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EDITORIAL

We endured. We move forward.

Launching a new scientific journal is rarely a quiet undertaking. The first issue of CJAIM was an act of trust — in the profession, in colleagues, and in the belief that knowledge should be shared openly and responsibly. Today, with a second issue in hand, we can state something simpler and truer: **we endured**. Not as a figure of speech, but as the outcome of shared work by authors, reviewers, the editorial board, and the institutions that recognised the value of this project.

In the meantime, a steady and encouraging stream of submissions has emerged. That does not make us complacent; it reminds us that there is a space where clinical experience, educational questions, and scientific curiosity can meet without unnecessary barriers. CJAIM does not belong to a single institution or a single city — it belongs to a clinical and scientific community centred on anaesthesiology and intensive care, yet open to colleagues whose work intersects with ours: internists, infectologists, cardiac surgeons, pain specialists, and others in Croatia, the region, and beyond. Our duty is to preserve that space: transparently, ethically, and open to criticism.

This issue reflects that diversity. Alongside original research on medical students' knowledge and practical experience in airway management (Plaftak et al.), we publish review articles that connect everyday practice with a broader context: ketamine in spinal surgery (Krezić et al.), the role of photoplethysmography in anaesthesiology and intensive care (Džaja et al.), and approaches to infections in the ICU (Đurić et al.). The issue closes with a letter to the editor by Tomić Mahečić on central venous catheter complications — a reminder that even routine procedures deserve critical scrutiny, especially when things do not go as planned.

Case reports remain at the heart of what connects us to the hospital. Jiang et al. describe the safe and effective use of esketamine in a difficult paediatric intubation scenario; Brigljević Kniewald et al. discuss urosepsis after endoscopic surgery for a staghorn calculus; Sabo et al. highlight delayed spinal cord injury following high-voltage electrical burns; Piršljin et al. report a generalised tonic–clonic seizure associated with sufentanil in a patient with pituitary macroadenoma. Each of these contributions carries a lesson that cannot be reduced to an algorithm — yet may save the next patient if it reaches the right hands.

We are particularly encouraged by the generational breadth of our specialty reflected in this issue. We deliberately make room for young authors at the beginning of their path, not only at its end. A first manuscript is rarely perfect; it is often, however, the most important one. The editorial office and reviewers are not merely a filter, but companions — with clear standards, but also with support. The sense of community we speak of is not a slogan on the cover; it is daily practice: feedback that builds, reviews that teach, and publications that give younger colleagues legitimacy to speak in science.

On behalf of the editorial board, we thank all authors who entrusted us with their work, the reviewers who placed their expertise in the service of quality, and the institutions and colleagues who support us. Our task remains the same: to preserve the credibility of scientific discourse and to promote a culture of learning, collaboration, and ethics in medicine.

We invite you to join us — by submitting manuscripts, reviewing, reading, and commenting. Write with courage, review with honesty, read with curiosity. Only in this way will CJAIM remain what we intend it to be: living proof that knowledge matters when it connects people.

Slobodan Mihaljević
Editor-in-Chief

Ivan Šitum
Managing Editor
Croatian Journal of Anaesthesiology and Intensive Medicine (CJAIM)

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ORIGINAL RESEARCH

Airway management education in medical students: a cross-sectional study of knowledge and practical experience

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ABSTRACT

INTRODUCTION:

Airway management is a fundamental clinical skill, and failure to secure the airway remains a major cause of morbidity and mortality.

OBJECTIVE:

To assess medical students' knowledge and practical competence in airway management.

METHODS:

A cross-sectional study was conducted among 79 medical students using a structured, anonymous questionnaire administered to 5th- and 6th-year students at the School of Medicine, University of Zagreb.

RESULTS:

Most students (94.9%) reported that endotracheal intubation should be included in undergraduate training. Basic airway maneuvers were well recognized, while advanced techniques such as laryngoscopy were identified by over 90% of participants. Fewer students (75.9%) recognized supraglottic airway devices. Practical experience was limited: 65.8% had placed a supraglottic airway device on a mannequin, but only 15.2% on a patient. Similarly, 59.5% had performed intubation on a mannequin compared with 19.0% on patients.

CONCLUSION:

While theoretical knowledge is strong, practical experience—particularly with advanced airway techniques—is limited. Enhanced structured and simulation-based training is needed to improve competence and patient safety.

Keywords: Airway Management; Students, Medical; Education, Medical, Undergraduate; Clinical Competence; Simulation Training

Introduction

Airway management is a key skill acquired during medical education and is widely used in various specializations, most notably in anesthesiology and emergency medicine (1). Failure to secure the airway remains a leading cause of patient morbidity and mortality. According to the Fourth National Audit Project of the Royal College of Anaesthetists and the Difficult Airway Society, the main reasons for that are poor judgement, inadequate skill, and unproductive behaviour (2). Good education is key to resolving this problem. It should start at the beginning of a medical career and be revisited throughout, to maintain and learn new upcoming skills (3). The main barriers to effective airway management training in undergraduate medical curricula for medical students include the lack of formal, structured curricula, insufficient hands-on exposure, limited access to

simulation resources, variability in training content and frequency, and inadequate assessment and feedback mechanisms. Most medical students report inadequate exposure to airway emergencies and altered airway anatomy, such as tracheostomy and laryngectomy care, which leads to low confidence and proficiency in managing these scenarios (4,5). Training is often opportunistic and relies on clinical rotations, resulting in inconsistent skill acquisition and retention (3,6). Simulation-based training, while effective, is not universally available or standardized, and many programs lack regular, competency-based assessment (7–9). Over the years, teaching strategies have changed, as well as student generations. It is shown that simulation is an effective way for the development of psychomotor skills and clinical judgment, allowing students to practice in a controlled environment without risking the patient harm (10,11). The traditional method of airway management education uses experiential learning during patient care in the operating room (3). Endotracheal intubation using a video laryngoscope may be appropriate in this context because it allows instructors to directly observe students' intubation attempts via the device's video screen (12). Another possibility, if acceptable for surgery, is the placement of a laryngeal mask airway, which is easier and faster. Despite its limitations, it is believed that simulator training before going to the operating room has a positive impact on students' acquisition of procedural and patient safety skills, although it has not yet been confirmed in published studies (13). It is said that the best learning is from mistakes; however, mistakes in the operating room are unacceptable. On the other hand, supervised mistakes in simulation labs are recommended. Effective training requires experienced instructors, high-fidelity simulators, and well-designed curricula (14). The problem is that high-fidelity simulators are expensive and not widely available. This creates an opportunity for implementing Artificial Intelligence (AI) in education, as it allows affordable virtual reality solutions. In a randomized controlled trial involving practicing on low-fidelity mannequins simulating difficult airway scenarios, students using the Vortex Approach demonstrated improved decision-making and reduced anxiety during airway management tasks (15). A systematic review and meta-analysis of advanced airway management training also found that stimulation techniques were associated with higher learner satisfaction and highlighted that curricula including course repetition, ongoing practice with or without evaluation and feedback, and use of self-regulated learning appear effective in airway management skill retention and should be incorporated for those requiring skills maintenance (7). In today's era of smartphones, anesthesiology learning applications have been developed. Some of them include Anesthesiologist (16), The Difficult Airway App (17), and NYSORA Anesthesia Assistant, which is powered by AI (18). Using these applications, students can better prepare for airway management training. Northwestern University has developed a virtual reality software application called iLarynx, which uses the accelerometer properties of the iPhone® or iPad® (Apple Inc., Cupertino, CA, USA) to mimic hand movements for performing fiberoptic skills (19). Their analysis showed a significant improvement in upper airway endoscopy skills among medical students.

At the University of Zagreb School of Medicine, these skills are part of the curriculum in several courses: First Aid in the 1st year, Anesthesiology and Reanimatology in the 5th year, and Fundamentals of Medical Skills throughout all six years of study (20). The lockdown during the COVID-19 pandemic taught us that high-tech learning has its advantages, but during other types of disasters, when infrastructure is disrupted, electricity is out, high-tech devices are not working or are unavailable, and patients are emerging, back-to-basic and old-school techniques are the only options available if we know how to use them. Having this in mind, during courses that teach airway management, we teach our students all available techniques, but most importantly, basic ones that can be used everywhere if you are confident in your skills. To find out the situation on the ground and potential gaps between curricula and real-life practice at the School of Medicine, University of Zagreb, the following study was performed.

Methods

Study design and setting:

This cross-sectional study was conducted during the 2024/2025 academic year at the University of Zagreb School of Medicine.

Participants:

Eligible participants were 5th- and 6th-year medical students. Participation was voluntary and anonymous. No exclusion criteria were applied.

Data collection and variables:

Data were collected using a structured, anonymous online questionnaire (Google Forms), distributed twice via the institutional learning management system and student WhatsApp groups, with approval from the Department of Anesthesiology, Reanimatology and Intensive Care Medicine of Surgical Specialties.

The questionnaire comprised seven items assessing: (1) year of study and attendance in the Anesthesiology and Reanimatology course; (2) attitudes toward inclusion of endotracheal intubation in undergraduate teaching; (3) knowledge of basic and advanced airway management techniques; and (4) perceived importance, acquisition, and setting of airway management skills.

Bias:

To reduce non-response bias, the survey was distributed twice through multiple communication channels.

Study size:

All eligible students were invited to participate; no formal sample size calculation was performed.

Statistical methods:

Data were analyzed descriptively and presented as frequencies and percentages in tables and figures.

Results

A total of 79 medical students participated in the survey out of 528 students enrolled in the 5th- and 6th-year. Table 1 shows participants' years of study and their attendance in the Anesthesiology and Reanimatology course. More than half of the participants were 5th-year medical students (N=43; 54.4%), and most participants completed the course at the School of Medicine (N=56; 70.9%).

Almost all participants thought that endotracheal intubation should be taught during medical school (N=75; 94.9%), while only 2.5% (N=2) disagreed. Solely 1.3% (N=1) thought that professors should only demonstrate the procedure without need for them to have any hands-on experience, and 1.3% (N=1) were unsure.

Results about basic airway management methods or maneuvers are shown in Figure 1. Regarding this question, all participants (N=79; 100.0%) identified head tilt, 94.9% (N=75) chin lift, and 93.7% (N=74) jaw trust. Placement of an oropharyngeal and nasopharyngeal tube was identified by 49.4% (N=39), and bag-valve-mask ventilation by 35.4% (N=28).

Figure 2 shows the results regarding which of the following are advanced airway management methods. Most participants recognized that endotracheal intubation using direct laryngoscopy (N=72; 91.1%) and indirect laryngoscopy (N=73; 92.4%) were advanced methods. Placement of a supraglottic device was selected by 75.9% (N=60), fiberoptic intubation by 74.7% (N=59), retrograde intubation by 50.6% (N=40), and cricothyroidotomy by 2.5% (N=2) of participants.

Table 2 shows what medical students think they should learn during their studies. Bag-valve-mask ventilation and endotracheal intubation using direct laryngoscopy were selected by 74 (93.7%) participants, while oropharyngeal tube placement by 77 (97.5%). Placement of a nasopharyngeal tube was chosen by 66 (83.5%) and a supraglottic device by 59 (74.7%). Almost half (N=38; 48.1%) would like to learn how to perform cricothyroidotomy. Interestingly, only 35.4% (N=28) wanted to learn endotracheal intubation using video laryngoscopy and only 15.2% (N=12) thought fiberoptic intubation should be taught.

The level of students' experience in airway management varied, as shown in Table 3. More than half of them (N=52; 65.8%) had placed a laryngeal mask airway device on a mannequin, mostly during the Fundamentals of Medical Skills course and the Anesthesiology and Reanimatology course. On the other hand, only 12 (15.2%) students had placed a laryngeal mask airway device on a patient under supervision. Endotracheal intubation using direct laryngoscopy on a mannequin was attempted by 47 (59.5%) students, while merely 15 (19.0%) attempted it on a patient under supervision. Endotracheal intubation using video laryngoscopy was endeavored by 8 (10.1%) students on a mannequin and by 9 (11.4%) on a patient under supervision. Both were performed during the Anesthesiology and Reanimatology course.

Table 1. Participant's year of study and attendance in the Anesthesiology and Reanimatology course

Question	Answer	Number (%)
Year of study	5th-year	43 (54.4)
	6th-year	36 (45.6)
Attendance in the Anesthesiology and Reanimatology course	Yes	56 (70.9)
	No	23 (29.1)

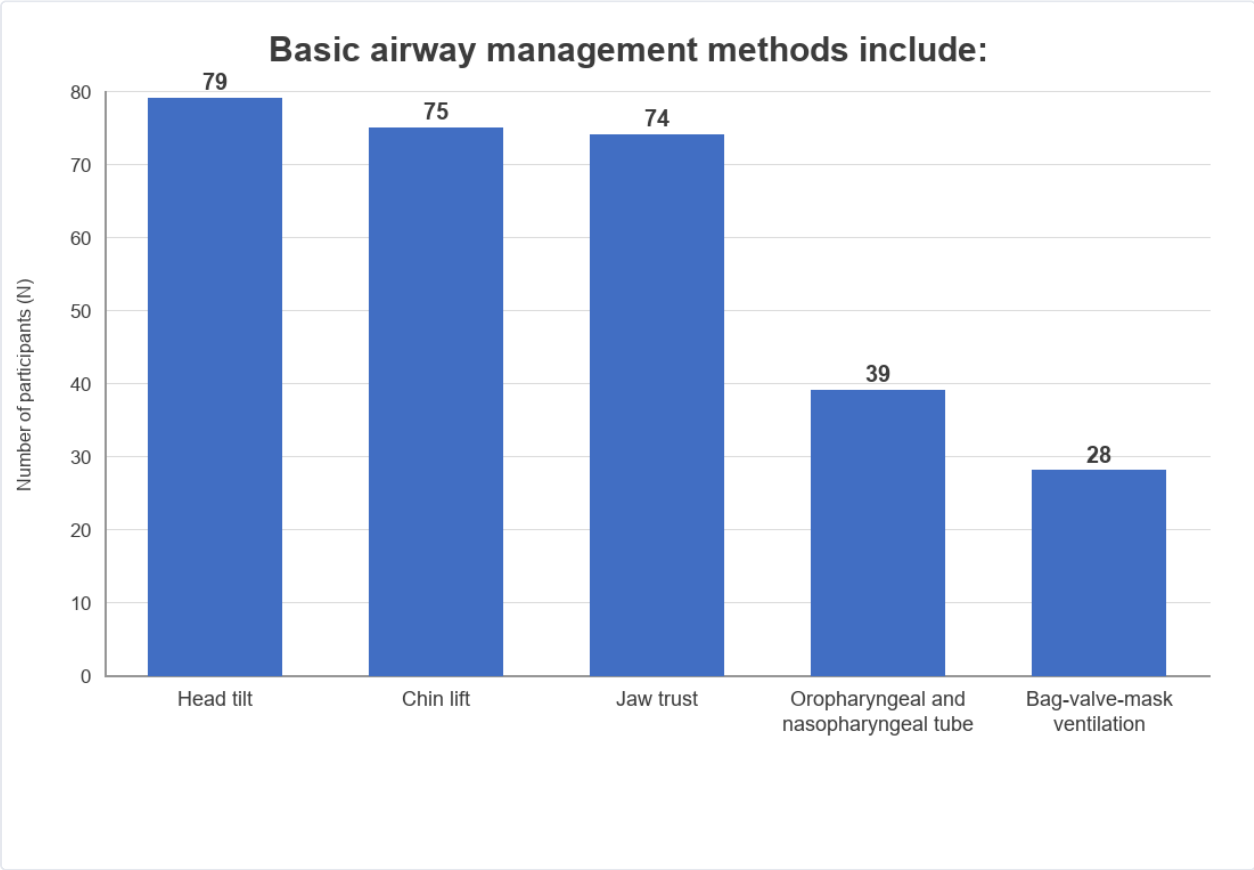

Figure 1. Participant's knowledge about basic airway management methods

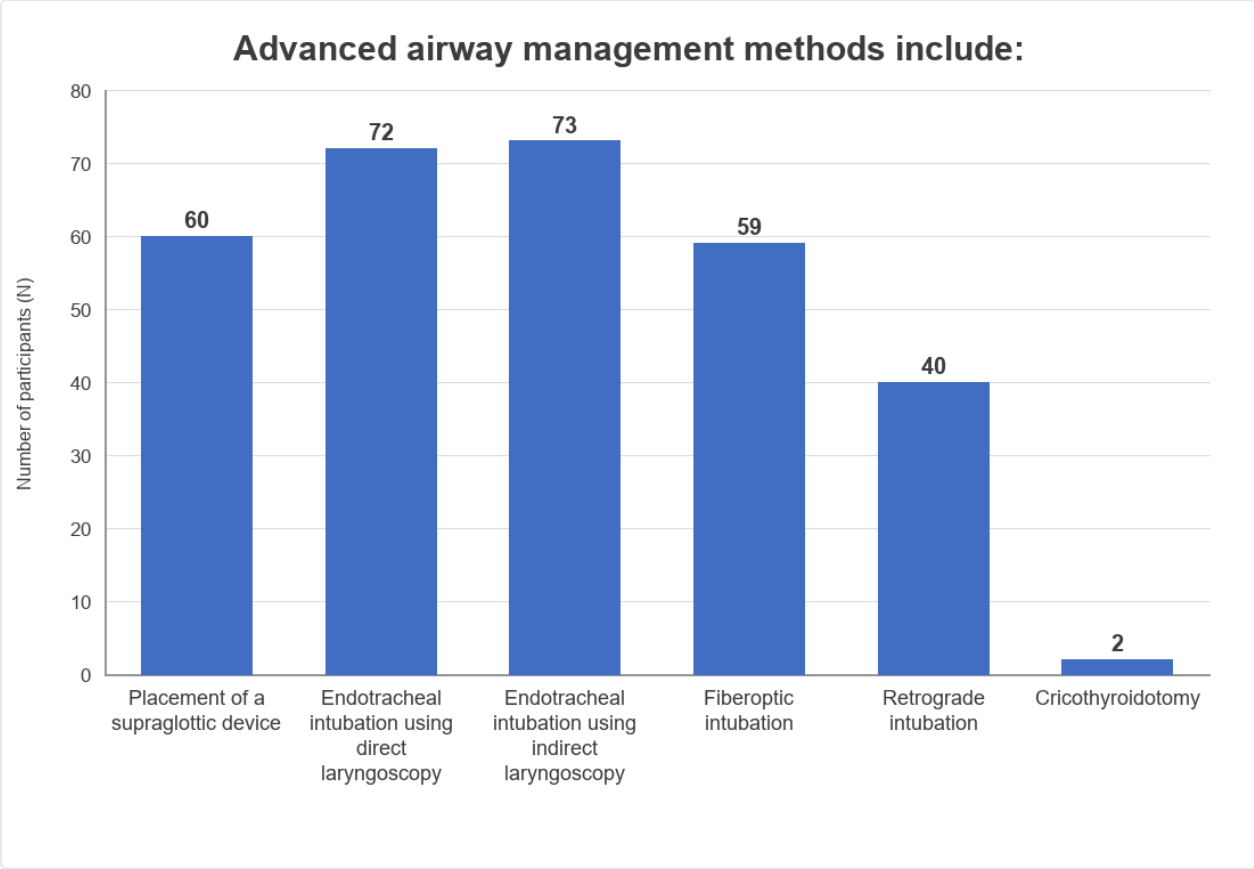

Figure 2. Participant's knowledge about advanced airway management methods

Table 2. Participants' opinion on what they should learn during medical school

I should learn in medical school:	Number (%)
Bag-valve-mask ventilation	74 (93.7)
Placement of a supraglottic device	59 (74.7)
Endotracheal intubation using direct laryngoscopy	74 (93.7)
Endotracheal intubation using indirect laryngoscopy	28 (35.4)
Cricothyroidotomy	38 (48.1)
Placement of an oropharyngeal tube	77 (97.5)
Placement of a nasopharyngeal tube	66 (83.5)
Fiberoptic intubation	12 (15.2)

Table 3. Participant's level of experience in airway management (LMA – laryngeal mask airway; DL – direct laryngoscopy; VL – video laryngoscopy)

	Yes	No	Yes, but unsuccessfully	Fundamentals of Medical Skills	First Aid	Anesthesiology and Reanimatology	Other
LMA on a mannequin	52 (65.8)	8 (10.1)	2 (2.5)	30 (40.0)	5 (6.3)	33 (41.8)	4 (5.1)
LMA on a patient under supervision	12 (15.2)	61 (77.2)	1 (1.3)	3 (3.8)	1 (1.3)	7 (8.9)	5 (6.3)
Endotracheal intubation using DL on a mannequin	47 (59.5)	10 (12.7)	3 (3.8)	34 (43.0)	1 (1.3)	31 (39.2)	6 (7.6)
Endotracheal intubation using DL on a patient under supervision	15 (19.0)	54 (68.4)	5 (6.3)	1 (1.3)	0	8 (10.1)	7 (8.9)
Endotracheal intubation using VL on a mannequin	8 (10.1)	66 (83.5)	0	0	0	3 (3.8)	7 (8.9)
Endotracheal intubation using VL on a patient under supervision	9 (11.4)	68 (86.1)	0	0	0	2 (2.5)	3 (3.8)

Discussion

This study demonstrates that medical students at the University of Zagreb School of Medicine possess strong theoretical knowledge of airway management. Most participants had attended the Anesthesiology and Reanimatology course and correctly identified both basic and advanced airway management techniques at the time of questionnaire distribution. In particular, nearly all respondents agreed that endotracheal intubation should be included in undergraduate training, reflecting awareness of its central role in airway management in both anesthesiology and emergency medicine.

