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Pharmacokinetics of Local Anesthetics in Fascial Plane Blocks: Clinical Implications and Safety Considerations-A Narrative Review

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Turkish Journal of Anaesthesiology & Reanimation

Beyond the Fascial Plane: An Open Invitation to Explore Mechanistic Uncertainties and Local Anesthetic Safety

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In this issue of the Turkish Journal of Anaesthesiology and Reanimation, we draw particular attention to an increasingly important aspect of regional anaesthesia: the pharmacokinetics and safety of local anesthetics used in fascial plane blocks. While Zengin et al.[1] provide a comprehensive review of local anesthetic pharmacokinetics in fascial plane blocks, Magoon and Choudhary[2] raise concerns regarding the safety of local anesthetic dosing in a previously published case report, prompting a response from Çiftçi et al.[3] As the Editorial Board, we consider these contributions an opportunity to revisit an issue that deserves greater attention.

Over the past decade, the rapid expansion of fascial plane blocks has substantially changed our approach to local anesthetic administration. Many fascial plane blocks use relatively large injectate volumes to facilitate spread toward the intended neural targets. This makes the relationship between volume, concentration, total dose, and systemic absorption particularly relevant to both efficacy and safety. This evolution raises an important question: have our understanding and consideration of local anesthetic pharmacokinetics kept pace with the growing use of high-volume fascial plane blocks? The recent systematic review by De Cassai et al.[4] examining local anesthetic pharmacokinetics after single-injection erector spinae plane block provides a focused contribution to this discussion.

A growing body of literature indicates that fascial plane blocks can reduce analgesic requirements in selected surgical settings, although their efficacy and sensory effects vary across techniques. Nevertheless, questions regarding the mechanisms underlying these beneficial effects have increasingly attracted the attention of clinicians and researchers. A relatively small but influential group of respected academics has raised the possibility that some of the analgesic effects attributed to fascial plane blocks may, in fact, result from the systemic analgesic action of absorbed local anesthetics rather than solely from their effects on targeted neural structures. Although this hypothesis has not gained widespread acceptance, it has introduced an important dimension to the ongoing scientific discussion. Local and systemic mechanisms need not be mutually exclusive, and their relative contributions may differ across techniques and local anesthetic regimens. Demonstrating systemic absorption alone, however, does not establish that it accounts for the observed analgesic benefit.

Our intention is not to take sides in this debate. We will continue to evaluate studies investigating the clinical efficacy of fascial plane blocks and publish those that meet our scientific and methodological standards. At the same time, we particularly welcome research exploring the pharmacokinetics of local anesthetics and the potential contribution of systemic absorption to the analgesic effects of fascial plane blocks. Such investigations are essential to advancing our understanding of these increasingly popular techniques.

The pursuit of innovation should never come at the expense of patient safety. As fascial plane blocks continue to evolve, we must maintain an appropriate balance between local anesthetic volume, concentration, and total dose. High volume does not necessarily imply a high total dose; these variables should be considered together. Local anesthetic administration should be

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individualized according to patient characteristics, surgical requirements, and the anatomical properties of the targeted fascial plane.

With patient safety as our foremost priority, we extend an open invitation to researchers to investigate whether, and to what extent, systemic absorption of local anesthetics contributes to the analgesic effects of fascial plane blocks. We particularly welcome experimental and clinical studies that use appropriate comparator groups to help distinguish local from systemic contributions to analgesia, supported by serial plasma concentration measurements, standardized sensory assessment, and clinically relevant analgesic outcomes. We also encourage investigations into the pharmacokinetic profiles of local anesthetics across different fascial plane blocks. As clinicians and researchers, we share this curiosity and look forward to studies that clarify mechanisms, inform dosing, and strengthen patient safety.

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Review Article
Perioperative Care

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Harnessing the Power of Education for a Low-carbon Future in Anaesthesia: A Narrative Review

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Abstract

Climate change poses a significant threat to public health, with the healthcare sector being a major contributor to greenhouse gas emissions. Anaesthesia and the operating room are notable contributors within this sector, particularly because of volatile inhalation gases such as desflurane and nitrous oxide. Therefore, improving sustainability in anaesthesia is a clinical and ethical imperative. This review examines recent advances in leveraging education to promote low-carbon anaesthesia practices. We summarize evidence on how various educational interventions and formats can reduce the carbon footprint of anaesthesia and discuss implementation strategies, challenges, and future directions. Many studies demonstrate that educational programs reduce the use of high global warming potential anaesthetic agents. Programs vary widely in scope, ranging from single-session lectures and surveys to multi-year sustainability task forces and formal policy changes, some of which have resulted in up to a 90% reduction in volatile agent emissions. Combining multiple techniques (such as lectures, posters, and vaporizer labeling) has been associated with substantial reductions in volatile agent emissions and with improved organizational readiness for sustainability initiatives. These education-driven shifts toward environmentally friendly approaches, such as low-flow techniques, total intravenous anaesthesia, and regional anaesthesia, have proven effective, cutting costs, maintaining patient safety, and reducing carbon emissions. Educational initiatives represent a practical and cost-efficient strategy to reduce carbon emissions in anaesthesia practice and in healthcare. By integrating environmental stewardship into anaesthesia training and policy, anaesthesiologists can lead the transition of healthcare to low-carbon care.

