with regard to age and duration of surgery. No statistically significant differences were observed between groups concerning baseline characteristics (Table 1.).

Table 1. Demographic and Operative Characteristics

Parameter	Opioid Group (n=50)	ESPB Group (n=50)	p value
Age (years)	51.9 ± 11.2 (21–78)	51.7 ± 14.1 (21–71)	0.918918
Operative duration (min)	201.8 ± 55.8 (150–400)	200.4 ± 51.5 (100–350)	0.896568
Male sex	37 (74.0%)	28 (56.0%)	0.0592
Female sex	13 (26.0%)	22 (44.0%)	0.0592

Distribution of Instrumented Levels The most commonly instrumented vertebral levels were L1 and Th12 (Table 2).

Table 2. Distribution of Fixation Levels

Level	Opioid Group n (%)	ESPB Group n (%)
L1	16 (32.0%)	22 (44.0%)
L2	8 (16.0%)	6 (12.0%)
L3	3 (6.0%)	4 (8.0%)
L4	4 (8.0%)	3 (6.0%)
L5	0	1 (2.0%)
Th3	1 (2.0%)	1 (2.0%)
Th4	1 (2.0%)	0
Th7	1 (2.0%)	1 (2.0%)
Th8	1 (2.0%)	1 (2.0%)
Th10	3 (6.0%)	0
Th11	1 (2.0%)	3 (6.0%)
Th12	11 (22.0%)	8 (16.0%)

Opioid Consumption

Patients receiving bilateral ESPB required significantly lower doses of fentanyl and tramadol (Table 3).

Table 3. Fentanyl and Tramadol Consumption

Parameter	Opioid Group	ESPB Group	p value
Fentanyl (μg)	480.0 ± 76.9	113.0 ± 24.3	<0.001
In-hospital tramadol (mg)	1010.0 ± 548.9	222.0 ± 154.2	<0.001
Total tramadol dose (mg)	412.0 ± 96.1	128.6 ± 48.8	0.000057

Postoperative Pain Intensity

Pain scores were significantly lower in the ESPB group throughout the first 48 postoperative hours (Table 4.)

Table 4. Postoperative NRS Pain Scores

Time after surgery	Opioid Group	ESPB Group	p value
1 hour	6.5 ± 0.8	3.2 ± 1.8	<0.001
4 hours	7.3 ± 0.6	4.1 ± 1.2	<0.001
8 hours	7.2 ± 0.7	4.1 ± 1.4	<0.001
12 hours	6.4 ± 0.9	3.6 ± 1.4	<0.001
24 hours	5.6 ± 0.9	3.0 ± 1.0	<0.001
36 hours	4.8 ± 0.7	2.7 ± 1.0	<0.001
48 hours	4.3 ± 0.8	2.6 ± 1.0	<0.001

Friedman ANOVA demonstrated a statistically significant reduction in pain scores over time in both groups ($p < 0.001$).

Length of Hospital Stay

Hospital stay was significantly shorter in patients receiving ESPB (Table 5.).

Table 5. Length of Hospital Stay

Parameter	Opioid Group	ESPB Group	p value
Hospital stay (days)	13.0 ± 3.9	10.1 ± 4.0	0.000561

Adverse Events and Safety Outcomes

Postoperative nausea and vomiting occurred significantly less in the ESPB group (Table 6.).

Table 6. Adverse Events

Outcome	Opioid Group	ESPB Group	p value
PONV – Yes	13 (26.0%)	5 (10.0%)	0.0373
PONV – No	37 (74.0%)	45 (90.0%)	0.0373
Vertigo/Nystagmus – Yes	1 (2.0%)	5 (10.0%)	0.0921
Vertigo/Nystagmus – No	49 (98.0%)	45 (90.0%)	0.0921

No severe block-related complications, including infection, hematoma, neurological deterioration, or local anesthetic systemic toxicity were observed.

Moderate positive correlations were identified between tramadol consumption and duration of hospital stay (Table 7.).

Table 7. Correlation Analysis

Correlation	r	p value
Tramadol consumption vs. hospital stay (OG)	0.4606	0.001
Tramadol consumption vs. hospital stay (ESPBG)	0.4605	0.001
Fentanyl dose vs. BMI (OG)	0.2891	0.042
Fentanyl dose vs. BMI (ESPBG)	-0.0064	0.965

Discussion

The present study demonstrated that bilateral erector spinae plane block (ESPB) provided superior postoperative analgesia and significant opioid-sparing effects in patients undergoing open thoracic and lumbar spinal fixation surgery. Compared with conventional intermittent opioid analgesia, patients receiving ESPB experienced significantly lower fentanyl and tramadol consumption, reduced postoperative pain scores, shorter hospital stay, and a lower incidence of postoperative nausea and vomiting.

The findings of the present investigation are consistent with the growing body of evidence supporting the use of ESPB in spine surgery and other major procedures (8,9,15,19).

Open spinal fixation surgery is associated with extensive tissue injury and activation of inflammatory pathways, resulting in severe postoperative pain (1,2). Inadequately controlled acute pain may impair rehabilitation and contribute to the development of chronic postsurgical pain through mechanisms involving peripheral and central sensitization (3,4).

The most prominent finding of the present study was the marked reduction in intraoperative fentanyl requirements. Mean fentanyl consumption in the ESPB group was approximately four times lower than that observed in the opioid group. These findings are consistent with the report by Chin and Lewis, who demonstrated successful opioid-free posterior spinal fusion surgery using ESPB as part of a multimodal analgesic regimen (19).

Similarly, Oh et al. performed a systematic review and meta-analysis and concluded that ESPB significantly reduced opioid consumption and postoperative pain intensity after lumbar spine surgery (15). Comparable results were reported by Fu et al., whose meta-analysis showed improved postoperative analgesia and lower opioid requirements in patients receiving ESPB (16).

More recently, Wilson et al. confirmed that ESPB significantly decreases cumulative opioid consumption and pain intensity following lumbar spine procedures (17). Likewise, randomized controlled studies conducted by Zhao et al. demonstrated superior analgesic efficacy and reduced rescue analgesic requirements after lumbar ESPB (18).

The mechanism of action of ESPB remains incompletely understood. Cadaveric and radiological investigations suggest cranio-caudal spread of local anesthetic with extension toward the dorsal rami, ventral rami, and paravertebral space (12,13). These anatomical characteristics explain ESPB's ability to provide multisegmental analgesia. Interfascial plane blocks have become essential components of modern regional anesthesia practice (14).

The favorable safety profile observed in our study deserves particular emphasis. No severe complications, including local anesthetic systemic toxicity, infection, hematoma formation, or neurological deterioration, were identified. Similar findings have been reported by Oezel et al., who reported a very low incidence of procedure-specific complications after lumbar ESPB (20).

The absence of major adverse events may be explained by the anatomical characteristics of the block. In contrast to epidural analgesia and paravertebral block, ESPB is performed in a superficial fascial plane remote from major vascular structures, pleura, and the neuraxis (9,10). Consequently, the technique is generally considered technically simple and relatively safe (10).

Patients receiving ESPB also experienced a significantly lower incidence of postoperative nausea and vomiting. This finding most likely reflects reduced opioid exposure. Opioid-related adverse effects remain among the principal obstacles to enhanced postoperative recovery (2,5).

The approximately three-day reduction in hospital stay observed in our study is clinically important. Enhanced Recovery After Surgery (ERAS) programs emphasize multimodal analgesia, opioid minimization, and early mobilization as key factors contributing to improved surgical outcomes (6,7). Kehlet and colleagues have repeatedly highlighted the importance of effective analgesia in promoting postoperative recovery and reducing morbidity (1,4,7).

Persistent postsurgical pain represents a significant long-term complication following spinal surgery (3,4). Chronic pain is believed to result from sustained nociceptive input and central sensitization mechanisms. Adequate perioperative analgesia and reduction of opioid exposure may contribute to lowering the incidence of chronic pain, although further prospective studies are necessary to confirm this hypothesis.

The moderate positive correlation observed between tramadol consumption and duration of hospital stay suggests that increased analgesic requirements may be associated with delayed recovery. Similar associations between pain severity and prolonged hospital stay have been reported in previous investigations (1,2).

Overall, the present study supports the integration of bilateral ESPB into multimodal perioperative analgesic protocols and ERAS pathways for spinal surgery. The technique provided effective analgesia, reduced opioid consumption, decreased opioid-related adverse effects, and demon-

strated a favorable safety profile consistent with contemporary literature (15–19).

Clinical Implications

The results of the present study have several important clinical implications.

First, bilateral ESPB may be incorporated into standardized multimodal analgesic protocols for thoracic and lumbar spinal fixation surgery.

Second, reduction of opioid consumption may decrease opioid-related complications and facilitate earlier mobilization and rehabilitation.

Third, the favorable safety profile observed in the present study supports broader implementation of ultrasound-guided ESPB in routine clinical practice.

Finally, integration of ESPB into ERAS pathways may contribute to shorter hospital stay and improved postoperative outcomes.

Study Limitations

Several limitations should be acknowledged.

First, the present study was based on aggregated statistical data and lacked complete access to individual patient-level variables.

Second, standardization of surgical procedures and postoperative rehabilitation protocols was limited.

Third, rare complications could not be adequately assessed because of the relatively small sample size.

Nevertheless, despite these limitations, the consistency of the results across multiple clinical outcomes strongly supports the beneficial effects of bilateral ESPB.

Conclusion

Bilateral erector spinae plane block demonstrated a favorable safety profile and significant analgesic efficacy in patients undergoing open thoracic and lumbar spinal fixation surgery.

Compared with intermittent opioid analgesia, ESPB was associated with significantly lower fentanyl and tramadol requirements, lower postoperative pain scores during the first 48 hours, shorter hospital stay, and reduced incidence of postoperative nausea and vomiting. No major block-related complications were observed.

These findings support the incorporation of bilateral ESPB into multimodal perioperative analgesic protocols and Enhanced Recovery After Surgery programs for spinal fixation procedures.

Further prospective randomized studies with larger patient populations are warranted to confirm these findings and to evaluate long-term outcomes.

Declarations

Ethics approval and consent to participate: The study has approval from the Ethics Committee for Research on Humans at the Faculty of Medicine - Skopje, approval no. 03-2031/9 dated 16.04.2024 The present study was performed using anonymized clinical and statistical data without personal identifiers. The investigation was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki and Good Clinical Practice guidelines.

Informed consent: Written informed consent was obtained from all participants included in the study.

Conflict of Interest: The author declares that there are no conflicts of interest related to this study.

Funding: No external funding was received for the conduct of this study, preparation of the manuscript, or publication of the results.

Availability of data and materials: The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Authors' contributions: A.D contributed to the study design, data collection, analysis, interpretation of results, and manuscript preparation.

Acknowledgments: The author would like to express gratitude to all colleagues and healthcare professionals involved in the perioperative management and postoperative care of patients included in this study.

Special appreciation is extended to the members of the surgical, anesthesiology, and intensive care teams for their dedication to the successful treatment of these patients.

Artificial Intelligence (AI) statement: ChatGPT (OpenAI) was used exclusively for language translation and linguistic editing of the manuscript. The authors reviewed and edited the output as necessary and take full responsibility for the content of the manuscript.

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REVIEW ARTICLE *UDK: 616.3-089:616.15*

www.doi.org/10.67214/dwrdp339

HEMODYNAMIC MONITORING AND GOAL-DIRECTED THERAPY IN MAJOR ABDOMINAL SURGERY: CURRENT CONCEPTS AND FUTURE DIRECTIONS

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Abstract

Objective: Major abdominal surgery is frequently associated with substantial physiological stress, fluid shifts, inflammatory activation, and perioperative hemodynamic instability, all of which may contribute to postoperative organ dysfunction and increased morbidity.

Over recent decades, perioperative hemodynamic management has evolved from reliance on static physiological variables toward individualized, physiology-driven optimization strategies.

Materials and Methods: This narrative review summarizes current concepts in perioperative hemodynamic monitoring and GDT in major abdominal surgery. The physiological basis of tissue perfusion, preload responsiveness, and cardiovascular optimization is discussed together with the clinical role of static and dynamic monitoring variables, including mean arterial pressure, central venous pressure, lactate, pulse pressure variation, stroke volume variation, and passive leg raising. Contemporary monitoring technologies such as arterial waveform analysis, minimally invasive cardiac output monitoring, and perioperative echocardiography are also reviewed.

Discussion: Contemporary perioperative medicine increasingly integrates dynamic hemodynamic monitoring, minimally invasive cardiac output assessment, arterial waveform analysis, ultrasound-based evaluation, and goal-directed therapy (GDT) protocols to optimize tissue perfusion while avoiding both hypovolemia and fluid overload. Current evidence suggests that individualized GDT strategies integrating fluids, vasopressors, and inotropic therapy may reduce postoperative complications, shorten hospital stay, and optimize perioperative outcomes in selected abdominal surgery populations. Emerging technologies including artificial intelligence, predictive analytics, and machine learning-assisted monitoring systems may further transform future perioperative management through precision-based physiological optimization.

Conclusion: Current evidence suggests that individualized GDT strategies integrating fluids, vasopressors, and inotropic therapy may reduce postoperative complications, shorten hospital stay, and optimize perioperative outcomes in selected abdominal surgery populations.

Keywords: *Dynamic hemodynamic monitoring; fluid responsiveness; goal-directed therapy; hemodynamic monitoring; major abdominal surgery; perioperative medicine.*

Introduction

Major abdominal surgery remains associated with significant perioperative morbidity and mortality despite major advances in surgical techniques, anesthetic management, and perioperative care pathways. Procedures involving the gastrointestinal, hepatobiliary, colorectal, and upper abdominal systems are characterized by substantial physiological stress, intravascular fluid redistribution, inflammatory activation, vasodilation, blood loss, and perioperative cardiovascular instability. These alterations may impair tissue perfusion and oxygen delivery, thereby contributing to postoperative complications such as acute kidney injury, pulmonary dysfunction, postoperative ileus, prolonged hospitalization, sepsis, and increased mortality (1).

Over the last several decades, perioperative medicine has undergone a major transition from traditional empiric fluid administration toward physiology-driven hemodynamic optimization. Historically, perioperative management relied predominantly on static physiological variables such as mean arterial pressure (MAP), heart rate, central venous pressure (CVP), urine output, and serum lactate. Although these variables remain clinically important, accumulating evidence has demonstrated that static indices often fail to accurately predict intravascular volume status, tissue perfusion, or fluid responsiveness (2).

This limitation has contributed to the emergence of dynamic hemodynamic monitoring and goal-directed therapy (GDT).

Goal-directed therapy refers to the use of predefined physiological targets to optimize tissue oxygen delivery and organ perfusion through individualized administration of fluids, vasopressors, and inotropic agents. Multiple randomized controlled trials and meta-analyses have evaluated the role of GDT in major abdominal surgery, demonstrating variable but generally favorable effects on postoperative morbidity, gastrointestinal recovery, and length of hospital length (3–5).

Modern perioperative management increasingly emphasizes individualized physiology-based optimization rather than generalized hemodynamic thresholds. Dynamic monitoring variables such as pulse pressure variation (PPV), stroke volume variation (SVV), cardiac output (CO), cardiac index (CI), and tissue oxygenation assessment are progressively replacing traditional static variables in high-risk surgical populations (6). In parallel, substantial technological advances have expanded perioperative monitoring capabilities through minimally invasive cardiac output systems, arterial waveform analysis, esophageal Doppler monitoring, microcirculatory assessment, and artificial intelligence-assisted predictive analytics.

Recent developments involving predictive monitoring systems such as the Hypotension Prediction Index (HPI) reflect a broader transition from reactive hemodynamic correction toward anticipatory hemodynamic optimization (7). Furthermore, enhanced recovery after surgery (ERAS) protocols have integrated perioperative hemodynamic optimization into multimodal recovery pathways aimed at reducing complications and accelerating postoperative rehabilitation (8).

The contemporary framework of perioperative hemodynamic optimization is illustrated in Figure 1, which summarizes the interaction between surgical stress, physiological determinants of

tissue perfusion, monitoring strategies, therapeutic interventions, and postoperative outcomes.

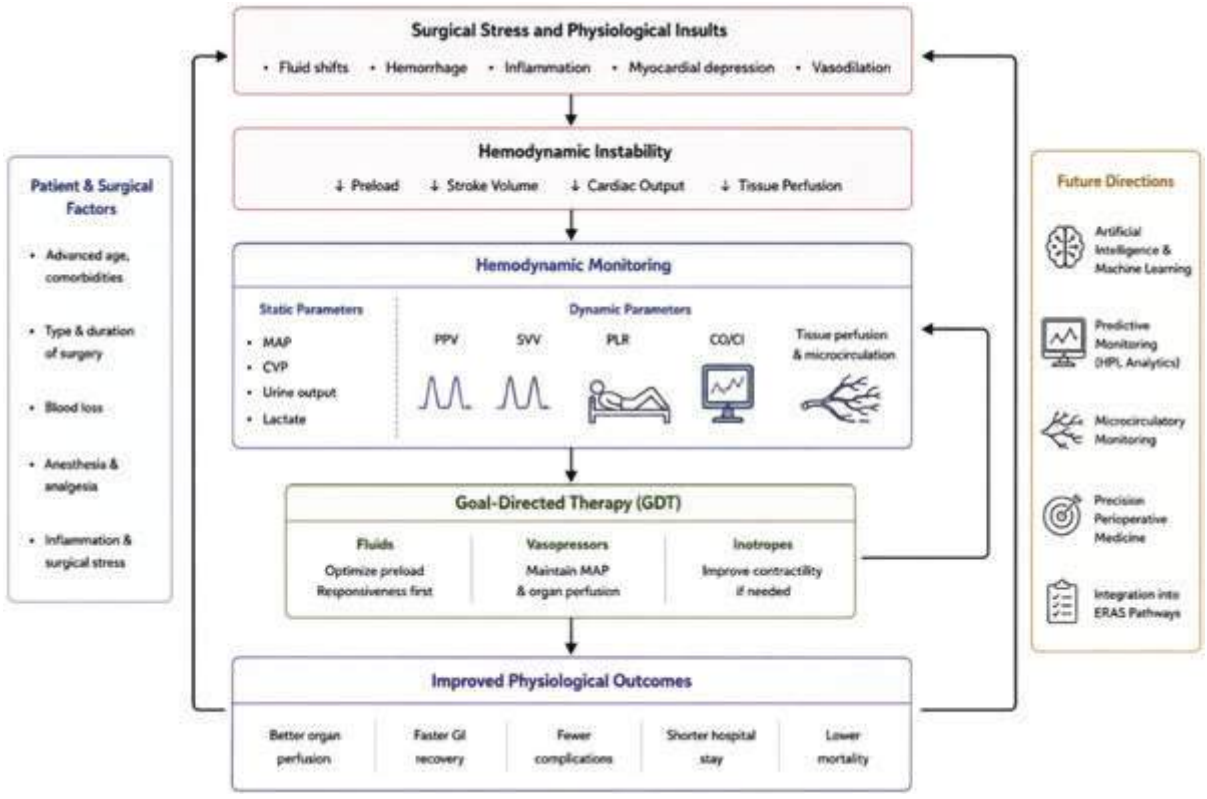

Figure 1. Conceptual framework of perioperative hemodynamic monitoring and goal-directed therapy in major abdominal surgery.

Major abdominal surgery causes physiological stress responses that may lead to hemodynamic instability and impaired tissue perfusion. Contemporary perioperative management combines static and dynamic hemodynamic monitoring to guide individualized goal-directed therapy with fluids, vasopressors, and inotropes. Emerging technologies, including artificial intelligence and predictive analytics, may further improve perioperative hemodynamic optimization and postoperative outcomes.

The objective of this review is to summarize current concepts in perioperative hemodynamic monitoring and goal-directed therapy in major abdominal surgery, with particular emphasis on physiological principles, dynamic monitoring modalities, monitoring technologies, clinical evidence, ERAS integration, and future directions involving artificial intelligence and precision perioperative medicine.

Discussion

Physiological Basis of Hemodynamic Monitoring

- Oxygen Delivery and Tissue Perfusion

The primary objective of perioperative hemodynamic management is preservation of adequate tissue oxygenation and organ perfusion. During major abdominal surgery, physiological home-

ostasis may be substantially disrupted through sympathetic activation, inflammatory cytokine release, vasodilation, blood loss, endothelial dysfunction, and intravascular fluid shifts. These alterations directly influence oxygen delivery and tissue metabolism. Oxygen delivery (DO2) represents the amount of oxygen transported to tissues per minute and depends primarily on cardiac output and arterial oxygen content. Oxygen delivery may be expressed mathematically as: When oxygen delivery becomes insufficient relative to tissue metabolic demand, anaerobic metabolism ensues, leading to lactate accumulation, mitochondrial dysfunction, cellular injury, and, ultimately, organ failure. Consequently, modern perioperative hemodynamic management focuses not only on maintaining blood pressure but also on ensuring sufficient global and regional tissue perfusion. Major abdominal surgery is associated with considerable hemodynamic instability due to anesthesia-induced vasodilation, fluid redistribution into the interstitial space, blood loss, and inflammatory activation (9).

Excessive perioperative hypotension may compromise renal, intestinal, hepatic, and myocardial perfusion, thereby increasing postoperative morbidity.

Goal-directed therapy attempts to maintain physiological equilibrium by optimizing preload, stroke volume, cardiac output, and oxygen delivery while simultaneously minimizing unnecessary fluid administration and tissue edema. Meta-analyses have demonstrated improved postoperative recovery and reduced complications when hemodynamic optimization is guided by dynamic physiological assessment rather than empiric fluid administration alone (3,4,10).

The relationship between surgical stress, oxygen delivery, hemodynamic monitoring, and postoperative outcomes is illustrated in Figure 1.

- Preload, Afterload, Cardiac Output

Cardiac output is determined by preload, afterload, contractility, and heart rate, all of which are essential components of perioperative hemodynamic management. Preload reflects ventricular filling and intravascular volume status, while excessive preload may contribute to pulmonary and bowel edema. Afterload represents ventricular resistance during systole and is primarily influenced by systemic vascular resistance and arterial pressure. Contractility reflects myocardial performance independent of loading conditions and may be impaired during anesthesia, inflammation, ischemia, or sepsis. Importantly, hypotension does not necessarily indicate hypovolemia, nor does normal blood pressure guarantee adequate tissue perfusion, which explains the limitations of static hemodynamic variables alone (1,2). Consequently, contemporary perioperative management increasingly utilizes dynamic monitoring techniques to assess preload responsiveness and guide individualized hemodynamic optimization.

- Microcirculation and Organ Perfusion

Recently, there has been growing attention focused on the role of microcirculation in perioperative physiology. Even when macrohemodynamic parameters such as MAP and cardiac output appear preserved, impaired microvascular flow may compromise oxygen delivery and tissue utilization. Microcirculatory dysfunction may result from endothelial injury, inflammatory activation, capillary leakage, vasoconstriction, or impaired autoregulation, potentially contributing to organ dysfunction despite apparently adequate systemic hemodynamics. Flick et al. (11) found significant alterations in sublingual microcirculation during major abdominal surgery, highlighting the potential disconnect between systemic hemodynamics and tissue-level perfusion.

Similarly, Coeckelenbergh et al. (12) observed improved microvascular flow during assisted fluid management in high-risk abdominal surgery.

These findings suggest that future perioperative management may increasingly incorporate microcirculatory endpoints in addition to traditional macrohemodynamic variables.