Basic airway maneuvers, including head tilt, chin lift, and jaw thrust, were widely recognized, likely reflecting their early introduction during first aid training and reinforcement throughout the curriculum, consistent with previous studies (3,21,22). In contrast, fewer students identified certain techniques such as bag-valve-mask ventilation and supraglottic airway devices, suggesting variability in exposure and retention of these skills. Similarly, although most participants recognized endotracheal intubation, fewer were familiar with less commonly performed advanced techniques such as fiberoptic or retrograde intubation (23,24), which are typically not emphasized in undergraduate training.

Despite strong theoretical knowledge, practical experience was limited. While many students reported experience with airway techniques on mannequins primarily during structured courses (25) fewer than one in five had performed procedures such as laryngeal mask airway placement or endotracheal intubation on patients under supervision (26). This gap may reflect limited clinical exposure, time constraints during rotations, and restricted access to operating room training opportunities.

Students identified key airway management skills that should be included in undergraduate education, particularly basic airway techniques, supraglottic device placement, and direct laryngoscopy. These findings support the need for structured, competency-based training. Simulation-based education plays a crucial role in addressing limited clinical exposure, enabling repeated practice in a safe environment; however, it does not fully replace supervised clinical experience. It enables contact with decision-making under stress, complication management, and non-technical skills such as teamwork and situation-awareness, while having an expert supervision to step-in during difficult airway situations.

Overall, the findings highlight a gap between theoretical knowledge and practical competence. Addressing this gap through enhanced, structured, and simulation-based training combined with increased opportunities for supervised clinical practice may improve skill acquisition, confidence, and ultimately patient safety. To achieve this, Department could propose structured training pathways, minimum procedural requirements, or integration of longitudinal airway training across different years of study. Another solution is to implement objective assessment methods like objective structured clinical examination (OSCE) or simulation scoring on mannequins at the end of the Anesthesiology and Reanimatology course (27).

This study provides a focused evaluation of both knowledge and practical exposure to airway management among senior medical students within a defined curriculum. It captures perspectives from students at a critical stage of training, integrating both cognitive and experiential aspects of learning. The use of a structured questionnaire enabled consistent data collection across participants, offering insight into current educational outcomes and areas for improvement.

Limitations:

The findings should be interpreted in light of the relatively low response rate (79/528), which may introduce non-response bias and limit generalizability. The survey was distributed twice via the institutional learning management system and WhatsApp groups; however, participation remained limited. Additionally, the data is self-reported, and participants might underestimate or overestimate their competence.

Conclusion

Medical students demonstrate strong theoretical knowledge of airway management, including advanced techniques; however, practical experience—particularly with procedures such as endotracheal intubation—remains limited. These findings highlight a gap between knowledge and clinical performance. Expanding structured, supervised, and simulation-based training within undergraduate curricula is essential to improve competence, confidence, and patient safety.

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REVIEW ARTICLES

Ketamine and Spine Surgery – Review

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ABSTRACT

INTRODUCTION:

Various multimodal analgesic approaches have been proposed for spine surgery. This article aims to review the evidence regarding the effect of perioperative ketamine on postoperative opioid consumption, pain scores, and side effects.

MATERIALS AND METHODS:

We included clinical trials in the adult population. Our primary outcome was pain management. Randomized controlled trials published in the English language from January 1995 to September 2025 assessing postoperative pain after spine surgery were identified from the MEDLINE database.

RESULTS:

A total of 16 clinical trials were selected for inclusion in the Review.

CONCLUSION:

Perioperative low doses of ketamine demonstrated analgesic and opioid-sparing effects with no increased adverse events after spine surgery. Further studies of qualitative randomized controlled trials are required to assess the optimal protocol of ketamine administration for postoperative pain relief.

Keywords: ketamine; spine surgery; opioids; pain management

Introduction

Spine surgeries are among the most commonly performed surgical procedures. (1) Worldwide, there is a significant increase in the overall number of spinal decompression and spinal fusion surgical procedures performed for degenerative lumbar spine disease. (2) Many of these patients suffer from chronic postoperative pain, and nearly 20% of those undergoing spine surgery will require secondary surgery for persistent pain or surgery-related complications during subsequent years. (2) Severe pain often accompanies major spine surgery. (3) In a study comparing pain scores in 179 surgical procedures, 3 of the 6 surgeries with a median pain score of 7 on postoperative day 1 (rated on a scale of 0 to 10) were major spinal procedures. (4) Patients undergoing spinal fusion surgery are at high risk for moderate-to-severe postoperative pain and associated complications. (5) Risk factors for severe postoperative pain include preexisting neuropathic pain, preoperative opioid use, perioperative anxiety/mood disorders, level of invasiveness of the surgery, spine segments involved, and degree of difficulty in exposing the surgical field. (1,5) Inadequate analgesia results in poor surgical outcomes, delayed mobilization and rehabilitation, higher rates of readmission, and poor patient satisfaction. (6)

Opioid medications, have historically served as the mainstay for acute postoperative pain management, particularly in procedures associated with severe pain intensity such as spinal surgery. While opioids are effective for managing moderate-to-severe pain, their use carries significant risks, including the development of

tolerance, respiratory depression, physical dependence, pruritus, hallucination, nightmare, sedation, urinary retention, gastrointestinal dysfunction such as ileus, which can result in prolonged hospital length of stay and subsequent delayed rehabilitation. (6–8) There is also a clear association between prolonged preoperative opioid use and adverse postoperative outcomes, including delayed wound healing, higher readmission rates, and increased mortality. (7) Additionally, opioids do not always fully relieve pain, and patients often develop a tolerance. (9) In addition to these acute adverse events, another complication of opioid use is opioid induced hyperalgesia (OIH), a condition where opioid exposure leads to an increased sensitivity to painful stimuli, higher postoperative analgesic requirements and an elevated risk of chronic postsurgical pain (CPSP). (9,10) Although the precise mechanism of OIH is not yet fully understood, proposed mechanisms include an enhanced nociceptive response from sensitized spinal neurons and decreased reuptake of neurotransmitters from primary afferent nociceptive fibers. (9) OIH is believed to be responsible for the decreased effectiveness of opioid medications in certain patients, particularly those without a known underlying pathology or disease progression. (9) Additionally, perioperative opioid use is a significant risk factor for persistent postoperative opioid use (PPOU), defined as continued opioid consumption beyond 90–365 days after surgery. (10)

In recent years, clinicians have employed multimodal analgesic regimens which employ agents with varying mechanisms of action to reduce reliance on opioids and their adverse effects. (5–7) Agents that are antagonists of the NMDA receptor may provide particular analgesic benefit in this patient population via an inhibition of sensitization of nociceptive pathways, prevention of opioid-related activation of pro-nociceptive systems, and attenuation of opioid tolerance and hyperalgesia. (6) NMDA antagonists can provide specific treatment of central hypersensitivity, given the involvement of the NMDA receptor in the generation of neuronal hyperexcitability (11). One such non-opioid agent is ketamine, which has been noted to prevent opioid-induced hyperalgesia. (12,13)

Ketamine is a non-competitive, NMDA receptor antagonist that prevents the induction of synaptic potentiation. (11) While all of the exact mechanisms have not been entirely agreed upon, the primary effect of the drug is related to its NMDA receptor antagonism. (14) This interaction decreases the activation of NMDA receptors, leading to a reduction in neuronal excitability, which plays a crucial role in its ability to alleviate pain. (15) The analgesic effects of ketamine do not end with NMDA receptors. Ketamine enhances opioid-induced analgesia through its binding to spinal μ receptors, which increases the effectiveness of opioid signaling and supports an opioid-sparing effect. (15) At high ketamine concentrations, sigma opioid receptors and muscarinic receptors are also affected. (16)

While it was initially developed as a unique anesthetic drug in the 1950s, clinicians later realized its potential for treating various forms of pain with sub-anesthetic doses, including post-operative pain, chronic pain, complex regional pain syndrome, phantom limb pain, and other analgesia-requiring neuropathic conditions. (4) Ketamine may be administered as a single-dose, continuous intravenous (IV) infusion, IV patient-controlled analgesia (IV-PCA), or epidural infusion. (13) It may be administered preoperatively, intraoperatively, and/or postoperatively. (13) Esketamine is a dextrose isolated from ketamine, with a greater potency and stronger analgesic effect, about twice as much as conventional ketamine. (17) Esketamine mildly depresses respiration and has mild excitatory effects on the circulatory system, mildly increasing blood pressure and heart rate. (17)

Although supplemental ketamine has been studied broadly in a variety of procedures and operations, there is no consensus regarding the effectiveness of adjunctive ketamine analgesic use specifically in spine surgery. (13) This review has been designed to present evidence from clinical trials about the efficacy and safety of the application of perioperative ketamine for the prevention and management of pain after spine procedures.

Materials and Methods

Search strategy: This review was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement recommendations. Publications listed in PUBMED were considered to identify clinical trials suitable for inclusion in this systematic review. The following keywords were used: spine surgery AND ketamine AND adults.

Study selection and inclusion criteria: Inclusion criteria were: clinical trials in adult population (older than 18 years old); about analgesia in spine procedures (i.e. including studies regardless of the anatomical sites and number of levels of the spine, accomplished after both open and percutaneous procedures, microdiscectomy, spine fusion and laminectomy); ketamine was administered; the article described a clinical trial; postoperative analgesia and pain scores were reported; general anesthesia was administered. (1,13,18) Only full papers in the English language that included human data were considered for eligibility. Articles that met any of the following exclusion criteria were excluded from the analysis: the article described a non-human study; non-spine surgery was conducted; the article did not describe a clinical trial; postoperative analgesia and pain scores were not reported; general anesthesia was not administered; abstracts and meeting/symposium proceedings. (1,13,18)

Results

A total of 58 full-text articles were assessed. Eventually, a total of 16 studies were eligible for inclusion in the review. Specific totals from database, and reasons for exclusion, can be found in the diagram (Figure 1).

In a clinical trial, a combination of ketamine and methadone led to reduced use of hydromorphone during the first 24 postoperative hours, and the time until first hydromorphone rescue in the PACU was longer in the methadone/ketamine group compared to the methadone group. (5) Pain scores at rest, with coughing, and with movement were lower in the methadone/ketamine group. Patient-reported satisfaction scores were high in both study groups. (5) After induction of the anesthesia, in methadone group patients were applicated 0.2 mg/kg methadone or 0.2 mg/kg methadone intraoperatively and a ketamine infusion (0.3 mg/kg/h infusion, without bolus, intraoperatively and then 0.1 mg/kg/h for next 48 h (both medications dosed at ideal body weight) in the methadone/ketamine group. (5)

In another study, perioperative ketamine–methadone combination significantly decreased opioid consumption by PCA (the patients who received combined methadone and ketamine (MK) required around 70% less opioid and had similar analgesia degree as the patients treated with methadone alone (M)). (19) Differences in side effects between the study groups were not found. However, the intraoperative administration of ketamine did not improve immediate post-operative analgesia. In the MK group, a ketamine bolus (0.5 mg/kg) was given after tracheal intubation, followed by an infusion of 0.15 mg/kg/h, or a saline bolus plus infusion in the M group. Postoperative analgesia – during 48 h – was provided by patient-controlled analgesia (PCA), delivering a bolus containing the following: ME 0.25 mg plus ketamine 0.5 mg in the MK group or ME 0.5 mg in the M group. (19)

In one investigation, ketamine improved postoperative pain, reduced side effects, and fentanyl use after cervical spine surgery, but could not do so after lumbar surgery. (20) The patients were divided into three groups: the ket-1 group (bolus ketamine 1 mg/kg before incision followed by continuous ketamine 0.042 mg/kg/h for 24 h), the ket-2 group (bolus ketamine 1 mg/kg followed by continuous ketamine 0.083 mg/kg/h for 24 h), control group (isotonic saline was administered). The PCA was programmed to deliver 0.5 μg/kg/h of fentanyl on basal infusion and 0.5 μg/kg on demand with 6 minute lockout for 48 h. Ketamine 2 protocol enhanced the analgesic effects of PCA fentanyl, reduced side effects, and increased patient satisfaction in cervical spine surgery. (20)

Zhang et al published the trial in which they investigated the combination of esketamine–dexmedetomidine combination to supplement analgesia for patients after scoliosis correction surgery. (21) The incidence of moderate-to-severe pain during the first 72 h was significantly lower in the supplement group than the control group (65.7% vs. 86.0%). Subjects who received the supplement experienced less pain at some time points and improved sleep quality without increasing adverse events, including sedation and psychiatric symptoms. (21) In this randomised controlled trial, patients were randomised to patient-controlled sufentanil analgesia (4 μg/kg in normal saline) with either a combined supplement (esketamine 0.25 mg/ml and dexmedetomidine 1 μg/ml) or placebo. (21)

Similar results were provided by Garg et al in who studied ketamine and dexmedetomidine infusion for postoperative analgesia in spine surgery. (22) Both ketamine (ketamine bolus 0.25 mg/kg followed by infusion of 0.25 mg/kg/h with midazolam bolus 10 μg/kg and infusion of 10 μg/kg/h mixed in the same infusion pump) and dexmedetomidine (dexmedetomidine bolus 0.5 μg/kg followed by 0.3 μg/kg/h infusion) in small infusions, provide good and safe analgesia, decreasing morphine requirement and increasing the pain-free period during the postoperative period. (22)

In one clinical trial, they investigated different dosages of esketamine and its effect on pain management. (17) Low-dose esketamine relieves patients' early postoperative pain, reduces the perioperative dose of sufentanil, improves intraoperative circulatory stability of elderly patients, reduces the risk of postoperative respiratory depression, without increasing the risk of adverse events, such as psychiatric symptoms, in the first 5 days after surgery. (17) The doses of 0.2 mg/kg at induction and 0.25 mg/kg/h infusion maintenance during operation were more effective. (17)

In contrast to previous studies, Brinck et al. showed that neither a 0.12 nor a 0.6 mg/kg/h infusion of intraoperative IV S-ketamine was superior to the placebo in reducing oxycodone consumption at 48 hours after lumbar fusion surgery in an opioid-naïve adult study population. (3) Differences in the occurrence of adverse events between study groups were nonsignificant. (3)

In one randomized, double-blind, placebo-controlled study, they evaluated the effect of adding incremental doses of S-ketamine to oxycodone PCA in patients who underwent major lumbar spinal fusion surgery. (23) Patients who received oxycodone: S-ketamine ratio 1:0.75 (a bolus containing oxycodone 1 mg + S-ketamine 0.75 mg per ml) for postoperative analgesia consumed significantly less oxycodone postoperatively compared with participants who received lower S-ketamine doses or oxycodone alone. (23) There was a significant opioid sparing effect long after the S-ketamine was removed from PCA at 24 h postoperatively among patients who received an oxycodone: S-ketamine ratio of 1:0.75 compared with participants in other groups. (23) The occurrence of adverse events was similar among the groups. (23)

One study examined the role of oral ketamine in improving recovery after major spine surgery. (4) Ketamine was given orally ketamine (30 mg) or a matching placebo for three days (nine doses total) or until hospital discharge. (4) Patients in the ketamine group spent significantly fewer days on oral opioids and tended to be discharged from the hospital earlier. (4) The incidence of psychotomimetic side effects in the ketamine group was not significantly different compared to the control group. (4)

Czarnetzki and coauthors investigated ketamine in patients with neuropathic lower back pain. (2) In this patient population undergoing major lower back surgery, a perioperative intravenous low-dose ketamine infusion did not affect the prevalence and intensity of neuropathic lower back pain at 6 or 12 months postoperatively. (2) They used intravenous ketamine 0.25 mg/kg after induction, followed by 0.25 mg/kg/hr intraoperatively, and 0.1 mg/kg/hr from 1 hr before the end of surgery until the end of recovery room stay. (2)

In one trial, Nielsen et al. found that opioid-dependent patients who received esketamine during spine surgery reported reduced opioid consumption, pain, and improved labour market attachment one year after

ery as compared to patients who received a placebo. (24) The protocol for esketamine was a perioperative esketamine bolus of 0.5 mg/kg followed by esketamine 0.25 mg/kg/h infusion. (24)

Nitta and associates investigated the combination of intravenous ketamine and oral clonidine. Although either ketamine (bolus of ketamine (10 mg) during the induction of anesthesia and 2 mg/kg/hour thereafter during the operation) or clonidine (preoperative 4 μg/kg orally) alone had not reduced the postoperative PCA morphine in patients undergoing spine surgery, the combination of oral clonidine premedication and intra- and postoperative subanesthetic ketamine administration reduced the IV-PCA morphine requirements. (25) In the postoperative period, patients were arranged to use IV-PCA mode for administration of drugs, which was programmed to deliver a bolus dose of 2 mg morphine (control and clonidine group), or boluses of 2 mg morphine and 2 mg ketamine (groups ketamine and ketamine/clonidine). (25)