Keywords: Sustainable anaesthesia, volatile anaesthetics, carbon footprint, environmental education, low-flow anaesthesia

Main Points

- Educational interventions consistently reduce volatile anaesthetic use without policy mandates or compromised patient safety.
- Low-flow anaesthesia, total intravenous anaesthesia (TIVA), and regional techniques significantly reduce emissions, cut costs and improve operational efficiency.
- Implementation barriers such as knowledge gaps, safety misconceptions, and resource constraints are surmountable through integrated medical school curricula, evidence-based safety training, and transparent carbon tracking systems.
- Sustainable anaesthesia education requires context-specific strategies: high-income countries should promote TIVA and advanced systems, while low- and middle-income settings should prioritize cost-effective interventions such as avoiding desflurane and minimizing fresh gas flows.

Introduction

Climate change is an ongoing concern, primarily attributable to emissions from manufacturing and automobiles. However, a major contributor on which experts have only recently focused is the healthcare system, specifically the use of volatile inhalational anaesthetics.[1] There are two common measurements for evaluating the environmental impact of various compounds, global warming potential (GWP) and carbon dioxide equivalents (CO_2e). GWP is an index representing the heat trapped by one kg of a compound compared to one kg of CO_2 during a 100-year period. CO_2e represents how many kg of CO_2 equivalents are generated by one kg of a compound. Higher values for both GWP and CO_2e indicate greater warming effects. Nitrous oxide, a commonly used inhalational anaesthetic, is a major contributor to ozone depletion and has a high GWP of 298.[2] Desflurane, another common volatile anaesthetic, has a GWP of 2,540 and CO_2e of 3,909 kg mL^{-1} which when

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used in one seven hour operation is equivalent to driving a car 7,850 kilometers.[3] Another commonly used inhalation anaesthetic, sevoflurane, has a smaller but still impactful effect at 0.408 CO_2e kg mL^{-1}.[3] Inhaled agents, which are more commonly used, tend to have a much higher CO_2e when compared to alternative administration methods, such as total intravenous anaesthesia (TIVA), which has a CO_2e of 0.017 kg mL^{-1}.[3] Regional anaesthesia does not have a defined CO_2e; rather, its environmental impact primarily arises from disposable packaging and instrument sterilization processes, for which environmental measurements remain limited.

The use of volatile anaesthetics contributes substantially to the carbon footprint of operating rooms and the healthcare system. Educational interventions targeting both clinicians and administrative staff have been shown to reduce this impact.[4] This review examines how such educational initiatives within anaesthesia departments and hospitals influence the choice of anaesthetic agents, delivery techniques, the use of volatile anaesthetics, and broader perioperative practices to reduce carbon emissions.

This study is a narrative review of educational interventions to promote environmentally sustainable anaesthesia practice. We conducted a targeted search of PubMed, Scopus, and PubMed Central for articles published between 2015 and 2025 using combinations of terms related to anaesthesia (e.g., "anaesthesia," "perioperative"), education (e.g., "education," "training"), and environmental impact (e.g., "carbon footprint," "global warming potential"). A total of 221 titles and abstracts were screened for relevance to anaesthesia, educational interventions, and environmental outcomes (n=37). Included studies were from countries with significant healthcare systems and documented sustainability programs, including the United States (US), Germany, the Netherlands, the United Kingdom, Australia, and South Korea. Full-text articles were then assessed for inclusion based on relevance and methodological contribution. The final article selection was reached by consensus through discussion (n=25, see Figure 1). Reference lists of key articles were also reviewed to identify additional sources. For our core studies (see Table 1), we included twelve English-language retrospective, interventional, cohort, qualitative, and review articles that involved anaesthesia, including perioperative anaesthesia, described an educational intervention, and reported environmental outcomes. We also included foundational papers on greenhouse gas emissions, barriers, and global epidemiology to provide context and guide the discussion. In total, 25 peer-reviewed articles were included.

Why Change is Needed?

Modern anaesthesia is safe and effective for a wide range of surgical procedures. However, its marked increase in use has revealed its negative environmental consequences. Volatile inhalation anaesthetics, such as desflurane, sevoflurane, isoflurane, and nitrous oxide, are recognized as major greenhouse gases.[4] Their widespread use, combined with fairly low induction efficiency (95% remaining unaltered) results in massive daily releases of these greenhouse gases into the environment.[5] This has led to anaesthesia being one of the leading sources of hospital-related emissions, with studies estimating emissions close to 5%, a disproportionately large share relative to the number of procedures that use these inhalation anaesthetics.[6,7]

The overall impact of emissions and climate change is not confined to the environment. It plays a direct role in human health, including heat-related illnesses and respiratory issues from pollution.[8,9] Thus, addressing the major role of anaesthetics in CO_2 emissions is imperative to improving the health of patients. Moreover, many of the environmentally friendly practices in anaesthesia, such as local anaesthetics and low-flow anaesthesia, align with broader administrative goals of patient safety and cost-efficiency, thereby boosting incentives to change practice.