Static Hemodynamic Parameters

- Central Venous Pressure

Central venous pressure (CVP) has historically been one of the most commonly used perioperative hemodynamic variables and was traditionally considered a surrogate marker of preload and intravascular volume status. Consequently, perioperative fluid administration strategies frequently relied on predefined CVP targets, particularly in critically ill and high-risk surgical patients.

However, accumulating physiological and clinical evidence has challenged the reliability of CVP as an indicator of fluid responsiveness.

Numerous investigations have demonstrated poor correlation between CVP values and actual intravascular volume status or cardiac preload responsiveness (2). Static filling pressures are strongly influenced by ventricular compliance, venous tone, intrathoracic pressure, mechanical ventilation, right ventricular function, and pulmonary vascular resistance. As a result, patients with similar CVP values may exhibit markedly different responses to fluid administration.

The limited ability of CVP to predict fluid responsiveness contributed to the transition toward dynamic hemodynamic monitoring.

Elevated CVP does not necessarily indicate adequate preload, while low values do not always imply hypovolemia. Moreover, excessive fluid administration targeting arbitrary CVP thresholds may increase postoperative morbidity through pulmonary and bowel edema.

Despite these limitations, CVP monitoring may still provide useful contextual physiological information in selected high-risk surgical populations. In patients with severe cardiovascular disease, pulmonary hypertension, major fluid shifts, or right ventricular dysfunction, CVP trends may contribute to overall hemodynamic assessment when interpreted alongside additional physiological variables. Nevertheless, contemporary perioperative guidelines emphasize that CVP should not be used in isolation to guide fluid therapy decisions (1). The decline in routine CVP-guided therapy reflects a broader shift from static physiological assessment to dynamic, individualized hemodynamic optimization. Modern perioperative medicine increasingly prioritizes direct assessment of fluid responsiveness and tissue perfusion rather than reliance on isolated static preload variables.

- Mean Arterial Pressure

Mean arterial pressure (MAP) remains one of the most important perioperative hemodynamic parameters because adequate arterial pressure is essential for maintaining organ perfusion during major surgery. Sustained intraoperative hypotension has been associated with postoperative myocardial injury, acute kidney injury, stroke, and increased mortality. However, universal blood pressure thresholds may not be appropriate for all patients, as individuals with chronic

hypertension, diabetes, or vascular disease may require higher perfusion pressures to maintain adequate organ blood flow (13).

Therefore, recent perioperative investigations have increasingly explored individualized blood pressure management strategies. The IMPROVE-multi randomized clinical trial evaluated individualized perioperative blood pressure targets in major abdominal surgery, reflecting growing interest in patient-specific hemodynamic optimization (11). Although individualized strategies remain an evolving area of research, these investigations emphasize the limitations of rigid universal MAP thresholds.

Intraoperative hypotension may result from vasodilation, hypovolemia, blood loss, myocardial depression, or inflammatory vasoplegia. Importantly, treatment requires identifying the underlying physiological disturbance rather than indiscriminate fluid administration, as excessive crystalloids may worsen tissue edema and postoperative recovery. Contemporary perioperative management, therefore, increasingly combines arterial pressure monitoring with dynamic assessment of stroke volume, cardiac output, and tissue perfusion to guide individualized use of fluids, vasopressors, and inotropes.

The emergence of predictive technologies such as the Hypotension Prediction Index further illustrates the growing importance of arterial pressure monitoring in modern perioperative medicine.

These systems aim to identify impending hypotension before clinically significant hemodynamic deterioration develops, thereby enabling proactive intervention (7).

- Urine Output

Urine output remains a widely used indicator of organ perfusion and intravascular status in perioperative medicine. Although oliguria during major abdominal surgery traditionally prompted aggressive fluid administration, contemporary understanding recognizes that urine output is influenced by multiple physiological factors beyond hypovolemia, including sympathetic activation, hormonal responses, inflammation, and reduced renal perfusion pressure. Consequently, oliguria may occur without true volume depletion, while preserved urine output does not necessarily guarantee adequate tissue perfusion.

Excessive fluid administration solely in response to transient oliguria may contribute to positive fluid balance, pulmonary edema, bowel edema, impaired wound healing, and delayed gastrointestinal recovery. Egger et al. (14) found an association between intraoperative fluid balance and perioperative complications in major oncologic surgery, further emphasizing the importance of balanced fluid management.

Current perioperative management therefore evaluates urine output within the broader context of overall hemodynamic assessment, including dynamic monitoring variables and tissue perfusion indicators. Although urine output remains clinically useful as a marker of renal perfusion and function, contemporary perioperative medicine discourages isolated interpretation of oliguria as an indication for indiscriminate fluid administration.

- Lactate

Serum lactate is an important marker of tissue perfusion and metabolic stress in perioperative medicine. Although elevated lactate traditionally indicates anaerobic metabolism from inad-

equate oxygen delivery, it may also result from adrenergic stimulation, impaired clearance, or inflammatory activation. During major abdominal surgery, persistent hyperlactatemia has been associated with postoperative complications, organ dysfunction, prolonged hospitalization, and mortality. Contemporary perioperative management therefore evaluates serial lactate trends within integrated hemodynamic assessment, as elevated lactate may occur despite apparently preserved systemic hemodynamics due to occult tissue hypoperfusion or microcirculatory dysfunction (11,12).

Dynamic Hemodynamic Monitoring

- Pulse Pressure Variation

Pulse pressure variation (PPV) is one of the most extensively studied dynamic predictors of fluid responsiveness in perioperative medicine. It reflects respiratory-induced changes in arterial pulse pressure during positive pressure ventilation caused by heart-lung interactions. During inspiration, increased intrathoracic pressure transiently reduces venous return and ventricular preload, leading to fluctuations in stroke volume and arterial pulse pressure. These variations are more pronounced in preload-responsive patients and attenuated in patients operating on the flat portion of the Frank-Starling curve.

PPV has consistently demonstrated superior predictive accuracy compared with static preload variables such as CVP. Salzwedel et al. (6) conducted a multicenter prospective randomized study that showed a reduction in postoperative complications with PPV-guided goal-directed therapy during major abdominal surgery.

Similarly, Cesur et al. (15) reported improved intraoperative fluid optimization with pleth variability index-guided therapy in colorectal surgery. Ochiai et al. (16) additionally demonstrated variability between pulse wave transit time-derived stroke volume variation and arterial waveform-derived measurements, emphasizing the importance of cautious interpretation when integrating advanced arterial waveform technologies into perioperative decision-making.

The advantages of PPV include continuous real-time assessment of fluid responsiveness and integration into arterial waveform monitoring systems commonly used during high-risk surgery. PPV-guided fluid optimization may help avoid both hypovolemia and unnecessary fluid administration.

However, accurate interpretation requires controlled mechanical ventilation, sinus rhythm, adequate tidal volume, and preserved chest wall compliance, while arrhythmias, spontaneous breathing activity, and elevated intra-abdominal pressure may reduce reliability. Despite these limitations, PPV remains a key component of contemporary goal-directed therapy protocols.

- Stroke Volume Variation

Stroke volume variation (SVV) is another major dynamic parameter used to predict fluid responsiveness during major surgery. SVV measures cyclic respiratory-induced fluctuations in stroke volume occurring during positive pressure ventilation. Similar to PPV, SVV exploits cardiopulmonary interactions to identify preload-responsive patients.

The physiological rationale underlying SVV monitoring is based on the observation that mechanically ventilated patients with preload dependency exhibit substantial respiratory changes

in ventricular filling and stroke volume.

High SVV values generally suggest that cardiac output may increase following fluid administration, whereas low SVV values imply limited preload responsiveness. Li et al. (17) demonstrated the predictive value of SVV during gastrointestinal surgery, while Sun et al. (18) reported shorter hospital stays and improved postoperative gastrointestinal recovery with SVV-guided fluid optimization in major abdominal surgery. These findings support the growing role of SVV-guided therapy within contemporary perioperative hemodynamic management.

SVV-guided strategies may improve perioperative care by promoting individualized fluid optimization and reducing unnecessary crystalloid administration, which has been associated with bowel edema, pulmonary complications, delayed gastrointestinal recovery, and prolonged hospital stays.

Modern minimally invasive monitoring systems increasingly integrate continuous SVV analysis with cardiac output estimation and arterial waveform interpretation to enable real-time hemodynamic assessment. However, SVV reliability may be reduced by arrhythmias, spontaneous respiratory effort, low-tidal-volume ventilation, or altered thoracic compliance (16,17).

- Passive Leg Raising

Passive leg raising (PLR) is a reversible endogenous fluid challenge that transiently increases venous return without intravenous fluid administration. A positive hemodynamic response suggests preload responsiveness, whereas the absence of significant cardiac output augmentation indicates limited benefit from additional fluids. PLR is especially useful when PPV or SVV become unreliable, including spontaneous breathing activity, arrhythmias, or low tidal volume ventilation (1).

- Fluid Responsiveness

Fluid responsiveness is a central concept of modern goal-directed therapy and refers to the ability of cardiac output or stroke volume to increase following fluid administration. Importantly, not all hypotensive patients are preload responsive, and unnecessary fluid administration may contribute to pulmonary dysfunction, bowel edema, impaired oxygen diffusion, and delayed recovery.

Therefore, contemporary perioperative medicine increasingly prioritizes identification of patients likely to benefit from fluid administration using dynamic monitoring variables such as PPV, SVV, PLR response, together with cardiac output assessment, rather than empiric fluid loading (3,6).

Static hemodynamic variables remain useful for general cardiovascular assessment; however, contemporary perioperative medicine increasingly prioritizes dynamic monitoring parameters because of their superior ability to predict fluid responsiveness and guide individualized hemodynamic optimization.

A comparative overview of static and dynamic hemodynamic monitoring modalities is presented in Figure 2.

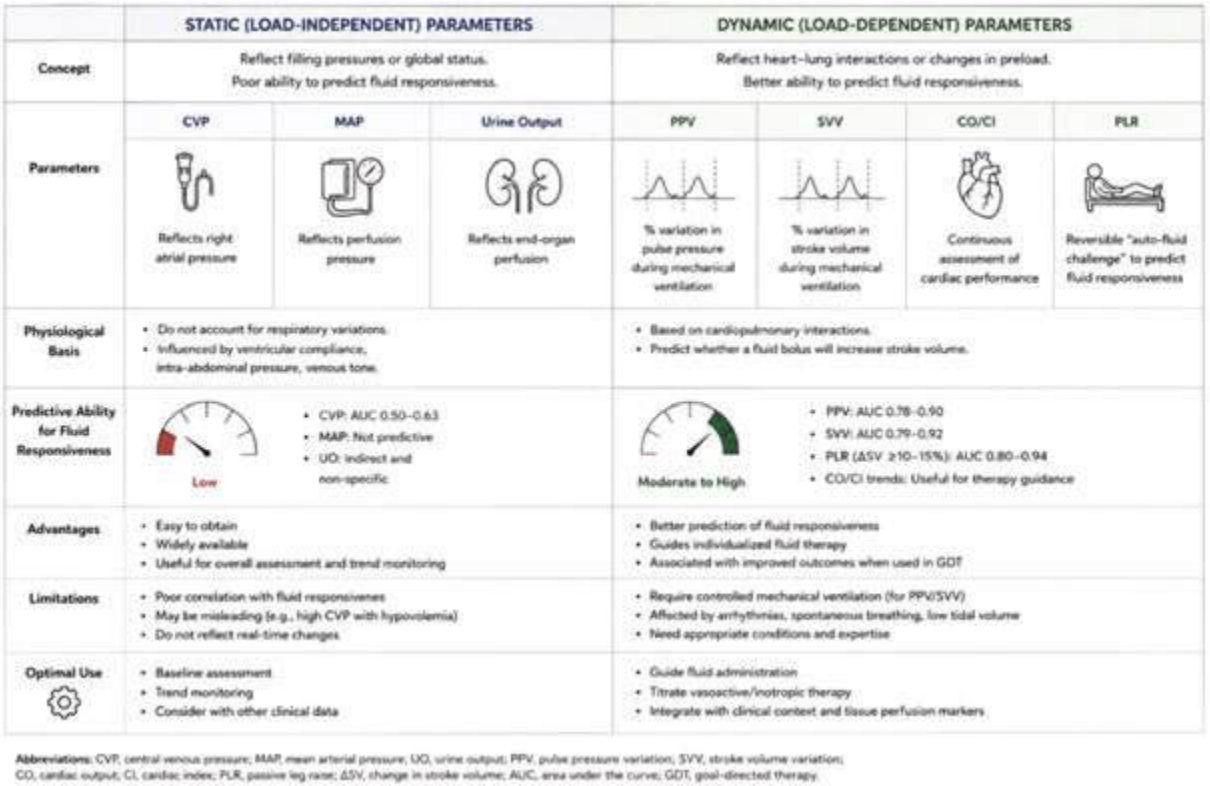

Figure 2. Comparison of static and dynamic hemodynamic monitoring parameters in perioperative goal-directed therapy.

Static hemodynamic parameters such as central venous pressure (CVP), mean arterial pressure (MAP), and urine output provide general physiological information but have limited ability to predict fluid responsiveness. Dynamic parameters, including pulse pressure variation (PPV), stroke volume variation (SVV), passive leg raising (PLR), and cardiac output/cardiac index (CO/CI) assessment, are based on cardiopulmonary interactions and provide superior prediction of preload responsiveness and individualized fluid optimization. Contemporary perioperative goal-directed therapy increasingly integrates dynamic monitoring strategies to improve tissue perfusion and postoperative outcomes (1,3,4).

Goal-Directed Therapy (GDT)

Principles of GDT

Goal-directed therapy (GDT) is a structured perioperative hemodynamic strategy that optimizes tissue perfusion and oxygen delivery by setting individualized physiological targets. Unlike traditional empirical fluid administration, GDT integrates continuous hemodynamic monitoring with protocolized fluid, vasopressor, and inotrope administration.

The concept emerged from the recognition that perioperative hypoperfusion contributes substantially to postoperative organ dysfunction, including acute kidney injury, pulmonary complications, myocardial injury, bowel dysfunction, and prolonged hospital stay. Therefore, cContemporary perioperative medicine increasingly emphasizes individualized hemodynamic optimization guided by dynamic monitoring variables such as pulse pressure variation, stroke volume variation, cardiac output, and cardiac index assessment (3,4,19).

Several landmark trials have evaluated perioperative GDT during major abdominal surgery. Pearse et al. (19) investigated cardiac output-guided hemodynamic therapy during major gastrointestinal surgery, whereas the OPTIMISE II Trial Group (20) evaluated contemporary cardiac output-guided protocols in elective gastrointestinal surgery.

Although results have varied, meta-analyses generally indicate improved postoperative recovery and reduced morbidity when appropriately implemented GDT strategies are implemented (3,4).

Importantly, GDT should not be interpreted as a single universal protocol but rather as a broader physiological framework emphasizing individualized optimization based on continuous hemodynamic assessment.

Variability in study results likely reflects differences in patient populations, monitoring technologies, fluid strategies, vasopressor use, surgical complexity, ERAS implementation, and definitions of perioperative optimization.

The contemporary framework of perioperative goal-directed therapy integrates dynamic monitoring, individualized fluid optimization, vasopressor support, and continuous reassessment of tissue perfusion. A proposed perioperative hemodynamic optimization algorithm based on current GDT and ERAS principles is presented in Figure 3.

Major clinical studies evaluating perioperative GDT in abdominal surgery are summarized in Table 1.

Major abdominal surgery causes physiological stress responses that may lead to hemodynamic instability and impaired tissue perfusion. Contemporary perioperative management combines static and dynamic hemodynamic monitoring to guide individualized goal-directed therapy with fluids, vasopressors, and inotropes.

Emerging technologies, including artificial intelligence and predictive analytics, may further improve perioperative hemodynamic optimization and postoperative outcomes. *Algorithm synthesized from contemporary perioperative hemodynamic optimization and goal-directed therapy literature (1,3,4,8).*

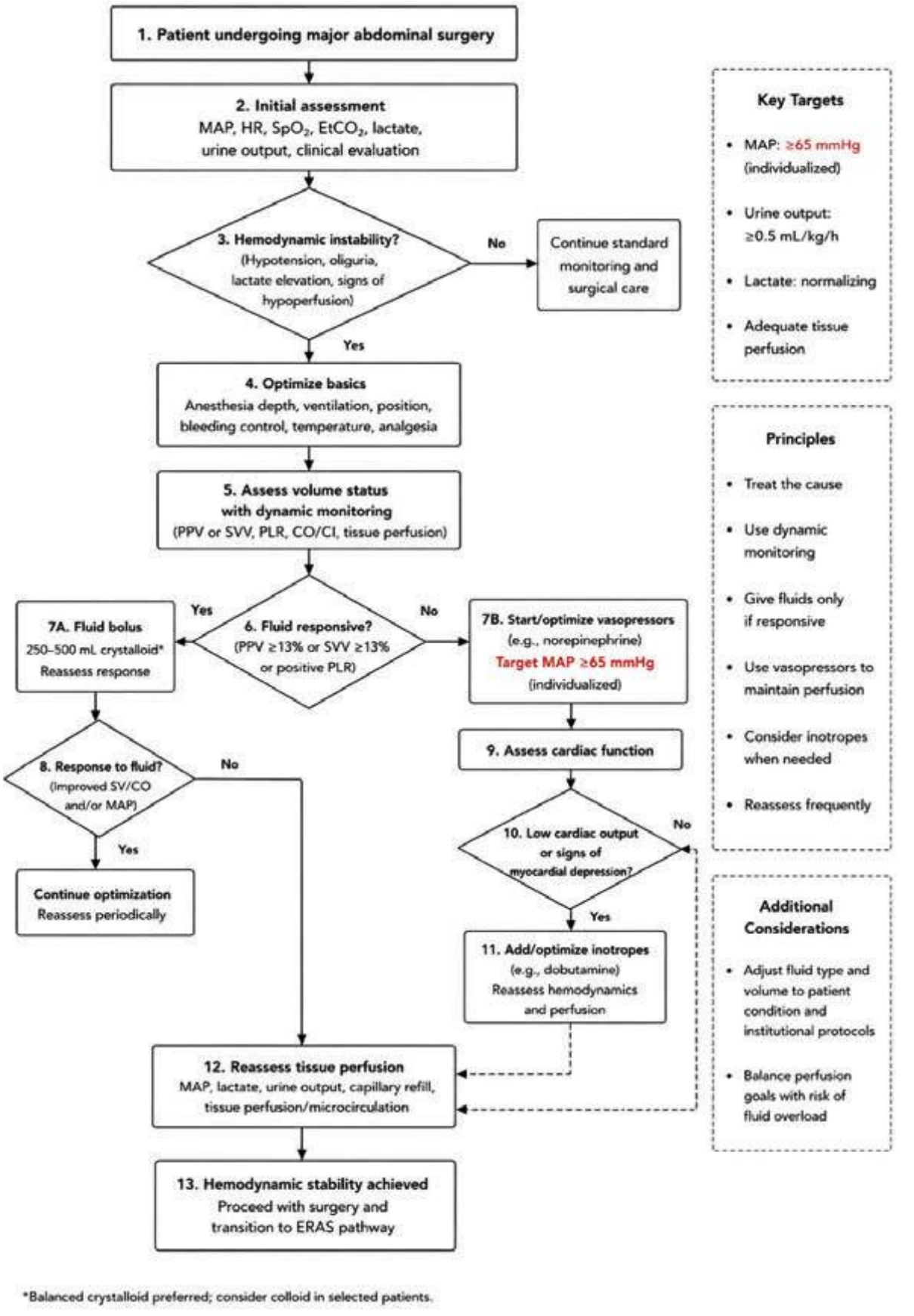

Figure 3. Suggested perioperative hemodynamic optimization algorithm in major abdominal surgery.

Table 1. Key clinical evidence on goal-directed hemodynamic therapy and perioperative hemodynamic optimization in major abdominal and gastrointestinal surgery

Study	Design/ population	Monitoring or intervention	Comparator	Main finding	Relevance to the review
Pearse et al., 2014 (19)	Multicenter RCT; high-risk major gastrointestinal surgery	Cardiac output-guided hemodynamic therapy algorithm based on fluid administration and inotrope support	Usual care	Did not significantly reduce composite complications and 30-day mortality, although updated meta-analysis suggested fewer complications	Landmark trial showing both the promise and limitations of cardiac output-guided GDT
Salzwedel et al., 2013 (6)	Multicenter prospective randomized study; major abdominal surgery	PPV, cardiac index trending, and MAP-guided GDT	Standard perioperative management	Reduced postoperative complications	Supports dynamic, protocolized hemodynamic optimization in major abdominal surgery
OPTIMISE II Trial Group, 2024 (20)	Large multicenter RCT; major elective gastrointestinal surgery	Cardiac output-guided hemodynamic therapy	Usual care	No reduction in the primary composite outcome compared with usual care	Important modern negative trial; suggests GDT benefit is context-dependent
Sun et al., 2017 (3)	Systematic review and meta-analysis of RCTs; major abdominal surgery	Perioperative goal-directed hemodynamic therapy	Conventional therapy	Suggested improved postoperative recovery	Provides pooled evidence supporting GDHT, while highlighting heterogeneity
Chong et al., 2018 (4)	Systematic review and meta-analysis; perioperative surgery	Goal-directed hemodynamic and fluid therapy	Standard care	Evaluated whether GDHT improves perioperative outcomes	Useful for summarizing broader perioperative evidence
Gómez-Izquierdo et al., 2017 (21)	RCT; elective laparoscopic colorectal surgery	Goal-directed fluid therapy	Standard perioperative fluid therapy	Did not reduce primary postoperative ileus	Demonstrates that GDT may not benefit all patients, especially within optimized ERAS settings

Study	Design/ population	Monitoring or intervention	Comparator	Main finding	Relevance to the review
Cesur et al., 2019 (15)	Elective colorectal surgery	PVI-guided goal-directed fluid management	Conventional fluid management	Compared crystalloid administration, lactate levels, and creatinine concentrations during surgery	Supports discussion of non-invasive dynamic monitoring in colorectal surgery
Sun et al., 2023 (18)	RCT; major abdominal oncologic surgery	SVV- and cardiac index-guided GDFT using FloTrac/Vigileo	Conventional management	Shorter hospital stay and faster gastrointestinal recovery	Strong recent evidence for SVV-guided fluid optimization
Coeckelenbergh et al., 2025 (12)	RCT; high-risk abdominal surgery	Assisted fluid management-guided GDFT	Standard GDFT	Higher sublingual microvascular flow during surgery	Introduces microcirculatory endpoints beyond macrohemodynamic targets
Ripollés-Melchor et al., 2025 (22)	Multicenter RCT; moderate- to high-risk elective abdominal surgery	HPI-guided hemodynamic therapy	Standard care	Did not reduce postoperative AKI or overall complications	Important cautionary evidence for predictive monitoring technologies
Yoshikawa et al., 2024 (7)	RCT; major non-cardiac surgery	Hypotension Prediction Index-guided management	Conventional goal-directed hemodynamic management	Reduced cumulative intraoperative hypotension	Supports HPI as a tool for reducing hypotensive burden
Saugel et al., 2024 (1)	Guideline; adult non-cardiac surgery	Intraoperative hemodynamic monitoring and management recommendations	Not applicable	Provides structured recommendations for perioperative monitoring	Authoritative basis for clinical recommendations
Saugel et al., 2025 (13)	European Society statement; adult non-cardiac surgery	Intraoperative hemodynamic monitoring and management	Not applicable	Consensus guidance on contemporary hemodynamic management	Strengthens the review's guideline-based framework

Study	Design/ population	Monitoring or intervention	Comparator	Main finding	Relevance to the review
Saugel et al., 2025 / IMPROVE - multi (23)	RCT; major abdominal surgery	Individualized perioperative blood pressure management	Routine blood pressure management	Did not support individualized targets based on preoperative nighttime MAP	Important recent evidence questioning simplified individualized BP strategies
Pasta et al., 2025 (24)	Major oncologic surgery	Progressive implementation of AI-based hemodynamic monitoring and decision-support tools	Earlier-stage monitoring strategies	Suggested decreasing intraoperative hypotension with increasing AI-assisted support	Supports future-perspective discussion on AI-guided perioperative care

Fluid Optimization

Fluid therapy remains a critical component of perioperative management in major abdominal surgery, as appropriate intravascular volume optimization is essential for maintaining cardiac output and tissue perfusion. However, both hypovolemia and fluid overload may contribute to postoperative complications. While hypovolemia may impair organ perfusion and oxygen delivery, excessive fluid administration may promote pulmonary and bowel edema, delayed gastrointestinal recovery, and prolonged hospital stay. Contemporary perioperative medicine, therefore, increasingly favors individualized fluid optimization over liberal empiric fluid administration (14,25).