In a prospective, double-blind, randomized controlled study, a subanaesthetic dose of ketamine mixed with fentanyl-based IV-PCA (patients received either ketamine 0.3 mg/kg i.v. or normal saline after anaesthetic induction with fentanyl-based IV-PCA either with or without a ketamine mixture (3 mg/kg in 180 ml) reduced the postoperative 48 h cumulative fentanyl consumption in high-risk patients for PONV undergoing lumbar spinal surgery on PONV but did not reduce the incidence of PONV. (26) Moreover, ketamine administration was associated with an increase in the severity of nausea, incidence of dizziness, and the occurrence of psychomimetic side-effects. (26)

Loftus et al had demonstrated that intraoperative ketamine reduces opioid consumption in the acute postoperative period by 37% in opioid-dependent patients with chronic pain who are undergoing back surgery. (27) Ketamine also reduced pain intensity postoperatively in the PACU and at 6 weeks and reduced consumption of morphine at the first postoperative visit. (27) This benefit is without an increase in side effects. Ketamine was administered 0.5 mg/kg intravenously on induction of anesthesia, and a continuous infusion at 0.6 mg/kg/h was begun on induction and terminated at wound closure. (27)

In the study by Aveline et al, the study documented that, in lumbar disk surgery, a combined bolus of morphine (0.1 mg/kg) and ketamine (0.15 mg/kg) after anaesthetic induction improved postoperative analgesia, and resulted in a significant reduction in titrated morphine dose in the PACU, and in the PCA morphine 24 h consumption compared to a bolus of each single agent. (28) The incidence of postoperative nausea and vomiting was decreased in the combined treatment group compared to the morphine group. (28)

Subramanian reported that the addition of continuous very low-dose ketamine IV infusion (patients in the treatment group received IV bolus ketamine 0.15 mg/kg at induction and continued on 0.12 mg/kg/h IV ketamine infusion intraoperatively and postoperatively for 24 hours) did not improve postoperative analgesia in patients taking opioids preoperatively. Side effects were not increased with low-dose ketamine. (12)

Various multimodal analgesic approaches have been proposed for spine surgery. One of them was a combination of single preoperative oral doses of acetaminophen 1,000 mg and gabapentin 600 mg, an infusion of ketamine 0.3 mg/kg/h throughout surgery, and an infusion of lidocaine 1.5 mg/kg/h intraoperatively and during the initial hour of recovery. The multimodal analgesic pathway did not improve day 3 Quality of Recovery or reduce pain scores or 48-h opioid consumption in patients who had multilevel spine surgery. (29)

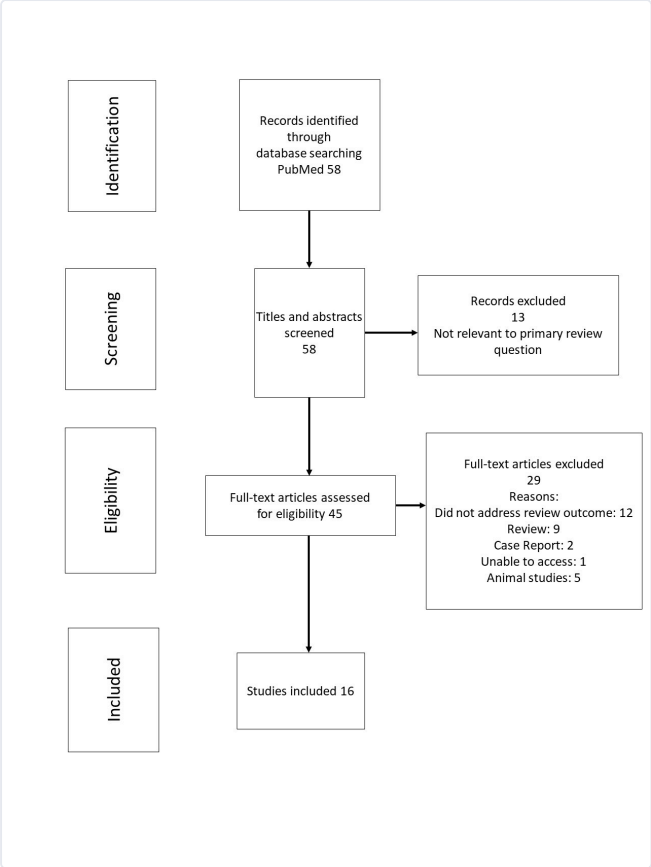

Figure 1. Flowchart depicting the literature review, search strategy, and selection process.

Discussion

Spinal procedures constitute perhaps some of the most painful surgical interventions, as they often encompass extensive muscle dissection, tissue retraction, and surgical implants, as well as prolonged operative duration. (11) Postoperative analgesic management remains a major challenge in spine fusion surgery, given the severity of associated pain. (4) Pain management in this population is further complicated by the number of patients with chronic pain, as well as the paucity of patients who have never received treatment with an opioid. (11) Inadequate postoperative analgesia or excessive pharmacotherapy may lead to diminished functional capacity and prolonged hospitalization. (11)

In this study, we investigated perioperative use of ketamine for pain management in spine surgery. Ketamine was historically used primarily as an anesthetic agent during surgery and is now used for analgesia in the postoperative period in intensive care, postoperative care units, and emergency departments. (15) The evidence supports the beneficial influence of ketamine in controlling postoperative pain, increasing time to first analgesic request, and decreasing overall opioids consumption. Applied as an intravenous continuous infusion during surgery and resumption during postoperative period (as continuous infusion or in combination with opioids in the PCA pump) for the first 48-72 postoperative hours, ketamine appears to be the most effective modality for postoperative pain control. Our finding was consistent with the results of a previous meta-analysis who reported that to obtain the analgesic effect and morphine-sparing effect, only ketamine administrated in postoperative period or through the perioperative period could prolong the analgesic time up to 48 h postoperatively. (15) In contrast to other hypnotics, such as propofol, ketamine has strong analgesic and sedative effects, but absence of significant cardiovascular and respiratory depression effects. It can be used for analgesia and sedation, alone or in combinations with other hypnotic, not only in the operat-

ion room but also in the intensive care and postoperative care units, in the emergency department, in the ambulance during transportation, and even in battlefields. (15)

The available literature in our research does not provide enough evidence to determine the most effective dose of ketamine due to the broad variation in dosing, differences in timing, or mode of ketamine application among trials and inconsistent efficacy outcomes. In several studies ketamine dosage was reduced in the postoperative period compared with the intraoperative dose, or the ketamine infusion was canceled. Furthermore, in several trials, continuous IV infusions during the intraoperative period were replaced by IV-PCA postoperatively, introducing variables such as patient decision-making and differences in lockout intervals. (13)

The other conclusion that can be drawn from the aforementioned studies is that although ketamine was effective in many of the trials, other trials showed that it provided no benefit when compared to a placebo. While ketamine holds a place in the prevention and treatment of postoperative pain, more large, high-quality controlled studies are necessary in order to determine which procedures it is best suited for and at what dosages and frequencies it should be administered. Future research could focus on determining the optimal ketamine dose and treatment duration, as well as its long-term effects, to improve perioperative outcomes and pain management efficiency. (15) More research needs to be performed to look at what doses, amounts (single bolus vs. multiple boluses), and what diferences exist between different patient populations (opioid naive vs. opioid dependent and patients with chronic pain). (9)

The lack of consistent findings concerning efficacy of the ketamine potentially resulting from the different types of surgical procedures. The types of spine surgery varied (lumbar or cervical) as well as the magnitude of incision (large or small), which were likely to affect the postoperative pain. (25) The more complex and painful spine procedures were the ones most likely to be associated with ketamine administration as a continuous infusion. (30)

The side effects most commonly associated with higher doses of ketamine, including vomiting, nausea, hallucinations, vivid dreams, and dissociation, are a significant concern and often limit its use. In contrast, when low doses of ketamine are used for the treatment of acute pain, studies show that there is no significant difference in the incidence of side effects compared with morphine, suggesting that lower doses may offer an effective alternative with a similar safety profile. (15)

Postoperative pain management in opioid users remains challenging. In this study, opioid-naive patients were largely enrolled, who consumed small amounts of opioid medications and were reasonably comfortable in the postoperative period, making it difficult to assess the impact on the reduction in analgesic consumption and on the opioid-related side effects, (27) what would it mean that ketamine may be most efficacious in patients who consume higher amounts of preoperative opioid medications. (27) It is well known, that preoperative opioid use is an important risk factor for severe acute postoperative pain and the development of chronic postsurgical pain. (31) Underlying mechanisms for increased pain and opioid consumption include those related to opioid-related tolerance and hyperalgesia. Hyperalgesia is associated with an up-regulation of NMDA receptors induced by activation of opioid receptors. Due to NMDA receptor involvement in opioid-related modulation responsible for hyperalgesia, ketamine as NMDA receptor blocker is suggested to be a reasonable adjuvant in the multimodal analgesia regime, especially for long term opioid tolerant patients. (31) The systematic review showed that in patients with preoperative opioid intake perioperative ketamine has no or only slight effects on pain intensity during movement or at rest 24 h after surgery. (31) However, perioperative ketamine reduced cumulative mean opioid consumption associated with a reduced risk for postoperative sedation and without increased harm. (31) In literature we can see that perioperative there are different dosage of opioid analgetic with emphasis that this often includes diverse opioids (fentanyl, remifentanil, morphine, hydromorphone, methadone). (5) Quantification of opioid requirements would

have been simplified if a single opioid had been given. Furthermore, intraoperative dosing of opioids is at the discretion of the anesthesia care provider. (5)

In conclusion, this review presents that intraoperative and postoperative administration of low doses of ketamine reduces opioid consumption during the perioperative time in patients who have undergone spine surgery. There are no differences regarding the assessed side effects. Furthermore, there was significant heterogeneity associated with the trials that were included in this study. The optimal ketamine administration regimen remains to be determined, as well as patient population characteristics that will benefit the most from perioperative ketamine.

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REVIEW ARTICLES

Principles and role of photoplethysmography in anesthesiology and intensive care medicine

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ABSTRACT

Photoplethysmography (PPG) is a non-invasive optical method that detects blood volume changes in the skin microcirculation. Since its first description in 1938, PPG has evolved from a research tool into a key component of clinical monitoring, particularly with pulse oximetry. This narrative review summarizes the principles, waveform characteristics, contemporary theories, and future applications of finger PPG in anesthesiology and intensive care medicine. A literature search was conducted using PubMed and Google Scholar with the keywords "photoplethysmography," "anesthesiology," and "intensive care medicine." OpenEvidence AI was used as a supplementary tool. Retrieved articles were independently reviewed for relevance and methodological quality. Finger PPG signals comprise pulsatile and non-pulsatile components, reflecting the cardiac cycle. Waveform morphology is influenced by microcirculatory blood volume, arterial pressure, autonomic tone, and vascular compliance. Clinically, PPG underlies pulse oximetry and provides information on nociceptive stimuli, anesthesia depth, and sympathetic activity. Parameters such as perfusion index (PI), pulse transit time (PTT), and area under the photoplethysmographic curve (AUCPPG) have been explored to assess regional anesthesia efficacy and volume status. Emerging technologies enable continuous, non-invasive arterial pressure and cardiac output monitoring via algorithmic interpretation of PPG-derived signals. Finger PPG is a versatile, non-invasive tool with established and emerging applications in anesthesiology and critical care. Advances in signal analysis and device technology are expanding its role in continuous hemodynamic monitoring, potentially enhancing patient management and safety in perioperative and intensive care settings.

Keywords: Anesthesiology; Intensive Care Medicine; Photoplethysmography

Introduction

Photoplethysmography (PPG) is a non-invasive optical method that uses infrared light to assess blood flow within the microcirculation of the skin (1,2). The term „photoplethysmography" originates from Greek words „plethysmos", meaning „to increase", and „graph", meaning „to write". The history of PPG began in 1938, when Alrick Hertzman observed that the amount of infrared light absorbed and reflected by tissue varies according to blood volume within the examined area (1,3). The most significant clinical application of PPG emerged several decades later with the development of pulse oximetry, which remains an essential component of standard monitoring during anesthetic procedures, surgical and invasive procedures, and intensive care treatment (4). Although the basic principles of PPG are well known for almost a century, advances in signal analysis during recent decades have led to improved understanding of the physiological mechanisms underlying the finger PPG waveform (5). As methods for waveform analysis have evolved, the potential clinical applications of PPG have expanded beyond conventional pulse oximetry. Today, non-invasive PPG is used for advanced and minimally invasive haemodynamic monitoring, assessment of nociceptive stimuli and depth

of anesthesia during surgical procedures, and evaluation of sympathetic blockade during central neuraxial blocks and peripheral nerve blocks (6–10). Continued technological development may additionally contribute to further advancement of continuous non-invasive blood pressure monitoring based on finger PPG-derived parameters (11).

Methodology

This study was a narrative literature review that conducted a literature search using the keywords „photoplethysmography", „anesthesiology", and „intensive care medicine" in the PubMed and Google Scholar databases in order to identify relevant publications on the use of photoplethysmography in anesthesiology and intensive care medicine. The study was conducted from February 2026 to March 2026. The primary search terms included the aforementioned keywords used individually and in combination. Approximately 70 articles relevant to the topic were identified and reviewed. No restrictions regarding publication year were applied in the initial search process. Following the database search, an additional targeted review was conducted using OpenEvidence AI as a supplementary artificial intelligence-assisted search tool to identify additional relevant publications from the previous 10 years addressing specific subtopics within the field: regional anesthesia and photoplethysmography, advanced hemodynamic monitoring and assessment of volume status, assessment of depth of anesthesia and nociceptive stimuli, and respiratory monitoring. Articles were selected based on their relevance to the clinical application of photoplethysmography in anesthesia and intensive care settings. Both original research articles and review papers were considered. The collected literature was analyzed descriptively, with emphasis placed on current clinical applications, technological advances, and emerging monitoring strategies involving photoplethysmography. All articles identified through OpenEvidence were subsequently verified through conventional database sources, primarily PubMed and Google Scholar, before inclusion in the review, to ensure scientific validity and relevance.

Principle of photoplethysmography

A non-invasive PPG device consists of a light-emitting diode, which transmits infrared light into the tissue, and a photodetector, which senses the amount of transmitted or reflected light. When the light-emitting diode and photodetector are placed on the same side of the examined tissue, the device operates in reflectance mode by detecting light that is reflected from the tissue. When positioned on the opposite side of the examined tissue, the device operates in transmission mode by detecting transmitted light (2,5). The light-emitting diode and photodetector are specific for infrared light because haemoglobin absorbs infrared light more readily than other skin structures (7). Due to strong absorption, blood vessels reflect substantially less light during systole, compared to reflection occurring during diastole (7,12). Consequently, the systolic amplitude of the finger PPG waveform correlates with the end-diastolic phase of the cardiac cycle (6,7,12). The PPG signal consists of two components: a pulsatile alternating current (AC) component and a non-pulsatile direct current (DC) component. The AC component arises from synchronised heartbeats and consequent periodic changes in microcirculatory blood volume, whereas the DC component reflects lower-frequency physiological processes, including respiration, sympathetic nervous system activity, and skin thermoregulation. Otherwise stated, the AC component is a consequence of heart frequency and the DC component is a consequence of frequencies lower than heart frequency (7,2,13,14). Analysis of these waveform components has enabled broader clinical interpretation of PPG signals beyond conventional pulse oximetry.

Contemporary theory on the origin of the curve of finger photoplethysmography

Since Alrick Hertzman's discovery in 1938, numerous studies have confirmed an inversely proportional relationship between blood volume within the examined tissue and the amount of transmitted or reflected in-

nisms underlying the relationship between cardiovascular dynamics and changes in infrared light absorption still remain a matter of scientific debate. Kamshilin et al. proposed that cyclic changes in transmural arterial pressure during the cardiac cycle lead to elastic deformations of dermis, resulting in relative changes in microcirculatory blood volume (5,18). During systole, increased transmural pressure in large arteries leads to compression of dermal tissue. Although the dermis predominantly contains non-pulsatile capillaries, tissue compression decreases the distance between capillaries, thereby increasing relative capillary density during the systolic phase of the cardiac cycle (5,19,20). Consequently, absorption of infrared light increases during systole due to the relatively greater blood volume within the examined tissue (5). Nevertheless, it remains unclear whether variability in infrared light absorption during different phases of the cardiac cycle primarily reflects periodic changes in microcirculatory blood volume or alterations in transmural arterial pressure (5,18). This ongoing uncertainty illustrates that, although the clinical applicability of PPG is well established, some physiological mechanisms responsible for the generation of the finger PPG waveform remain incompletely elucidated.

Curve of the finger photoplethysmography

The finger PPG waveform reflects pulsatile movement from the heart toward the peripheral circulation at the site of probe placement. The shape of the PPG curve may be influenced by numerous physiological and clinical factors, including heart rhythm and heart rate, stroke volume, circulating blood volume, extremity position, autonomic nervous system activity, vascular wall compliance, and administration of vasoactive drugs (1). According to contemporary theories of PPG curve origin, individual tissue characteristics may also influence the shape of the curve (5). Such variability indicates that the interpretation of PPG waveforms may depend on multiple physiological mechanisms acting simultaneously.

The finger PPG curve consists of two main parts: the ascending component (anacrota) and the descending component (catacrota). The dicrotic notch, located on the descending portion of the curve, corresponds to closure of the aortic valve (1). A typical appearance of the finger PPG curve is presented in Figure 1 (21).

Because changes in the PPG signal may be difficult to detect at waveform inflection points, Takazawa et al. introduced automatic digital processing of the basal PPG signal in 1998 to enable calculation of parameters derived from the curve (1,22). Digital processing generates the first or second derivative of the original signal and is currently incorporated into most contemporary PPG devices (1,22). Interpretation of the PPG signal therefore, relies not only on the basal waveform itself, but also on signal processing techniques used for the extraction of curve characteristics and calculation of derived diagnostic parameters (1). Figure 2 presents the basic diagnostic structure of finger PPG analysis (23).