The roadmap for implementing change is extensive. Major opportunities include switching from high-GWP to low-GWP inhalation induction agents; minimizing fresh gas flow (FGF) during inhalation anaesthesia and using low-flow or rebreathing systems; switching from inhalation induction to TIVA or regional blocks; and prioritizing reusable products. With evidence of financial incentives and clinical evidence demonstrating improved patient safety, education becomes the next step in implementing these changes in practice.

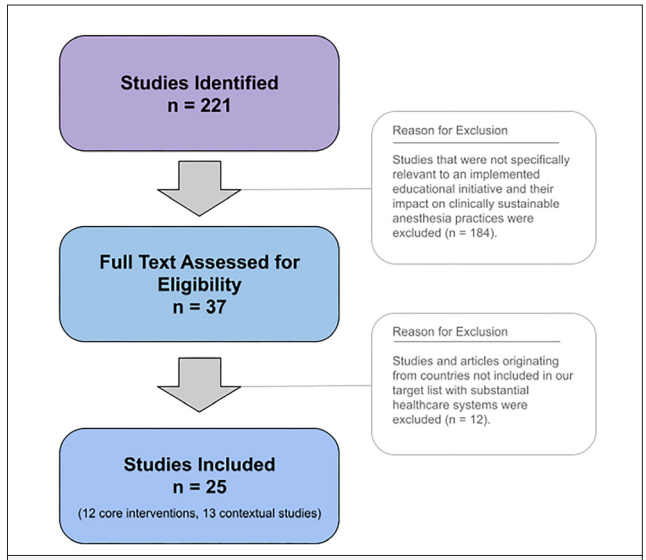


Figure 1. Selection criteria. Outline of the process for excluding and selecting studies to be included in the narrative review.

Educational Strategies to Promote Low-carbon Anaesthesia Worldwide

Studies from across the globe describe several educational strategies that have been shown to reduce the environmental impact of anaesthetic use.

European Educational Strategies

One effective approach involves lecture-based interventions and grand rounds within departmental teaching. In one German study, repeated lectures were delivered across three hospital campuses, after which volatile anaesthetic–related emissions reportedly dropped by 90%.[4] These sessions emphasized the GWP of commonly used anaesthetics, particularly desflurane highlighting that its GWP is 2,540. They also proposed the use of sevoflurane and TIVA as lower-impact alternatives. Following these educational sessions, the use of desflurane in the examined hospitals declined markedly and was nearly phased out by late 2023.[4]

Building on these results, the same hospital system at Charité in Germany banned the use of desflurane through a top-down, policy-backed approach. These guideline changes, which removed vaporizer usage, updated ordering protocols, and enforced minimal-flow techniques, were all paired with reiterative sustainable anaesthetic practice education. While lecture-based education alone was effective, top-down education and policy change produced the most rapid and durable reduction in carbon output compared with the bottom-up voluntary education approach.[4]

Similar outcomes were seen in four French hospitals that created "sustainable anaesthesia groups," or "green teams," which were groups of anaesthesia personnel that organized information campaigns, distributed posters, and provided feedback on staff awareness and habits via online surveys. Despite participation from only 19% of staff, desflurane and sevoflurane use dropped significantly, with monthly CO_2 emissions decreasing by about 14.16 tons following the campaign.[5]

North American Educational Strategies

In North America, one intervention employed visual cues and behavioral nudges, including informational posters in break rooms and hallways, reference charts at work stations, and stickers on anaesthetic vaporizers.[10] These reminders increased clinician awareness of desflurane's GWP and encouraged lower-carbon anaesthetic choices, with providers reporting greater awareness and greater application of sustainable practices.[10]

Rather than relying solely on extracurricular groups, some departments have directly incorporated sustainability education into residency training and Continuing Medical Education programs. These efforts focused on the "5 Rs" (reduce, reuse, recycle, rethink, research) and applied circular design principles to promote a more sustainable operating room.[2] The implementation of each component has reduced anaesthesia-related carbon emissions, and therefore integrating this circular design approach may yield greater long-term change and improve readiness for sustainable practices in anaesthesia and the broader operating-room environment.[2,11]

Additionally, one study demonstrated the effectiveness of an audit-feedback system in which residents received weekly emails with their total FGF relative to an American Society of Anesthesiologists low-dose standard and to the performance of other residents. In just a four-week period, this audit-feedback program resulted in a 22% reduction in FGF, with nearly 56% of resident survey respondents indicating that the personalized data motivated a decrease in their volume usage of environmentally harmful anaesthetics.[12] These findings suggest that timely, case-by-case reports of individual performance in anaesthetic use could contribute to reducing GWP in the operating room.