Egger et al. (14) demonstrated significant associations between intraoperative fluid balance and perioperative complications during major oncologic surgery. Similarly, Sun et al. (18) reported improved gastrointestinal recovery and shorter hospital stay with stroke volume variation-guided fluid optimization strategies.

Dynamic hemodynamic monitoring plays a central role in modern fluid optimization because it allows identification of patients likely to benefit from fluid administration. Rather than administering empiric fluid boluses based solely on hypotension or oliguria, contemporary protocols increasingly assess preload responsiveness using PPV, SVV, or cardiac output response assessment.

The concept of "fluid responsiveness" is fundamental to GDT. Fluid administration should ideally produce meaningful augmentation of stroke volume or cardiac output. If no significant hemodynamic improvement occurs following volume expansion, additional fluids may simply accumulate within the interstitial space without improving tissue perfusion. The type of administered fluid also remains clinically important. Crystalloids remain the primary perioperative fluid choice due to their widespread availability, favorable safety profile, and lower cost. However, excessive crystalloid administration may promote tissue edema through redistribution into the extracellular compartment. Colloid solutions may provide more efficient plasma volume expansion but remain controversial because of potential renal and coagulation effects.

Huisman et al. (25) additionally highlighted the importance of balancing fluid administration and vasopressor therapy during colorectal surgery to avoid both hypoperfusion and fluid overload. Yates et al. (26) compared crystalloid- and colloid-based fluid strategies during colorectal surgery within goal-directed protocols, emphasizing ongoing debate over the optimal perioperative fluid composition.

Contemporary perioperative management increasingly favors balanced, individualized fluid administration guided by physiological monitoring rather than fixed liberal or restrictive strategies.

Vasopressors and Inotropes

Vasopressors and inotropes are essential components of modern perioperative hemodynamic management, as anesthesia-induced vasodilation, inflammatory vasoplegia, and blood loss frequently contribute to hypotension during major abdominal surgery. While hypotension was historically treated primarily with aggressive fluid administration, recognition of the harmful effects of fluid overload has shifted practice toward earlier and more individualized vasopressor use.

Norepinephrine has emerged as the preferred vasopressor because it increases vascular tone and perfusion pressure while generally preserving cardiac output and limiting excessive fluid administration (13,27).

Vokuhl et al. (27) showed improved arterial pressure stability when applying continuous norepinephrine administration during induction of general anesthesia in high-risk surgical patients. These findings support the growing interest in implementing proactive vasopressor strategies during perioperative hemodynamic optimization.

Importantly, vasopressor therapy should not replace appropriate volume assessment. Hypotension secondary to severe hypovolemia may worsen if treated exclusively with vasoconstrictive agents. Consequently, integrated physiological assessment remains essential for distinguishing preload deficiency from vasodilatory hypotension or myocardial dysfunction.

Inotropic agents may become necessary when cardiac output remains inadequate despite optimization of preload and perfusion pressure. Reduced myocardial contractility may occur during major surgery due to anesthesia, ischemia, sepsis, or inflammatory myocardial depression. In such situations, augmentation of cardiac contractility may improve oxygen delivery and organ perfusion.

Modern perioperative medicine increasingly emphasizes balanced hemodynamic optimization integrating fluids, vasopressors, and inotropic agents according to individualized physiological requirements rather than rigid universal protocols.

Individualized Hemodynamic Targets

One of the most important developments in contemporary perioperative medicine is the transition from generalized hemodynamic thresholds toward individualized physiological targets. Traditional perioperative management often relied on fixed MAP values or standardized fluid administration algorithms regardless of baseline patient physiology.

However, autoregulatory capacity and cardiovascular reserve vary substantially among surgical patients. Individuals with chronic hypertension, diabetes mellitus, advanced age, vascular disease, or impaired cardiac function may require different perfusion pressures to maintain adequate organ blood flow.

Recent studies have therefore increasingly explored personalized hemodynamic optimization strategies. The IMPROVE-multi randomized clinical trial evaluated individualized perioperative blood pressure management during major abdominal surgery, reflecting growing recognition that "one-size-fits-all" hemodynamic targets may be physiologically inadequate (13).

Materials and Methods

Similarly, modern GDT protocols increasingly incorporate patient-specific variables including baseline cardiovascular physiology, comorbidities, surgical complexity, and predicted postoperative risk. The emergence of predictive monitoring technologies further supports this individualized approach. Hypotension Prediction Index-guided management permits anticipatory intervention before clinically significant hemodynamic deterioration develops. Yoshikawa et al. (7) demonstrated reduced cumulative hypotension with HPI-guided therapy during non-cardiac surgery. Precision perioperative medicine aims to further expand individualized management through integration of physiological monitoring, predictive analytics, artificial intelligence, and potentially genomic or biomarker-based risk stratification. The movement toward individualized hemodynamic optimization represents a major paradigm shift within modern anesthesiology and perioperative medicine.

Monitoring Technologies

Arterial Waveform Analysis

Arterial waveform analysis has become a major tool for perioperative hemodynamic assessment by deriving dynamic variables such as pulse pressure and stroke volume variation from invasive arterial pressure monitoring. Based on cardiopulmonary interactions during positive-pressure ventilation, these systems provide continuous real-time assessment of preload responsiveness, cardiovascular reserve, cardiac output, and systemic vascular resistance, facilitating individualized hemodynamic intervention during surgery.

Salzwedel et al. (6) showed reduced postoperative complications with PPV-based goal-directed therapy during major abdominal surgery. Similarly, Sun et al. (18) reported improved gastrointestinal recovery and a shorter hospital stay with stroke volume variation-guided fluid optimization.

Arterial waveform systems offer several advantages, including continuous monitoring capability, relatively low invasiveness, and integration with modern perioperative workstations. However, interpretation requires awareness of important physiological limitations, including arrhythmias, spontaneous respiratory effort, low-tidal-volume ventilation, impaired chest wall compliance, and altered right ventricular physiology.

Despite these limitations, arterial waveform analysis remains central to contemporary goal-directed therapy protocols and modern perioperative hemodynamic optimization strategies.

Esophageal Doppler

Esophageal Doppler monitoring provides a minimally invasive assessment of descending thoracic aortic blood flow velocity and stroke volume. A specialized Doppler probe placed within the esophagus enables real-time evaluation of cardiovascular function during surgery.

The principal advantage of esophageal Doppler technology is its ability to continuously estimate stroke volume and cardiac output without requiring a pulmonary artery catheter. This allows individualized fluid optimization and direct assessment of hemodynamic response to therapeutic intervention.

Esophageal Doppler monitoring played a major role in the early development of perioperative goal-directed therapy protocols and has been extensively studied in abdominal surgery. De Pascale et al. (28) compared esophageal Doppler monitoring with non-invasive bioreactance technologies during major abdominal-pelvic surgery and showed important methodological differences between the monitoring systems.

Advantages of esophageal Doppler monitoring include relatively rapid setup, minimally invasive application, and real-time cardiac output assessment. However, important limitations include operator dependency, probe positioning challenges, motion artifacts, and variable signal acquisition.

Although newer arterial waveform and minimally invasive monitoring technologies have become increasingly widespread, esophageal Doppler monitoring remains an important and physiologically valuable tool in perioperative hemodynamic management.

Minimally Invasive Cardiac Output Monitoring

Over the past two decades, technological advances have driven the development of minimally invasive cardiac output monitoring systems that provide continuous hemodynamic assessment with lower procedural risk than traditional pulmonary artery catheterization. Contemporary technologies include pulse contour analysis, bioreactance devices, pulse wave transit time analysis, and noncalibrated arterial waveform systems, which estimate cardiac output using arterial waveform or thoracic bioimpedance analysis.

Bioreactance monitoring is among the most widely studied noninvasive cardiac output technologies. This method analyzes phase shifts in thoracic electrical currents generated by pulsatile blood flow. De Pascale et al. (28) compared noninvasive bioreactance monitoring with esophageal Doppler assessment during major abdominal-pelvic surgery and reported important differences between the methodologies.

The principal advantages of minimally invasive cardiac output monitoring include reduced procedural complications, continuous real-time physiological assessment, simplified perioperative integration, and broader applicability outside specialized intensive care settings. These technologies facilitate dynamic evaluation of stroke volume response, cardiac output trends, preload responsiveness, and therapeutic intervention effects during surgery.

Minimally invasive monitoring also has important limitations, as accuracy may be affected by arrhythmias, vasoplegia, arterial waveform distortion, mechanical ventilation settings, obesity, and severe hemodynamic instability. Nevertheless, these systems have become central to mod-

ern goal-directed therapy because contemporary perioperative management increasingly prioritizes continuous physiological assessment and individualized optimization over intermittent static measurements. Recent integration of predictive analytics and machine learning may further expand their clinical utility.

Ultrasound and Echocardiography

Point-of-care ultrasound (POCUS) and perioperative echocardiography have assumed an increasingly important role in modern hemodynamic assessment because they enable rapid bedside evaluation of ventricular function, intravascular volume status, and structural abnormalities. Unlike isolated numerical variables, echocardiography provides direct visualization of cardiac physiology and may identify causes of hemodynamic instability, including ventricular dysfunction, hypovolemia, vasoplegia, or obstructive pathology. Ultrasound assessment of the inferior vena cava has also emerged as a potential tool for estimating preload responsiveness, although its interpretation remains affected by ventilation and intrathoracic pressure changes. Contemporary perioperative medicine increasingly integrates ultrasound alongside conventional monitoring technologies to improve individualized hemodynamic management (13).

Hemodynamic Optimization in Major Abdominal Surgery

Colorectal Surgery

Colorectal surgery is one of the most extensively investigated areas of perioperative hemodynamic optimization and goal-directed therapy because these procedures are associated with significant fluid shifts, inflammatory activation, and postoperative gastrointestinal dysfunction. Although colorectal surgery historically favored liberal fluid administration, excessive crystalloids are now recognized to contribute to bowel edema, delayed gastrointestinal recovery, pulmonary complications, and prolonged hospital stay. Consequently, contemporary perioperative management increasingly emphasizes individualized fluid optimization guided by dynamic hemodynamic monitoring (15,29,30).

Cesur et al. (15) compared conventional fluid management with pleth variability index-guided goal-directed therapy during elective colorectal surgery and reported improved intraoperative fluid optimization. Similarly, Resalt-Pereira et al. (29) evaluated goal-directed fluid therapy during laparoscopic colorectal surgery within ERAS pathways.

Gómez-Izquierdo et al. (21) examined goal-directed fluid therapy during elective laparoscopic colorectal surgery and reported no reduction in postoperative ileus despite protocolized optimization. These findings highlight ongoing controversy regarding the magnitude of the benefit associated with perioperative GDT within already optimized ERAS programs.

Zorrilla-Vaca et al. (30) conducted a propensity score-matched multicenter study, demonstrating improved postoperative outcomes when goal-directed fluid therapy was incorporated into enhanced recovery protocols for colorectal surgery.

Dynamic monitoring variables such as PPV and SVV remain particularly valuable during colorectal surgery because these procedures frequently involve significant fluid redistribution and prolonged operative duration. Individualized optimization strategies may therefore improve tissue perfusion while minimizing bowel edema and postoperative dysfunction.

The integration of perioperative hemodynamic optimization into ERAS pathways has become increasingly important in colorectal surgery, driven by the growing emphasis on accelerated recovery, reduced complications, and shorter hospitalization.

Hepatobiliary Surgery

Hepatobiliary surgery presents unique hemodynamic challenges due to complex hepatic vascular physiology and substantial blood loss risk. Excessive fluid administration may increase hepatic venous congestion and intraoperative bleeding, whereas excessive restriction may compromise organ perfusion. Consequently, contemporary hepatobiliary anesthesia emphasizes balanced hemodynamic optimization through dynamic monitoring, controlled fluid therapy, and individualized physiological targets (31).

Saito et al. (31) concluded that stroke volume variation-guided monitoring may reduce blood loss during hepatocellular carcinoma resection. These findings support the use of dynamic preload assessment during complex hepatic surgery.

Low central venous pressure anesthesia has historically been administered to minimize hepatic venous bleeding during liver resection. However, excessive preload reduction may impair renal perfusion and tissue oxygen delivery. Consequently, contemporary hepatobiliary management integrates individualized hemodynamic optimization to a greater extent rather than rigid CVP reduction alone.

Major hepatobiliary procedures are also frequently associated with prolonged operative duration, major fluid shifts, ischemia-reperfusion injury, inflammatory activation, and vasodilatory physiology. Advanced hemodynamic monitoring, therefore, plays a key role in maintaining physiological stability during these operations.

Dynamic monitoring strategies enable individualized balancing of adequate organ perfusion against avoidance of excessive venous congestion and tissue edema.

Emergency Abdominal Surgery

Emergency abdominal surgery patients represent a particularly high-risk perioperative population due to sepsis, hypovolemia, hemorrhage, intestinal ischemia, and inflammatory activation. Unlike elective surgical patients, many present with hemodynamic instability, metabolic acidosis, and organ dysfunction before anesthesia induction, substantially increasing perioperative morbidity and mortality. Consequently, contemporary perioperative management prioritizes rapid hemodynamic assessment and individualized optimization through dynamic monitoring, lactate assessment, vasopressor support, and goal-directed therapy, while avoiding indiscriminate crystalloid administration that may worsen bowel edema and pulmonary dysfunction (1,3).

ERAS Protocols

Enhanced Recovery After Surgery (ERAS) protocols (8) are one of the most significant contemporary developments in perioperative medicine. ERAS pathways integrate multimodal perioperative strategies designed to reduce surgical stress, minimize complications, and accelerate postoperative recovery.

Perioperative fluid and hemodynamic optimization constitute the central components of modern ERAS programs. Excessive crystalloid administration has been consistently associated with bowel edema, impaired gastrointestinal motility, pulmonary complications, delayed mobilization, and prolonged hospitalization. Consequently, ERAS pathways promote balanced individualized fluid therapy rather than liberal fluid administration.

McLain et al. (32) highlighted that goal-directed fluid therapy has become a major component of contemporary ERAS implementation due to its ability to individualize fluid administration according to dynamic physiological assessment.

Colorectal surgery remains one of the most extensively researched ERAS populations, with multiple studies demonstrating improved postoperative recovery through integration of individualized fluid optimization and minimally invasive perioperative strategies (29,30).

Ripollés-Melchor et al. (8) described the growing integration of perioperative hemodynamic optimization within ERAS protocols in surgical oncology.

Dynamic monitoring strategies allow for a more physiologically targeted fluid administration and may improve postoperative recovery within enhanced recovery pathways.

Goal-directed therapy has therefore become incorporated into ERAS frameworks because individualized physiological optimization aligns closely with broader ERAS objectives, including reduced complications, earlier feeding, accelerated mobilization, and shorter hospital stay.

Importantly, implementation of ERAS pathways may influence the observed effects of perioperative GDT in contemporary studies. Because modern ERAS care already reduces postoperative morbidity through multimodal optimization, additional incremental benefits from hemodynamic protocols may become more difficult to demonstrate.

Nevertheless, contemporary perioperative medicine recognizes perioperative hemodynamic optimization as a fundamental component of successful enhanced recovery strategies.

Future Directions

Artificial Intelligence

Artificial intelligence (AI) has emerged as one of the most rapidly expanding fields within perioperative medicine and hemodynamic monitoring. Advances in machine learning, predictive analytics, automated physiological interpretation, and real-time computational modeling have accelerated the development of AI-assisted perioperative management.

Traditional perioperative hemodynamic management has largely relied on clinician interpretation of physiological variables after hemodynamic deterioration has occurred. In contrast, AI-assisted monitoring systems aim to predict impending instability before clinically significant deterioration becomes apparent.

This anticipatory approach represents a major conceptual shift from reactive correction toward proactive prevention of hemodynamic compromise.

The Hypotension Prediction Index (HPI) is among the most widely studied AI-assisted perioperative monitoring technologies. HPI utilizes machine learning algorithms, analyzing subtle

arterial waveform characteristics to predict impending intraoperative hypotension before significant blood pressure decline occurs. These systems continuously process large quantities of physiological data beyond what is typically recognizable through conventional visual waveform interpretation.

Yoshikawa et al. (7) reported reduced cumulative intraoperative hypotension with HPI-guided management during non-cardiac surgery. Similarly, Ripollés-Melchor et al. (22) evaluated HPI-guided hemodynamic management during abdominal surgery, reflecting the growing interest in predictive perioperative monitoring strategies.

Artificial intelligence technologies may offer several major advantages in perioperative care. Early identification of impending instability may allow timely intervention before prolonged tissue hypoperfusion develops. Potentially, this may reduce postoperative complications including acute kidney injury, myocardial injury, neurological dysfunction, and gastrointestinal impairment.

Pasta et al. (24) investigated the progressive implementation of AI-assisted predictive hemodynamic management during major oncologic surgery and reported improvements in perioperative hemodynamic stability through integration of advanced monitoring systems.

In addition to hypotension prediction, future AI systems may potentially integrate multiple physiological domains, including cardiac output trends, microcirculatory assessment, lactate kinetics, tissue oxygenation, inflammatory biomarkers, ventilatory parameters, and patient-specific risk factors. Such multidimensional integration could substantially improve individualized perioperative decision-making.

Despite these promising developments, several important challenges remain. Artificial intelligence systems require extensive physiological validation across diverse surgical populations and varying hemodynamic conditions. Concerns also remain regarding algorithm transparency, clinician overreliance on automated systems, cost-effectiveness, and integration into routine perioperative workflows.

Importantly, AI-assisted technologies should not replace clinical judgment but rather augment physiological interpretation and support individualized decision-making. Future perioperative medicine will likely involve collaborative interaction between clinician expertise and advanced computational monitoring systems.

Predictive Analytics

Predictive analytics is an emerging field in perioperative hemodynamic optimization that aims to forecast physiological deterioration through continuous data analysis and machine learning algorithms rather than simply displaying current hemodynamic values. By integrating arterial waveform morphology, heart rate variability, cardiac output trends, and additional physiological variables, these systems may identify evolving instability before overt clinical manifestations develop.

This transition toward predictive monitoring reflects the growing emphasis on prevention of intraoperative hypotension and organ hypoperfusion rather than delayed correction of hemodynamic deterioration (7,8).

Ripollés-Melchor et al. (22) evaluated HPI-guided hemodynamic management in abdominal surgery populations, while Yoshikawa et al. (7) demonstrated reduced cumulative hypotension through predictive monitoring-guided intervention. These studies suggest that predictive technologies may improve perioperative hemodynamic stability, although long-term outcome benefits remain under active investigation.

Predictive analytics may also become integrated with perioperative risk stratification systems. Future monitoring platforms may potentially combine baseline patient characteristics, comorbidities, laboratory data, imaging findings, genomic information, and real-time physiological monitoring into individualized predictive models.

Another important area of development involves predictive fluid responsiveness assessment. Dynamic monitoring variables such as PPV and SVV already provide real-time estimation of preload responsiveness, but future systems may potentially forecast evolving fluid requirements before clinically significant instability develops.

Microcirculatory monitoring may similarly become integrated into predictive analytics frameworks. Because tissue hypoperfusion may precede macrohemodynamic deterioration, incorporation of microvascular assessment could potentially improve early identification of organ perfusion abnormalities.

Although predictive technologies remain an evolving field, their integration into perioperative medicine is likely to expand substantially over the coming decade.

Precision Perioperative Medicine

Precision perioperative medicine represents a transition toward individualized physiological management based on patient-specific characteristics rather than generalized treatment protocols. Unlike traditional approaches relying on standardized fluid regimens and fixed blood pressure thresholds, contemporary perioperative care increasingly integrates dynamic monitoring, predictive analytics, artificial intelligence, and individualized cardiovascular assessment.

Recent studies on personalized blood pressure optimization during major abdominal surgery further support this shift toward precision physiology, recognizing that universal hemodynamic targets may not adequately reflect individual patient requirements (13). As perioperative technologies continue to evolve, future anesthesiology practice will likely become personalized, predictive, and physiology-driven.

Conclusion

Hemodynamic monitoring and goal-directed therapy have become central components of modern perioperative medicine in major abdominal surgery. Contemporary perioperative management prioritizes dynamic assessment of fluid responsiveness and tissue perfusion through pulse pressure variation, stroke volume variation, cardiac output monitoring, and individualized hemodynamic optimization. Goal-directed therapy protocols including fluids, vasopressors, and inotropes have yield important benefits including reduced postoperative morbidity, improved gastrointestinal recovery, and shorter hospitalization. In addition, ERAS pathways, predictive analytics, artificial intelligence, and precision perioperative medicine are further advancing in-

dividualized physiology-driven care aimed at preserving tissue perfusion, oxygen delivery, and organ function.

Declarations

Ethics Approval and consent to participate: Ethical approval was not required for this narrative review article because no human participants, patient data, or experimental interventions were involved.

Informed consent: Not applicable.

Conflict of Interest: The authors declare that there is no conflict of interest regarding the publication of this manuscript.

Funding: The authors received no financial support for the research, authorship, or publication of this article.

Availability of data and materials: No new datasets were generated or analyzed during the preparation of this review article. All information discussed is derived from previously published sources cited in the manuscript.

Author Contributions: H.S. contributed to the conceptualization of the review, literature research, manuscript drafting, figure preparation, and overall coordination of the manuscript. M.S., N.B., M.B., and A.G.B. contributed to literature interpretation, critical revision of the manuscript, scientific supervision, and improvement of the intellectual content. All authors reviewed and approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

Acknowledgments: The authors would like to express their gratitude to all colleagues and collaborators who contributed through academic discussion and professional support during the preparation of this review article.

Artificial Intelligence (AI) Statement: Artificial intelligence (AI)-assisted tools were used exclusively for assistance in generating and refining the graphical figures included in this manuscript. All scientific content, interpretations, and final figure selection were reviewed and approved by the authors, who take full responsibility for the integrity and accuracy of the work.

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REVIEW ARTICLE *UDK: 336.58:614.2(497-15)*

www.doi.org/10.67214/66y5t474

HEALTH FINANCING SYSTEMS: THE WESTERN BALKANS CASE

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Abstract

Objective: Reforms introduced in the 1990s aimed at sustainability amidst high out-of-pocket costs and low public funding. Over the past three decades, the Western Balkans (WB) countries have undergone profound transformations. The aspiration to join the European Union (EU) strongly shapes health financing policies in the Western Balkans, encouraging reforms focused on equity, efficiency, and financial sustainability. The aim of this paper is to analyze and compare health expenditure levels and financing structures across Western Balkan countries.