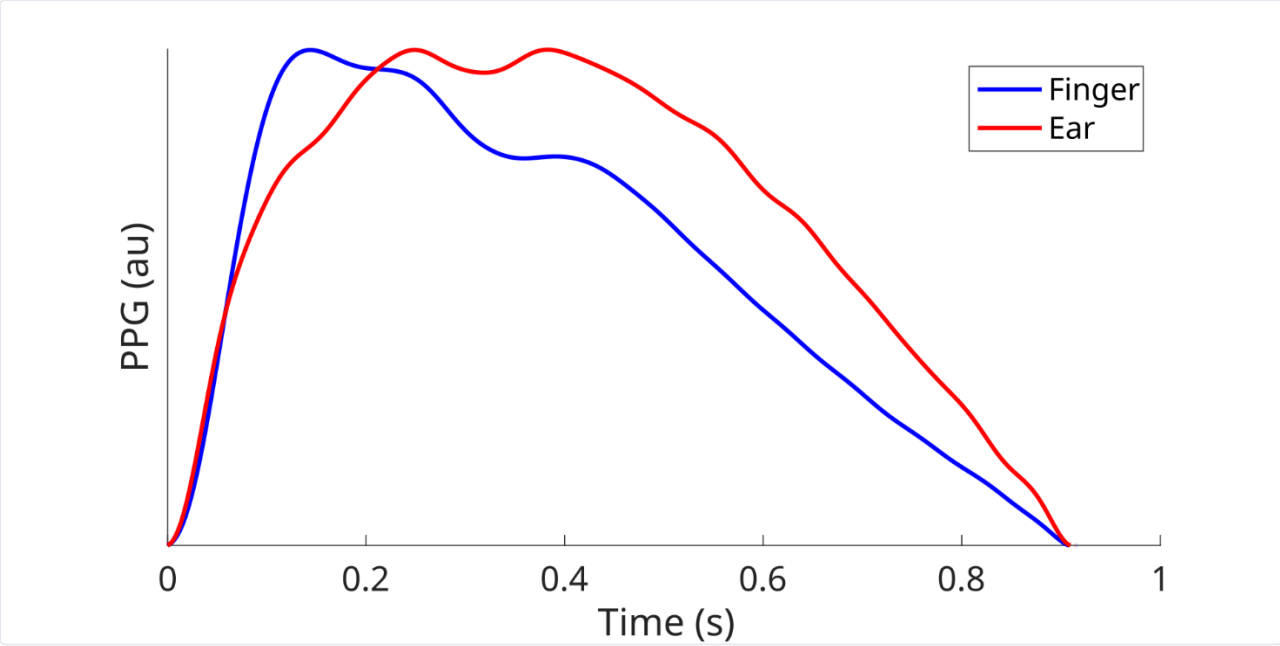

Figure 1. Finger photoplethysmography waveform. Reproduced from Charlton PH. Finger vs ear photoplethysmogram (PPG) pulse waves. Wikimedia Commons; 2016. CC BY 4.0.

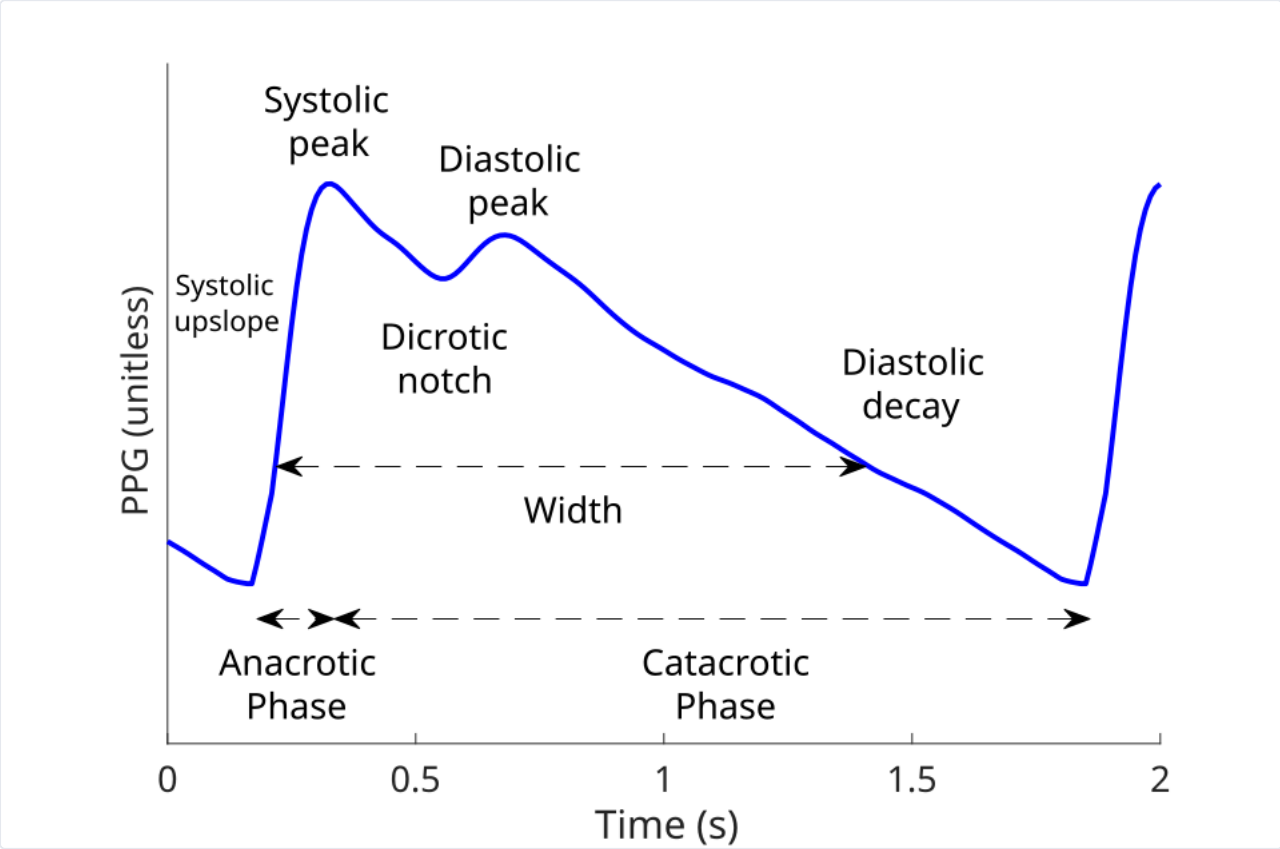

Figure 2. Diagnostic structure of finger photoplethysmography. Reproduced from Charlton PH. Photoplethysmogram (PPG) pulse wave. Wikimedia Commons; 2021. CC BY 4.0.

Respiratory monitoring

The most significant clinical application of finger photoplethysmography remains pulse oximetry, which has represented an essential component of standard monitoring during anesthetic procedures and intensive care

treatment for almost half a century. In 1972, Takuo Aoyagi discovered that tissue oxygen saturation depends on the strength of the measured pulse signal (4). Discovery led to the development of pulse oximetry, which combines finger photoplethysmography and oximetry. Oximetry is based on the Lambert-Beer law, according to which oxygenated and reduced haemoglobin differ in their absorption of red and infrared light. By combining oximetry and finger photoplethysmography, it became possible to differentiate pulsatile arterial blood from non-pulsatile venous blood and thereby indirectly estimate arterial oxygen saturation (24).

Beyond pulse oximetry, PPG has been increasingly investigated for additional applications in respiratory monitoring. PPG signals contain respiratory-induced variations (RIVs), including baseline wander, amplitude modulation, and frequency modulation, which may be used for continuous non-invasive respiratory rate estimation in both clinical and wearable device settings. Several algorithms based on these signal modulations have demonstrated results comparable with capnography and thoracic belt measurements under different body positions and low sampling rates (25–33). Nevertheless, these applications remain dependent on signal quality and processing methodology.

PPG waveform analysis has also been investigated in sleep-related breathing disorders. Variations in the PPG signal may differentiate between apneas and hypopneas during sleep, and machine learning models trained on PPG-derived features have demonstrated the ability to classify such events with reasonable accuracy (34). These findings suggest potential utility of wearable PPG devices in sleep monitoring, although broader clinical applicability continues to require further evaluation.

In addition, PPG-derived parameters have been used for assessment of respiratory effort through analysis of amplitude, baseline, and pulse transit time (PTT) modulations. Reported correlations between these parameters and airway pressure or respiratory load suggest possible application in non-invasive assessment of respiratory mechanics and upper airway dynamics (35).

Respiratory synchronous variation in the PPG waveform, including the pleth variability index (PVI), has also been utilized in the prediction of fluid responsiveness in mechanically ventilated patients (25,36). This application leverages the respiratory modulation of the PPG signal to inform hemodynamic management (25,36).

Recent technological advances have additionally enabled remote PPG-based respiratory rate estimation for telemedicine and unobtrusive monitoring in ambulatory and elderly care settings (28,29). Overall, these developments indicate expanding clinical interest in respiratory applications of PPG; however, the degree of clinical utility may vary depending on patient population, monitoring conditions, and applied signal-processing techniques (25–36).

Assessment of depth of anesthesia and nociceptive stimulus

Finger PPG has been investigated as a potential tool for assessment of anesthesia depth during surgical procedures (7). Zhang et al. compared various parameters derived from the finger PPG curve with the Cerebral State Index (CSI) during general anesthesia and concluded that finger PPG is inferior to CSI for direct assessment of anesthesia depth. However, the same study suggested that finger PPG may be useful for assessment of analgesia during balanced general anesthesia (37). Krishnamohan et al. demonstrated a significant correlation between perfusion index (PI), derived from finger PPG, and minimum alveolar concentration (MAC) values, suggesting potential utility of PI in monitoring anesthetic depth, particularly in pediatric populations (38). Nevertheless, PI primarily reflects peripheral vasodilation and sympathetic nervous system activity, both of which may be influenced by hypnotic and analgesic components of anesthesia. Consequently, the interpretation of PI as an isolated indicator of anesthetic depth may be limited.

Several studies have therefore focused on the use of finger PPG for assessment of nociceptive stimulus during surgical procedures, with reported positive correlation between the PPG-derived parameters and

ive stimulus (8,39,40). One of the most established PPG-derived parameters in this context is the surgical pleth index (SPI), which is calculated from pulse amplitude and pulse frequency obtained by pulse oximetry (41). In 2018, Choi et al. proposed the nasal photoplethysmography index (NPI) as a potential parameter for assessment of nociception during surgery and concluded that its performance was comparable to SPI in evaluating nociceptive stimulus (9).

Pulse transit time (PTT) has additionally been investigated as a marker of nociceptive response. Sigtermans et al. applied PTT during both laparoscopic and open abdominal surgery and reported successful detection of nociceptive impulses (39). Similarly, Singham et al. proposed PTT as a surrogate marker for nociceptive stimulus during gynecological surgery and concluded that PTT changes adequately reflected sympathetic nervous system responses to nociceptive stimulation and fluctuations in anesthesia depth, independently of heart rate changes (40). Beyond nociception monitoring, intraoperative trends in PTT have also been proposed as potential surrogate markers for estimation of blood loss during surgery (42).

Recent multimodal approaches integrating PPG with electroencephalographic and electrocardiographic signals using deep learning models have demonstrated additional potential for intraoperative nociception monitoring; however, these approaches have not yet become part of standard clinical practice (43). Overall, current evidence suggests that PPG-derived parameters may be more applicable for assessment of nociceptive and autonomic responses during anesthesia than for direct assessment of hypnotic depth. In comparison with electroencephalography-based monitors such as CSI, Bispectral Index (BIS), and Patient State Index (PSI), the role of PPG in direct monitoring of anesthetic depth remains more limited (8,9,39–41,43).

Regional anesthesia

The ability of finger PPG to indirectly reflect changes in systemic vascular resistance has resulted in numerous studies investigating its application in regional anesthesia. PPG-derived parameters have been used for assessment of sympathectomy following administration of peripheral nerve blocks and central neuraxial blocks, as well as for evaluation of clinical adequacy of administered nerve blocks (7,44–52).

Area under the curve of the finger photoplethysmography (AUCPPG) has been described as an indicator of changes in vascular tone (53). Babchenko et al. explained that decreased sympathetic activity following epidural block increases vascular compliance, which subsequently affects pulse wave propagation (50,54,55). Although systolic amplitude and width of the PPG waveform are more commonly investigated, several studies have evaluated AUCPPG as an independent parameter for assessment of systemic vascular resistance during anesthetic procedures. Seitsonen et al. described AUCPPG as a potential parameter for assessment of nociception during abdominal hysterectomy under balanced general anesthesia (56), while La Yang et al. proposed its possible utility in postoperative pain assessment (57). However, clinical experience with AUCPPG as an isolated monitoring parameter remains relatively limited.

Pulse oximeter perfusion index (PI) has also been investigated as a marker of sympathectomy after neuraxial blockade. Ginosar et al. examined changes in PI following epidural administration of bupivacaine and concluded that PI may represent a more sensitive indicator of sympathectomy compared with changes in mean arterial pressure and skin temperature (44). PI is calculated from pulse oximetry as the ratio between pulsatile and non-pulsatile signal components (AC/DC x 100) (58).

PTT is another frequently investigated PPG-derived parameter in regional anesthesia. Babchenko et al. demonstrated that increases in PTT after epidural administration of bupivacaine reflected sympathectomy more sensitively than conventional clinical indicators such as mean arterial pressure and skin temperature (50). Kortekaas et al. additionally proposed increasing PTT trends after axillary block as a potential marker of successful brachial plexus blockade (46). Similar approaches have been described for the assessment of successful caudal block in children and blockade of the lumbar sympathetic ganglion in neuropathic pain

treatment (48,49). Several studies have also used PTT for evaluation of sympathectomy after epidural anesthesia during surgical procedures (7,50).

In obstetric anesthesiology, PTT has mainly been investigated as a marker of cardiovascular changes after spinal anesthesia for cesarean delivery (51,52). Sharwood-Smith et al. reported that a 20% increase in PTT after spinal anesthesia predicted a decrease in mean arterial pressure greater than 10% from baseline with 74% sensitivity and 70% specificity (53). Approximately one decade later, Bolea et al. reported similar findings describing 76% sensitivity, 70% specificity, and 72% overall accuracy of PTT in the prediction of hypotension following spinal anesthesia for cesarean delivery (52). PPG-derived signals have also been successfully applied in the evaluation of sympathectomy after epidural analgesia during vaginal delivery (59).

Despite the promising results reported in multiple studies, PPG-derived parameters are still not part of standard clinical monitoring in regional anesthesia. Proposed limitations include technical barriers, complexity of signal interpretation, increased use of ultrasound guidance, and susceptibility of PPG-derived parameters to confounding factors (i.e., patient anxiety, systemic medications, etc.). Consequently, conventional clinical methods, including assessment of sensation to cold, touch, and pinprick testing, remain the standard techniques for evaluation of peripheral and central neuraxial block success in everyday clinical practice (60).

Advanced hemodynamic monitoring and assessment of volume status

Middleton et al. described the successful application of PPG for the assessment of peripheral circulation in septic patients, thereby introducing the possibility of non-invasive hemodynamic monitoring in this population (61). In this context, a case report describing the use of esophageal PPG in a patient with diffuse peritonitis additionally demonstrated potential application of PPG for assessment of hemodynamic coherence (62).

PPG-derived parameters have also been investigated for the assessment of volume status in critically ill patients. Established methods of advanced hemodynamic monitoring, including lithium dilution cardiac output (LiDCO) systems, have been used for many years to calculate parameters such as stroke volume variation (SVV) and pulse pressure variation (PPV) in order to evaluate hemodynamic response following intravenous fluid administration (10). Similarly, parameters derived from the finger PPG curve, including pulse amplitude variation (PAV) and PVI, have been proposed as non-invasive alternatives for assessment of volume status in critically ill patients (63,64).

Over recent decades, there has been substantial development of hemodynamic monitoring technologies utilizing PPG for minimally invasive or non-invasive cardiac output assessment, including previously mentioned LiDCO systems (10,65). However, it should be emphasized that several commonly used advanced hemodynamic monitoring systems, such as LiDCO, Pulse Index Contour Continuous Output (PiCCO), and FloTrac, still require placement of a peripheral arterial catheter for cardiac output calculation (66,67). In contrast, estimated continuous cardiac output (esCCO) monitoring represents a completely non-invasive approach that calculates cardiac output algorithmically by measuring PTT, also referred to as pulse wave transit time (PWTT) (68). Several reports have described successful clinical utilization of esCCO monitoring. For example, esCCO was used in one case report to detect a reduction in cardiac output following administration of epidural analgesia during vaginal delivery (69). Nevertheless, comparative clinical trials evaluating esCCO have reported conflicting results regarding its accuracy when compared with more conventional monitoring techniques (70,71). These findings indicate that, although non-invasive PPG-based cardiac output monitoring demonstrates promising potential, its clinical performance may vary depending on methodology and reference standard.

Additional PPG-based technologies include the Biobeat BB-613WP medical-grade patch-monitor, which utilizes a reflective PPG sensor and PTT analysis calibrated against cuff-based blood pressure measurements.

Clinical studies comparing this device with invasive pulmonary artery catheter measurements have demonstrated its capability for non-invasive monitoring of cardiac output and systemic vascular resistance (72).

Another example is the volume-clamp method, implemented in devices such as Finapres and related systems. These devices use finger cuffs to continuously measure arterial blood pressure and derive cardiac output from the arterial pressure waveform according to the Penaz principle. Reported measurements have shown comparability with conventional brachial pressure measurements (39).

Experimental systems integrating spectrometry, PPG, and arterial pressure measurement have also been developed. These systems combine time-resolved and wavelength-resolved optical fingertip signals under externally applied pressure in order to derive hemodynamic information from both macrovascular and microvascular circulation (73,74).

In parallel, wearable devices and bedside monitoring systems, incorporating advanced signal processing and calibration protocols, are becoming increasingly available. However, their clinical utility and accuracy continue to be evaluated against invasive reference methods (72,73,75).

Due to the possibility of estimating arterial blood pressure from PTT measured by finger PPG, continued development of continuous non-invasive blood pressure monitoring technologies may be expected in forthcoming years (7,11,19).

Conclusions

Since its initial discovery in the first half of the twentieth century, the most established clinical application of PPG has remained pulse oximetry, particularly in anesthesiology and intensive care medicine. Advancements in signal analysis and monitoring technology during the second half of the twentieth century enabled a broader understanding of the physiological principles underlying the PPG signal and contributed to the expansion of its potential clinical applications. Beyond pulse oximetry, finger PPG has been investigated for assessment of nociceptive stimulus during surgical procedures, evaluation of sympathetic blockade following peripheral nerve blocks and central neuraxial anesthesia, respiratory monitoring, and advanced hemodynamic assessment. Several studies have demonstrated promising results for these applications; however, many PPG-derived parameters continue to be primarily used in research and experimental settings rather than as part of routine clinical monitoring.

Among emerging applications, advanced hemodynamic monitoring represents one of the most significant areas of ongoing development. Numerous technologies based on finger PPG and pulse transit time analysis have demonstrated potential for minimally invasive or non-invasive assessment of cardiac output, volume status, and cardiovascular changes. Nevertheless, variability in methodology, technical limitations, and conflicting results in comparative studies indicate that further clinical evaluation remains necessary before broader standardization and implementation can be achieved.

Overall, current technological progress suggests continued expansion of PPG-based monitoring systems, including further development of continuous non-invasive arterial blood pressure monitoring derived from the finger PPG signal.

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REVIEW ARTICLES

Tackling Infections in Intensive care unit setting

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ABSTRACT

Infections within the intensive care unit (ICU) continue to be a major contributor to morbidity and mortality throughout Europe. Critically ill patients, oftentimes presenting with organ failure, having frequent interactions with invasive medical devices, and by receiving multiple antimicrobial agents are particularly susceptible to infections. Having knowledge of pathogen-specific epidemiology in ICUs across Europe and their antimicrobial resistance patterns is of utmost importance to choosing the right empirical therapy. Challenge posed by multidrug-resistant organisms, especially Gram-negative bacteria, is easier to tackle with infection prevention strategies, antimicrobial stewardship initiatives, and collaborative multidisciplinary care in place within the ICU setting.

Keywords: ICU; infections; MDRO

Introduction

Healthcare-associated infections (HAIs) represent one of the most significant challenges in intensive care medicine. Intensive care unit (ICU) patients experience infection rates that are several times higher than patients in general hospital wards (1). It is mostly due to the immune dysfunction and high prevalence of invasive procedures done on patients in ICU. Infections are associated with prolonged ICU stay, increased healthcare costs, and excess mortality, particularly when caused by multidrug-resistant organisms (MDROs)(2).