Global/Asian Educational Strategies

In a Korean study, short-term awareness campaigns, similar to the green teams, included departmental briefings and educational handouts summarizing the environmental impact of desflurane, sevoflurane, and other techniques. These interventions led to a 50% decrease in desflurane use and significantly dropped CO_2 emissions in the span of just one month.[5,6]

On a global scale, professional societies have contributed to the push toward environmentally friendly healthcare practices. For instance, the World Federation of Societies of Anesthesiologists (WFSA) issued a 2022 statement urging anaesthesia programs to integrate environmental sustainability into their curricula.[13] A global consensus among 45 anaesthesia leaders held that educating providers on sustainability is both achievable worldwide and crucial to reducing anaesthesia's footprint. To date, the literature has not explicitly evaluated whether the WFSA 2022 statement has led to measurable changes in curricula, institutional policies, or clinical practice.

Evidence of Impact

Recent studies have provided encouraging evidence that educational interventions are effective in reducing the carbon footprint of anaesthesia practice. One of the major effects is the sharp reduction in the use of desflurane, the inhalation anaesthetic with the highest GWP. In multiple studies, education on the negative environmental effects of desflurane, particularly through departmental programs and the creation of sustainable anaesthesia groups, led to about a 50% decrease in use.[3-6] Many of these changes were made without policy mandating bans on desflurane, because the evident effect on carbon emissions, safe and effective

alternatives such as sevoflurane, and the price reduction alone provided sufficient incentive to change practice. When top-down changes were implemented through policy, the greatest decrease in desflurane use was observed.

Educational interventions also shifted induction practices away from high-flow techniques toward increased use of low-flow techniques. In particular, a German study using an educational bundle of lectures, posters, and stickers resulted in a self-reported 14% increase in low-flow anaesthetic use, with financial incentives and patient safety playing major roles in the switch.[14] The education focused on informing providers about the advantages of low-flow anaesthesia, dispelling myths about patient safety and reduced gas use, and training providers in low-flow delivery skills. Another study quantified the effects of education by calculating carbon emissions, finding that reducing sevoflurane flow rates from 3 L min^{-1} to 1 L min^{-1} can reduce them by more than 50%.[10] Low-flow techniques therefore illustrate the measurable impact of educational initiatives on reducing the carbon footprint of anaesthesia.

One of the largest reductions in emissions in anaesthesia practice was achieved through education on the use of TIVA and regional anaesthesia instead of inhalation anaesthetics. TIVA does not use inhalation anaesthetics, which confers a major environmental benefit compared with inhalation agents such as desflurane and sevoflurane, which do not provide efficient induction and thus produce significant environmental emissions. Furthermore, TIVA and inhalational induction have been shown to be equally effective and safe.[14,15] As a result, through educational programs and sustainability task forces within hospitals, there was a major increase in TIVA use and associated decrease in anaesthesia-related emissions, with one study showing a 20-fold decrease, from 48.85 kg CO_2 to 2.42 kg CO_2.[3] When accounting for standard clinical dosing patterns, a single hour of desflurane anaesthesia generates approximately 179,055 grams CO_2e vs. propofol-based TIVA at around 231 grams CO_2e, demonstrating TIVA's environmental benefit.[16] Similarly, the method of anaesthetic administration has been shown to significantly affect the carbon footprint associated with its use in operating rooms. In a neurosurgical practice study that measured its carbon footprint in usage of general anaesthesia and spinal anaesthesia, the results showed a nearly 67-fold reduction from 4,745 g CO_2 to 70 g CO_2 in carbon footprint when switching to spinal administration from general anaesthesia. The highly significant difference in footprint measurements suggests substantial potential for footprint reduction by altering administration techniques through education.[17]

Along with the direct environmental benefits of changing anaesthesia practice, the importance of an added financial incentive should not be underestimated. Transitioning from high-cost volatile anaesthetics to lower-volume, lower-cost techniques such as TIVA and regional anaesthesia has facilitated top-down policy implementation and has resulted in substantial annual cost savings, with high-flow volatile anaesthetics (such as sevoflurane) costing approximately $7.99 per hour, compared with about $2.00 per hour for low-flow anaesthesia and TIVA.[15] For instance, in the Netherlands, a nationwide professional guideline promoting "TIVA when possible, inhalation when necessary" helped catalyze a rapid shift in practice across multiple hospitals.[18] What truly drove its successful adoption, however, were its strong educational outreach and framing that emphasized its cost savings and clinical safety.[18] This combination of environmental and economic incentives provided a compelling rationale for institutional investment in sustainable anaesthesia practices, underscoring the value of integrating financial considerations into climate-conscious healthcare strategies.