Materials and Methods: The analysis is based on data from the World Health Organization HFA-DB and the World Bank, supplemented by Health in Action reports for the selected countries. Public health approach has been applied.

Results: In 2023, health expenditure ranged from 7% of GDP in Albania to 9.7% in Montenegro. Despite this growth, per capita spending remains substantially below EU levels (US$4,153), with Albania reporting the lowest (US$590) and Montenegro the highest (US$1,147). A common regional challenge is the high reliance on out-of-pocket (OOP) payments, exceeding 30% in most countries and reaching over 40% in Albania and North Macedonia, well above the EU average (14,8%).

Conclusion: Health financing systems in the Western Balkans show increasing expenditure but continue to face limited financial protection and persistent inequities. High reliance on out-of-pocket payments and unmet healthcare needs continue to expose populations to financial risk, particularly among lower-income groups. Strengthening public financing, improving risk pooling, and enhancing system efficiency are essential to accelerate progress toward universal health coverage in the region.

Keywords: *efficiency; health financing systems; Western Balkans.*

Introduction

Health care financing is a function of the health system that mobilizes, accumulates, and allocates financial resources to cover the health needs of people, individually and collectively (1). At its core, health financing constitutes a simple but integral function of a health system: raising and spending money on health care (2).

Health expenditure constitutes a major policy concern for economies worldwide, placing significant pressure on public budgets while reflecting governments' investment in the health and

well-being of their populations. These challenges are especially acute in the Balkan region, where countries continue to face the combined effects of the global economic downturn over the past decade and the enduring socioeconomic consequences of past conflicts (3).

The health system traces its infrastructure and organization to the period when the countries were part of former Yugoslavia. Most Western Balkan countries operate under a Bismarck-type social health insurance system, characterized by social health insurance and universal coverage principles. This model emphasized universal coverage, solidarity, and public provision of services. However, the economic and political transitions of the 1990s led to structural reforms aimed at decentralization, cost containment, and system sustainability (4).

Although Albania was not part of Yugoslavia, its healthcare system, similar to those in other former communist countries of Central and Eastern Europe (CEE), is based on the Soviet "Semashko" model.

The legacies of the Semashko system remain visible, especially in the state ownership of public healthcare institutions, the public provision of services, and funding from the general tax base (especially for secondary and tertiary care) (5).

After an initial phase focused on macroeconomic stabilization and reconstruction, reforms are now focusing on enhancing economic growth, promoting employment, and encouraging the containment and efficiency of public spending (6).

The shared aspiration of the Western Balkan countries to join the European Union (EU) significantly shapes their policy decisions. In particular, the EU integration process influences health financing reforms by encouraging alignment with key principles such as equity, efficiency, transparency, and financial sustainability. This includes reducing out-of-pocket payments, improving resource allocation, and strengthening financial management systems (7).

Despite these efforts, the region faces persistent challenges, including limited fiscal space, demographic pressures, and high out-of-pocket payments. Understanding financing patterns and expenditure trends is essential for improving system performance and achieving universal health coverage. The aim of this paper is to analyze and compare health expenditure levels and financing structures across Western Balkan countries.

Materials and Methods

The analysis is based on data from the World Health Organization HFA-DB and the World Bank, supplemented by Health in Action reports for the selected countries. Public health approach has been applied.

Results

Health expenditure has increased steadily across the region, both as a share of GDP and in absolute terms. However, this growth is driven largely by rising demand, aging populations, and increased costs rather than systemic improvements.

Gross domestic product (GDP) as an economic indicator which measures the economic power of a country, is an important indicator of the financial state of one country and is a way to compare countries with each other.

Health expenditure (% of GDP) among observed countries was highest in Montenegro with 9.7% and lowest in Albania with 7% in 2023. (Figure 1) (Table 1) (9)

Table 1. Health expenditure (% of GDP) for Albania, Bosnia and Herzegovina, Montenegro, North Macedonia and Serbia (2019 - 2023)

Countries	2019	2020	2021	2022	2023
Albania	6,8	7,5	7,4	7,5	7
Bosnia and Herzegovina	8,9	9,7	9,6	8,7	8,9
Montenegro	8,3	11,4	10,6	10,2	9,7
North Macedonia	7,1	7,7	8,4	7,4	7,4
Serbia	8,3	8,3	9,2	8,6	8,0
European Union	9,8	10,8	10,8	10,3	10

Source: Global Health Expenditure Database, updated December 12th, 2025, World Health Organization (WHO), uri: apps.who.int/nha/database (9)

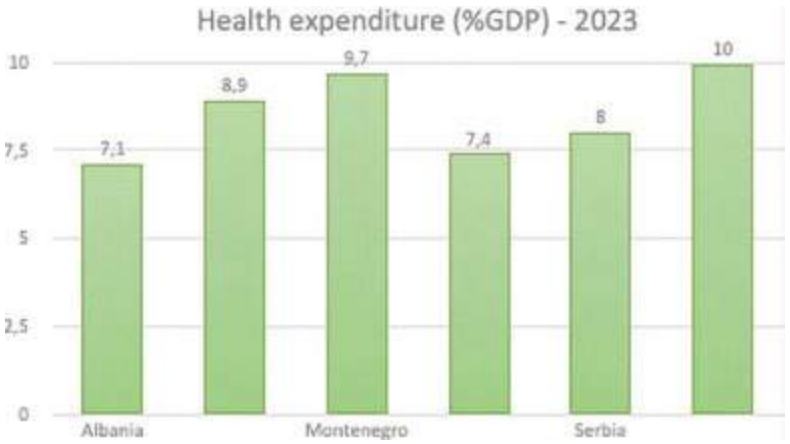

Figure 1. Health expenditure (% GDP) for Albania, Bosnia and Herzegovina, Montenegro, North Macedonia, Serbia and European Union (2023). Source: Global Health Expenditure Database, updated December 12th, 2025, World Health Organization (WHO), uri: apps.who.int/nha/database (9)

In 2023 in Albania, per capita health spending remained the lowest among Western Balkan countries, standing at US$590,6, despite a gradual increase over the past decade. (Figure 2) (10)

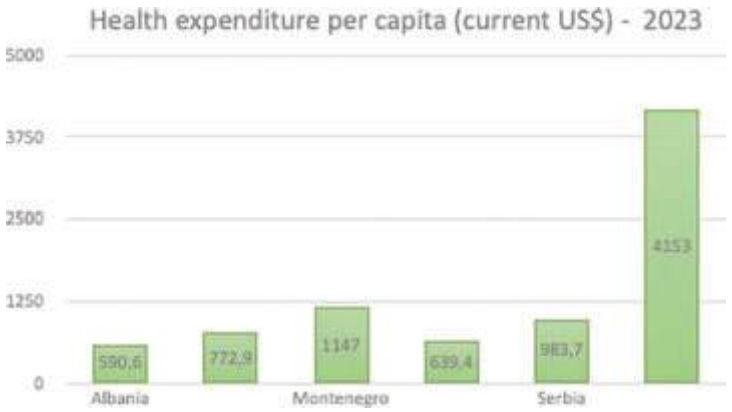

Figure 2. Health expenditure per capita (current US$) for Albania, Bosnia and Herzegovina, Montenegro, North Macedonia, Serbia and European Union (2023). Source: Global Health Expenditure Database, updated December 12th, 2025, World Health Organization (WHO), uri: apps.who.int/nha/database (10)

Out-of-pocket (OOP) payments represent a substantial share of total health expenditure, accounting for 48.3% in 2023, significantly above the European Union (EU) average of 14.8%. (Figure 3) (11) These expenditures are primarily driven by outpatient medicines, informal payments, and the use of private healthcare services. As a result, financial protection remains limited, with more than 12% of households experiencing catastrophic health expenditure, disproportionately affecting lower-income groups.

Bosnia and Herzegovina allocated 9.6% of its GDP to health expenditure in 2021, with this share decreasing to 8.9% in 2023. (Figure 1) (Table 1) (9) Health expenditure per capita (current US$) in 2023 is lower than (772.9) compared to the European Union (EU) (4,153) (Figure 2) (10). Financial protection remains a concern, with catastrophic health spending disproportionately affecting lower-income households. This is largely driven by out-of-pocket (OOP) payments, particularly for outpatient medicines, which accounted for 30.9% of total health expenditure in 2023. (Figure 3) (11)

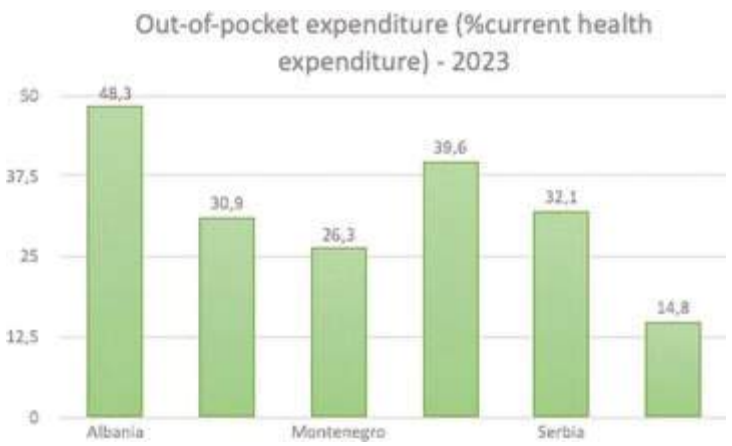

Figure 3. Out-of-pocket expenditure (% of current health expenditure) for Albania, Bosnia and Herzegovina, Montenegro, North Macedonia, Serbia and European Union (2023). Source: Global Health Expenditure Database, updated December 12th, 2025, World Health Organization (WHO), uri: apps.who.int/nha/database (11)

Public health expenditure in Montenegro increased markedly during the COVID-19 pandemic, reaching 10.6% of the gross domestic product (GDP) in 2021, before declining to 9.7% in

2023. (Figure 1) (Table 1) (9) In the same year, health expenditure per capita was amounted to US$1,147, the highest in the region. (Figure 2) (10) Out-of-pocket (OOP) payments represented approximately 38% of health expenditure in 2021, largely driven by spending on non-reimbursed medicines and private services, often chosen to avoid waiting times. Although the share of OOP spending fluctuated from 2011 to 2021, it remained consistently high before dropping notably to 26.3% in 2023. (Figure 3) (11)

North Macedonia's health expenditure increased from 7.1% of GDP in 2019 to 8.4% in 2021, following a trend observed across Europe during the COVID-19 pandemic, before declining to 7.4% in 2023. (Figure 1) (Table 1) (14) Health expenditure per capita (current US$) in 2023 for North Macedonia is relatively low (639.4) in comparison to the European Union (4,153). (Figure 2) (10) OOP payments account for over 40% of total health spending. Despite increases in public spending on health, OOP spending accounted for 39.6% of health spending in 2023, which was far above the average of EU countries (14.8%). (Figure 3) (11)

Health expenditure in Serbia reached a peak of 9.2% of gross domestic product (GDP) in 2021, primarily due to economic contraction and heightened emergency spending during the COVID-19 pandemic, before declining to 8% in 2023. (Figure 1) (Table 1) (9) In the same year, health expenditure per capita amounted to US$983.7, well below the European Union (EU) average of US$4,153. (Figure 2) (10) The system remains heavily reliant on out-of-pocket (OOP) payments, which account for the majority of private health spending. OOP payments as a share of health expenditure nearly doubled from 2002 to 2017, then eased after 2018 but remained elevated, standing at 32.1% in 2023, compared to the EU average of 14.8%. (Figure 3) (11). According to 2024 data from Eurostat, Albania reported the highest percentage of unmet healthcare needs (15%), followed by Serbia (8%), North Macedonia (6%), and Montenegro (3%). (Figure 4) (14) Unmet healthcare needs remain a significant equity and access challenge in the Western Balkans, particularly among low-income populations.

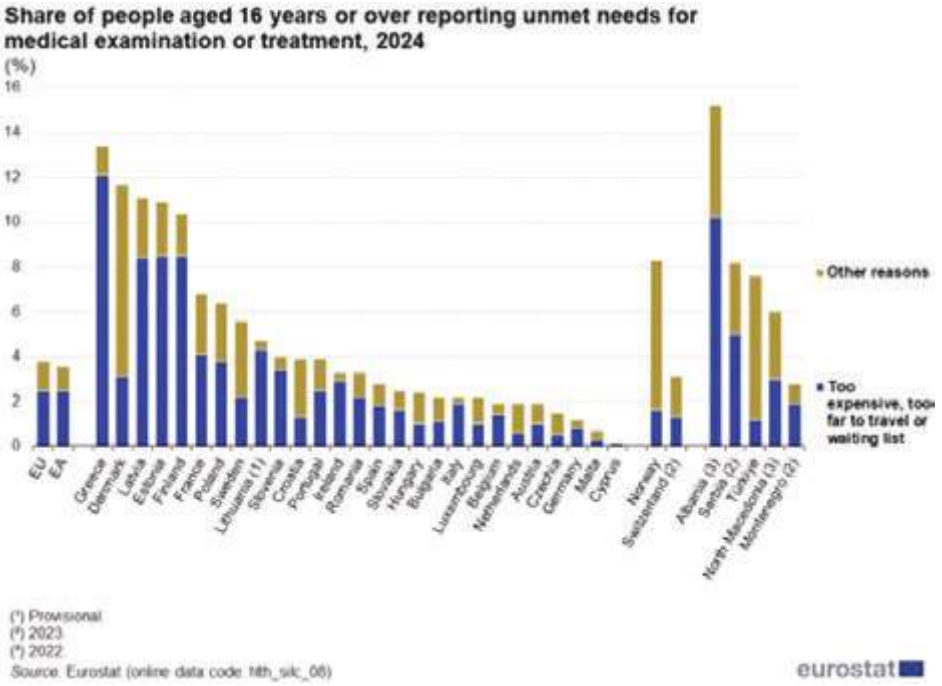

Figure 4. Share of people aged 16 years or over reporting unmet needs for medical examination or treatment, 2024 (%). Source: Eurostat, 2024 (hlth_silc_08) (14)

According to WHO "Health Systems in Action" reports, Western Balkan countries continue to experience barriers to timely access to healthcare services, despite relatively high levels of formal insurance coverage in some systems. WHO analyses across the region consistently highlight that financial barriers are the main driver of unmet healthcare needs, with low-income groups being disproportionately affected. High reliance on out-of-pocket payments increases the likelihood that individuals will delay or forgo necessary care, particularly medicines and specialist services. In North Macedonia, for example, more than 90% of the population is covered by social health insurance, yet unmet need persists, especially among poorer households due to cost-related barriers and high out-of-pocket payments for outpatient medicines and specialist care (14).

Discussion

Albania's health system is financed through a combination of compulsory health insurance contributions from employees and employers, supplemented by allocations from the state budget. The Compulsory Health Insurance Fund (ISKSH) pools these resources and finances publicly provided healthcare services, reimburses insured individuals for prescription medicines, and contracts selected services from private providers (8).

In Bosnia and Herzegovina, due to the organization of the state itself, the financing of healthcare providers is different and more complex. There is no centralized health insurance, so healthcare providers sign contracts and are paid by a specific Fund to which the insured are registered depending on where they live. In the Federation of Bosnia and Herzegovina, the insured of the respective cantonal Health Insurance Fund can receive publicly paid primary and secondary services only from that canton's contracted cantonal providers, and not from providers from other cantons of the Federation of Bosnia and Herzegovina. In the Republika Srpska and the Brčko District of Bosnia and Herzegovina, the insured can receive publicly paid health services from contracted providers in the whole entity/district. The Federation of Bosnia and Herzegovina established a minimum services package that has to be provided in all cantons, in addition to a list of complex services and expensive medicines that are financed by the Federation's Health Insurance and Reinsurance Fund (12).

Montenegro's health system is highly centralized, with the Ministry of Health responsible for governance, regulation, and administration, while the Health Insurance Fund (HIF) serves as the sole public purchaser of health services. In 2022, under the Montenegro Economic Reform Programme 2022-2024 and the "Europe Now" initiative, the financing model transitioned from a contribution-based social health insurance system to a fully tax-funded system (13). This reform aimed to enhance labour market competitiveness and reduce informality.

North Macedonia's health system is largely financed through a social health insurance scheme operated by a single-payer Health Insurance Fund (HIF) that acts as the main purchaser of publicly funded health services (14).

Serbia's principal purchaser of publicly financed health services is the National Health Insurance Fund (NHIF), predominantly funded through payroll contributions (15).

Health expenditure remains a central concern in public policy across countries, as it consumes a significant share of government budgets while also serving as an indicator of state investment in population health and welfare. In the Western Balkans, this challenge is even more evident,

largely due to the lingering effects of the global financial crisis over the past decade and the persistent socioeconomic repercussions of earlier conflicts in the region (16).

Despite convergence in expenditure growth, substantial cross-country disparities persist. Montenegro reports the highest THE as a share of GDP and per capita spending, reflecting recent financing reforms and increased fiscal commitment. In contrast, Albania remains at the lower end of both relative and absolute spending, indicating constrained fiscal capacity. Across North Macedonia, Serbia, and Bosnia and Herzegovina, per capita expenditure remains significantly below European Union levels, highlighting persistent resource gaps. This supports earlier findings that relatively high GDP shares may mask low absolute investment due to limited economic capacity (17).

A defining structural feature of the region is the persistently high reliance on out-of-pocket (OOP) payments. Medicines remain the principal driver of OOP expenditure, with inadequate coverage and pricing inefficiencies limiting affordability. Complementary evidence shows that while essential medicines are generally available, access varies significantly across countries, as well as prescribing restrictions, particularly in primary care, where cost may increase and reduce system efficiency.

The case of North Macedonia illustrates both the problem and potential policy response. WHO evidence shows that limited coverage of outpatient medicines has been a major driver of financial hardship, while the recent expansion of the positive medicines list has improved affordability and treatment adherence (18).

High OOP spending has important implications for equity, as it is strongly associated with catastrophic and impoverishing health expenditure (19).

This is particularly evident in Albania and Bosnia and Herzegovina, where financial protection remains weak despite formal coverage arrangements. Fragmented financing structures, especially in Bosnia and Herzegovina, further exacerbate inequities by limiting risk pooling and creating disparities in access across administrative units.

Consequently, a considerable share of households experiences financial hardship and catastrophic health expenditure, highlighting ongoing inequities in access to essential health services.

Policy efforts in the Western Balkans should prioritize strengthening public financing mechanisms, expanding benefit coverage, improving purchasing efficiency, and reducing reliance on out-of-pocket payments to enhance equity, financial protection, and system sustainability. Institutional arrangements play a critical role in shaping these outcomes. Centralized systems, such as those in Montenegro and North Macedonia, may facilitate coordinated purchasing but do not necessarily reduce financial barriers.

Conversely, decentralized systems introduce inefficiencies and inequities due to fragmentation.

Transitioning from contribution-based to tax-funded models, as observed in Montenegro, may improve equity in principle, while international evidence suggests that financing reforms alone are insufficient without parallel improvements in benefit design and purchasing efficiency. Although various reforms have been introduced, including adjustments to financing models and incremental increases in public spending, these efforts have not yet resulted in substantial reductions in OOP expenditures or significant improvements in financial protection (20).

Conclusion

Health expenditure in the Western Balkan region reflects a complex interplay of economic capacity, demographic pressures, and ongoing health system reforms. Although health spending has increased gradually in recent years, the region continues to lag behind European Union averages in both total and per capita health expenditure.

Substantial disparities persist across countries, with Albania consistently recording the lowest and Montenegro the highest levels of health spending.

Across the region, health systems continue to be characterized by limited financial protection and a persistently high reliance on out-of-pocket payments, which remain significantly above EU levels. This high level of direct payment at the point of service contributes to unmet healthcare needs, particularly among low-income and other vulnerable population groups.

Overall, the findings suggest that increasing health expenditure alone is insufficient to achieve universal health coverage objectives. Sustainable progress in the Western Balkans will depend not only on increasing health expenditure but also on ensuring that available resources are used more effectively to achieve better health outcomes and greater system resilience.

Declarations

Ethics approval and consent to participate: Not applicable.

Informed consent: Not applicable.

Conflict of interest: The authors declare no conflict of interest.

Funding: This research received no external funding.

Availability of data and materials: Data used in this study are publicly available from the World Bank, WHO HFA-DB, Eurostat.

Authors' contribution: H.V: literature review, writing, analysis, editing;

M.S: analysis, editing; F.T: supervision

Acknowledgements: None

Artificial Intelligence (AI) statement: No AI tools were used to prepare this manuscript.

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QUESTIONNAIRE-BASED SCREENING FOR PRIMARY HYPEROXALURIA IN HEMODIALYSIS PATIENTS: CLINICAL IMPLICATIONS AND A PRACTICAL PERSPECTIVE

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Abstract

Primary hyperoxaluria (PH) is a rare inherited metabolic disorder that is frequently underrecognized in adult patients, particularly those undergoing chronic hemodialysis. Diagnostic challenges arise from the reduced reliability of biochemical markers in advanced kidney failure, often leading to delayed or missed diagnosis and the development of systemic oxalosis. Recent studies have proposed a simple clinical prediction model based on readily available "red flags" for identifying patients at increased risk of PH1 in dialysis populations. Building on this approach, we propose implementing a questionnaire-based screening strategy adapted for routine clinical use. The potential applicability of this strategy in North Macedonia is further outlined, as a significant proportion of patients receiving kidney replacement therapy have an unknown primary renal disease. Given the existing dialysis care system, systematic screening using a simple questionnaire could be feasibly integrated into clinical practice. Such an approach may facilitate earlier identification of high-risk patients, enable targeted genetic testing, and improve clinical outcomes.

Keywords: *Hemodialysis; Primary Hyperoxaluria; Surveys; Questionnaires.*

Introduction

Primary hyperoxaluria (PH) is a group of rare autosomal recessive disorders of glyoxylate metabolism characterized by excessive endogenous oxalate production. Three types of PH have been described (PH1, PH2 and PH3), caused by defects in specific hepatic enzymes: alanine–glyoxylate aminotransferase (AGT, encoded by AGXT gene) in PH1, glyoxylate reductase/hydroxypyruvate reductase (GRHPR) in PH2, and 4-hydroxy-2-oxoglutarate aldolase (HOGA1) in PH3 (1). The pathophysiology of kidney injury in PH is driven by hepatic overproduction of oxalate, which is primarily excreted by the kidneys. Persistent hyperoxaluria leads to calcium oxalate supersaturation, resulting in recurrent nephrolithiasis, nephrocalcinosis, and progressive tubulointerstitial damage. As kidney function declines, plasma oxalate levels rise, exceeding renal clearance and leading to systemic oxalosis with multi-organ involvement (1,2).