The EPIC III study, involving ICUs across Europe and beyond, reported that 54% of ICU patients had suspected or confirmed infection, with 22% acquiring infection after ICU admission. That highlights the disease burden of ICUs, as more than half of the patients will be treated for an infection, and almost half of those patients will contract an infection in the ICU. Pneumonia accounts for most of the ICU infections, followed by bloodstream and urinary tract infections (3). European Centre for Disease Prevention and Control (ECDC) surveillance reports consistently identify ICUs as the hospital setting with the highest prevalence of HAIs. Approximately 15–25% of ICU patients develop at least one HAI during their stay, with considerable differences among countries. Mechanical ventilation, central venous catheterization, and urinary catheterization are strongly associated with increased risk of infection. More than 60% of ICU-acquired pneumonias are ventilator-associated, approximately one-third of bloodstream infections (BSIs) are central line-associated, and nearly all ICU-acquired urinary tract infections (UTI) occur in catheterized patients in Europe (Table 1.). Apart from bacterial infections, fungal and viral pathogens are increasingly recognized as contributing agents to an infectious burden in ICUs (4).

Widespread dissemination of bacterial strains harboring multiple resistance genes to antimicrobial agents has further complicated the management of ICU infections, with regards to empirical therapy and contact precautions regarding patients colonized or infected with those strains. Surveillance data from the European

Antimicrobial Resistance Surveillance Network (EARS-Net) outlines persistently high resistance rates among Gram-negative microorganisms, particularly *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and carbapenem-resistant Enterobacterales (5). These trends have important implications for induction of antimicrobial therapy, infection control measures and finally on clinical outcome in critically ill patients.

Table 1. Estimated prevalence of infectious syndromes in European ICUs.

Infectious syndrome	Estimated proportion of ICU HAIs (%)	Risk factor	References
Ventilator-associated pneumonia	40–50	Mechanical ventilation	Vincent et al. (2020); ECDC (2021); Koulenti et al. (2017)
Bloodstream infection	7–10	Central venous catheter	Munro et al. (2024); Tabah et al. (2012); ECDC (2021)
Catheter-associated urinary tract infection	3–5	Urinary catheter	ECDC (2021); Hooton et al. (2010)
Intra-abdominal infection	5–8	Surgical procedures, drains	Munro et al. (2024); Tabah et al. (2012)
Fungal infections (mainly candidemia)	5–10 (of BSIs)	Central venous catheter	Munro et al. (2024); Vincent et al. (2020); Pappas et al. (2016)

Ventilator-associated pneumonia in the ICU

Ventilator-associated pneumonia (VAP) remains the most frequently reported ICU-acquired infection in Europe. Although prevention strategies have reduced incidence in some settings, VAP continues to account for up to half of ICU HAIs (6,7). ICU patients oftentimes require prolonged mechanical ventilation and frequently exposed to multiple antimicrobial agents, both of which contribute to infections with difficult-to-treat microorganisms.

Gram-negative bacteria are the predominant cause of VAP in Europe (Table 3.). *Pseudomonas aeruginosa* is the most frequently isolated pathogen, followed by *Staphylococcus aureus*, *Klebsiella* spp., *Escherichia coli*, *Enterobacter* spp., and *Acinetobacter baumannii* (7,8). Antimicrobial resistance is common among VAP pathogens. Carbapenem resistance in *P. aeruginosa* and *A. baumannii* and ESBL production among Enterobacterales complicates empirical antimicrobial therapy, while being associated with increased ICU patient mortality (5). Further implications of difficulties when prescribing empirical therapy are carbapenem resistance among *P. aeruginosa* and *A. baumannii* isolates, with carbapenems being the agent of choice for ESBL producing Enterobacterales.

Table 2. Pathogens associated with VAP in European ICUs.

Pathogen	Estimated frequency among VAP isolates (%)	Resistance	References
Pseudomonas aeruginosa	20–30	carbapenem resistance	Koulenti et al. (2017)
Staphylococcus aureus	15–20	methicillin resistance	Vincent et al. (2020)
Klebsiella spp.	15–20	beta-lactam resistance	ECDC (2021)
Escherichia coli	10–15	beta-lactam resistance	Koulenti et al. (2017)
Enterobacter spp.	5–10	beta-lactam resistance	Koulenti et al. (2017)
Acinetobacter baumannii	5–10	extensive drug resistance	ECDC (2021)

Bloodstream infections in the ICU

Bloodstream infections represent one of the most severe ICU-acquired infections and are consistently associated with high mortality. Population-based and ICU-specific studies report mortality rates ranging from 30% to over 40%, depending on pathogen, resistance profile, and patient comorbidities (2,9).

It is estimated that ICU-acquired BSI incidence falls in the 1.5–3 episodes per 1,000 patient-days in Europe (10). The EUROBACT study demonstrated that the majority of ICU BSIs are secondary, most frequently originating from pneumonia, intra-abdominal infections, or urinary tract infections (11). Primary catheter-related BSIs remain common but can be curbed by active prevention programs (12).

Both Gram-positive and Gram-negative microorganisms cause BSIs in ICUs across Europe (Table 2.). Coagulase-negative staphylococci, *Enterococcus* spp., and *Staphylococcus aureus* are among most common Gram-positive isolates, while *Klebsiella* spp., *Escherichia coli*, *Pseudomonas aeruginosa*, and *Acinetobacter baumannii* are the most common Gram-negative isolates (2,3). Fungal pathogens, predominantly *Candida* spp., account for 5–10% of ICU BSIs and are associated with worse outcomes, especially when diagnosis or antifungal therapy is delayed (13).

Table 3. Bacterial and fungal pathogens causing ICU BSIs in Europe.

Pathogen	Approximate proportion of ICU BSIs (%)	Resistance	References
Coagulase-negative staphylococci	20–30	methicillin resistance	Munro et al. (2024); Tabah et al. (2012); Vincent et al. (2020)
Enterococcus spp.	10–15	vancomycin resistance	Lanaghan et al. (2024); ECDC (2021)
Staphylococcus aureus	10–15	methicillin resistance	Vincent et al. (2020)
Klebsiella spp.	8–12	beta-lactam resistance	Munro et al. (2024); ECDC (2021)
Escherichia coli	7–10	beta-lactam resistance	Munro et al. (2024)
Pseudomonas aeruginosa	5–10	carbapenem resistance	ECDC (2021)
Candida spp.	5–10	azole resistance	Munro et al. (2024); Pappas et al. (2016)
Acinetobacter baumannii	2–5	extensive drug resistance	Munro et al. (2024); ECDC (2021)

Other infection types in the ICU

Intra-abdominal infections represent a very high portion of ICU infections, with some estimates ranging from 5-20% of all ICU patients having one (14,15). Gram-negative bacteria are among the most isolated pathogens involved in intra-abdominal infections, with *E. coli* being the predominant pathogen isolated (16). *Enterococcus* spp. was the most common gram-positive isolate responsible for intra-abdominal infections in ICU. Mortality of patients with intra-abdominal infections is usually higher than of those associated with other infections (15).

ICU-acquired UTIs represent a smaller proportion of HAIs and are almost universally catheter-associated. Risk for contracting an infection increases with catheter duration and prior antimicrobial exposure (17). Common pathogens are *E. coli*, *Enterococcus* spp., *Klebsiella* spp., *P. aeruginosa*, and *Candida* spp. While mortality directly attributable to catheter associated UTI is lower than for BSI or VAP, these infections contribute to overuse of antimicrobial agents, consequential resistance selection in pathogens, and prolonged ICU stay of patients.

Fungal infections, particularly invasive candidiasis, have seen an increase in incidence in European ICUs. Risk factors for contracting an invasive fungal infection include usage of broad-spectrum antibiotics, presence of central venous catheters, parenteral nutrition, and immunosuppression of patients (13). Candidemia is associated with high mortality and prolonged hospitalization, emphasizing the importance of early diagnosis of invasive fungal infections, with subsequent appropriate and timely antifungal therapy induction.

Respiratory viruses are recognized as an important cause of ICU admission, which can further contribute to secondary bacterial infections in ICU patients. Influenza, SARS-CoV-2, and other respiratory viruses can cause severe pneumonia requiring mechanical ventilation (18,19). As stated, viral infection may predispose patients to secondary bacterial infection and complicate antimicrobial stewardship decisions (20). COVID-19

pandemic highlighted the vulnerability of ICU patients to secondary BSIs, with a severe impact on infection prevention programs due to system and personnel strain in healthcare systems across the world (21,22).

Antimicrobial resistance and prevention strategies in the ICU

Antimicrobial resistance remains a challenge in treating ICU infections, with understanding the local epidemiology and resistance patterns being of utmost importance in choosing the appropriate empirical therapy (Table 4.). MRSA remains prevalent in European ICUs, accounting for 15–25% of *S. aureus* isolates (3). Vancomycin-resistant *Enterococcus* is less common but increasing in some European regions (6). Gram-negative resistance poses the greatest threat to ICU infection management. EARS-Net data demonstrate high rates of carbapenem resistance in *A. baumannii* (60–85%), substantial resistance in *P. aeruginosa* (20–30%), and increasing carbapenemase production among Enterobacterales (5). Resistance patterns vary from country to country, underlying the need for knowledge of local epidemiology. Infections caused by resistant organisms are independently associated with increased mortality, delayed appropriate therapy, and excess healthcare costs (2).

Effective prevention strategies for reducing the impact of resistance include proper management of central line catheters, mechanical ventilation, doing proper hand hygiene in ICUs and appropriate environmental cleaning (12,23). Antimicrobial stewardship programs play a critical role in optimizing therapy, reducing unnecessary antibiotic exposure and limiting resistance to antimicrobials (10,24).

ICU-acquired infections remain a major burden across Europe, driven by specific high-risk pathogens and increasing antimicrobial resistance. Bloodstream infections, intra-abdominal infections and ventilator-associated pneumonia are the most dominant clinical entities comprising the landscape of ICU-acquired infections, with Gram-negative MDROs posing the greatest challenge regarding treatment choice. Sustained surveillance, prevention, and multidisciplinary management are essential to improve outcomes of these infections in critically ill patients. Further studies assessing the local and global epidemiological data are needed to guide empirical treatment and implementation of rapid microbiological testing could benefit individualised and targeted therapy for patients in the ICU setting.

Table 4. Antimicrobial resistance rates among ICU pathogens in Europe.

Pathogen	Resistance	Approximate prevalence (%)	References
Staphylococcus aureus	methicillin resistance	15–25	Vincent et al. (2020)
Enterococcus spp.	vancomycin resistance	5–15	ECDC (2021)
Pseudomonas aeruginosa	carbapenem resistance	20–30	ECDC (2021)
Klebsiella spp.	ESBL production	20–40	Munro et al. (2024); ECDC (2021)
Klebsiella spp.	carbapenem resistance	8–15	Munro et al. (2024); ECDC (2021)
Acinetobacter baumannii	carbapenem resistance	60–85	Munro et al. (2024); ECDC (2021)

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CASE REPORTS

From burn to paralysis: delayed spinal cord injury in high-voltage electrical burns

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ABSTRACT

Electrical burn injuries, though uncommon, can cause severe neurological complications, with sequelae observed in up to 67% of high-voltage cases. This report presents two cases of spinal cord injuries following high-voltage electrical burns in male patients aged 29 and 53. The first patient, a 29-year-old male, sustained 9% total body surface area (TBSA) burns. His initial neurological assessment was unremarkable, but post-injury he developed quadriplegia with preserved sensation. Imaging was inconclusive, and he required prolonged intensive care unit care, showing only modest neurological improvement over time. The second patient, a 53-year-old male, suffered 25% TBSA burns, initially presenting unconscious and requiring resuscitation. He developed delayed paraplegia, with electromyoneurography confirming severe bilateral lumbosacral plexus injury despite normal spinal imaging. Both patients underwent supportive treatment, surgical interventions, and rehabilitation, showing varying degrees of motor recovery. Neurological sequelae in electrical injuries may result from direct electrical damage, vascular injury, or ischemic changes. Despite no clear spinal abnormalities on imaging, significant neurological deficits were present. No specific treatment exists, and corticosteroid use remains controversial. These cases underscore the need for early neurological evaluation, awareness of long-term consequences, and further research to develop standardized treatment protocols.

Keywords: electrical injury; spinal cord injury; quadriplegia; paraplegia; neurologic deficit

Introduction

Electrical burn injuries, though relatively uncommon, can be devastating. They account for approximately 0.04% to 5% of burn unit admissions in developed countries and up to 27% in developing countries [1,2]. In adults, these injuries primarily affect men and are most often work-related [3,4]. Recent research from the World Health Organization's Global Burn Registry indicates that 8.8% of electrical burn injuries patients have a median age of 28 years, with 89.2% being male, and the majority sustaining injuries in the workplace [5]. At the burn Intensive Care Unit (ICU) of the Croatian Burn Unit, data from the past five years show that out of 130 total admissions, 9 (6.92%) were due to electrical burns, with a mean age of 32.22 ± 13.45 years—all of whom were male. This pattern aligns with trends observed in the literature. While electrical burn injuries are relatively uncommon, they pose a significant concern due to their impact on young, working-age individuals in high-risk industries. These injuries can result in severe consequences and impose a substantial socioeconomic burden on this demographic. Morbidity and mortality rates associated with electrical injuries are relatively high, with both short- and long-term physical and psychological consequences [6].

Electrical injuries can be defined as sequels due to accidental contact with electrical power and typically are categorized as low-voltage (LV, < 1000 volts) or high-voltage (HV, > 1000 volts). Injury occurs when electrical current travels through the body upon contact with an electrical source, causing damage through multiple

mechanisms. These include direct tissue injury due to electrical forces and indirect injury through heat generation. Resistance is an important concept in those injuries. Electricity tends to take the path of the least resistance, and when electrical current encounters resistance, heat is generated. Different tissues have varying resistance levels; nerves and blood vessels exhibit lower resistance than bones and fat, making them more susceptible to injury [7]. Significantly, the external appearance of an electrical burn usually does not correlate with the severity of internal damage, as deeper tissues and organs may be considerably more affected than the skin [4,8]. Numerous systems, including cardiac, respiratory, ocular, renal, and nervous systems, within the individual's body can be affected [7]. Neurological complications are observed in 67% of high-voltage and 50% of low-voltage injury cases [9]. These complications include cerebral, spinal, and peripheral nerve syndromes [9,10], with potential outcomes such as hemiplegia, aphasia, epilepsy, cerebellar dysfunction, and delayed spinal cord injury. Here, we present two cases of high-voltage electrical burns in male patients aged 29 (Figure 1) and 53 who developed neurological sequelae due to spinal cord injury.

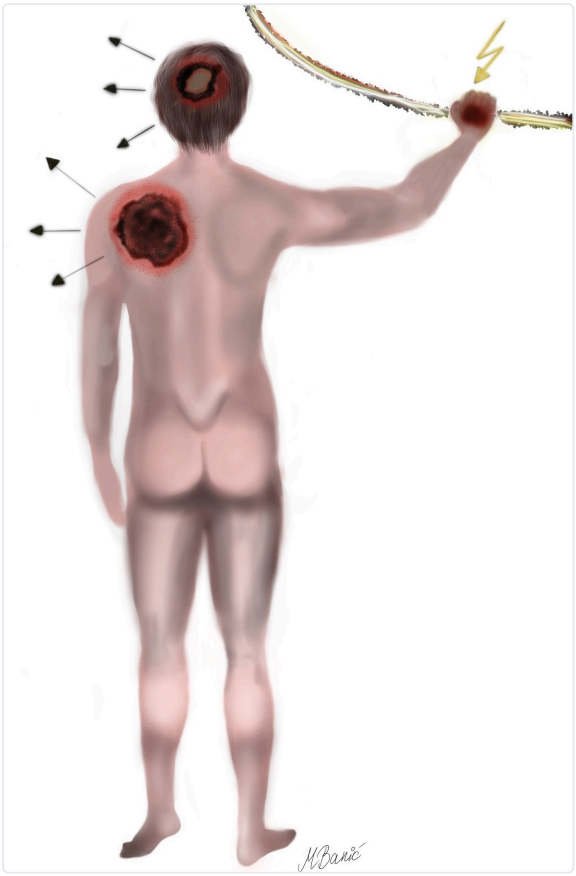

Figure 1. High-voltage electrical burn in a 29-year-old male.

Case 1

A 29-year-old male sustained a work-related high-voltage electrical injury while working on a powerline. His medical history was significant for a prior thyroidectomy, and he was on levothyroxine replacement therapy. On the initial examination, the patient was conscious but highly agitated. He was spontaneously breathing with a SpO2 of 89%, blood pressure of 115/80 mmHg, and a pulse rate of 112 bpm. Neurological assessments revealed no gross neurological deficits. His pupils were isochoric, but the eye bulbs were deviated to the right. Physical examination identified a full-thickness burn measuring 20 × 10 cm on his right upper back region (Figure 2a), a full-thickness burn measuring 10 × 10 cm on his head (Figure 2b), and a second-degree burn on the palm of his right hand. The total body surface area (TBSA) affected was estimated at approxim-

ately 9% (8% full-thickness burns, 1% partial-thickness burns). He was subsequently admitted to the ICU at Zadar General Hospital.

Upon admission, data regarding the fall was unknown, so a computed tomography (CT) scan of the brain, cervical, thoracic, and lumbar spine, as well as the abdomen and pelvis, was performed per the trauma protocol. Since the patient was extremely agitated, sedation was administered, and the patient was intubated and placed on mechanical ventilation for diagnostic purposes. The only notable findings included an interstitial pulmonary pattern suggestive of either pulmonary edema or contusion and a minor pneumocephalus. Later, it was revealed that the patient had not hit his head or fallen during the electric shock. On the second day after the injury, a repeat brain CT scan, performed due to pneumocephalus observed in previous imaging, revealed a hypodense lamellar extra-axial collection in the left frontal region. On the fifth post-injury day, the patient was transferred to the Burn Unit at Sestre Milosrdnice University Hospital Center for further management. Sedation was discontinued on days seven and fourteen, and the patient was extubated on both occasions. However, both extubating attempts were unsuccessful due to respiratory fatigue, necessitating reintubation on the same day. On post-injury day twenty, a tracheostomy was performed, and mechanical ventilation was ultimately discontinued on post-injury day twenty-two. Thereafter, the patient maintained spontaneous respiration. On post-injury day fourteen, following sedation discontinuation and extubation, it was noted that the left pupil was slightly larger than the right. A neurological deficit was also observed, characterized by an inability to move both upper and lower extremities. Sensory examination revealed preserved sensation in all four limbs; however, assessment was limited due to light sedation with dexmedetomidine and sufentanyl. Further neurological workup included a brain CT, cervical spine CT, CT angiography of the head and neck, and magnetic resonance imaging (MR) of the brain and cervical spine, none of which revealed significant pathological findings. The previously noted extra-axial collection on the initial CT scan had been resolved entirely. The laboratory workup for thyroid hormones revealed a TSH level of 94.69 mIU/L, FT4 of 11.5 pmol/L, and FT3 of 1.9 pmol/L, indicating severe hypothyroidism. Treatment was initiated with higher doses of levothyroxine to correct thyroid function, along with vitamin B1, B6, and B12 supplementation.