Beyond quantifiable metrics such as cost or gas volume, education has had a positive effect on the mindset in anaesthesia departments and on the willingness to implement change. Most participants in educational programs reported in post-education surveys that they were more likely to prioritize environmental considerations in their work and to be open to new practices.[6] While this cultural change is considerably more difficult to measure, it is critical to long-term sustainability efforts, as it encourages sustainability-related initiatives even after the educational programs end.

Overall, the available literature indicates that educational interventions are effective in reducing anaesthesia-related greenhouse gas emissions. Whether it is through sustainability groups, educational programs, or other methods, educating anaesthesia providers has led to measurable reductions in anaesthesia-related CO_2 emissions, often accompanied by other ancillary benefits like reduced costs and cultural changes.

Barriers and Challenges

Despite the effectiveness of various educational interventions to reduce the impact of volatile anaesthetics on the operating room's carbon footprint, systemic barriers have been shown to persist at the system, provider, and institutional levels. Understanding these obstacles, along with their potential solutions, is important for creating sustainable and impactful change initiatives.

The first and most fundamental issue in implementing educational programs is that informing providers about the climate impact of anaesthetics is not part of the standard medical education curriculum. Thus, the initial encounter with an anaesthesiologist who has received formal instruction on the GWP of their anaesthetic use will take place during

residency or fellowship, if at all. For instance, providers often lack awareness of desflurane's high GWP.[4] As a result, knowledge gaps and misconceptions persist, interfere with informed decisions regarding environmental impact, and may lead to resistance to change due to unfamiliarity.[4] A solution in this case may be to incorporate environmental training and GWP information earlier in anaesthesia training and, preferably, into medical school curricula.[19]

Another critical misconception pertinent to efforts to reduce the environmental impact of anaesthetic use in the operating room concerns patient safety and often deters providers from such practices. The idea is that reducing fresh anaesthetic gas flow, which is a primary strategy in decreasing volatile agent emissions, leads to an increase in compound A and carbon monoxide, which are toxic to humans, thereby raising concerns about patient harm and neurotoxicity.[2] This is a theoretical idea that there will be increased byproduct accumulation when volatile anaesthetics interact with CO_2 absorbents. However, only excessively low flow rates may result in increased production of compound A and carbon monoxide.[2] Modern absorbents are engineered to prevent these risks at clinically appropriate flow rates (0.5-1.0 L/min). Although it is a worthy concern for patient safety, worrying about trace byproducts from minimal-flow anaesthesia is disproportionate compared with other clinical risks. Therefore, educational solutions must be incorporated to teach updated absorbent physiology and evidence-based safety thresholds, to amend this misconception, and to verify low-flow anaesthesia as a useful practice for reducing the environmental impact of volatile agents.[2]

Similar concerns exist regarding the use of TIVA in clinical settings. TIVA has been proven to be an effective technique to reduce operating room greenhouse gas emissions, but it introduces the issue of drug waste. More than half of drugs prepared for clinical use go unused, and propofol makes up approximately 45% of this waste, which is considered environmentally unsustainable.[2] This is because propofol is known to persist in aquatic ecosystems and to accumulate in animal tissues. Although the footprint of propofol is concerning based on available data, assessments reveal that its life cycle has a significantly lower impact than those of desflurane or nitrous oxide.[2] Therefore, TIVA is still better than using high-GWP volatiles despite its aquatic costs, but it remains a non-zero-impact solution to the problem. Thus, it is important to provide anaesthesia personnel with comprehensive lifecycle education rather than oversimplified usage messaging.

While knowledge gaps and misconceptions continue hindering adoption of environmentally sustainable practices in the operating room, these challenges are compounded by cultural resistance and limited clinician engagement. Low voluntary participation continues to be a driving force behind the lack of adaptation and the limited adoption of greener techniques.[5] This suggests that anaesthesia personnel and providers perceive education regarding sustainable anaesthetic use as optional rather than integral to practice. Arguably, this could be addressed with the reporting and tracking of volatile usage and of correlated GWP and environmental impact, an additional issue facing this topic. Most hospital systems lack visible tracking or targets for anaesthetic carbon footprints, thereby reducing the urgency to change practice. Reporting also lacks standardization, preventing meaningful comparisons across settings.[2]

The adoption of greener techniques also faces limitations in infrastructure and resources. TIVA, regional anaesthesia, and enhanced monitoring equipment require substantial capital investment and increased drug costs. With the US and many other countries already facing access-to-care issues, one might expect that these techniques may not rank high on providers' priority lists. This is a significant barrier, as the cost of implementing this change limits its adoption in resource-limited environments.[2] Another component is the use of scavenging systems, which are not only designed to vent gases to the outside atmosphere but also, in higher-end models, incorporate technology to absorb, neutralize, or recycle these agents.[2] Most hospitals utilize basic scavenging systems that vent rather than capture and recycle, thereby missing an opportunity to implement environmentally friendly practices. If advanced scavenging systems were made more cost-efficient, accessible, and standardized, their adoption could help reduce the environmental impact of volatile agents.