Despite this well-established pathophysiology, PH remains underdiagnosed, particularly in adult patients. Clinical heterogeneity and often subtle early manifestations contribute to delayed recognition. Diagnostic delay is substantial, with reports suggesting a median delay of 3–5 years from symptom onset to diagnosis, and a significant proportion of patients being diagnosed only after

progression to advanced chronic kidney disease or end-stage kidney disease (ESKD) (3,4). Our real-world experience further illustrates this challenge. A case from North Macedonia demonstrated that PH may remain unrecognized until after kidney transplantation, when early graft failure led to the diagnosis, following detection of calcium oxalate deposition on graft biopsy (5). Such cases highlight the critical implications of missed diagnosis, particularly given that isolated kidney transplantation without correction of the underlying metabolic defect is associated with rapid disease recurrence and graft loss. Moreover, a subset of patients undergoing chronic hemodialysis with presumed unknown etiology of kidney failure may, in fact, have unrecognized PH or clinically significant hyperoxaluria. Although the exact prevalence remains uncertain, prediction models suggest that a substantial proportion of dialysis patients exhibit clinical "red flags" for PH, underscoring the need for simple and accessible PH screening strategies in this high-risk population (3). Recently published national evidence-based guidelines for primary hyperoxaluria (2025) provide a structured framework for disease management; however, they do not specifically address systematic screening of patients undergoing chronic hemodialysis (6).

Clinical Importance of Identifying PH in Dialysis Patients

Recognition of PH in patients undergoing chronic dialysis remains critically important despite the presence of advanced kidney failure. Ongoing hepatic overproduction of oxalate persists even in the absence of renal function, leading to progressive systemic oxalosis with deposition of calcium oxalate in multiple organs, including bone, myocardium, retina, and vascular tissues, resulting in significant morbidity and mortality (2,4). Establishing the diagnosis of PH in dialysis patients directly influences dialysis management strategies in HD units. Current recommendations by ERKNet and OxalEurope emphasize the need for intensified and individualized dialysis regimens in patients with PH, as conventional schedules are insufficient to control the oxalate burden. This includes the use of high-flux hemodialysis with maximal blood flow, as well as increased dialysis sessions frequency, tailored to plasma oxalate levels and clinical manifestations of systemic oxalosis in order to improve patients' survival (2).

Failure to establish the diagnosis of PH prior to kidney transplantation carries major clinical consequences. Isolated kidney transplantation in undiagnosed PH is associated with a high risk of early graft failure due to rapid oxalate deposition in the allograft, as demonstrated in clinical reports (4,5). Importantly, identification of PH has implications beyond the individual patient. Given the autosomal recessive inheritance pattern, early diagnosis enables targeted family screening and detection of affected carrier relatives, allowing timely intervention and prevention of disease progression in other family members (2,7). In addition, the emergence of novel disease-modifying therapies, including RNA interference–based treatments that reduce hepatic oxalate production, further emphasizes the value of early and accurate diagnosis even in advanced disease stages (2).

Taken as a whole, these considerations highlight that diagnosing PH in dialysis patients is not merely of academic interest, but has direct implications for prognosis, transplant strategy, family counseling and therapeutic decision-making.

From Diagnostic Challenges to Practical Solutions: Questionnaire-Based Screening

The biochemical diagnosis of PH in patients on dialysis is limited by several fundamental pathophysiological and analytical constraints. In advanced kidney failure, urinary oxalate excretion is no longer a reliable marker, as reduced glomerular filtration leads to decreased urinary elim-

ination despite ongoing hepatic overproduction of oxalate (4,8,9). In this setting, plasma oxalate becomes the principal marker; however, its diagnostic specificity is significantly reduced. Plasma oxalate levels increase in all patients with kidney failure due to reduced clearance, and values may overlap between PH and non-PH populations. Importantly, plasma oxalate levels exceeding the supersaturation threshold of approximately 30–50 μmol/L are associated with systemic oxalosis, but this threshold may be reached in both primary and secondary hyperoxaluria in dialysis patients (9,10). Moreover, plasma oxalate concentrations are highly dependent on dialysis-related factors, including dialysis modality, frequency, membrane type, and timing of sampling relative to dialysis sessions. Post-dialysis measurements may underestimate total body oxalate burden, whereas pre-dialysis levels may vary considerably, further complicating interpretation (2). These diagnostic limitations are further illustrated by reported cases of delayed diagnosis in dialysis patients, where PH remained unrecognized for years despite ongoing treatment. In one such case, the diagnosis was established only after the development of systemic oxalosis with severe multisystem involvement, highlighting the consequences of relying solely on conventional diagnostic approaches (11).

Differentiating primary from secondary hyperoxaluria represents an additional challenge in this population. Secondary causes, including increased intestinal absorption or dietary factors, may also lead to elevated plasma oxalate levels in patients with kidney failure, thereby reducing the specificity of biochemical markers alone (4,10) Although adjunctive markers such as plasma glycolate may support the diagnosis of PH1, their limited availability restricts their routine use. At the same time, pre-analytical issues, including oxalate precipitation in urine samples and strict requirements for plasma handling, further reduce the reliability of biochemical testing (9,10). Consequently, reliance on biochemical markers alone is insufficient for accurate diagnosis in dialysis populations. Importantly, the recently adopted national evidence-based guidelines for primary hyperoxaluria (2025) primarily focus on diagnostic and therapeutic strategies following established clinical suspicion, without addressing systematic screening in dialysis populations (6). Given that a significant proportion of dialysis patients have an unknown primary renal disease, this represents a clinically relevant gap. The questionnaire-based screening approach proposed in this study may serve as a practical and implementable strategy to bridge this gap by enabling early identification of high-risk patients. In this context, current expert recommendations emphasize genetic testing in patients with high clinical suspicion; however, given its cost and limited accessibility, initial patient selection using simple clinical tools, such as questionnaire-based screening, may represent a necessary and pragmatic first step (4,12).

Clinical Prediction Model and Questionnaire-Based Screening

A clinical prediction model for PH1 in adult dialysis patients has recently been developed based on five readily available clinical "red flags": active nephrolithiasis or nephrocalcinosis, prior graft loss, early initiation of hemodialysis (before 40 years of age), and family history of chronic kidney disease (3). Using these variables, a scoring system ("PH score") was developed, demonstrating excellent diagnostic performance, with strong discrimination ability (AUC 0.93 in the training cohort and 0.85 in validation). The score ranges from 0 to 3, with higher values indicating a greater probability of PH1. Importantly, even a low threshold (≥1 positive criterion) provides high sensitivity (up to 91%), supporting its role as an initial screening tool in dialysis populations (3).

The clinical applicability of this algorithm has also been demonstrated in a multicenter Italian cohort of adult dialysis patients with genetically confirmed PH1, in which at least one "red

flag" was present in 93% of patients, confirming the high sensitivity of the model in real-world settings (8). As shown in the results of this study, active nephrolithiasis was the most frequent feature (87%), followed by early dialysis initiation, nephrocalcinosis and family history of CKD, supporting the relevance of these variables for clinical screening.

Based on this model, we adapted a translated Macedonian version of the questionnaire suitable for routine clinical use, incorporating four key elements derived from the original "red flags": (1) history of active nephrolithiasis, defined as recurrent, early-onset (<25 years), bilateral, or familial stone disease; (2) early initiation of dialysis before 40 years of age, suggesting rapidly progressive kidney disease; (3) previous kidney graft loss without a clear alternative explanation; and (4) family history of chronic kidney disease, reflecting the inherited nature of the disorder. The original version of the questionnaire is available at https://qxmd.com/calculate/calculator_886/primary-hyperoxaluria-prediction-tool (3). Each positive response in the questionnaire contributes to a cumulative score, with the presence of at least one criterion indicating a high-risk profile that should prompt further diagnostic evaluation. Increasing number of positive responses is associated with higher PH specificity, reaching up to 100% when three criteria are present (3,8). The Macedonian version of the questionnaire is provided as supplementary material to this manuscript.

Implementation of a Questionnaire-Based Screening in North Macedonia

According to the ERA Registry Annual Report 2023, the prevalence of patients with the need for kidney replacement therapy (KRT) in North Macedonia is 974.1 per million population (pmp), corresponding to a total of 1,779 patients. Among them, 84.7% are treated with hemodialysis, 0.8% with peritoneal dialysis, and 14.5% have a functioning kidney transplant. Notably, 87.1 pmp (8.9%) of prevalent patients on KRT have an unknown primary renal disease. In 2023, the incidence of patients on KRT was 254.9 pmp, with a mean age of 65.2 years and a male predominance (57%). Among incident patients, 18.1 pmp (7.8%) have an unknown underlying kidney disease (13).

The dialysis care structure in North Macedonia provides a favorable framework for the implementation of systematic screening. Currently, there are 23 dialysis centers distributed across the country, each staffed with physicians responsible for the longitudinal care of patients undergoing chronic hemodialysis, with full access to their medical history (14). Within this structure, the proposed questionnaire-based screening could be readily integrated into routine clinical practice. Screening may be particularly valuable when performed at the initiation of dialysis, as well as during pre-transplant evaluation, where identification of undiagnosed primary hyperoxaluria has direct implications for transplant strategy and graft survival. The questionnaire would be administered by the treating nephrologist at the dialysis center, who would subsequently calculate the PH score for each patient. Particular focus should be placed on patients with unknown primary renal disease, as well as those with clinical features suggestive of PH, including a history of nephrolithiasis, early-onset kidney failure, or family history of kidney disease. Patients identified as high risk, based on a positive PH score, should be referred to the University Clinic of Nephrology in Skopje for further evaluation, including genetic testing to confirm the diagnosis. Such a structured, stepwise approach would allow efficient allocation of resources by prioritizing high-risk individuals for advanced diagnostics, while maintaining feasibility within the existing healthcare system.

Conclusion

Primary hyperoxaluria remains an underrecognized cause of kidney failure in dialysis populations, largely due to diagnostic limitations and clinical heterogeneity. Questionnaire-based screening represents a simple, low-cost, and scalable approach for identifying high-risk patients, particularly in settings with limited access to advanced diagnostics. In North Macedonia, where a notable proportion of patients on kidney replacement therapy have an unknown primary renal disease, and dialysis care is centralized within a structured network of centers, the implementation of such a screening strategy is both feasible and clinically justified. Integrating questionnaire-based screening into routine dialysis practice may facilitate earlier diagnosis, enable targeted genetic testing, and ultimately improve patient outcomes.

Declarations

Ethics Approval and consent to participate: Ethical approval was not required for this narrative review article because no human participants, patient data, or experimental interventions were involved.

Informed consent: Not applicable.

Conflict of Interest: The authors declare no conflicts of interest.

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Availability of data and materials: No datasets were generated or analyzed during the current study. The English and Macedonian versions of the questionnaire are provided as supplementary materials.

Author Contributions: V. K drafted the manuscript and performed data collection and analysis. N. Gj. conceived the study idea and developed the overall concept. P. D. V contributed through supervision, critical revisions, and important scientific guidance. All authors reviewed and approved the final version of the manuscript.

Acknowledgments: None

Artificial Intelligence (AI) Statement: Artificial intelligence (AI)-assisted tools were used exclusively for language editing and grammar correction.

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CASE REPORT *UDK: 618.19-002.3-073.763.5*

www.doi.org/10.67214/y7n2n013

BEYOND MASTITIS: MULTICENTRIC BREAST ABSCESS OF THE RIGHT BREAST DIAGNOSED BY MULTIMODAL IMAGING

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Abstract

Introduction: Breast abscess is a known complication of mastitis, however multicentric involvement in non-lactating patients is uncommon and may closely mimic malignancy, creating a diagnostic challenge and often necessitating advanced imaging.

Case Presentation: We report the case of a 28-year-old patient who was referred with a clinical diagnosis of right-sided mastitis following initial surgical evaluation. Ultrasound examination demonstrated a well-defined hypoechoic collection containing dense fluid, associated with a fistulous tract extending toward the para-mammary region, as well as findings suggestive of abscess formation. Given the complexity of the presentation, further evaluation with breast magnetic resonance imaging was performed. MRI revealed multiple multicentric lesions within the right breast, characterized by low signal intensity on T1-weighted images, high signal intensity on T2-weighted images, and peripheral rim enhancement following contrast administration, findings that are consistent with multicentric breast abscesses. No suspicious solid enhancing components were identified.

Conclusion: This case highlights the importance of a multimodal imaging approach in the assessment of atypical or extensive breast infections. While ultrasound remains the first-line modality for detection and guidance of intervention, MRI provides superior delineation of disease extent, identification of multicentric involvement, and improved differentiation from malignancy. Accurate imaging interpretation is essential for appropriate clinical management, avoiding unnecessary invasive procedures, and ensuring timely and targeted treatment.

Keywords: *breast abscess; breast infection; magnetic resonance imaging; mastitis; ultrasound.*

Introduction

Breast infections represent a heterogeneous group of inflammatory conditions ranging from simple mastitis to complex abscess formation and, in some cases, conditions associated with underlying malignancy. Breast abscess is defined as a localized collection of purulent material, most commonly arising as a complication of infectious mastitis, and occurs in approximately 5–11% of affected patients, particularly in lactating women, although non-lactational cases are increasingly recognized and clinically significant (1,2). In non-puerperal patients, breast abscesses often present with atypical clinical features and may be associated with risk factors such

as smoking, diabetes, or chronic inflammatory conditions, further complicating diagnosis and management (1,3).

Inflammatory breast diseases encompass a wide spectrum of entities, including infectious mastitis, granulomatous mastitis, and inflammation secondary to malignancy, all of which may demonstrate overlapping clinical and imaging features (3,4). This overlap creates a well-recognized diagnostic dilemma, as breast abscesses may mimic inflammatory breast carcinoma both clinically and radiologically, necessitating careful evaluation and, in some cases, histopathological confirmation (4,5). Failure to accurately differentiate these entities may lead to delayed diagnosis or inappropriate treatment.

Imaging plays a pivotal role in the evaluation of suspected breast infection. Due to its accessibility and ability to identify fluid collections, ultrasound (US) is the first-line modality, typically demonstrating hypoechoic or complex cystic lesions with internal echoes and posterior acoustic enhancement (2,6). However, in complex, recurrent, or atypical presentations, magnetic resonance imaging (MRI) provides superior soft-tissue contrast and enables more accurate assessment of lesion extent, multicentricity, and internal features, including rim enhancement patterns and surrounding inflammatory changes (7). These traits are essential in distinguishing abscesses from malignancies, which may present with similar enhancement characteristics.

Multicentric breast abscesses are relatively uncommon and often associated with prolonged disease course, delayed diagnosis, or systemic predisposition, and their imaging appearance may closely resemble malignant processes, requiring a high level of diagnostic suspicion and multimodal correlation (7,8). In this context, accurate interpretation of imaging findings is essential for appropriate clinical management and avoidance of unnecessary invasive procedures.

We present a case of a multicentric breast abscess of the right breast, initially referred as mastitis, in which multimodal imaging—ultrasound and MRI—played a decisive role in establishing the diagnosis and excluding malignancy.

Case presentation

A 28-year-old female patient was referred from the Department of Thoracic Surgery with a clinical diagnosis of right-sided mastitis (ICD-10: N61) despite ongoing antibiotic therapy.

The patient reported persistent localized breast discomfort and swelling, with only partial clinical improvement following intravenous antibiotic treatment, raising suspicion for a complicated or atypical inflammatory process. She had no known history of diabetes mellitus, prior breast disease, smoking, or other chronic inflammatory conditions. The patient was non-lactating and at presentation denied significant systemic symptoms, including fever or generalized malaise. Given the persistence of symptoms and the incomplete response to initial therapy, a multimodal imaging assessment was undertaken to further delineate the extent of disease and exclude an underlying malignant or extensive inflammatory process.

Ultrasound Findings - Breast ultrasound examination demonstrated:

- A well-defined hypoechoic collection located in the outer and lower quadrants of the right breast, Figure 1(b);

- Heterogeneous internal echoes, consistent with dense purulent content;
- Posterior acoustic enhancement, supporting fluid nature of the lesion;
- A fistulous tract extending laterally toward the para-mammary region, indicating a chronic or complicated abscess;
- Surrounding breast parenchyma without marked hyperemia on Doppler evaluation, suggesting subacute or partially treated inflammation, Figure 1(a);

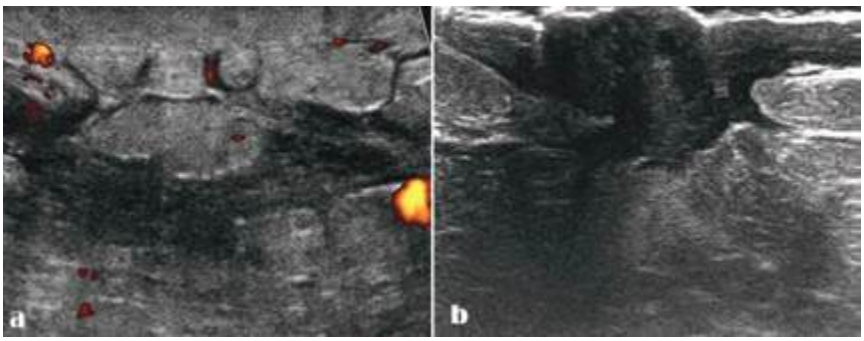

Figure 1. Ultrasound findings of right breast abscess.

(a) Ultrasound image demonstrating altered echogenicity of the right breast parenchyma with areas of increased echogenicity consistent with surrounding inflammatory changes and subcutaneous edema. **(b)** Non-lactational abscess in the right breast showing a well-defined hypoechoic collection with heterogeneous internal echoes, posterior acoustic enhancement, and a fistulous tract extending through the parenchymal planes, corresponding to abscess tracking within the breast tissue.

These findings were consistent with a localized breast abscess with fistulization. However, the full extent of disease and potential multifocal involvement could not be adequately assessed by ultrasound alone, prompting further evaluation with MRI.

MRI Findings

Breast MRI provided a comprehensive assessment of the disease extent and demonstrated:

- Multiple multicentric lesions involving the right breast, extending beyond the area identified on ultrasound;
- Lesions of variable size distributed across different quadrants, confirming multifocal and multicentric involvement;
- T1-weighted images: lesions appeared predominantly hypointense, consistent with fluid content, Figure 2(a);
- T2-weighted images: lesions were markedly hyperintense, reflecting fluid-rich collections with inflammatory components, Figure 2(b, c);
- Areas of intermediate signal intensity within some lesions, suggestive of proteinaceous or debris-containing material;
- Peripheral rim enhancement of the lesions following contrast administration, consistent with abscess cavities, Figure 3(a-f);

- No internal solid enhancing components, reducing suspicion for malignancy;
- Surrounding parenchymal enhancement, consistent with inflammatory changes;
- Mild associated parenchymal edema and inflammatory infiltration;
- No suspicious axillary lymph nodes or features suggestive of metastatic involvement, Figure 2(d).

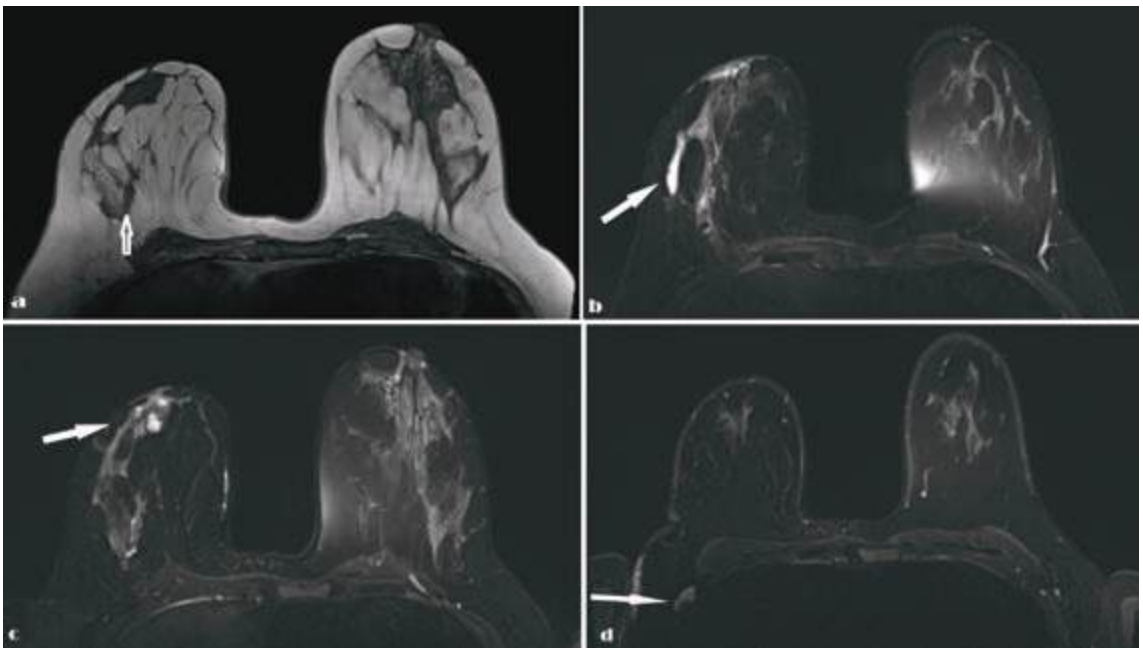

Figure 2. Breast MRI findings in multicentric right breast abscess.

(a) Axial T1-weighted image demonstrating a predominantly hypointense lesion in the right breast (arrow), consistent with a fluid-containing collection. **(b, c)** Axial T2-weighted SPAIR images showing multiple hyperintense multicentric lesions with heterogeneous internal signal, corresponding to proteinaceous or purulent fluid content, with surrounding parenchymal edema. **(d)** Axial T2-weighted SPAIR image demonstrating a reactive lymph node in the right axilla, with preserved morphology and signal characteristics.

MRI provided a significantly broader perspective than ultrasound, enabling accurate delineation of multicentric disease distribution, superior characterization of lesion composition, and confident exclusion of malignancy. These findings were consistent with multicentric breast abscesses, supporting a diagnosis of complicated infectious mastitis with multifocal involvement and guiding appropriate clinical management.

Based on imaging findings, the patient underwent targeted drainage and continued antibiotic therapy, with gradual clinical improvement during follow-up.

Given the atypical multicentric presentation and the need to document the complete therapeutic response, a follow-up breast MRI examination has been scheduled one month after completion of treatment. The purpose of the follow-up imaging is to assess the resolution of the inflammatory changes, confirm regression of the abscess cavities, and exclude any residual suspicious enhancing components.