Over time, the patient demonstrated modest neurological improvement. During his hospital stay, he underwent ten surgical procedures, including debridement, and skin grafting. On post-injury day eighty-six, he was discharged from the ICU to the general ward for further rehabilitation and management and is currently awaiting transfer to the stationary rehabilitation program. Four months after the injury, on the day this report is written, his neurological status has improved. Electromyoneurography (EMNG) shows a right brachial plexus lesion, peripheral polyneuropathy, and myopathy. The presence or level of a spinal cord lesion could not be confirmed or excluded due to inconclusive results. A neurological consultation suggested a probable combination of spinal cord injury and peripheral polyneuropathy with a right brachial plexus lesion. The hand grip in both of his hands has slightly improved. He is able to flex both arms at the elbows and dorsiflex his feet but is unable to lift his legs from the bed. Subjectively reports improvement in stability while sitting.

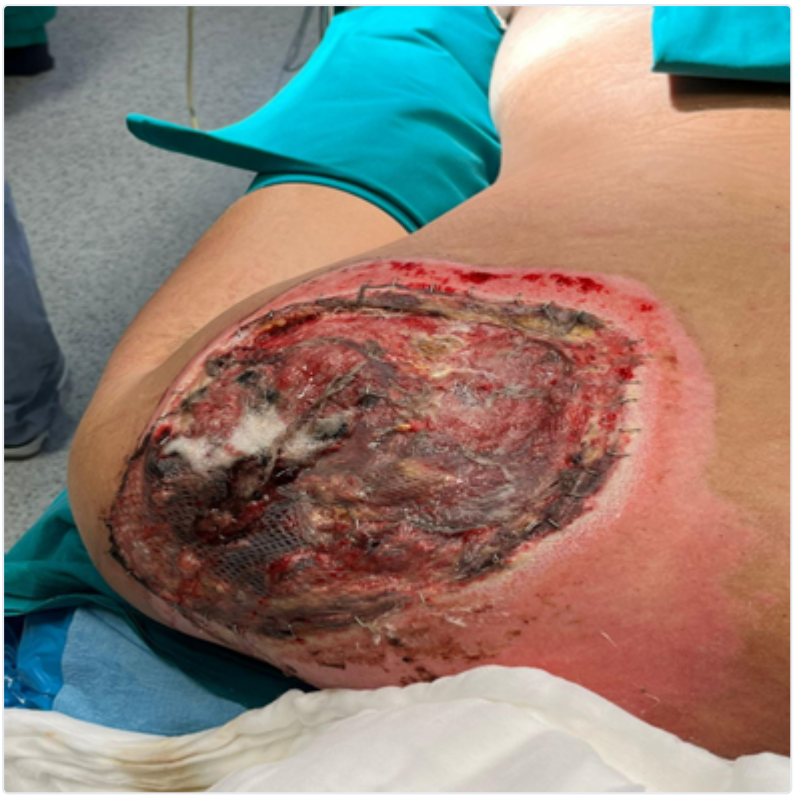

Figure 2a. A 29-year-old male with electrical burn injury: a full-thickness burn on his right upper back region.

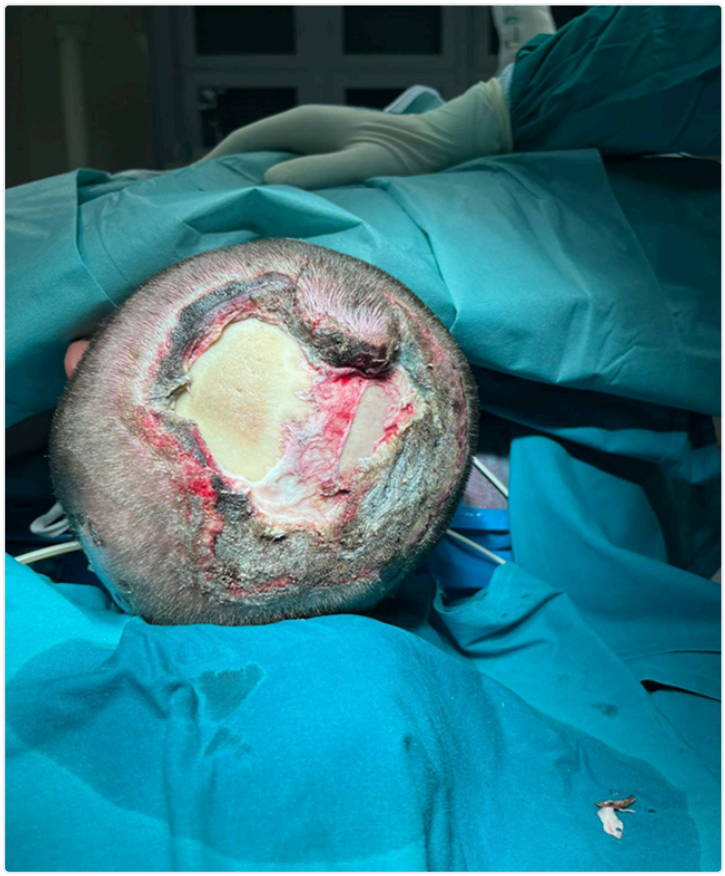

Figure 2b. A 29-year-old male with electrical burn injury: a full-thickness burn on his head.

Case 2

A 53-year-old male sustained a work-related high-voltage electrical injury while working on a powerline (Figure 3). It was unclear whether he fell during the incident. He was initially unconscious and required resuscitation by emergency medical services. Spontaneous breathing and circulation were restored. His past medical history was unremarkable. He sustained partial thickness, and full-thickness burn injuries affecting 25% TBSA, including the face, anterior side of the neck, left anterior thoracic wall, anteromedial side of the right thigh, anterior side of the lower leg, small areas on the right arm, and lower back.

He was admitted to the ICU of Vinkovci General Hospital. Upon admission, he was conscious, spontaneously breathing, and hemodynamically stable. A trauma computed tomography (CT) scan of the head, spine, thorax, abdomen, and pelvis was performed. The only pathological finding was the contusion of the right lung. On the fifth post-injury day, he was transferred to the Burn Unit at Sestre Milosrdnice University Hospital Center, for further treatment. Upon admission, paraplegia with dissociated sensory impairment for temperature sensation was noted. The only significant laboratory finding was severe hypokalemia. A nephrology consultation suspected hypokalemic transient paralysis, but no neurological improvement was observed after potassium levels correction. He received supportive treatment along with vitamin B1, B6, and B12 supplementation to address the neurological deficits and promote recovery. CT scans of the cervical, thoracic, and lumbar spine and MRI of the brain, cervical, thoracic, and lumbar spine showed no demyelination or significant injuries. EMNG revealed severe neurogenic muscle lesions in the right leg, with severe denervation of the peroneal musculature. The conclusion was a severe lesion of the lumbosacral plexus of the right leg. The left leg could not be examined initially due to burns, but after the resolution of burn injuries, an EMNG performed before hospital discharge revealed a severe bilateral lumbosacral plexus lesion.

During hospitalization, the patient exhibited significant improvement in neurological function over time. He underwent four surgeries, including three skin grafting procedures and plastic reconstruction of the hand. He spent 17 days in the ICU, for a total hospital stay of 145 days. After discharge, he was referred to inpatient medical rehabilitation. He continued to be followed for 10 months post-injury after returning home. During this period, he reported significant improvement, started verticalizing and walking, but was still unable to return to work.

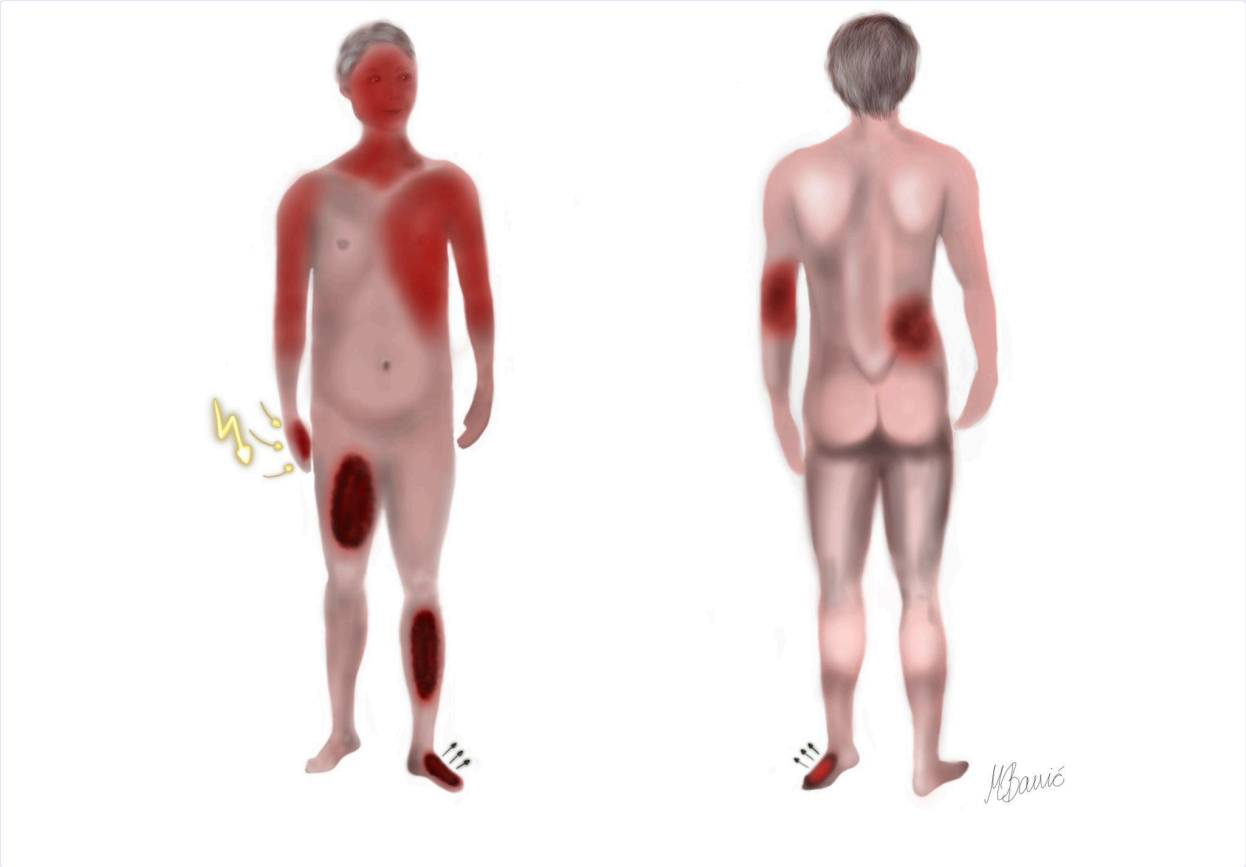

Figure 3. High-voltage electrical burn in a 53-year-old male.

Discussion

Neurological sequelae associated with electrical injuries occur at a high rate, likely due to the low resistance of nerves and blood vessels, which allows electrical current to flow along these structures. The pathophysiology of neurological sequelae following electrical injury remains poorly understood, and several mechanisms have been proposed. Injury may result from direct mechanical or thermal damage to nervous tissue or indirect effects. Commonly suggested mechanisms include vascular damage, pure electrical damage causing electrostatic separation of tissues, electroporation, and alterations in proteins, DNA, and lipids—particularly in myelin cells, leading to demyelination. Neurohumoral influences involving circulating substances such as cortisol have also been implicated [9]. Delayed spinal cord injury has been proposed to result from the degeneration of tiny blood vessels. Specifically, injury to the small branches of the anterior spinal artery, which supplies the anterior two-thirds of the spinal cord, has been suggested as an etiologic factor for delayed spinal cord injury. This hypothesis is supported by findings that motor nerve dysfunction predominantly characterizes delayed spinal cord injury [11]. Consistent with this, our patients presented with more significant motor deficits than sensory deficits.

In patients presenting with neurological sequelae after electrical injury, other possible treatable causes of neurological deficits should be excluded. Both of our patients underwent CT and MRI of the brain and spine, which ruled out vertebral fractures or spinal cord compression. The first patient was diagnosed with a combined central and peripheral neurologic deficit, reminding us that electrical current can damage both the central and peripheral nervous systems, and that such injuries can be combined. The right brachial plexus lesion was attributed to the current entry point, which could have directly damaged the brachial plexus. Additionally, the patient had severe hypothyroidism, raising suspicion of hypothyroid myopathy. Hypothyroid myopathy can occur in both congenital and acquired cases, presenting symptoms such as generalized myalgias, musc-

le weakness, and muscle pain or stiffness [12]. In this case, despite the correction of thyroid function, there was no improvement in neurological status; however, thyroid dysfunction may have contributed to motor weakness. The second patient presented severe hypokalemia upon admission, raising suspicion of hypokalemic periodic paralysis [13]. However, this was promptly excluded, as the patient had no history of muscle weakness and exhibited no resolution of paraplegia after potassium correction. After excluding other potential diagnoses, we concluded that both cases represented delayed-onset spinal cord injury due to electrical current exposure. In the first patient, neurological impairment was noticed on the fourteenth day after discontinuation of sedation and extubating, while in the second patient, it was observed on the fifth day, upon transfer to a specialized burn center. Due to prior sedation, the exact onset of the first patient's neurological deficit could not be determined. This highlights the importance of daily sedation breaks for neurological status examination, as sedation may mask neurological deficits.

Currently, there is no standardized treatment for electrical injury-induced spinal cord damage, and most management strategies are supportive. Corticosteroids are sometimes administrated therapy in periprocedural nerve damage (for example, during anesthesia or pain medicine procedures) [14]. High doses of corticosteroids are rescue therapy in acute traumatic spinal cord injury in selected cases due to their anti-inflammatory effect and reduction of membrane peroxidation. Although recent recommendations suggest that the potential risks may outweigh advantages without significant neurological improvement [15]. Corticosteroids increase the risk of infections, gastrointestinal bleeding, metabolic disturbances like hyperglycemia, and delay wound healing. When discussing electrical injuries, some reports in the literature describe neurological improvement following corticosteroid therapy [11,16]. The exact dosage, duration, and protocol in such cases of electrical injury remain undefined. Additionally, prostaglandin E1 has been mentioned as a potential treatment to improve ischemic tissue injury [11]. Since there is no specific treatment protocol for such injuries, given the absence of visible edema or ischemia on MRI in both patients, and considering potential complications, we decided against corticosteroid therapy.

The only specific therapy, aside from supportive treatment, that was initiated in both patients was vitamin B1, B6, and B12 supplementation after the diagnosis of neurological sequelae, due to their well-known neurotropic effects. Vitamin B plays a significant role in nerve repair and function; however, no research currently addresses its role in electrical injuries. Vitamin B1 (thiamine) contributes to nerve regeneration, vitamin B6 (pyridoxine) is involved in neurotransmitter synthesis, and vitamin B12 (cobalamin) plays a role in nerve regeneration, cell survival, and remyelination [17]. Due to its application, positive effect, and recommendation in other neuropathies and neurological diseases [18], vitamin supplementation was initiated. However, the actual effect of the treatment could not be fully evaluated, as the observed improvement may have been due to the natural course of the disease or rehabilitation therapy.

Outcomes for spinal cord injuries from electrical burns vary, with some patients achieving full recovery, while others experience permanent deficits. At the time of this article, the first patient was in the process of being transferred to inpatient rehabilitation, showing some improvement in motor function of the arms and legs. The second patient had completed inpatient rehabilitation with significant improvement in leg motor function but remained unable to return to work. These cases highlight the severe neurological impact of electrical injuries, emphasizing the need for comprehensive neurological evaluations upon admission, daily assessments for new-onset neurological impairment, greater awareness of long-term consequences, the impact on patients' quality of life after discharge, and further research into treatment protocols. We must always keep in mind the possibility of multiple injuries at both the central and peripheral levels, resulting from various mechanisms, and, when possible, rely on objective EMNG diagnostics.

Conclusions

Electrical injuries can lead to significant neurological complications, including delayed-onset spinal cord injury. A thorough neurological examination is essential in the acute phase, and patients should be monitored for delayed neurological deterioration. Further research is needed to establish standardized treatment protocols for electrical injury-induced spinal cord damage.

Informed consent

Written informed consent has been obtained from the patients to publish this paper.

Abbreviations

CT — Computerized tomography

EMNG — Electromyoneurography

ICU — Intensive care unit

MR — Magnetic resonance imaging

TBSA — Total body surface area

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Data availability. Data is available on request due to ethical and legal reasons.

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CASE REPORTS

Sufentanil-Associated Seizure-Like Tonic–Clonic Activity in a Patient with Pituitary Macroadenoma and Hypopituitarism: A Case Report

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ABSTRACT

BACKGROUND:

Opioid-associated convulsive episodes are exceedingly rare during anesthesia induction. When they occur, they typically manifest within seconds of intravenous opioid administration as generalized tonic–clonic movements without epileptiform EEG activity, suggesting a pharmacodynamic origin.

CASE:

We present a 67-year-old male with a pituitary macroadenoma and panhypopituitarism who developed generalized tonic–clonic seizure-like activity immediately after receiving 20 µg of sufentanil during anesthesia induction. The episode lasted approximately 30 seconds, accompanied by a blood pressure spike to 220/110 mmHg and oxygen desaturation to 65%. It resolved spontaneously with supportive care. Surgery was postponed, and the patient was monitored in the intensive care unit; later that day, neurological examination and EEG results showed no acute abnormalities.

CONCLUSIONS:

Even small doses of sufentanil may rarely be associated with seizure-like motor phenomena during anesthesia induction. Because EEG was not recorded during the event, definitive differentiation between an epileptic seizure and opioid-induced nonepileptic motor activity was not possible. Underlying endocrine dysfunction may have represented an additional vulnerability, although this association remains speculative.

Keywords: Sufentanil; Seizure-like activity; Hypopituitarism; Pituitary macroadenoma; Adrenal insufficiency; Anesthesia induction

Introduction

Opioids used during anesthesia induction are rarely associated with seizure-like activity, but such cases have been reported since the early 1980s (1). Subsequent reports described similar generalized tonic–clonic movements after alfentanil, sufentanil, and remifentanil (2). These episodes typically develop within seconds of intravenous opioid administration and may present as generalized tonic–clonic movements without epileptiform activity on electroencephalography (EEG), raising the possibility of opioid-associated excitatory motor phenomena rather than definite epilepsy (1–3).

Proposed mechanisms include acute disinhibition of GABAergic interneurons, opioid-induced muscle rigidity manifesting as convulsions, or activation of subcortical motor pathways (1–3, 5). Notably, fentanyl and sufentanil have no known convulsant metabolites, supporting the possibility of a direct pharmacodynamic contribution to these events (1–3).

Patient-specific factors such as metabolic or endocrine disorders may contribute to a lowered seizure threshold (4–7). In particular, adrenal insufficiency may reduce the production of neurosteroids that enhance GABA-mediated inhibition and is often associated with hyponatremia; both of these consequences of cortisol deficiency may predispose patients to seizure-like phenomena (4–7). Because intra-event EEG monitoring is rarely available during anesthesia induction, distinguishing epileptic seizures from opioid-associated nonepileptic motor phenomena may be challenging.

Case Presentation

A 67-year-old male (94 kg) with a 2.5 cm pituitary macroadenoma extending to the suprasellar area and compressing the optic chiasm was admitted for an elective transsphenoidal resection. The patient had no personal history of seizures or epilepsy. Informed consent was obtained from the patient prior to the preparation of this report.