Bottom-up education and the use of organized campaigns, lectures, posters, and green teams have proven to be an effective route to reducing GWP of anaesthetic agents, but they risk regression without repeated reinforcement. When healthcare systems incorporate these techniques, they should maintain educational efforts to achieve their goal of reducing environmental impact. On the other hand, top-down policy mandates, such as desflurane vaporizer removal, will achieve a more rapid uptake within three to six months and remain durable and efficient.[3]

Many of these obstacles were echoed in a large cross-sectional study of anaesthetists in Australia and New Zealand, where, despite broad support for sustainability, practitioners reported barriers including limited infrastructure, time pressure, and lack of educational support that prevented the widespread adoption of environmentally conscious practices.[20] Furthermore, this study found that a minority of respondents received any formal training on sustainability, highlighting the educational gap and the lack of standardization across anaesthesia curricula.

The primary clinical priorities are patient safety and positive

outcomes, and in emergencies many physicians may revert to high-flow techniques and agents such as desflurane and nitrous oxide because of their familiarity and experience, thereby sidelining sustainability goals. It is important that environmental education efforts frame sustainability in alignment with clinical excellence and safety, rather than as a competitive component. Creating a balance among patient benefit, safety, cost-effectiveness, and environmental responsibility is a key component of incorporating these greener techniques.[2]

In a healthcare system's mission to educate employees and providers about sustainable anaesthesia practices, barriers include legitimate knowledge gaps, misconceptions about techniques and lifecycle costs, cultural resistance and physician inertia, resource constraints, and competing clinical pressures. These obstacles are addressable, and several practical strategies have been proposed to overcome them. Effective educational interventions should clarify the evidence-based safety of low-flow techniques, explain the footprints and impacts of different volatile agents, demonstrate sustainability's alignment with patient safety and economic considerations, and incorporate change and accountability into healthcare institutions.

Table 1. Summarized Core References

Citation (authors, reference number, year)	Study type	Main focus	Key findings related to carbon footprint
Saadat and Raman[2], 2024	Narrative review	Conceptual framework for "sustainable anaesthesia"	Identifies desflurane and N_2O as major high-GWP contributors; outlines low-flow, TIVA/regional techniques, and equipment/waste changes as practical ways to reduce anaesthesia's climate impact while maintaining safety.
Bernat et al.[3], 2024	Large retrospective cohort	TIVA vs. volatile-based general anaesthesia	Demonstrates ≈20-fold lower CO_2e per case with TIVA (≈2.4 vs. 48.9 kg CO_2e) compared to a mixed volatile strategy, with similar clinical outcomes, supporting TIVA as a major mitigation option.
Schwiethal et al.[4], 2025	Before-after interventional study	Flagship education + policy example (Charité)	Repeated education with top-down desflurane removal achieved ≈90% reduction in volatile-related CO_2e and substantial drug cost savings without compromising clinical care.
Chambrin et al.[5], 2023	Retrospective multicenter cohort	"Green teams" and information campaigns	Formation of sustainable anaesthesia groups and campaigns led to significant drops in desflurane/sevoflurane use and a steeper decline in halogenated anaesthetic CO_2e (≈-14.16 tons/month).
Park et al.[6], 2024	Single-center retrospective study	Short-term focused education	One-month education on climate impact of inhaled agents reduced desflurane use by ~50%, increased sevoflurane, and significantly lowered OR-level anaesthetic CO_2e and costs.
Zuegge et al.[10], 2019	Before-after interventional study	Visual cues + education (vaporizer labeling)	Provider education and vaporizer labels reduced purchasing of high-GWP volatiles, resulting in decreased anaesthetic-gas-related CO_2e and drug expenditures.
MacNeill et al.[11], 2024	Narrative review	Perioperative systems context	Positions volatile anaesthetics as high-impact nodes within the perioperative carbon footprint and recommends low-flow, desflurane avoidance, TIVA, and regional techniques to reduce emissions.
Nordin et al.[12], 2024	Prospective educational intervention	Audit-and-feedba ck program for residents	Personalized FGF feedback emails to residents reduced average FGF by ~22% in four weeks, implying a meaningful decline in waste anaesthetic gas emissions during training.
White et al.[13], 2022	Global consensus statement	Professional endorsement of sustainability	WFSA consensus identifies volatile agents and N_2O as key GHG sources and calls for education and practice changes (low-flow, TIVA/regional, desflurane/N_2O avoidance) to reduce anaesthesia's carbon footprint worldwide.
Baumann et al.[14], 2025	Cross-sectional survey	Readiness for climate mitigation	Anaesthesiologists widely recognize the need to mitigate anaesthesia -related emissions but report inconsistent adoption of low-flow and desflurane-avoidance behaviors, highlighting an attitude-behavior gap.
Wang et al.[17], 2022	Comparative observational study	Regional vs general anaesthesia	In single-level TLIF surgery, spinal anaesthesia produced ≈67-fold lower anaesthetic-related CO_2e (70 g vs. 4,745 g) than general anaesthesia, illustrating the footprint impact of technique selection.
Kampman et al.[18], 2025	National implementation study	Dutch "decarbonising anaesthesia" program	Shows that a national "TIVA when possible, inhalation when necessary" strategy with education and guidelines reduced volatile gas use and associated emissions across Dutch hospitals.