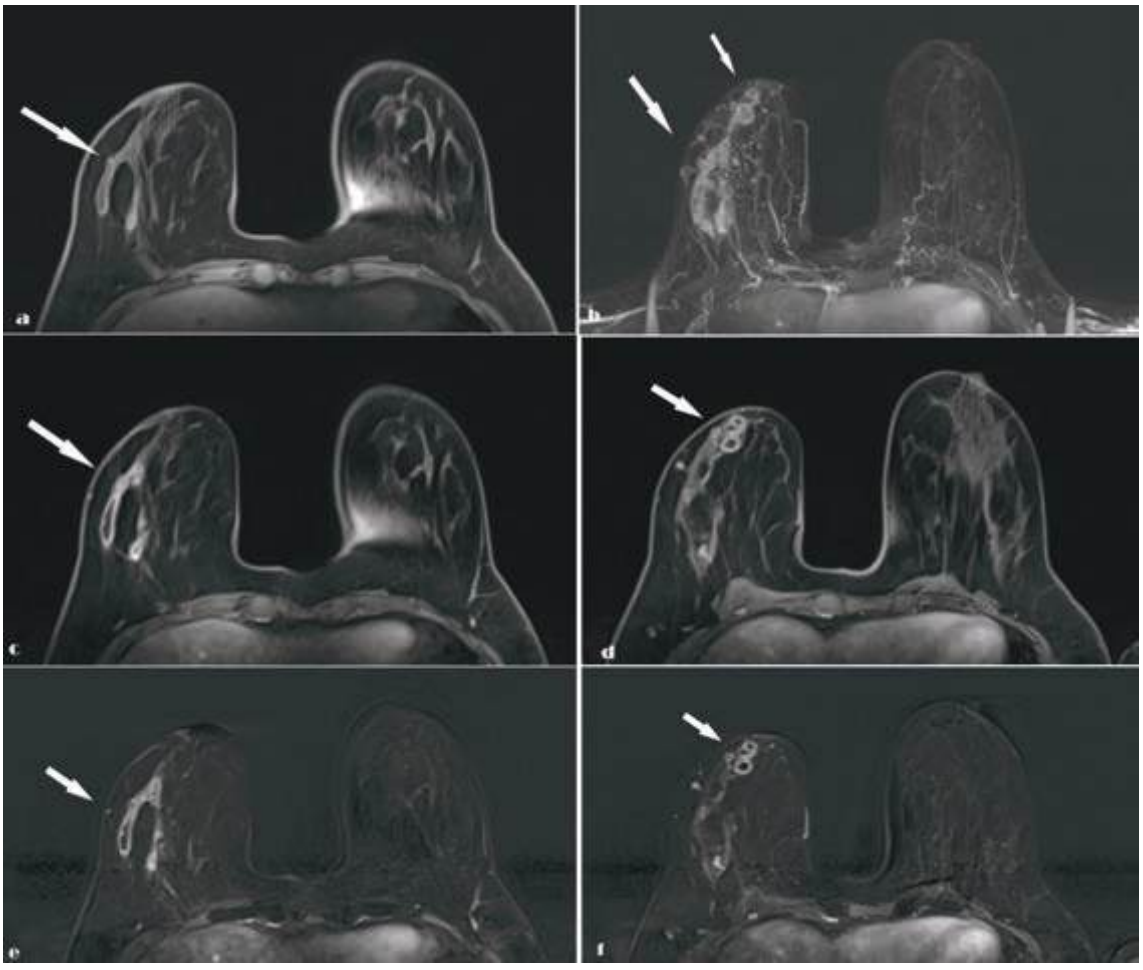

Figure 3. Contrast-enhanced breast MRI demonstrating multicentric abscesses in the right breast.

(a) Axial T1-weighted native image showing predominantly hypointense lesions corresponding to fluid-containing collections. **(b)** Maximum intensity projection (MIP) from post-contrast T1-weighted imaging demonstrating multifocal areas of enhancement in the right breast. **(c, d)** Axial dynamic post-contrast T1-weighted images showing multiple lesions with characteristic peripheral rim enhancement and absence of internal solid enhancing components. **(e, f)** Subtracted dynamic post-contrast T1-weighted images highlighting the rim-enhancing pattern of the lesions, with improved visualization of lesion margins and multicentric distribution.

Discussion

Breast abscess represents a well-recognized complication of infectious mastitis, most frequently encountered in lactating women, but increasingly reported in non-lactational settings where the clinical course may be more complex and prolonged (1,3). In such cases, imaging plays a central role not only in confirming the diagnosis but also in excluding malignancy, particularly inflammatory breast carcinoma, which may present with overlapping clinical and radiological features (3,4).

Ultrasound remains the initial modality of choice, allowing identification of fluid collections and guiding intervention. Typical findings include hypoechoic or complex cystic lesions with

internal echoes and posterior acoustic enhancement (2,6,9). In the present case, ultrasound detected a localized abscess and an associated fistulous tract; however, it underestimated the true extent of the disease. This limitation is well described, particularly in cases of multifocal or deep parenchymal involvement.

MRI provided a decisive diagnostic advantage by demonstrating the multicentric distribution of lesions, which were not fully visualized on ultrasound. The observed signal characteristics—T1 hypointensity, T2 hyperintensity, and peripheral rim enhancement—are consistent with previously reported MRI features of breast abscesses (7,9,10). Importantly, the absence of internal solid enhancement and the presence of a typical rim-enhancing pattern supported a benign inflammatory process rather than malignancy. Similar MRI findings have been described in rare reports of multiple breast abscesses in non-lactating patients, where imaging played a key role in avoiding unnecessary biopsy or surgical intervention (7,8,10).

Multicentric breast abscesses remain relatively uncommon and are often associated with delayed diagnosis or incomplete response to therapy (8). Compared to single abscesses, they may present with less pronounced inflammatory signs, as seen in this case, further complicating clinical assessment. This highlights the importance of considering advanced imaging when clinical evolution is atypical or when initial imaging findings do not fully explain the patient's symptoms.

Overall, this case reinforces the complementary role of ultrasound and MRI. While ultrasound is indispensable for initial detection and procedural guidance, MRI offers superior evaluation of disease extent and distribution, enabling confident differentiation from malignancy and more precise treatment planning.

Conclusion

This case highlights the importance of a multimodal imaging approach in the evaluation of breast infections. Ultrasound remains the first-line diagnostic tool, enabling rapid identification of fluid collections and guiding intervention. However, in complex or atypical presentations, particularly when multicentric involvement is suspected, MRI provides essential additional information by accurately delineating disease extent and characterizing lesion morphology. Careful interpretation of imaging findings is crucial for differentiating abscess from malignancy, especially in non-lactating patients, where diagnostic uncertainty is higher. Early recognition combined with appropriate imaging-guided management plays a key role in preventing complications and ensuring optimal clinical outcomes.

Declarations

Ethics approval and consent to participate: Not applicable.

Informed consent: Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Conflict of interest: The author declares no conflict of interest.

Funding: This research received no external funding.

Availability of data and materials: The data supporting the findings of this case report are available from the corresponding author upon reasonable request.

Authors' contributions: S.N. contributed to the conception and design of the study, data acquisition, image interpretation, drafting of the manuscript, and final approval of the version to be published.

Acknowledgements: The author would like to acknowledge the staff of the University Institute of Radiology, Skopje, for their support in the imaging procedures.

Artificial Intelligence (AI) statement: AI-assisted language support tools were used exclusively for linguistic refinement and grammar improvement during manuscript preparation. The author takes full responsibility for the scientific content, interpretation, and final version of the manuscript.

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www.doi.org/10.67214/zeahf840

EARLY-ONSET OSTEOPOROSIS IN ADULT TURNER SYNDROME: IMPORTANCE OF LIFELONG BONE MONITORING

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Abstract

Introduction: Turner syndrome (TS) is a common sex chromosome disorder associated with gonadal dysgenesis, chronic estrogen deficiency, and increased risk of impaired bone mineral acquisition. Reduced bone mineral density may remain under-recognized during the transition from pediatric to adult care.

Case presentation: We report a 29-year-old woman with TS due to monosomy X (45, X), diagnosed at 17 years of age, who was referred for endocrine evaluation and skeletal assessment. She had short stature (141 cm), low body weight (38 kg; BMI 19.1 kg/m^2), delayed puberty, primary ovarian insufficiency, and inconsistent adherence to cyclic estrogen–progestin replacement therapy. Hormonal evaluation showed hypergonadotropic hypogonadism, with elevated FSH and LH and low estradiol.

Thyroid evaluation confirmed autoimmune thyroiditis with stable thyroid function under levothyroxine replacement. DXA demonstrated bone mineral density below the expected range for her age, predominantly at the hip. Lumbar spine L1–L4 BMD was 0.901 g/cm^2 with a Z-score of −1.4, while total left and right femur Z-scores were −2.4 and −2.6, respectively. Femoral neck Z-scores ranged from −2.3 to −2.5. Vitamin D deficiency was also present. Although small bone size and short stature may contribute to underestimation of areal BMD by DXA, the markedly reduced femoral Z-scores, chronic hypoestrogenism, low body weight, inconsistent hormone replacement therapy, and vitamin D deficiency supported clinically relevant secondary skeletal impairment.

Conclusion: This case highlights the importance of lifelong skeletal surveillance in TS, including early DXA assessment interpreted with Z-scores, optimization of hormone replacement therapy, correction of vitamin D deficiency, adequate calcium intake, and fracture prevention strategies.

Keywords: *bone mineral density; HRT; osteoporosis; Turner syndrome.*

Introduction

Turner syndrome (TS) is one of the most common chromosomal disorders affecting females, with an estimated prevalence of approximately 1 in 2,000–2,500 live female births. It results from the complete or partial absence of one X chromosome and is characterized by a broad and

highly variable clinical phenotype involving multiple organ systems (1,2).

Common manifestations include short stature, gonadal dysgenesis, delayed puberty, infertility, cardiovascular abnormalities, autoimmune disorders, metabolic dysfunction, neurocognitive features, and skeletal complications (1,2). Although the clinical phenotype may vary according to karyotype and degree of mosaicism, primary ovarian insufficiency remains one of the most consistent endocrine features of TS and represents a major determinant of long-term morbidity (1,3).

Estrogen deficiency secondary to gonadal dysgenesis has a profound impact on skeletal development and bone metabolism. Adequate estrogen exposure during puberty is essential for normal bone mineralization and attainment of peak bone mass. Consequently, girls and women with TS are at increased risk of impaired bone accrual beginning in adolescence, which may persist into adulthood and predispose to reduced bone mineral density and fragility fractures (1,4).

In addition to hypoestrogenism, several other mechanisms contribute to compromised skeletal health in TS, including altered bone geometry, reduced cortical bone thickness, impaired trabecular bone quality, decreased muscle mass, vitamin D deficiency, low body weight, and reduced physical activity (1,4).

Reduced bone mineral density (BMD) and increased fracture risk are well-recognized manifestations of Turner syndrome. Recent reviews have reported that fracture risk in patients with TS may be approximately 1.4–2.2 times higher than in the general population, with hypogonadism and inadequate estrogen exposure representing major contributing factors (4). Vertebral fractures, impaired bone quality, and early skeletal deterioration have been described, even in relatively young patients (4,5).

Li et al. reported a severe case of TS-associated osteoporosis with multiple vertebral compression fractures requiring repeated percutaneous vertebroplasty, illustrating the potential severity of skeletal complications in the setting of prolonged estrogen deficiency (5). In addition, Rawat et al. described primary hyperparathyroidism in a young woman with TS who presented with hypercalcemia and renal stones, further emphasizing the need to evaluate endocrine comorbidities that may aggravate skeletal risk (6).

Despite advances in pediatric diagnosis and management, long-term follow-up during adulthood remains challenging. Clinical attention is often directed toward reproductive, cardiovascular, and metabolic complications, whereas skeletal health may be underestimated or insufficiently monitored (1,3). Delayed recognition of TS may contribute to prolonged untreated estrogen deficiency and preventable long-term complications. Recent case reports describing TS diagnosed in late adulthood, including at 61 and 76 years of age, underscore the variable presentation of the syndrome and the potential consequences of missed or delayed diagnosis (7,8).

Current international guidelines recommend lifelong multidisciplinary surveillance in girls and women with TS, including assessment of bone health, optimization of calcium and vitamin D intake, promotion of weight-bearing physical activity, and timely initiation and maintenance of estrogen–progestin hormone replacement therapy to support bone accrual and reduce future fracture risk (1). Recent clinical data have also demonstrated beneficial effects of hormone replacement therapy on BMD in adult women with TS, reinforcing the importance of adequate

hormonal management throughout life (9).

This case report describes markedly reduced bone mineral density below the expected range for a women aged 29 with Turner syndrome. The case highlights the importance of continuous skeletal surveillance beyond childhood and adolescence, appropriate DXA interpretation using Z-scores in young women, and timely interventions to preserve bone mass and reduce long-term fracture risk.

Case Presentation

A 29-year-old woman with a previously established diagnosis of Turner syndrome was referred for comprehensive endocrinological evaluation and assessment of skeletal health. Turner syndrome was diagnosed at the age of 17, based on cytogenetic analysis demonstrating monosomy X, 45,X.

Her clinical phenotype included short stature, delayed pubertal development, and primary ovarian insufficiency. The patient's final adult height was 141 cm, with a body weight of 38.0 kg and a body mass index of 19.1 kg/m^2. Growth hormone therapy had been administered during late adolescence, resulting in an approximate height gain of 5 cm.

The patient had a history of primary hypothyroidism diagnosed in 2013. She reported irregular adherence to levothyroxine therapy for several years, with treatment reinitiated in 2023. At the time of assessment, thyroid function was stable under levothyroxine replacement therapy.

Thyroid ultrasonography demonstrated a thyroid gland of normal size, shape, and anatomical position, but with heterogeneous and non-homogeneous parenchyma, anechoic areas suggestive of lymphocytic infiltration, and hyperechogenic reflections consistent with chronic autoimmune thyroiditis. No focal thyroid nodules were identified. The markedly elevated anti-thyroid peroxidase antibody level further supported the diagnosis of autoimmune thyroiditis, a common autoimmune comorbidity in Turner syndrome.

Reproductive history and hormonal evaluation were consistent with primary ovarian insufficiency secondary to gonadal dysgenesis. The patient had delayed pubertal development and had been prescribed cyclic estrogen–progestin hormone replacement therapy; however, adherence had been inconsistent over several years. Biochemical evaluation demonstrated markedly elevated gonadotropin concentrations, with follicle-stimulating hormone of 62 IU/L and luteinizing hormone of 53 IU/L, accompanied by low estradiol concentration of 28 pg/mL.

These findings were compatible with hypergonadotropic hypogonadism, which is characteristic of Turner syndrome.

Transvaginal ultrasonography revealed a hypoplastic uterus with thin endometrium and markedly reduced ovarian dimensions bilaterally, supporting the presence of longstanding gonadal dysgenesis and chronic estrogen deficiency.

Given the well-established association between Turner syndrome and impaired skeletal health, bone mineral density was evaluated using dual-energy X-ray absorptiometry. In view of the patient's young age, premenopausal status, and Turner syndrome as an underlying cause of sec-

ondary bone loss, DXA interpretation was primarily based on Z-scores rather than T-scores. Lumbar spine assessment showed a mean L1–L4 BMD of 0.901 g/cm², corresponding to a Z-score of −1.4, with individual vertebral Z-scores ranging from −0.9 to −1.6.

A more pronounced reduction in bone mineral density was observed at the hip. Total left femur BMD was 0.617 g/cm² with a Z-score of −2.4, while total right femur BMD was 0.591 g/cm² with a Z-score of −2.6. Femoral neck Z-scores ranged from −2.3 to −2.5 bilaterally, indicating bone mineral density below the expected range for the age. The greatest skeletal deficits were observed in Ward's and trochanteric regions, with Z-scores reaching −3.2 and −2.8, respectively.

These findings indicate markedly impaired peak bone mass acquisition in a young adult woman with Turner syndrome. The reduced bone mineral density is most likely multifactorial, related to chronic hypoestrogenism, delayed and inconsistent hormone replacement therapy, low body weight, reduced mechanical loading, vitamin D deficiency, and longstanding gonadal dysgenesis. In this clinical context, the skeletal impairment should be interpreted as secondary osteoporosis associated with Turner syndrome rather than primary or postmenopausal osteoporosis.

Body composition analysis demonstrated a low body weight, fat mass of 15.9%, and lean mass of 84.1%. The patient denied smoking, excessive alcohol intake, glucocorticoid or anticonvulsant use, and there was no reported family history of osteoporosis or fragility fractures.

Biochemical assessment showed serum calcium and phosphorus within reference ranges, with normal renal and liver function tests. However, 25-hydroxyvitamin D levels were markedly reduced, ranging from 6 to 14 ng/mL, consistent with significant vitamin D deficiency and representing an additional modifiable contributor to impaired bone health. No additional major contributors to secondary bone loss were identified apart from Turner syndrome–related hypogonadism, low body weight, and vitamin D deficiency.

Other endocrine and metabolic parameters were unremarkable. Prolactin was within the reference range. Fasting plasma glucose and fasting insulin levels were normal, without evidence of impaired glucose metabolism or insulin resistance at the time of evaluation. Dehydroepiandrosterone sulfate, total testosterone, and morning cortisol concentrations were also within the expected reference ranges.

Serum growth hormone and insulin-like growth factor 1 levels were appropriate for adulthood following previous growth hormone therapy, with no biochemical evidence of persistent growth hormone deficiency.

Although the patient had been followed endocrinologically for Turner syndrome-associated comorbidities, bone mineral density assessment had not been performed earlier in adulthood. She had no previous history of fragility fractures; however, the presence of markedly reduced bone mineral density at the age of 29 years suggests increased future fracture risk.

This case emphasizes that skeletal surveillance in Turner syndrome should extend beyond childhood and adolescence and should be incorporated into lifelong multidisciplinary care. Early DXA assessment, interpretation using Z-scores in young women, optimization of hormone replacement therapy, correction of vitamin D deficiency, adequate calcium intake, and long-term monitoring are essential for reducing future skeletal complications in this high-risk population.

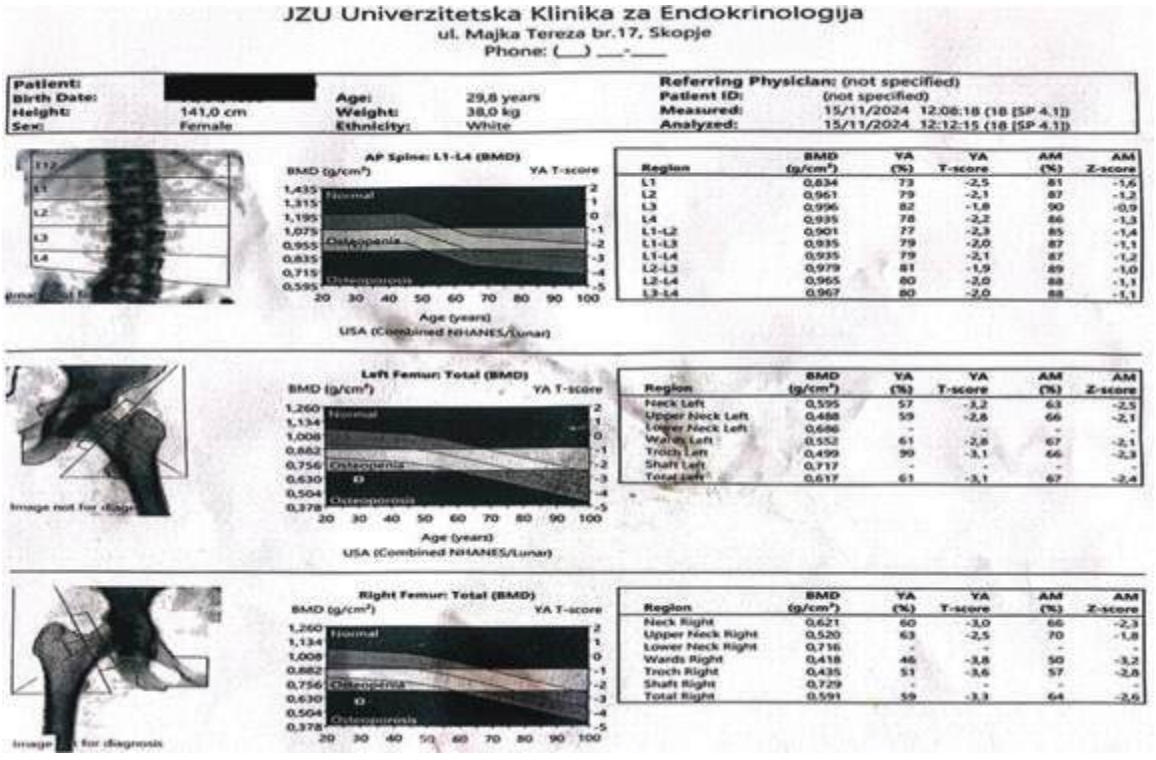

Figure 1. DXA scan showing reduced bone mineral density in a 29-year-old patient with Turner syndrome. Z-scores demonstrated lumbar spine reduction (L1–L4 Z-score −1.4), with more pronounced femoral involvement, including total left femur Z-score −2.4 and total right femur Z-score −2.6, consistent with bone mineral density below the expected range for age.

Discussion

Turner syndrome is a lifelong multisystem disorder in which skeletal health represents an important, but often under-recognized, component of long-term morbidity. Although short stature, gonadal dysgenesis, infertility, cardiovascular anomalies, and autoimmune disorders are commonly emphasized in clinical follow-up, reduced bone mineral density and increased fracture risk are also well-established complications (1,4).

The present case illustrates early-onset impairment of bone health in a young adult woman with Turner syndrome, emphasizing the need for systematic skeletal assessment beyond childhood and adolescence (1,4).

The main finding in this patient was significantly reduced bone mineral density at the age of 29, with the greatest impairment observed at the hip. Because the patient was young and premenopausal, and because Turner syndrome itself represents an underlying cause of secondary osteoporosis, interpretation of DXA findings should primarily rely on Z-scores rather than T-scores (1,4). In this case, lumbar spine BMD was reduced but less severely affected, with an L1–L4 Z-score of −1.4. In contrast, femoral involvement was more pronounced, with total left femur and total right femur Z-scores of −2.4 and −2.6, respectively. These values indicate bone mineral density below the expected range for the age and suggest clinically relevant impairment of peak bone mass acquisition (1,4).

An additional consideration in the interpretation of DXA findings in Turner syndrome is the influence of short stature and small bone size on areal BMD measurements. DXA provides a two-dimensional estimate of bone mineral density and may underestimate volumetric bone density in individuals with smaller bones (4,10,11). Therefore, in patients with Turner syndrome, particularly those with marked short stature, reduced areal BMD should be interpreted with caution and in the context of body size, pubertal history, estrogen exposure, and clinical risk factors. Adjustment methods such as bone mineral apparent density, height-for-age Z-scores, or interpretation according to height age rather than chronological age may provide additional information and help distinguish true skeletal fragility from size-related underestimation of BMD (4,10,11). Nevertheless, in the present case, the markedly reduced femoral Z-scores, chronic hypoestrogenism, inconsistent hormone replacement therapy, low body weight, and vitamin D deficiency support clinically relevant skeletal impairment rather than a purely size-related DXA artifact.

Several mechanisms may explain the reduced bone mineral density observed in this patient. The most important factor is chronic estrogen deficiency due to primary ovarian insufficiency, which is one of the hallmark endocrine features of Turner syndrome (1,12). Estrogen plays a central role in pubertal bone mineralization, epiphyseal maturation, maintenance of bone mass, and regulation of bone remodeling (9,12,13). Inadequate estrogen exposure during adolescence and early adulthood may prevent optimal acquisition of peak bone mass, thereby increasing the risk of premature osteoporosis and future fragility fractures (8,9,12,13,14). In the present case, delayed pubertal development and inconsistent adherence to estrogen–progestin hormone replacement therapy likely contributed substantially to skeletal impairment.

Low body weight may have further aggravated bone loss. The patient had a BMI of 19.1 kg/m^2 and low body weight, which may reduce the mechanical loading of bone and negatively affect bone strength. Mechanical loading is an important determinant of bone formation, and reduced lean mass or low body mass may contribute to lower bone mineral density, particularly in patients already exposed to chronic hypoestrogenism (11,12,14).

Therefore, the skeletal phenotype in this case is likely multifactorial, resulting from the combined effects of gonadal dysgenesis, inadequate estrogen exposure, low body weight, reduced mechanical stimulation, and vitamin D deficiency.(1,4,11,14)

Vitamin D deficiency represented an additional modifiable risk factor in this patient. Although serum calcium and phosphorus were within reference ranges, 25-hydroxyvitamin D levels were markedly reduced. Vitamin D deficiency may impair calcium absorption, contribute to secondary alterations in bone metabolism, and further compromise bone mineralization. In a patient with Turner syndrome and already reduced bone mass, correction of vitamin D deficiency is essential as part of comprehensive bone-protective management (1).