Preoperative endocrine evaluation revealed secondary adrenal insufficiency and central hypothyroidism consistent with hypopituitarism. He was stabilized with hormone replacement therapy. As part of perioperative management, 100 mg of hydrocortisone was administered intravenously one hour before induction. No sedative premedication was administered. Standard monitors were applied (ECG, noninvasive blood pressure, pulse oximetry, and bispectral index). Initial vital signs were stable: oxygen saturation 99%, heart rate 78/min, and blood pressure 135/80 mmHg.

Following preoxygenation, induction began with an intravenous dose of 20 µg sufentanil administered over 20 seconds. No hypnotic or neuromuscular blocking agent had been administered before the event. Within seconds of injection, the patient developed generalized tonic–clonic seizure-like activity characterized by generalized rigidity, tonic extension, clonic limb movements, upward gaze deviation, and loss of consciousness. The episode lasted approximately 20–30 seconds. During the event, arterial pressure increased to 220/110 mmHg, and oxygen saturation decreased to 65%. Assisted mask ventilation with 100% oxygen was initiated, and 5 mg of intravenous midazolam was administered. The episode resolved spontaneously and transient nonsustained arrhythmias were observed on ECG monitoring. After stabilization, anesthesia was deepened with propofol and rocuronium, and the trachea was intubated uneventfully.

Following the event, surgery was aborted, and the patient was transferred to the intensive care unit for observation. On admission, his neurological examination was normal with no focal deficits. Serum sodium, glucose, calcium, and magnesium levels were within normal ranges before and after the event. An EEG performed later that day showed no epileptiform activity, although this did not exclude a transient peri-induction epileptic event. A postoperative head CT scan showed no acute intracranial abnormalities, and neurological examination remained normal without focal deficits. In light of these findings, the procedure was postponed for one week.

One week later, anesthesia induction was modified, given the prior adverse event: no sufentanil bolus was used, and anesthesia was maintained with target-controlled infusions of propofol and remifentanil. The second induction and surgery were uneventful, and the patient made a full recovery.

Discussion

The close temporal relationship between sufentanil administration and symptom onset strongly suggests an association between sufentanil exposure and the observed event. However, because no intra-event EEG was available, definitive differentiation between epileptic seizure activity and opioid-induced nonepileptic motor phenomena was not possible. Similar episodes have been documented with fentanyl and sufentanil during induction; these episodes were usually brief and self-limited (1–3).

The differential diagnosis includes transient epileptic seizure, opioid-induced rigidity, opioid-induced myoclonus, hypoxia-related convulsive activity, metabolic disturbances, and psychogenic nonepileptic activity. Metabolic causes were considered unlikely given normal glucose and electrolyte values before and after the episode. Hypoxia-related motor activity was also considered less likely because oxygen desaturation occurred after the onset of abnormal movements. Opioid-induced rigidity remains a plausible alternative explanation, particularly given the temporal relationship with opioid administration and the presence of generalized tonic posturing.

Underlying endocrine dysfunction may have represented an additional vulnerability in this patient. Adrenal insufficiency has been associated with altered neurosteroid-mediated GABAergic inhibition and lowered seizure threshold in experimental and clinical settings. However, the patient had received perioperative hydrocortisone replacement and had normal electrolyte and glucose values at the time of the event. Therefore, any contribution of hypothalamic–pituitary–adrenal axis dysfunction remains speculative. Structural epilepsy related to the pituitary macroadenoma could not be definitively excluded, although the patient had no previous seizure history, postoperative neurological examination was normal, and head CT imaging showed no acute intracranial abnormalities. A psychogenic nonepileptic event was considered unlikely in the context of abrupt onset immediately following intravenous opioid administration during anesthesia induction.

In comparison with previously reported cases of opioid-associated seizure-like activity, the present case shares several key features. Across published reports, including the review by El-Karamany (1) and the case described by Silva-dos-Santos et al. (2), the characteristic pattern consists of generalized tonic–clonic movements beginning within seconds of intravenous opioid administration at low or standard doses, resolving spontaneously within 30–60 seconds, and—when EEG was simultaneously available—showing no concurrent epileptiform activity. Tonic–clonic activity specifically following sufentanil administration has been documented since at least 1987 (1), and comparable events have been reported with fentanyl, alfentanil, and remifentanil. The present case is consistent with this established pattern in all major respects: onset within seconds of a 20 µg sufentanil bolus, generalized tonic–clonic semiology with rigidity and upward gaze deviation, and spontaneous resolution within approximately 30 seconds. A distinguishing feature of the current case, not uniformly reported in the literature, is the severity of hemodynamic compromise (arterial pressure 220/110 mmHg, oxygen desaturation to 65%) and the concurrent endocrine vulnerability. The absence of prior seizure history and the unremarkable post-event neurological evaluation and neuroimaging further align with the nonepileptic pattern characteristic of most reported opioid-associated motor events (1, 2).

The marked hypertension, oxygen desaturation, and transient arrhythmias observed during the episode emphasize the importance of prompt airway and hemodynamic support when unusual motor phenomena occur during anesthesia induction. Although EEG monitoring is not routinely used during anesthesia induction, additional neurophysiological monitoring may help characterize similar events in selected high-risk patients.

When the surgery was rescheduled, the anesthetic plan was adjusted—notably avoiding a rapid sufentanil bolus. Anesthesia was maintained with titrated infusions of propofol and remifentanil, and the second surgery proceeded without incident. The uneventful second procedure after modification of the anesthetic plan supports the practical value of avoiding rapid sufentanil bolus administration following a suspected opioid-associated neuroexcitatory event, although it does not establish definitive causality.

Conclusion

Sufentanil may rarely be associated with seizure-like tonic–clonic activity during anesthesia induction. In the absence of intra-event EEG monitoring, distinction between true epileptic seizure and opioid-induced nonepileptic motor activity may be impossible. Careful opioid titration, avoidance of rapid bolus administration, optimization of endocrine status, and readiness for immediate airway and hemodynamic support may improve perioperative safety in vulnerable patients.

Table 1. Timeline of peri-induction events

Time/Event	Clinical findings and interventions
Preoperative evaluation	Pituitary macroadenoma with secondary adrenal insufficiency and central hypothyroidism diagnosed; patient stabilized with hormone replacement therapy
1 h before induction	100 mg intravenous hydrocortisone administered
Baseline monitoring	Blood pressure 135/80 mmHg; heart rate 78/min; oxygen saturation 99%
Induction initiated	20 µg intravenous sufentanil administered over 20 seconds; no hypnotic or neuromuscular blocking agent given prior to event
Seconds after sufentanil administration	Generalized tonic–clonic seizure-like activity: generalized rigidity, tonic extension, clonic limb movements, upward gaze deviation, and loss of consciousness
During the episode	Blood pressure increased to 220/110 mmHg; oxygen saturation decreased to 65%; transient nonsustained arrhythmias observed
Immediate management	Assisted mask ventilation with 100% oxygen; 5 mg intravenous midazolam administered
After resolution of the episode	Anesthesia deepened with propofol and rocuronium; tracheal intubation performed uneventfully
Post-event management	Surgery aborted; patient transferred to intensive care unit for observation
Same-day evaluation	Neurological examination normal; laboratory findings unremarkable; EEG showed no epileptiform activity; head CT showed no acute intracranial abnormalities
One week later	Repeat anesthesia without sufentanil bolus using target-controlled infusions of propofol and remifentanil
Final outcome	Second surgery uneventful; patient recovered without neurological sequelae

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Ethics approval. For every elective and urgent procedure in our Hospital, it is required to obtain an informed consent form. The patient had signed the informed consent form and therefore gave the Hospital permission to perform procedures as well as use the data for scientific purposes with strong protection of personal information. Written informed consent for publication was obtained as part of the institutional consent procedure.

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CASE REPORTS

Urosepsis Complicated by Septic Shock After Endoscopic Combined Intrarenal Surgery for a Staghorn Calculus: A Case Report

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ABSTRACT

Endoscopic combined intrarenal surgery (ECIRS) is used for complex renal stones because it combines retrograde and percutaneous access and may allow complete stone clearance in a single session. Infectious complications are recognised after stone surgery. Rapid progression to septic shock, however, is not expected after an apparently uncomplicated procedure, and patients are usually managed postoperatively on the ward.

We present a 51-year-old woman with a right-sided staghorn calculus and multiple documented antibiotic allergies who developed urosepsis complicated by septic shock after ECIRS. The procedure was technically successful, but septic shock developed approximately 10 hours postoperatively, requiring intensive care unit admission. Treatment included fluid resuscitation, noradrenaline, oxygen therapy, and antimicrobial therapy based on the patient's microbiological history and allergy profile.

This case supports better preoperative identification of patients at risk and early recognition of postoperative deterioration after ECIRS.

Keywords: ECIRS; urosepsis; septic shock; staghorn calculus

Introduction

Urolithiasis is a common condition, and its incidence continues to increase worldwide. This has led to ongoing efforts to improve surgical strategies for renal stone management. (1) Percutaneous nephrolithotomy (PCNL) has changed considerably over recent decades. Improvements in renal access, endoscopic equipment, lithotripsy devices, and drainage strategies have all contributed to this development. Supine and modified supine positions have further expanded the procedure, mainly by improving anaesthesiological safety and allowing retrograde intrarenal surgery to be performed at the same time. Endoscopic combined intrarenal surgery (ECIRS) can therefore be adapted to the patient's anatomy, the collecting system, and the size and complexity of the stone burden.

By using both antegrade percutaneous and retrograde ureteroscopic access, ECIRS has become an accepted treatment option for large renal stones. Compared with PCNL alone, it may be associated with lower radiation exposure and less bleeding. (1,2) Infectious complications remain an important concern after ECIRS. This is expected, as the procedure combines elements of both PCNL and ureteroscopy, and both approaches carry a risk of urinary tract infection (UTI). (3–5) Perioperative complications occur in approximately one-third of patients undergoing PCNL/ECIRS. Urinary tract infections are among the most common infectious

complications and have been reported in 10.4-39.8% of cases. (3,6,7) Because available data are limited, there are still no ECIRS specific recommendations for preoperative antibiotic regimens. There is also no clear consensus on how to define patients at high risk for infectious complications. (5,8–10) ECIRS allows antegrade and retrograde endoscopic treatment to be performed during the same procedure. In our institution, patients are usually transferred to the ward after surgery for continued antibiotic prophylaxis, with discharge planned after a short hospital stay, unless their clinical condition requires intensive care unit admission. However, severe infectious complications can still occur after ECIRS, including septic shock.

Case Presentation

We present the case of a 51-year-old female patient (body mass index 27.5 kg/m²) who was scheduled for elective ECIRS due to a staghorn calculus in the right kidney. Her comorbidities included cholelithiasis, autoimmune thyroiditis, and documented multiple antibiotic allergies, and she was classified as American Society of Anesthesiologists (ASA) physical status II. Preoperatively, a urine culture (UC) was obtained and confirmed sterile, and antimicrobial prophylaxis with ciprofloxacin was administered prior to the procedure. A fluoroquinolone was selected because the patient's documented multiple antibiotic allergies precluded beta-lactam–based prophylaxis, and ciprofloxacin is an established, guideline-supported option for antimicrobial prophylaxis in endourological stone surgery. (1,9)

The procedure was performed under general anaesthesia (GA) with a total operative time of 4 hours and 30 minutes. Standard monitoring included non-invasive blood pressure (NIBP), electrocardiography (ECG), pulse oximetry (SpO_2), and end-tidal CO_2 ($EtCO_2$). The patient was positioned in the standard Valdivia position. A flexible ureteroscope was introduced into the right renal collecting system, revealing a staghorn calculus with a characteristic golden-yellow appearance. Under combined ultrasound and fluoroscopic guidance, puncture of the medial calyx was performed, with high-pressure urine backflow noted upon access. The calculus was subsequently disintegrated and extracted nephroscopically.

Final ureteroscopic inspection confirmed complete stone clearance with no residual fragments. A JJ ureteral stent was then positioned, and a percutaneous nephrostomy tube was placed and secured. The immediate postoperative outcome was uneventful. The patient was transferred to the ward in a haemodynamically stable condition with adequate spontaneous breathing, with instructions for continued antibiotic prophylaxis administration at regular intervals. Approximately 10 hours postoperatively, the patient's clinical condition rapidly deteriorated, with abrupt onset of shivering, somnolence, nausea, and vomiting. NIBP was 73/45 mmHg, corresponding to a mean arterial pressure (MAP) of approximately 54 mmHg, and remained refractory to an initial crystalloid bolus of 1000 mL administered on the ward, prompting immediate escalation of care. The patient was tachypnoeic, with SpO_2 maintained at approximately 96% on supplemental oxygen via nasal cannula (NC). In view of suspected septic shock, the patient was emergently transferred to the intensive care unit (ICU). Upon ICU admission, the patient remained spontaneously breathing and maintained adequate oxygenation on supplemental oxygen via NC at 4 L/min, without the need for endotracheal intubation or mechanical ventilation. Invasive blood pressure (IBP) monitoring was established immediately, and a central venous catheter (CVC) was inserted. Vasopressor support with noradrenaline (NA) was then initiated promptly through the CVC at 0.2 mcg/kg/min, targeting a MAP ≥ 65 mmHg. Blood cultures (BCs) and a UC were obtained at ICU admission. The most recent preoperative UC had been sterile, but the patient's earlier UCs had repeatedly grown *Escherichia coli*. Empirical therapy was therefore directed against a likely gram-negative organism while awaiting the culture result.

The patient had a clear history of severe hypersensitivity to penicillin antibiotics, including anaphylactic shock with angioedema upon re-exposure, as well as documented allergies to trimethoprim–sulfamethoxazole, tetracyclines, and chloramphenicol. She had previously been evaluated by a clinical pharmacologist,

with a clear recommendation to avoid these antibiotic classes. Antibiotic selection was significantly limited by the patient's documented multiple antibiotic allergies, necessitating a multidisciplinary approach to antimicrobial management.

Amikacin and fosfomycin were selected because the patient had no documented allergy to either and because they provided appropriate coverage for the suspected gram-negative infection. Treatment was started in consultation with a clinical microbiologist (amikacin 600 mg IV every 12 hours; fosfomycin 4 g IV every 8 hours). Initial laboratory evaluation in the ICU demonstrated severe metabolic acidosis. Arterial blood gas (ABG) analysis showed a pH of 7.10 , pCO_2 of 3.97 kPa, HCO_3^- of 11 mmol/L, and a base excess (BE) of -12.4 mmol/L. Serum lactate was 3.4 mmol/L. Inflammatory markers were markedly elevated, with a white blood cell (WBC) count of 24.3 × 10^9/L, C-reactive protein (CRP) of 228 mg/L, and procalcitonin (PCT) of 56 ng/mL. Urea was 6.7 mmol/L and serum creatinine was 92 µmol/L. ECG showed sinus tachycardia, with heart rate up to 120 beats per minute.

Over the following 24 hours, aggressive fluid resuscitation was continued, with a total crystalloid volume of 3500 mL administered, and NA was gradually tapered. Haemodynamic stability was achieved within 24 hours, with MAP maintained at 83 mmHg. Urine output was monitored hourly and remained adequate at 2 mL/kg/h. Serum sodium levels and renal function were closely monitored during the following days. Despite haemodynamic improvement, inflammatory markers remained markedly elevated, with CRP increasing to 445 mg/L and PCT remaining >50 ng/mL. WBC was 22.3×10^9/L. Serum lactate decreased to 1.1 mmol/L. BCs remained sterile. The UC grew *Escherichia coli* >10^5 CFU/mL, with the result available after two days. The isolate was susceptible to fosfomycin, gentamicin, nitrofurantoin and cephalosporins, and resistant to ciprofloxacin and other fluoroquinolones, ampicillin, amoxicillin–clavulanic acid and trimethoprim–sulfamethoxazole.

The regimen was then changed to meropenem 1 g IV every 8 hours, following consultation with a clinical pharmacologist. NA was discontinued by ICU day 3.

Inflammatory markers declined progressively over the following days, with CRP decreasing to 34 mg/L and PCT to 1.3 ng/mL by ICU day 4. A follow-up UC was sterile on ICU day 5. The patient recovered well and was discharged after 14 days of hospitalisation.

Discussion

Sepsis is defined as life-threatening acute organ dysfunction caused by a dysregulated host response to infection, with septic shock representing a subset characterised by circulatory dysfunction conferring higher mortality risk, as established by Sepsis-3 and reaffirmed by the Surviving Sepsis Campaign 2026 guidelines. (5,11–13) Urosepsis, the most serious infectious complication of endourological procedures, refers to sepsis originating from the urogenital tract. (5,11,14,15) Historically, sepsis was described as a systemic inflammatory response syndrome (SIRS) to infection, and several studies investigating infectious complications following endourological procedures, including ECIRS, have used SIRS-based criteria to define urosepsis. (11) Mariappan et al. (9) and Bag et al. (16) defined urosepsis as fever >38°C and/or leukocyte counts >12,000, after exclusion of alternative sources. The EDGE Consortium applied broader criteria, including temperature abnormalities, tachycardia, tachypnoea, altered mental status, hypotension, and abnormal white blood cell counts assessed at least 12 hours postoperatively. (12) In our patient, the clinical course was consistent with sepsis progressing to septic shock according to the Sepsis-3 definition. Treatment was therefore initiated without delay. This included IV crystalloid resuscitation, early NA support to maintain a MAP of at least 65 mmHg, and antimicrobial therapy within one hour of recognition. Following these measures, haemodynamic stability was restored. (12–15)

Multiple risk factors for infectious complications following endourological procedures have been identified. According to systematic reviews by Corrales et al. and Bhojani et al., independent risk factors for urosepsis include positive preoperative urine culture, female sex, diabetes mellitus, older age, preoperative stent placement, stone size, high irrigation pressure, longer operative time, and ischemic heart disease. (13–15) Bhojani et al. reported a pooled postoperative urosepsis incidence of 5.0% following ureteroscopy, with preoperative stent placement (odds ratio [OR] 3.94) and positive preoperative UC (OR 3.56) being the strongest predictors (14,15). Similarly, infectious complications following PCNL have been reported in 10.4–39.8% of cases, with risk factors including positive preoperative UC, staghorn calculus, prolonged operative time, and preoperative nephrostomy tube use. (3,4,6–8)

A meta-analysis of randomized controlled trials demonstrated that the overall risk of infectious complications following endourological stone treatment ranges from 0-13%. (5) Notably, patient positioning, tract size, obesity, and solitary kidney do not appear to significantly influence infectious complication rates. (3,14) However, several investigators consider patients to be at high risk when stone size exceeds 20 mm and/or collecting system dilatation is present, even with sterile urine, as well as when a positive preoperative UC has been documented within three months of the procedure, or when an indwelling stent or nephrostomy tube is present at surgery. (4,8,14,15) The role of preoperative antibiotic prophylaxis in ECIRS patients remains debated, with no specific recommendations due to insufficient data. (8–10,13) Despite appropriate prophylaxis, infected stones may harbour bacterial biofilms. Bacteria within the stone matrix may be released during endoscopic manipulation and lithotripsy, regardless of preoperative urine sterility. (14,17)

In our case, several established risk factors for urosepsis were identified. The patient was female, which has been consistently reported as an independent risk factor. (14,15) She presented with a staghorn calculus, associated with a higher risk of harbouring bacteria within the stone matrix and recognised as a significant risk factor for postoperative infection. (3,7,14) The procedure lasted 4 hours and 30 minutes, which was well beyond the 60-minute threshold after which the risk of infectious complications has been reported to double. (14,15) The stone itself was also clinically relevant. Its golden-yellow colour was suggestive of an infection-related calculus; therefore, even in the presence of a sterile preoperative urine culture, bacteria embedded in biofilm within the stone matrix may have been released during lithotripsy and caused postoperative urosepsis. (14,15,17)

The combined endoscopic approach may have played a role in this case. Prolonged operative time, continuous irrigation, and the high-pressure urinary backflow noted at puncture could have transiently raised intrarenal pressure and possibly favoured systemic release of bacteria from the infected stone matrix, despite a sterile preoperative urine culture. Several of the usual risk factors were not present in this patient. There was no diabetes mellitus, no preoperative stent, no positive immediate preoperative UC, and no ischemic heart disease. Antibiotic management was particularly challenging because of the patient's severe, multiple documented allergies. Amikacin and fosfomycin were chosen as empirical therapy, as the patient had no documented allergy to either and both offered appropriate coverage for a suspected gram-negative infection, in consultation with a clinical microbiologist. Meropenem was considered, but the patient gave an unclear, undocumented account of a possible previous reaction to it; although the likelihood of a true reaction was low, this uncertainty had to be respected, and all beta-lactams, including carbapenems, were therefore avoided initially, accepting the trade-off of relying on a more nephrotoxic aminoglycoside.