TIVA, total intravenous anaesthesia; GWP, global warming potential; CO_2e, carbon dioxide equivalents; FGF, fresh gas flow

Special Considerations for Training and Global Equity

Because of the varying attributes of healthcare systems and settings, education in sustainable anaesthesia cannot follow a one-size-fits-all model. Settings in which anaesthetics are used and that involve different professional groups and training levels require tailored approaches that balance clinical reality, resource availability, and environmental goals. To achieve these environmental goals, it is imperative that all anaesthesiologists receive education in greening the operating room.[2] Framing sustainability as a core clinical competence, rather than an optional ethical add-on, teaches trainers about the environmental impact of agents, alongside safety and efficacy considerations. Establishing sustainable practice as the norm will identify the overlap among cost, clinical safety, and environmental benefit.

Also, physicians who have been practicing for longer, typically attendings, hold leadership roles and have more experience. However, established providers face barriers, being entrenched in habitual practices and skeptical of new systemic changes.[21] Education must emphasize both the environmental and economic benefits to address this cultural resistance from the top down. When institutional leaders and senior staff model sustainable practices, junior colleagues such as residents and new providers follow suit.[3] These efforts must extend beyond physicians' roles. Operating room staff such as Certified Registered Nurse Anesthetists (CRNAs), Certified Anesthesiologist Assistants, and other support staff play critical roles in waste management, equipment handling, and gas scavenging. Education for these staff members should focus on practical, actionable steps, such as waste segregation and reuse protocols.[2]

A major consideration for global equity is addressing differences in practice environments between high-, middle-, and low-income (LIC) countries. Countries like France and other high-income countries (HIC) have infrastructure for TIVA, advanced monitoring, reusable equipment cleaning systems, and modern absorbents for CO_2. In these countries, education can confidently promote low flow techniques, sevoflurane minimization and regional administration without facing major resource and accessibility barriers.[4-6] The adoption of TIVA and low-flow techniques may be hindered in resource-limited environments in LIC and middle-income countries (MIC). Healthcare systems often lack capital for TIVA pumps and infusion systems, reliable supply chains for injectable regional agents, and infrastructure for advanced waste scavenging. Rather than using TIVA and low-flow techniques as the universal solution, educational efforts should be location-specific and provide context-appropriate guidance.

Another concern regarding regional infrastructure is power-grid dependency, because carbon emissions from reusable equipment depend primarily on the local area. For instance, in countries that rely on coal-based energy, such as Australia, the use of reusable equipment may increase carbon emissions.[2] Therefore, educational programs must be regionally calibrated to account for their power-grid composition. For example, cleaning equipment with water and increasing its reuse may actually have a negative impact on climate change if conducted in an area that does not have much water to begin with.[2] Local accessibility and resources are therefore key components in evaluating the effectiveness of sustainability efforts.

Importantly, sustainability is not typically achieved by a single entity but rather through the collective efforts of multiple groups. All stakeholders must act to ensure an effective response, including hospitals, medical and nursing societies, and state, local, and federal governments. It is important that the HICs with resources pioneer sustainable anaesthetic practices and share knowledge, equipment, and financial support with LICs and MICs. HICs and their prominent healthcare systems should develop and disseminate contextualized educational toolkits for LICs and MICs, and advocate for technology transfer and equipment donation programs. Lobbying for policy development, such as supporting desflurane bans, would also further sustainability efforts in LICs and MICs. Wealthier institutions can model and subsidize sustainability investments, thereby creating pathways for others to follow.[2]

Effective sustainable anaesthesia education must be tailored to individual operating room environments to account for substantial differences in infrastructure and resources. HICs can confidently promote TIVA and reusable equipment, while LICs and MICs benefit most from high-impact, low-cost interventions (avoiding desflurane and using minimal flows). Implementation must balance safety, cost-effectiveness, resource availability, and environmental responsibility specific to each location.[2]

Education and Waste Management

While this review focuses primarily on the use of education in anaesthetic choice and technique, waste management is a complementary domain in which education can further reduce anaesthesia's environmental footprint. Educational efforts should therefore target these three high-impact areas: reusable vs. single-use equipment, drug waste reduction, and waste segregation practices.

Life-cycle assessments consistently demonstrate that reusable devices generate lower greenhouse gas emissions and less solid waste per use compared with their single-use equivalents, while also reducing long-term costs.[22] Therefore, implementing the aforementioned educational initiatives that emphasize safety, environmental benefits, and proper use of reusable instruments may be an effective strategy for reducing anaesthetic-related carbon emissions.