Another important aspect of this case is the presence of autoimmune thyroiditis. Autoimmune thyroid disease is frequently associated with Turner syndrome and in this patient, it was supported by elevated anti-thyroid peroxidase antibodies and ultrasound features compatible with chronic autoimmune thyroiditis (1). At the time of evaluation, thyroid function was stable under levothyroxine replacement therapy. Although uncontrolled hyperthyroidism or excessive levothyroxine replacement may negatively affect bone metabolism, this was not evident in the present case. Nevertheless, regular monitoring of thyroid function remains important, as both thyroid dysfunction and overtreatment may influence skeletal health over time (1).

The gynecological and hormonal findings further support the role of longstanding gonadal dysgenesis. Elevated FSH and LH levels with low estradiol confirmed hypergonadotropic hypogonadism, while transvaginal ultrasonography demonstrated a hypoplastic uterus with thin endometrium and markedly reduced ovarian dimensions. These findings are consistent with chronic estrogen deficiency and provide a pathophysiological explanation for impaired bone mass acquisition (1,13). They also reinforce the importance of continuous and adequate hormone replacement therapy in women with Turner syndrome, not only for induction and maintenance of secondary sexual characteristics, but also for preservation of skeletal health (8,9,12-14).

This case also highlights an important gap in adult follow-up. Although the patient had regular endocrinological care for Turner syndrome-associated comorbidities, bone mineral density assessment had not been performed earlier in adulthood.

The absence of previous fragility fractures may have contributed to the underestimation of skeletal risk. However, osteoporosis and low bone mass may remain clinically silent until a fracture occurs (1,4,5). Therefore, relying only on symptoms or fracture history may delay diagnosis and intervention. Early DXA screening and periodic reassessment are necessary, especially in patients with delayed puberty, poor adherence to hormone replacement therapy, low body weight, vitamin D deficiency, or other risk factors for reduced bone mass (1,10).

The case also underscores the importance of terminology in young women with Turner syndrome. In postmenopausal women, osteoporosis is commonly classified using T-scores. However, in premenopausal women and younger individuals, particularly those with secondary causes of bone loss, Z-scores are more appropriate for interpretation (10). Therefore, the skeletal impairment in this patient should be described as bone mineral density below the expected range for the age and secondary osteoporosis associated with Turner syndrome, rather than primary postmenopausal osteoporosis. This distinction is clinically relevant because it directs attention to the underlying mechanism, namely, impaired peak bone mass acquisition due to estrogen deficiency and other Turner syndrome-related factors (1,4,10).

From a therapeutic perspective, management should focus on correcting modifiable risk factors and preventing future fractures. Optimization of estrogen–progestin hormone replacement therapy is central, provided there are no contraindications (1,8,9,12-14). Adequate replacement may help maintain bone mass and reduce further skeletal deterioration. Correction of vitamin D deficiency, ensuring sufficient calcium intake, optimizing nutrition, and encouraging regular weight-bearing and muscle-strengthening physical activity are also essential (1). In addition, follow-up DXA assessment should be planned to evaluate the skeletal response to treatment and monitor progression.(1,10)

Pharmacological anti-osteoporotic therapy in young women requires individualized consideration. In this patient, the first priority should be optimization of hormone replacement therapy and correction of vitamin D deficiency, because the underlying cause is mainly hypoestrogenism-related impaired bone accrual (1,8,9,12-14). Antiresorptive or anabolic therapy may be considered only after careful evaluation of fracture risk, persistence of very low BMD despite correction of reversible factors, presence of fragility fractures, or additional risk factors. The patient's reproductive potential, long skeletal retention of some medications, and long-term safety considerations should be taken into account before initiating such treatment.(1)

Overall, this case demonstrates that clinically significant skeletal impairment may be present in young adults with Turner syndrome even in the absence of fragility fractures.(1,4,5) It reinforces the need for lifelong multidisciplinary care, with bone health assessment integrated into routine adult follow-up (1). Timely DXA evaluation using Z-scores, consistent hormone replacement therapy, correction of vitamin D deficiency, adequate calcium intake, lifestyle measures, and regular monitoring are essential to reduce long-term fracture risk (1,8,10). The case therefore contributes to the growing recognition that skeletal surveillance should be considered a core component of adult Turner syndrome management, rather than an optional or secondary concern.

Conclusion

This case highlights early-onset skeletal impairment in a young woman with Turner syndrome, most likely resulting from longstanding hypoestrogenism, delayed and inconsistent hormone replacement therapy, low body weight, vitamin D deficiency, and impaired peak bone mass acquisition. The markedly reduced femoral Z-scores demonstrate bone mineral density below the expected range for the age and support the interpretation of secondary osteoporosis in the context of Turner syndrome.

The case emphasizes that bone health assessment should be an integral component of lifelong multidisciplinary follow-up in patients with Turner syndrome, extending beyond childhood and adolescence into adult care. DXA interpretation in young women should primarily rely on Z-scores rather than T-scores, particularly when secondary causes of bone loss are present. Although small bone size related to Turner syndrome and short stature may contribute to underestimation of areal BMD by DXA, the markedly reduced femoral Z-scores, together with chronic hypoestrogenism, inconsistent hormone replacement therapy, low body weight, and vitamin D deficiency, support clinically relevant secondary skeletal impairment.

Early recognition of reduced bone mineral density, optimization of estrogen–progestin replacement therapy, correction of vitamin D deficiency, adequate calcium intake, and promotion of weight-bearing physical activity are essential strategies to preserve bone mass and reduce future fracture risk.

Declarations

Ethics approval and consent to participate: According to institutional policy, ethics committee approval is not required for single case reports. Not applicable. All procedures were performed as part of routine clinical practice.

Conflict of interest: The authors declare that they have no conflicts of interest related to this manuscript.

Funding: The authors received no financial support for this work.

Informed consent: Written informed consent was obtained from the patient for publication of this case report and accompanying data.

Availability of data and materials: All data generated or analyzed during this study are included in this article. Additional anonymized data are available from the corresponding author upon reasonable request.

Authors' contributions: M.T.S. contributed to study design, data collection, and manuscript preparation. I.M.S. contributed to data interpretation and manuscript revision. A.G.V. contributed to clinical evaluation and manuscript revision. All authors approved the final manuscript.

Acknowledgements: None.

Artificial Intelligence (AI) statement: Artificial intelligence (AI) tools were used exclusively for language editing and formatting assistance during manuscript preparation. No AI tools were used to generate clinical data, perform analyses, interpret results, or draw scientific conclusions. The authors take full responsibility for the accuracy, integrity, and originality of the content.

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www.doi.org/10.67214/t8wk5g53

BILOMA AFTER SUBTOTAL CHOLECYSTECTOMY-A RARE BUT EXPECTED COMPLICATION

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Abstract

Introduction: Biloma is an encapsulated intrahepatic or extrahepatic collection of bile that most commonly occurs as a consequence of iatrogenic biliary injury following cholecystectomy. Diagnosis is primarily based on imaging, with computed tomography (CT) and magnetic resonance cholangiopancreatography (MRCP) playing a central role in the detection of postoperative collections and associated biliary leaks. Management is frequently minimally invasive, with image-guided percutaneous drainage, representing an effective therapeutic option.

Case Presentation: We report the case of a 56-year-old female patient who developed an intrahepatic biloma with secondary abscess formation following subtotal cholecystectomy performed for chronic calculous cholecystitis. Initial ultrasound examination suggested a postoperative biloma, which was further characterized by contrast-enhanced CT demonstrating multiple fluid collections, the largest measuring 15 × 10 cm, with features of early abscess formation.

CT-guided percutaneous drainage was performed, with evacuation of purulent material. Empiric intravenous antibiotic therapy was initiated, resulting in progressive clinical improvement and normalization of inflammatory markers. Follow-up CT demonstrated significant regression of the collections, while MRCP confirmed a patent biliary tree without evidence of active bile leakage. No ERCP or surgical re-intervention was required.

Conclusion: This case highlights the importance of multimodal imaging in the evaluation and management of postoperative biliary complications and demonstrates that selected patients can be successfully managed with a minimally invasive, conservative approach.

Keywords: *Biloma; bile leak; MRCP; percutaneous drainage; subtotal cholecystectomy.*

Introduction

Biloma represents a localized accumulation of bile either within or outside the liver parenchyma, situated beyond the confines of the biliary system and typically enclosed by a well-defined fibrous capsule. The most common underlying cause is iatrogenic injury to the biliary tract, most frequently occurring during cholecystectomy, while blunt abdominal trauma represents the second leading cause (1).

Clinical manifestations may include abdominal pain, fever, jaundice, leukocytosis, or prolonged postoperative recovery; however, symptoms are often nonspecific, potentially delaying diagnosis (2).

Postoperative bile leakage following laparoscopic cholecystectomy may result from common bile duct injury, inadequate cystic duct closure, or anatomical variations involving accessory biliary ducts (3). When infected, bilomas may progress to hepatic abscess formation and potentially lead to systemic infection if not promptly recognized and treated.

Subtotal cholecystectomy is recognized as an important bail-out procedure in difficult gallbladder surgery, particularly when the critical view of safety cannot be achieved because of severe inflammation, distorted anatomy, or dense adhesions (4). Although this approach decreases the risk of major bile duct injury, it is associated with a higher incidence of postoperative bile leakage and related complications (5).

Ultrasound examination is usually the initial imaging modality used in suspected biloma; however, CT provides superior evaluation of the extent of collections and their relationship to surrounding anatomical structures (6). MRCP offers high sensitivity and specificity for detecting biliary leaks while simultaneously providing detailed visualization of the biliary anatomy (3).

The differential diagnosis of biloma includes lymphocele, abscess, hematoma, pancreatic pseudocyst, hepatic cyst, seroma, and cystic metastatic lesions (7). These conditions should be considered when evaluating postoperative hepatobiliary fluid collections because of overlapping imaging findings and clinical presentation.

Case Presentation

A 56-year-old female patient with a history of chronic calculous cholecystitis underwent subtotal cholecystectomy due to dense adhesions and difficult operative anatomy. The immediate postoperative course was initially uneventful, and the patient was discharged home.

Three days after surgery, the patient developed persistent right upper quadrant abdominal pain associated with mild nausea. Abdominal ultrasound performed at a local hospital demonstrated a heterogeneous subhepatic fluid collection suggestive of postoperative biloma, and the patient was referred to our tertiary care center for further evaluation.

Laboratory investigations revealed mild leukocytosis and elevated C-reactive protein levels, consistent with an inflammatory process.

Contrast-enhanced CT of the abdomen demonstrated a large subhepatic fluid collection measuring approximately 15 × 10 cm with heterogeneous content and an air-fluid level. Areas of wall thickening suggested early abscess formation. Adjacent to the inferior liver margin, an additional organized collection measuring approximately 25 × 40 mm was identified. A smaller loculated collection measuring 18 × 11 mm was also present in the right paracolic gutter. Mild surrounding fat stranding and adjacent tissue edema were noted. These findings were consistent with postoperative biloma complicated by secondary abscess formation.

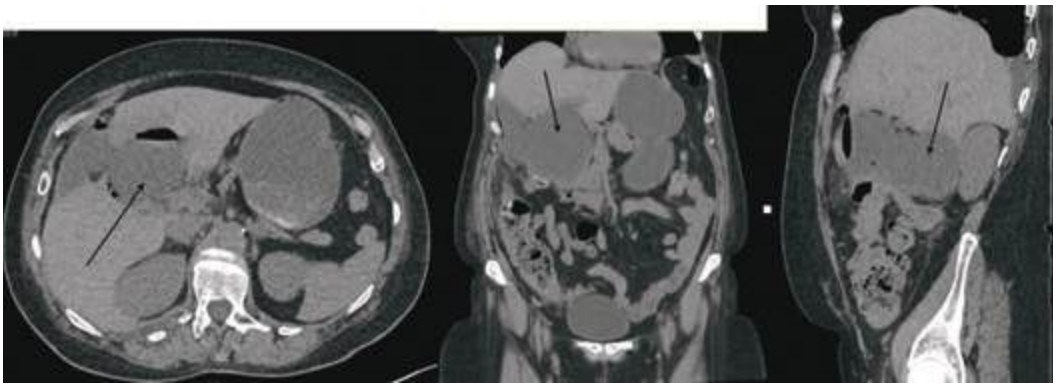

Figure 1. Contrast-enhanced CT images demonstrating a large subhepatic biloma with an air-fluid level (black arrow), consistent with secondary abscess formation. Smaller adjacent collections are also visible.

Following confirmation of the diagnosis, CT-guided percutaneous drainage was performed. After local preparation and administration of local anesthesia, a 12 Fr drainage catheter was inserted into the largest collection under CT guidance. Purulent material was immediately evacuated, confirming the infected bile collection. The drainage catheter was initially positioned deeply within the cavity and was partially withdrawn during follow-up to optimize drainage of residual fluid collections.

Empiric intravenous antibiotic therapy with ceftriaxone and metronidazole was initiated to provide broad-spectrum coverage against common biliary pathogens. The patient demonstrated gradual clinical improvement, with reduced inflammatory markers and resolution of abdominal pain.

Follow-up contrast-enhanced CT demonstrated significant regression of the previously drained collection, with only a small residual fluid component remaining. No newly formed collections were identified.

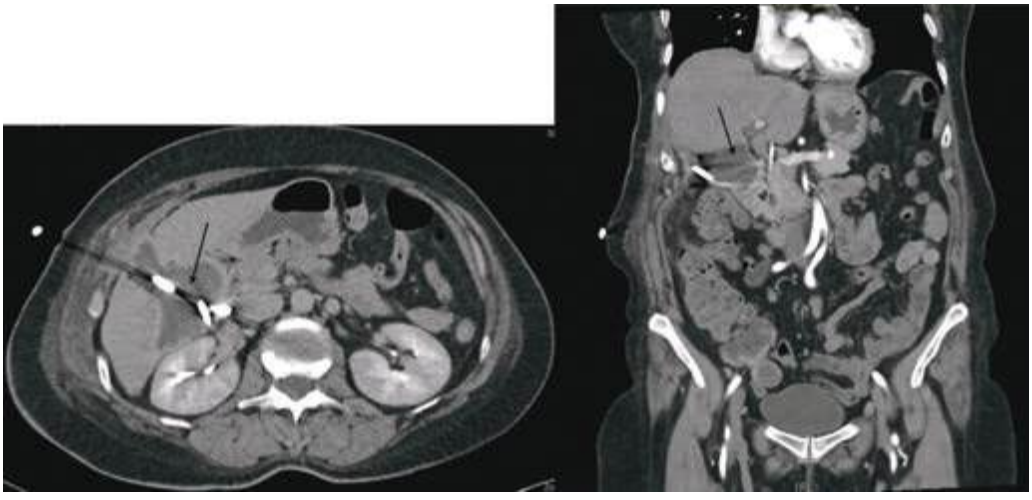

Figure 2. Follow-up contrast-enhanced CT demonstrating significant regression of the previously drained biloma with the drainage catheter in situ. Only minimal residual fluid remains (arrow).

MRCP was subsequently performed for further evaluation of the biliary anatomy. The examination demonstrated patent intrahepatic and extrahepatic bile ducts without evidence of obstruc-

tion, choledocholithiasis, or active bile leakage. The cystic duct stump and a small gallbladder remnant were visualized.

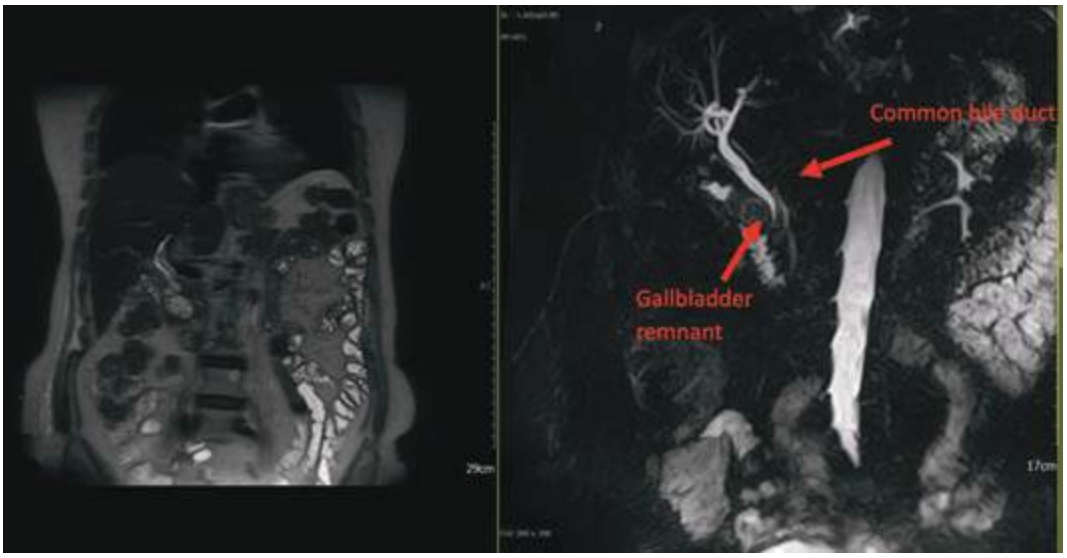

Figure 3. MRCP demonstrating patent intrahepatic and extrahepatic bile ducts without evidence of obstruction or filling defects. The common bile duct measured 7 mm (arrow). The cystic duct stump and a small gallbladder remnant are visualized (arrow).

Conservative treatment was continued, including catheter drainage, intravenous antibiotics, and clinical monitoring. The patient remained hemodynamically stable throughout hospitalization and showed progressive clinical recovery. Follow-up laboratory findings demonstrated normalization of inflammatory markers. No ERCP or surgical re-intervention was required.

At outpatient follow-up, the patient remained asymptomatic, with no evidence of recurrent fluid collections or biliary complications.

Discussion

Subtotal cholecystectomy is widely accepted as a safe alternative in difficult gallbladder surgery when identification of the biliary anatomy is compromised. Although this approach significantly reduces the risk of major bile duct injury, postoperative bile leakage remains one of the most commonly reported complications (4,5). Biloma formation may result from leakage from the cystic duct stump, remnant gallbladder, or small accessory biliary branches.

Previous reports have demonstrated that postoperative bilomas may present with nonspecific clinical symptoms, including abdominal pain, fever, nausea, and elevated inflammatory markers, thereby delaying diagnosis (1,2). In the present case, early postoperative abdominal pain prompted imaging evaluation, allowing timely identification of this complication before progression to severe sepsis.

CT plays a central role in evaluating postoperative biliary complications because it accurately defines the size, extent, and characteristics of fluid collections while guiding minimally invasive drainage procedures (6). In our patient, CT findings of heterogeneous fluid with an air-fluid

level and wall thickening suggested secondary infection and early abscess formation, supporting the need for prompt intervention.

Several studies have emphasized the value of percutaneous drainage combined with antibiotic therapy as first-line treatment for large or infected bilomas (6,8). Previous reports describe biloma as a potentially serious postoperative complication requiring prompt radiological diagnosis and minimally invasive management. Several published cases have demonstrated successful conservative treatment with percutaneous drainage in clinically stable patients, whereas others have required invasive biliary intervention because of persistent leakage or ongoing obstruction. Similar to previously reported cases, our patient demonstrated rapid clinical improvement following CT-guided drainage and broad-spectrum intravenous antibiotic therapy. However, unlike several published reports in which ERCP with biliary stenting was necessary, our patient achieved complete resolution without endoscopic intervention, emphasizing the importance of individualized imaging-based management.

MRCP has emerged as a valuable non-invasive modality for evaluating the biliary tree in postoperative patients. In contrast to ERCP, MRCP avoids procedure-related complications while still providing excellent visualization of biliary anatomy and potential sites of leakage (3). Previous reports have shown that many patients with resolving collections and no evidence of ongoing bile leakage can be managed successfully without endoscopic intervention.

In many published cases of postoperative biloma, ERCP with biliary stenting was required because of persistent leakage or ongoing biliary obstruction (3,8). Reports involving postoperative bile leaks after subtotal cholecystectomy frequently describe the need for combined endoscopic and radiological management to achieve complete resolution. In contrast, our patient was successfully managed conservatively with CT-guided drainage, antibiotics, and close imaging follow-up alone. MRCP confirmed the absence of active bile leakage, thereby avoiding unnecessary invasive endoscopic intervention.

This case highlights the complementary roles of CT and MRCP in the management of postoperative biliary complications. CT enables accurate diagnosis and image-guided treatment, whereas MRCP provides a detailed assessment of biliary anatomy and helps select patients who may not require ERCP. Furthermore, this case emphasizes the importance of follow-up imaging in documenting regression of collections and confirming their resolution.

Conclusion

Biloma with secondary abscess formation represents a clinically significant complication following subtotal cholecystectomy and requires prompt recognition and appropriate management.

CT-guided percutaneous drainage remains the cornerstone treatment for large or infected bilomas, while MRCP provides valuable non-invasive assessment of the biliary tree and may help determine the need for further intervention.

In selected patients, conservative management combining drainage, antibiotic therapy, and imaging follow-up may achieve complete resolution while avoiding unnecessary endoscopic or surgical procedures.

Declarations

Ethics Approval and consent to participate: This study was approved by the Ethics Committee of the University Clinic for Surgical Diseases "St. Naum Ohridski", Skopje, North Macedonia. For the publication of this case report and accompanying images, a written informed consent was obtained from the patient.

Informed consent: Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Conflict of Interest: The authors declare no conflict of interest.

Funding: This research received no external funding.

Availability of Data and Materials: The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Authors' Contributions: M. M. – primary author; manuscript preparation, image acquisition, analysis, and interpretation. P. T. – supervision, critical revision, and final approval of the manuscript. R. K. – data collection. E. A. – literature review. T. A. – manuscript drafting. D. T. – manuscript editing and final preparation

Artificial Intelligence (AI) Statement: ChatGPT was used exclusively for English language editing and formatting assistance. The authors take full responsibility for the scientific content and accuracy of the manuscript.

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www.doi.org/10.67214/cgpgnv67

ILIOPSOAS ABSCESS SECONDARY TO PYELONEPHRITIS WITH SUBSEQUENT UNILATERAL SACROILIITIS PRESENTING AS LOW BACK PAIN IN A YOUNG ADULT

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Abstract

Introduction: Iliopsoas abscess is a rare but potentially life-threatening condition. Secondary iliopsoas abscess following pyelonephritis is rarely reported, and contiguous spread to the sacroiliac joint resulting in sacroiliitis is an uncommon complication. Early detection is crucial, as initial symptoms may mimic low back pain, hip or gluteal discomfort, or genitourinary tract infection, often leading to delayed diagnosis.

Case Presentation: We report a case of a young adult who presented with severe low back pain radiating to the right lower extremity. Pyelonephritis was initially diagnosed based on CT imaging and laboratory tests, including blood tests and urinalysis. Almost two months after symptom onset, MRI revealed a unilateral iliopsoas abscess with contiguous involvement of the sacroiliac joint, resulting in secondary sacroiliitis. Methicillin-resistant Staphylococcus aureus (MRSA) was identified as the causative organism. The patient underwent percutaneous core biopsy and culture-guided antimicrobial therapy, leading to complete recovery.

Conclusion: This case underscores the importance of considering retroperitoneal and sacroiliac infections in patients with persistent, immobilizing low back pain, even when laboratory abnormalities are transient. Prompt imaging and timely management are essential to prevent morbidity and mortality associated with iliopsoas abscess and secondary sacroiliitis.