The staghorn morphology and infection-related appearance of the stone supported this choice, as such calculi often harbour biofilm-embedded bacteria that may be released during fragmentation despite a sterile preoperative urine culture. (14,17) Fosfomycin was particularly relevant for its reported anti-biofilm activity.

The culture confirmed an *Escherichia coli* susceptible to fosfomycin and gentamicin, supporting the empirical regimen. The isolate was resistant to ciprofloxacin, the agent used for prophylaxis, which may have cont-

ributed to the breakthrough infection.

After two days, the regimen was switched to meropenem, with faster recovery thereafter. In retrospect, given the very low penicillin–carbapenem cross-reactivity (<1%), meropenem could have been introduced earlier. (18) Routine avoidance of carbapenems in penicillin-allergic patients is no longer justified and may push clinicians toward more toxic alternatives such as aminoglycosides. By clearing the entire stone in a single session, ECIRS removed the infective source, which likely supported the favourable outcome.

Conclusion

ECIRS is an effective and well-established procedure for complex renal stone disease, usually followed by an uneventful recovery and a short hospital stay. Postoperative urinary infections are generally mild and manageable on the ward. This case, however, is a reminder that an apparently routine, technically successful procedure can be followed within hours by rapidly progressive urosepsis and septic shock. The key message is the need for a high index of suspicion, early Sepsis-3–based recognition, and a low threshold for intensive care, especially in patients at higher risk of severe postoperative infection. Antimicrobial prophylaxis in this setting remains uncertain, particularly when multiple allergies limit standard options, and prospective studies are needed to define evidence-based prophylaxis and postoperative risk stratification. (8–10)

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Use of artificial intelligence. ChatGPT (OpenAI, GPT-5.5) was used only for grammar correction and language refinement. It was not used to generate scientific content, clinical data, results, interpretations, or references. The authors reviewed and approved the final manuscript.

Ethics approval. Formal ethics committee approval was not required for this case report according to institutional policy. Written informed consent for the surgical and anaesthetic procedures was obtained from the patient, and the consent form included permission for the use of anonymized clinical data for scientific and educational purposes. The manuscript was prepared in accordance with the principles of the Declaration of Helsinki. Patient anonymity has been preserved.

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CASE REPORTS

Use of Esketamine Combined with Dexmedetomidine for Difficult Tracheal Intubation in an Uncooperative Pediatric Patient with Severe Trismus: A Case Report

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ABSTRACT

Managing difficult airways in pediatric patients with severe trismus and poor cooperation is challenging because conventional sedatives may suppress spontaneous respiration. We report a case of a 15-year-old girl (weight 50 kg) with recurrent rhabdomyosarcoma causing severe trismus (0-finger mouth opening) and facial deformity. After premedication with atropine and methylprednisolone, sedation was achieved with a slow infusion of dexmedetomidine (20 μg over 10 minutes) followed by intravenous esketamine (20 mg, 0.4 mg/kg). This regimen preserved spontaneous breathing with oxygen saturation maintained at 99–100% throughout the procedure. Topical anesthesia of the nasopharynx was performed using 2% lidocaine spray (total dose 100 mg, approximately 2 mg/kg) via spray-as-you-go technique. Fiberoptic nasotracheal intubation was then successfully accomplished without coughing, body movement, or hemodynamic instability. No adverse events such as emergence reactions or hallucinations occurred. This multimodal sedation approach may offer a safe and effective alternative when preserving spontaneous respiration is critical in uncooperative pediatric patients with severely restricted mouth opening.

Keywords: Airway Management; Child; Dexmedetomidine; Esketamine; Fiberoptic Intubation; Rhabdomyosarcoma; Trismus

Introduction

Fiberoptic bronchoscopic (FB) intubation is a cornerstone for managing anticipated difficult pediatric airways, particularly when trismus and poor cooperation limit direct laryngoscopy (1). Success depends on maintaining spontaneous respiration and adequate airway topicalization while avoiding respiratory depression. Conventional sedatives such as propofol, midazolam, or opioids may suppress ventilatory drive, increasing hypoxia risk in patients with severe trismus and tumor-related airway distortion (2,3). Esketamine, the S-enantiomer of ketamine, preserves spontaneous breathing and pharyngeal reflexes, making it theoretically advantageous (4). Dexmedetomidine, a highly selective α2-adrenoceptor agonist, provides sedation and analgesia without significant respiratory depression and has been used successfully for awake fiberoptic intubation in both adults and children (5–7). However, the combined use of dexmedetomidine and esketamine for sedated fiberoptic intubation in uncooperative pediatric patients with severe trismus remains undocumented. In this case, a 15-year-old female with recurrent rhabdomyosarcoma presented with 0-finger mouth opening, facial deformity, and an ulcerated intraoral tumor. To secure the airway while preserving spontaneous ventilation, a dexmedetomidine-esketamine sedation regimen was employed.

Case Presentation

A 15-year-old female (weight 50 kg) presented with a diagnosis of left temporal rhabdomyosarcoma in August 2025. The planned procedure was excision of the temporal mass and reconstruction with a left anterolateral thigh musculocutaneous flap. Her past medical history included surgical resection, radiotherapy, and chemotherapy for left temporo-sphenoidal rhabdomyosarcoma. She was unable to eat orally, received enteral nutrition via a gastrostomy tube, and was malnourished.

Physical examination revealed a large mass in the left temporal region with local ulceration communicating with the oral cavity. Mouth opening was 0 finger-widths, indicating severe restriction (Fig. 1A). Jaw protrusion was impossible, and trismus prevented tongue protrusion, making Mallampati classification unfeasible. Neck extension and rotation were normal. Head and neck CT demonstrated a residual soft tissue mass measuring approximately 62 × 26 mm, with destruction of the left temporal bone, sphenoid wing, orbital floor, and zygomatic arch. The left foramen ovale was expanded, with tumor infiltration into the left maxillary sinus and mastoid air cells.

Based on these findings, the patient was anticipated to have a difficult airway. Her uncooperativeness for awake sedation intubation, combined with complete inability to open the mouth, made airway management extremely challenging. Fiberoptic bronchoscope-guided nasotracheal intubation under preserved spontaneous respiration was ultimately planned.

Given that traditional opioids and midazolam could lead to respiratory depression, and to provide adequate sedation while preserving spontaneous respiration, esketamine was chosen. Premedication included intravenous atropine (0.2 mg) and methylprednisolone (10 mg). Dexmedetomidine was administered as a slow infusion (20 μg over 10 minutes), followed by pre-oxygenation. Intravenous administration of 20 mg esketamine (0.4 mg/kg) was given. After the patient lost consciousness, topical anesthesia of the nasopharynx was performed with 2% lidocaine spray (total dose 100 mg, approximately 2 mg/kg) using a spray-as-you-go technique through the fiberoptic bronchoscope working channel. During this process, vital signs remained stable, breathing was steady, and oxygen saturation was maintained at 99–100%. Fiberoptic bronchoscope-guided nasotracheal intubation was then performed using a size 6.0 endotracheal tube, with no significant body movement or coughing. The endotracheal tube was secured after immediate confirmation by end-tidal CO_2 waveform, and SpO_2 remained above 99% throughout. After securing the airway, GA was induced with Sufentanil (0.2 μg/kg), Propofol (1.5 mg/kg), and Rocuronium (0.6 mg/kg). Then mechanical ventilation was initiated. General anesthesia was maintained intraoperatively with sevoflurane inhalation, continuous intravenous infusions of propofol and remifentanil, and rocuronium as needed. Surgery proceeded uneventfully for approximately 6 hours with stable hemodynamics and no airway complications. Fluid administration and blood loss were within expected limits. The patient was extubated in the post-anesthesia care unit and regained consciousness within 15 minutes. Vital signs remained stable, respiratory function was satisfactory, and she was transferred back to the ward in stable condition. She was eventually discharged after recovery without adverse memories related to the intubation.

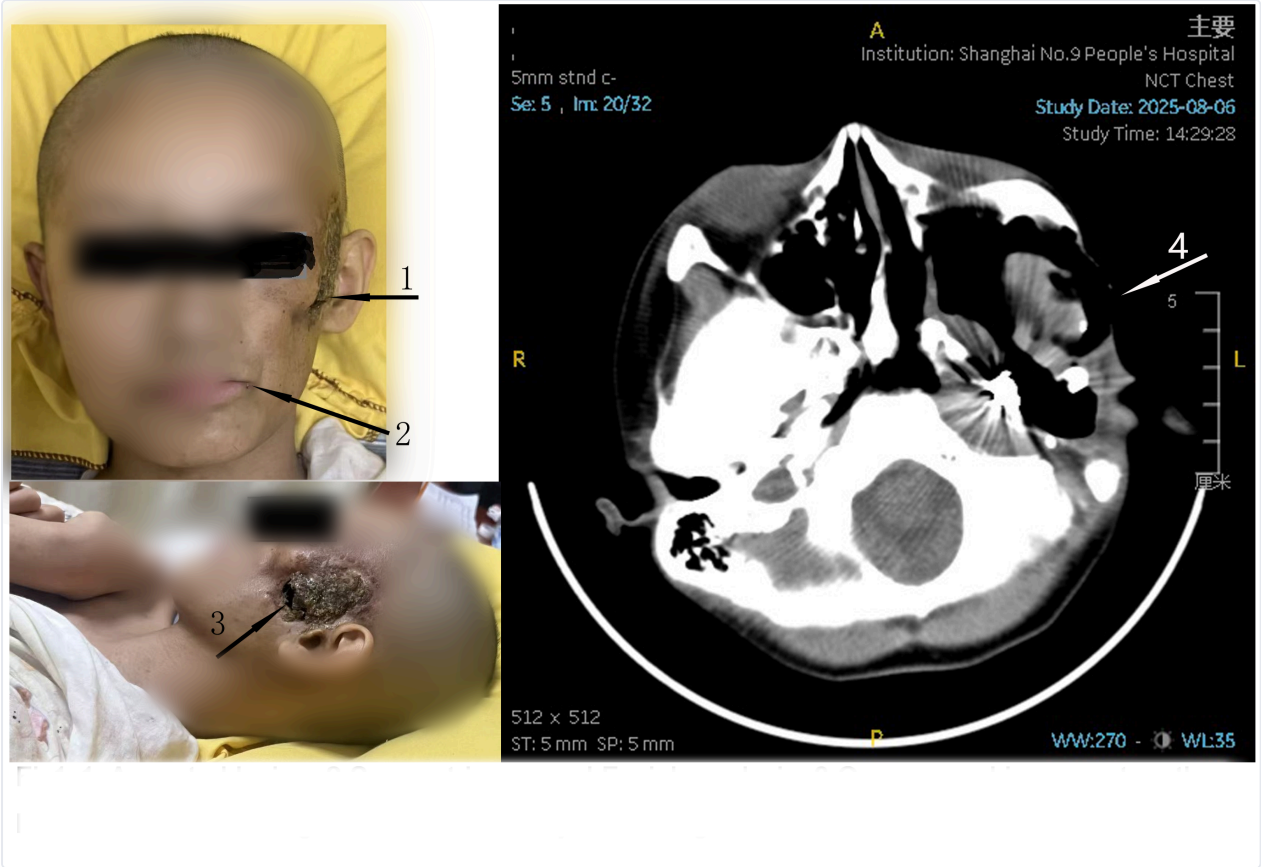

Figure 1. 1 A crusted lesion; 2 Severe trismus and Facial paralysis; 3 Open wound is present on the left face,communicating with the oral cavity; 4 CT image shows oronaoculaneous fistula.

Informed Consent

Written informed consent was obtained from the patient's guardian for publication of this case report and any accompanying images.

Discussion

Awake fiberoptic bronchoscope-guided intubation under preserved spontaneous respiration is the gold standard for anticipated difficult airways (1,8). However, for patients with mouth opening restriction who may be impossible to mask-ventilate — as in this case where facial tumor ulceration communicated with the oral cavity — hypoxia is difficult to avoid once respiratory depression occurs. Esketamine, the S-enantiomer of ketamine, provides potent analgesia and sedation while preserving spontaneous respiration (4). It does not affect the hypoxic ventilatory response. Previous studies have demonstrated its efficacy in pediatric sedation (9,10). Potential risks include emergence reactions, hallucinations, and increased secretions. Appropriate use of dexmedetomidine can effectively reduce these adverse reactions (11).

The rationale for selecting low doses of dexmedetomidine and esketamine in this case deserves further elaboration. We used a low-dose dexmedetomidine infusion (20 μg over 10 minutes, equivalent to approximately 0.4 μg/kg loading) followed by a single bolus of esketamine 0.4 mg/kg. These doses are at the lower end of the recommended ranges for procedural sedation. Low-dose dexmedetomidine (≤0.5–1.0 μg/kg) has been shown to preserve spontaneous ventilation and airway reflexes while providing adequate sedation and hemodynamic stability (5,6). Similarly, sub-dissociative doses of esketamine (0.2–0.5 mg/kg) maintain pharyngeal tone and spontaneous breathing, reduce the risk of apnea, and have a favorable safety profile (4). The combination allows synergy: dexmedetomidine provides baseline sedation and attenuates

esketamine-induced sympathetic stimulation and emergence phenomena, while esketamine contributes analgesia and deeper sedation without compromising respiratory drive. This balanced approach enabled us to perform fiberoptic intubation smoothly with no episodes of hypoxia, coughing, or hemodynamic instability. We believe this regimen is particularly advantageous in uncooperative pediatric patients with severe trismus, where any loss of spontaneous ventilation could be catastrophic.

Conclusion

For managing complex airways involving difficult mask ventilation and severe mouth opening restriction in an uncooperative adolescent, esketamine-assisted fiberoptic intubation with preservation of spontaneous respiration is a promising technique. More clinical studies are needed to validate its safety and efficacy in diverse patient populations.

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LETTERS TO THE EDITOR

A knotted central venous catheter discovered at removal: when resistance should prompt imaging, not traction

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Letter

Dear Editor,

Central venous catheter (CVC) placement is routine in acute care, yet mechanical complications remain clinically important. Most attention rightly focuses on arterial puncture, pneumothorax, infection, and thrombosis. Knot formation at the distal end of a standard multilumen CVC is uncommon and easily missed when the line functions normally during use.

We wish to report a case that illustrates this hazard.

A patient required central venous access for prolonged intravenous therapy. A double-lumen catheter was inserted into the right internal jugular vein without immediate complications; blood aspiration and infusion through both lumens were satisfactory. No post-procedure chest radiograph was obtained. The catheter remained in place for one week and delivered treatment without dysfunction.

On planned removal, the operator encountered firm resistance over the final 5–6 cm of the catheter. Further withdrawal was stopped. A bedside ultrasound in the operating room showed the catheter still within the vein, with neither inflow nor outflow through the lumens. After cautious attempts at non-operative removal failed, a vascular surgeon was consulted.

Operative exploration under local anaesthesia confirmed the presence of a knot at the distal end of the catheter (Figure 1). The line was removed intact. The patient recovered without haemorrhage or infection.

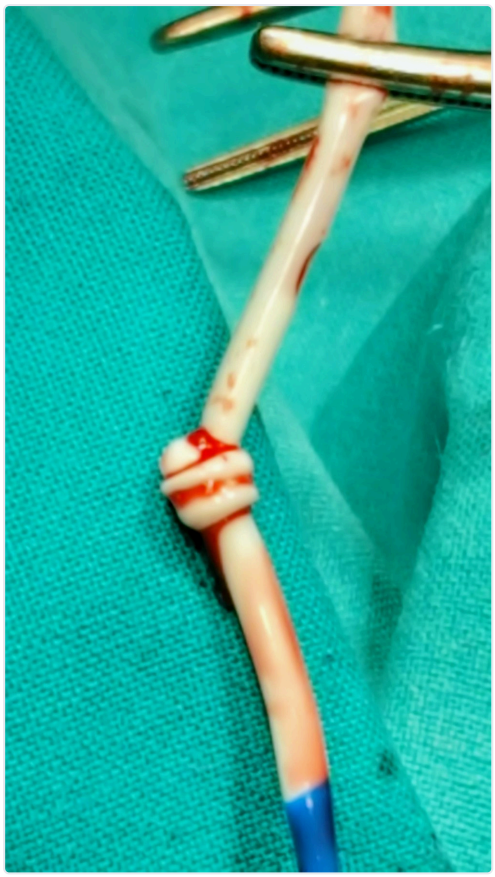

Figure 1. The explanted double-lumen central venous catheter, held on forceps, showing a knot at its distal end confirmed at operative exploration.

Although CVC knotting is rare and is described mainly in case reports and small series (1,2), it is not merely theoretical. Proposed mechanisms include guidewire looping, vascular tortuosity, excessive catheter length with intravascular coiling, and loop tightening during withdrawal (3). Reports of knotting in pulmonary artery catheters suggest incidences of roughly 0.2–2.5% in selected settings (3); comparable figures for routine CVCs are not well established, which may contribute to under-recognition.

This case supports several practical points. First, resistance during removal should be treated as a mechanical problem until proven otherwise; forced traction risks fracture and embolisation (3,5). Second, imaging—ultrasound or radiography—should precede further manipulation when withdrawal is not smooth (3,5). Third, routine post-insertion imaging may disclose malposition or coiling before the catheter is used for days without symptoms (2,3). In our patient, normal function during infusion did not exclude a distal abnormality that became apparent only at removal.

Operator experience and ultrasound guidance reduce many insertion-related complications (4), but they do not eliminate rare mechanical events (1,3). Clinicians should remain aware that a CVC which appears to work well may still harbor a distal knot (1,2).

We hope this report encourages colleagues to stop, image, and seek specialist input when catheter removal is unexpectedly difficult.

Sincerely,

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