Keywords: *Iliopsoas abscess; Low back pain; MRSA; Pyelonephritis; Sacroiliitis.*

Introduction

Sacroiliitis in young adults is an uncommon but clinically important cause of low back pain (1). Its presentation frequently overlaps with musculoskeletal lumbar pain, hip and gluteal pain, or even symptoms of genitourinary tract infection. Because of this nonspecific pattern, sacroiliitis may initially be misdiagnosed, leading to delayed treatment and prolonged morbidity in those patients (2).

Iliopsoas abscess is a rare clinical entity with a recent reported incidence of approximately 1.21 per 100,000 population per year (3). Although rare, it remains a potentially life–threatening condition, with a high mortality rate, reported as 2.4% for primary iliopsoas abscess, and up

to 18.9% for secondary abscess, particularly in patients with delayed diagnosis or underlying comorbidities (3,4).

Iliopsoas abscesses are classified as primary or secondary. In a primary iliopsoas abscess, the causative microorganism spreads hematogenously or via lymphatic dissemination from a distant site of infection, whereas in a secondary abscess, there is an identifiable contiguous source of infection. Secondary abscesses may arise from gastrointestinal disease, spinal infections, suppurative urinary tract infections, or other adjacent sources and account for approximately 70% of iliopsoas abscesses. Skeletal origin is among the most frequently reported source of secondary iliopsoas abscess formation (4).

Although cases of iliopsoas abscess complicated by sacroiliitis have been documented, contiguous spread of infection from the kidney through the iliacus and psoas muscle and sacroiliac joint remains exceptionally rare (5-8).

We present a case of unilateral sacroiliitis with associated iliopsoas abscess in a young adult patient presenting with intense low back pain radiating to the right lower extremity. The patient underwent treatment for pyelonephritis for nearly two months before she was diagnosed with sacroiliitis caused by MRSA.

Case Presentation

A 20-year-old female with no prior medical history presented to the general surgery department in a secondary care hospital in her hometown with complaints of intermittent lower abdominal pain, which had previously undergone a gynecological evaluation that excluded a gynecologic source of symptoms. Upon examination, the attending surgeon concluded that the patient had no signs of acute abdominal distress and suspected a urinary tract infection. Abdominal ultrasonography was performed, and laboratory tests and urinalysis were ordered. Microscopic examination of the urine revealed 30–100 leukocytes per high-power field, consistent with pyuria, with a negative urine culture. The patient was discharged the same day and referred for further urological and gynecological evaluation. Abdominal ultrasonography was unremarkable.

Four weeks after symptom onset, the patient underwent repeat gynecological evaluation, which was also unremarkable, and showed no free fluid in the pouch of Douglas. However, speculum examination revealed signs of vaginitis and macroscopic herpes simplex infection, for which treatment was initiated according to standard clinical practice.

Approximately five weeks after initial symptom onset, the patient was evaluated by an orthopedic surgeon with complaints of persistent and gradually worsening low back pain radiating to the right gluteal region. There was no history of trauma. No clinical or radiological evidence suggestive of a significant musculoskeletal pathology was identified upon clinical evaluation, and the patient was referred for infectious disease and internal medicine assessment.

Upon examination by an infectious disease specialist, the patient was found to be febrile (38.8 °C), with stable vital signs, but unable to ambulate. Laboratory tests revealed markedly elevated inflammatory markers (CRP 339 mg/L; ESR 56 mm/h; WBC 9.60×10^3/μL; NEUT 8.89×10^3/μL). Chest, abdominal, and pelvic CT imaging was performed.

CT of the abdomen found no evidence of obstruction or nephrolithiasis; however, a striated nephrogram of the lower renal poles, more pronounced on the right, was observed, suggestive of acute pyelonephritis. There was also delayed contrast excretion with mild right ureteral dilatation.

Acute pyelonephritis was diagnosed based on clinical, laboratory, and imaging findings despite sterile urine cultures, likely due to prior broad-spectrum antibiotic therapy.

The patient was subsequently hospitalized and treated with empirical intravenous antibiotic therapy, including meropenem, intravenous fluids, analgesics, corticosteroids, proton pump inhibitors, and prophylactic low-molecular-weight heparin. Serological testing for Brucella (Rose Bengal/agglutination testing) was negative. Orthopedic consultation during the initial hospitalization did not reveal clinical or radiological evidence of septic arthritis of the right hip.

The patient was discharged after an 8-day hospitalization, afebrile and in good general condition. Laboratory results at discharge showed improvement in inflammatory markers (CRP 21.43 mg/L; WBC 10.19×10^3/μL; NEUT 6.69×10^3/μL; PCT 0.10 ng/mL). No pathogens were isolated from blood, urine, and gynecological cultures.

Approximately 2 months after the initial onset of symptoms, the patient consulted a neurosurgeon due to persistent lumbar pain radiating to the right gluteal region. Neurological examination revealed radicular pain, with a positive Lasègue test at 45 degrees on the affected side, preserved sensation in both lower limbs, and intact sphincter control. MRI of the lumbosacral spine was performed and was unremarkable. However, abnormalities were identified in the right sacroiliac joint, prompting a dedicated pelvic MRI, which revealed findings indicative of suppurative sacroiliitis of the right sacroiliac joint.

As there was no indication for neurosurgical intervention and the patient reported worsening pain in the right leg and pelvis, consultation with the orthopedic department recommended urgent referral to a center with higher diagnostic and treatment capacity.

The patient was subsequently admitted to the referred center, where comprehensive clinical, radiological (conventional X-ray, contrast-enhanced CT, and MRI), and laboratory investigations were performed. All routine laboratory parameters were within normal reference ranges. On admission, vital signs were stable. Clinically, the patient exhibited limited hip flexion due to pain and a positive FABER test. No neurological deficits in the lower extremities were observed.

Contrast-enhanced CT of the abdomen and pelvis revealed a multiloculated, hypodense intramuscular collection centered in the right iliacus muscle with extension into the psoas muscle, showing peripheral rim enhancement and a central necrotic component, consistent with an intramuscular abscess. Several additional punctate necrotic foci measuring up to 3 mm were identified within the iliacus muscle, representing microabscesses. The primary collection extended along the right sacroiliac joint, most prominently along its distal aspect, where communication with the joint capsule was observed.

The right sacroiliac joint exhibited cortical remodeling, multiple cortical erosions, distal osseous fragmentation incorporated into the joint space, and asymmetric joint space widening. Secondary involvement of the obturator internus muscle was also noted. These findings were consistent with an iliopsoas–iliacus muscle abscess complicated by secondary sacroilitis of the right sacroiliac joint. (Figure 1).

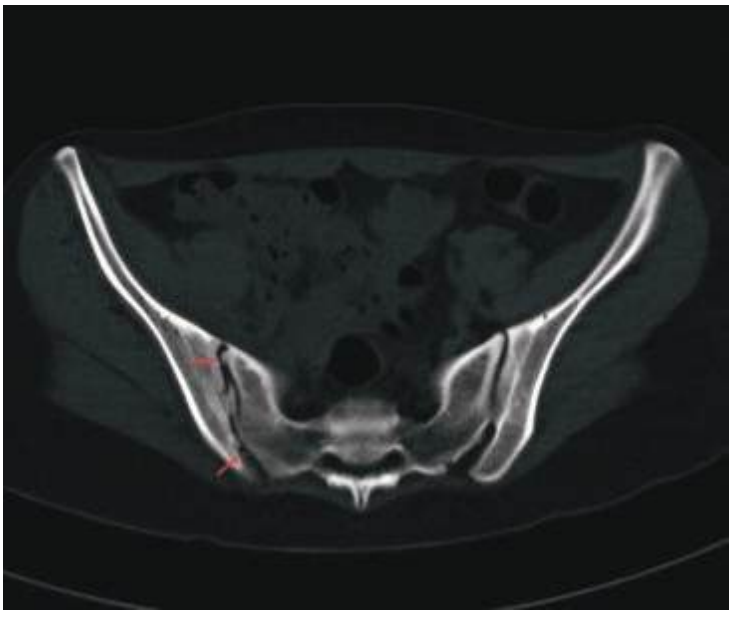

Figure 1. Axial CT image demonstrating unilateral right sacroiliac joint irregularity and cortical erosions, most pronounced inferiorly, consistent with sacroiliitis (arrow).

MRI of the sacroiliac joint demonstrated right sacral bone edema involving the sacroiliac joint and iliac wing, with cortical remodeling, erosions, and bony fragments.

A 25 × 11.5 mm encapsulated collection was seen in the iliacus and psoas muscles, in close posterior contact with the iliac cortex without evidence of cortical bone destruction, showing central necrosis and peripheral pathological enhancement, consistent with an abscess. Associated edema extended into the distal sacroiliac joint, piriformis, and gluteal muscles, with reactive synovial changes. (Figures 2 and 3).

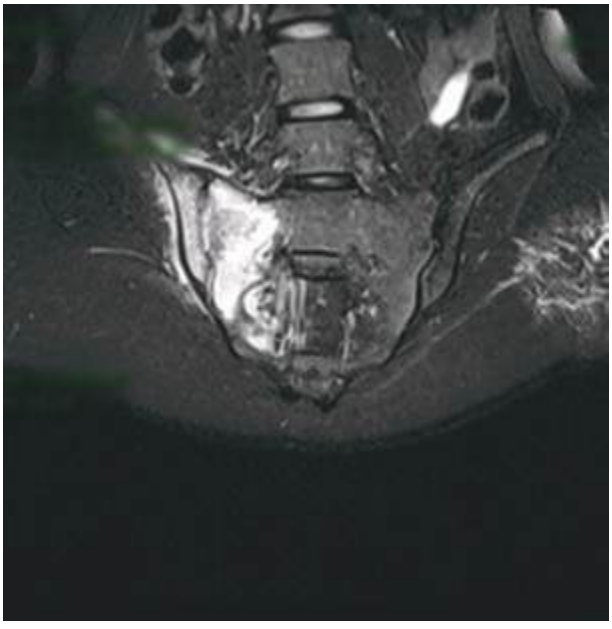

Figure 2. Coronal T2-weighted MRI displaying extensive hyperintense bone marrow edema and inflammatory changes involving the right sacroiliac joint and adjacent sacral ala, consistent with active sacroiliitis.

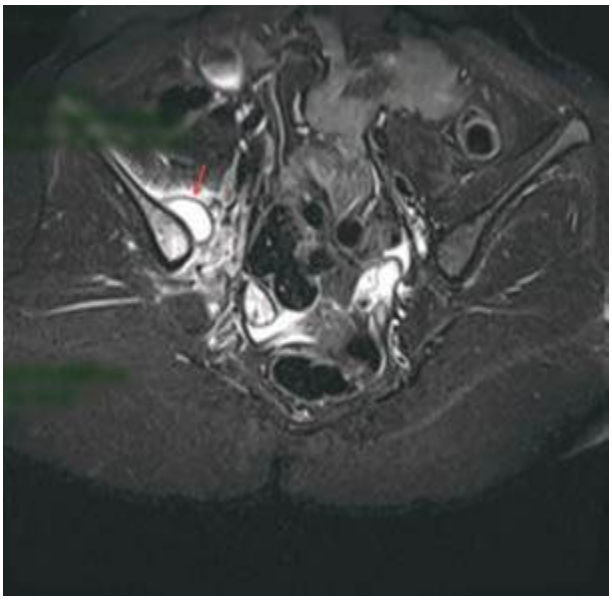

Figure 3. Coronal T2-weighted MRI showing a well-defined hyperintense fluid collection adjacent to the right sacroiliac joint with surrounding inflammatory changes extending into the iliopsoas region, consistent with an iliopsoas abscess (arrow).

During the second hospital stay, a biopsy of the lesion was performed 15 days after admission. Under fluoroscopic guidance, a percutaneous vertebroplasty needle (11 Gauge) was advanced to the posterior synovial portion of the right sacroiliac joint via a posterolateral approach, and sufficient tissue was obtained for histopathological examination. Approximately 1 cc of purulent fluid was obtained from the cytological sediment and submitted for cytological analysis. Smears were prepared and stained with H&E, Papanicolaou, and Giemsa. Examination revealed a proteinaceous, amorphous background containing numerous lymphocytes, plasma cells, and neutrophilic leukocytes, consistent with an inflammatory process.

Microbiological analysis of the biopsied material isolated methicillin-resistant Staphylococcus aureus (MRSA), and targeted antimicrobial therapy was initiated according to susceptibility testing, as prescribed by an infectious disease specialist. Initial treatment consisted of imipenem/cilastatin 1 g IV every 8 h, clindamycin 600 mg IV every 6 h, and amikacin 500 mg IV every 8 h for 5 days.

The regimen was subsequently continued for an additional 10 days and modified to amikacin 500 mg IV every 8 h, ciprofloxacin 400 mg IV every 12 h, and fosfomycin 4 g in 10% dextrose solution IV every 6 h.

Throughout the treatment course, the patient received supportive therapy, including intravenous fluids, probiotics, and gastroprotective medication.

Drainage was not performed because the patient remained clinically stable and responded favorably to antimicrobial therapy, with progressive improvement in symptoms and inflammatory markers.

Upon discharge, oral outpatient therapy prescribed by an infectious disease specialist included: levofloxacin 750 mg once a day for 2 weeks, combined with oral intake of linezolid 600 mg twice

a day for 2 weeks, followed by an oral intake of trimethoprim/sulfamethoxazole 400/80 mg twice a day for 2 weeks.

Physical therapy was initiated during the hospital stay and continued after discharge, to maintain hip mobility and strength. The patient was discharged in good general condition with improved pain control, with all inflammatory markers within normal limits (e.g., CRP 0.6 mg/L). Blood and urine cultures remained negative during both hospital stays.

The first follow-up was performed 19 days after discharge following the second hospital stay. A subsequent follow-up was conducted approximately six months later.

The patient showed progressive clinical improvement, with markedly reduced pain and full recovery of mobility. Follow-up MRI demonstrated complete bony remodeling of the right sacroiliac joint, consistent with the findings upon admission. Mild cortical irregularity and minimal intra-articular fluid were noted. The bone marrow signal was normal. (Figure 4). Overall, there was complete regression of the previously documented sacroiliitis.

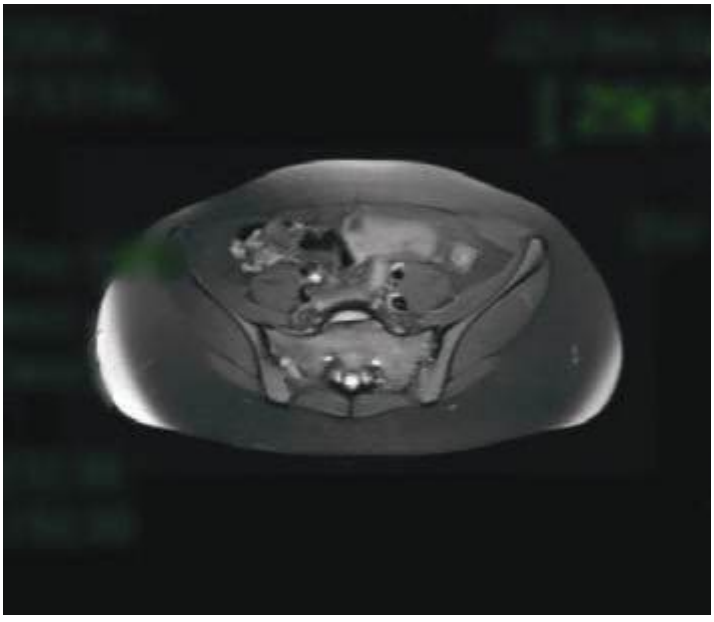

Figure 4. Follow-up axial MRI at the level of the sacroiliac joints exhibits preserved joint morphology and absence of inflammatory changes, consistent with complete regression of previously observed sacroiliitis.

Discussion

This case underscores the importance of maintaining a high index of suspicion for sacroiliitis and iliopsoas abscess in patients presenting with persistent, immobilizing low back pain, particularly following urinary tract infections (4,5). The clinical diagnosis of acute pyelonephritis with subsequent isolation of MRSA from the sacroiliac region likely reflects secondary infectious involvement of the iliopsoas and sacroiliac region in the setting of acute pyelonephritis via recognized retroperitoneal and hematogenous pathways (4). However, the exact pathogenetic mechanism linking the initial pyelonephritis and the subsequent development of MRSA iliopsoas abscess and sacroiliitis cannot be definitively established. Although iliopsoas abscess with secondary sacroiliitis has been described (5-8), to our knowledge, reports documenting such a

progression following pyelonephritis are limited, further emphasizing the uncommon nature of this presentation.

Clinicians should be aware that laboratory abnormalities may be transient and that resolution of urinary symptoms does not exclude secondary infectious complications; therefore, imaging remains essential for accurate diagnosis and assessment (4).

Reported outcomes of iliopsoas abscess in the literature are generally favorable when early diagnosis and appropriate antimicrobial therapy are initiated; however, morbidity remains significant, and a substantial proportion of patients require percutaneous or surgical drainage, particularly in cases with larger collections or inadequate response to antibiotics alone (3,4,9). Complications may include sepsis, prolonged hospital stay, and contiguous spread to adjacent structures, including vertebral and sacroiliac involvement (4,5).

Standard management typically involves a combination of targeted antimicrobial therapy and drainage when indicated (10-12). However, in the present case, a conservative approach with intravenous antibiotics guided by susceptibility testing was chosen based on the patient's clinical stability and radiological findings, along with close clinical follow-up. The patient demonstrated progressive clinical and radiological improvement without the need for invasive drainage procedures, highlighting the variability in disease course and the importance of individualized management strategies.

Conclusion

Early recognition and prompt, individualized management with culture-guided antimicrobial therapy are critical for achieving full recovery and preventing serious complications, long-term disability, and potential mortality associated with iliopsoas abscess and secondary sacroiliitis.

Declarations

Ethics Approval and consent to participate: Not applicable.

Informed Consent: Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Conflict of Interest: The authors declare no conflict of interest.

Funding: This research received no external funding.

Availability of Data and Materials: Data are available from the corresponding author upon reasonable request.

Author Contributions: All authors contributed to manuscript preparation and approved the final version.

Acknowledgements: None

Artificial Intelligence Statement: No AI tools were used in the preparation of this manuscript.

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www.doi.org/10.67214/g9qrns48

SCIENTIFIC EXCHANGE, PRACTICAL LEARNING, AND PROFESSIONAL DEVELOPMENT: REFLECTIONS FROM THE 47TH INTERNATIONAL MEDICAL STUDENTS' CONGRESS

As a fourth-year medical student, I have learned over the years that scientific congresses offer valuable experiences beyond traditional medical education. The 47th International Medical Students' Congress (IMSC) took place in Ohrid, North Macedonia, bringing together students, researchers, and healthcare professionals from various countries to exchange knowledge, develop practical skills, and establish professional connections. As an active participant presenting a clinical case report, I was honored to be selected by the Scientific Committee to present my work, titled "Acute Stanford Type A Aortic Dissection as the Initial Manifestation of Suspected Marfan Syndrome." The experience allowed me to learn to professionally present complex medical cases to a distinguished scientific audience, discuss clinical findings with experts, and confidently defend and debate a case not typically found in textbooks. Presenting my case report was both challenging and rewarding. Preparing for the presentation involved a thorough literature review, a detailed analysis of clinical findings, and learning how to explain medical information in a simple and clear way.

Alongside the scientific presentations, the congress also offered practical workshops in fields such as surgery and anesthesiology, allowing us medical students to gain hands-on experience in areas of particular clinical interest. These sessions showed us the importance of teamwork, communication, and attention to detail, while also connecting theoretical knowledge with everyday clinical practice. What I found particularly meaningful was the opportunity to interact with professors and experts from North Macedonia, Serbia, and Turkey. Through their lectures and personal clinical experiences, they created discussions that were not only educational but also genuinely inspiring for young medical students. Listening to experienced physicians speak so passionately about their profession further strengthened my motivation to continue learning and growing in medicine.

At the same time, the congress created an environment that encouraged interaction between students from diverse universities and international backgrounds, fostering the exchange of ideas and experiences across different educational and cultural settings. . During scientific sessions, workshops, and informal discussions, we shared a strong enthusiasm for medicine and a genuine desire to learn from each other. These exchanges, together with discussions about future careers and new friendships, showed that professional growth extends beyond academic achievements. The connections made at such events often provide valuable support, motivation, and opportunities for future collaboration.

Reflecting on this experience, I became more aware of how important environments like these are in shaping young medical professionals. Beyond the academic program itself, the congress created a space where knowledge, experience, and diverse perspectives were openly shared among students and physicians from various backgrounds.

Participating in discussions, observing different approaches to medicine, and engaging with people who share the same dedication to healthcare made the entire experience both memorable and motivating.

The 47th International Medical Students' Congress not only broadened my perspective on medicine but also reinforced my enthusiasm for continued learning and professional growth.

Sincerely,
Jordanoski Matej
Medical Student, Faculty of Medicine
University of "Ss. Cyril and Methodius"
Skopje Republic of North Macedonia

GUIDELINES FOR AUTHORS

Macedonian Journal of Anaesthesia (MJA) is a scientific journal of the Macedonian Society of Anaesthesia (MSA) and Macedonian Society of Critical Care Medicine (MSCCM). The aim of this specialized medical journal is to speed and promote scientific achievements, novelties', clinical experience's, reviews, controversial topics in anesthesia, reanimation and intensive care, as well as other correlated medical branches .

The Journal is published four times a year (April, June, October and December), but additional supplements might be published when needed. MJA publishes original articles in basic and applied research, review articles, case studies, therapeutic and technological innovation, discussions, critics, surveys, impressions from meetings, information for international conferences and reviews of new books or variate.

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Dag Stat. Mackinnon A. Available from :http//www.mhri.cdu.au/biostats.Accessed May 5th 2006.

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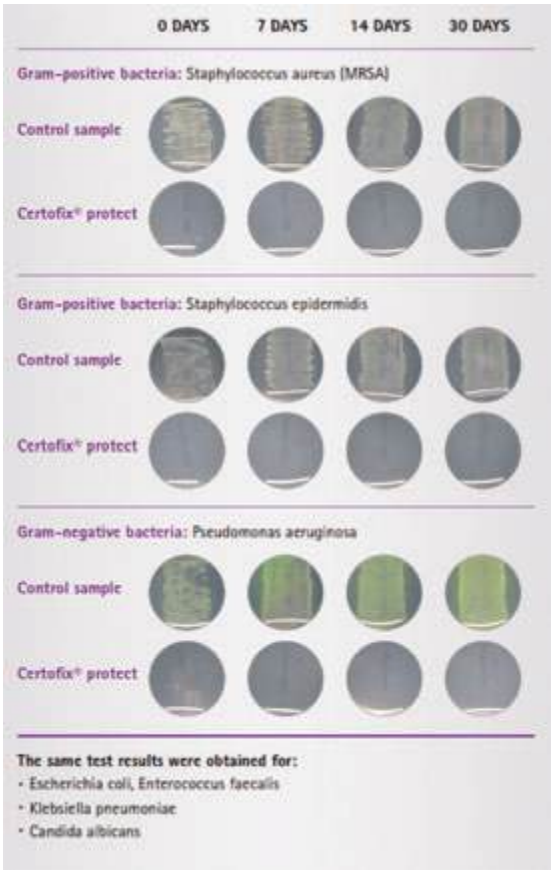

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