Over-preparation of propofol and other agents and improper disposal also contribute to increased anaesthetic-related environmental impact; a survey of 118 anaesthesiologists and CRNAs showed that many practitioners disposed of unused anaesthetic agents down drains and into trash bins.[23] These improperly disposed compounds may lead to downstream effects, including aquatic toxicity and other negative environmental impacts.[23] Thus, developing educational interventions that encourage the use of smaller vials, tailoring preparation to case-specific needs, and promoting proper waste segregation may help reduce drug waste and, consequently, environmental impact.[23] Overall, limited evidence exists regarding the impact of educational interventions on anaesthesia-related waste management strategies, indicating a need for further research in this field.

Future Directions

While substantial progress has been made in achieving low-carbon anaesthetic practice, there are still many questions for future research. A major example is the determination of the long-term efficacy of these educational interventions. Do the decrease in desflurane use and the increase in TIVA last over 5-10 years after the educational program ends? Because many of these interventions have occurred within the last few years, there have been no major studies addressing this question. Follow-up studies and surveys could explore the lasting impact of educational interventions, as well as show the potential benefits of "booster" educations to reinforce sustainable practice.

Another direction for implementing sustainable practice is to standardize sustainability education. This could take several forms, such as developing a sustainability curriculum within anaesthesia departments or residency programs, which could include interactive exercises or lunch lectures. Additionally, including anaesthesia-related environmental impact in professional exams could improve providers' awareness of these issues. Stemming from this idea, a multi-specialty initiative has advocated for embedding sustainability into perioperative medical education and board certification, recognizing that formal training is key to empowering clinicians to lead environmental change.[24] However, resistance is likely, given the already-packed training schedules of anaesthesia providers.

Technological innovations also offer a promising means of reducing the carbon footprint, largely without changing anaesthesia practice. A major example is the improvement of anaesthesia gas capture and recycling systems. This would reduce the total amount of anaesthesia purchased and used, thereby providing a financial incentive for hospital systems to invest in their development. In particular, technologies that capture and reprocess waste sevoflurane have shown early promise, with experimental systems demonstrating the ability to reclaim a significant proportion of the exhaled anaesthetic for reuse.[25] These approaches could mitigate the environmental impact while maintaining clinician familiarity and workflow. Additionally, developing novel induction methods or alternative synthetic agents could greatly reduce the environmental impact and the cost of anaesthesia. Xenon, for example, is an excellent anaesthetic and has no negative environmental impact.[15] However, its high cost and limited availability have restricted its use. Research into its recycling and production could be an effective approach to reducing carbon emissions while supporting the provision of care.

While top-down measures have the greatest impact on changes in practice, the impact of a bottom-up approach, beginning with advocacy by anaesthesiologists, should not be underestimated. Equipping anaesthesiologists with the knowledge and confidence to engage in healthcare policy could amplify the demand for sustainable anaesthesia practices and ultimately lead to change.

Finally, addressing which anaesthesia strategy is safe and provides optimal patient care is vital to justify changes to current practice. If an alternative induction agent or method is more environmentally friendly but carries a greater risk of complications during surgery, no provider will be willing to risk patient harm or their license by changing their anaesthetic practice. On the other hand, if there is clinical evidence that an alternative induction agent or method is safer than the current standard, practicing anaesthesiologists and hospital administrators will be much more likely to adopt the practice. Thus, research to understand the specific clinical implications of alternative induction agents can be crucial to adopting environmentally friendly anaesthesia practices.

Exploring these future directions makes it clear that the quest for sustainable anaesthesia remains an ongoing endeavor. Pushback can be resolved only through additional research and evidence, which will, in turn, facilitate education and implementation. The anaesthesia field has been cognizant of the need for change toward sustainable anaesthesia, and many changes have already been institutionalized.[3] By staying informed and proactive, the field of anaesthesia will remain at the forefront of both medical advances and environmental responsibility.

Conclusion

Anaesthesiology stands at an inflection point where clinical excellence is becoming inseparable from environmental stewardship. This review demonstrates that education is a practical and scalable method for transforming anaesthesia practice toward low-carbon care. Through deliberate educational interventions, ranging from residency training in low-flow techniques to multi-year departmental sustainability campaigns and audit-and-feedback systems, anaesthesia departments have consistently achieved substantial reductions in greenhouse gas emissions from volatile anaesthetic agents.

Further, these reductions have been accomplished without sacrificing patient safety or clinical outcomes, and many of these low-carbon practices align with improved cost-effectiveness and operational efficiency.

For anaesthesiologists, the implications are both clear and actionable. Incremental changes in daily practice—avoiding high-GWP agents, minimizing FGFs, optimizing technique selection, and reducing pharmaceutical waste—result in measurable environmental gains. Departmental leadership must prioritize sustainability education within residency and quality improvement programs. By integrating environmental stewardship into training, measurement systems, and institutional policies, anaesthesiologists can lead healthcare's transition to low-carbon care while maintaining clinical excellence. The evidence is now compelling enough that sustainable anaesthesia should be treated as a quality improvement standard, ensuring we care for patients today while safeguarding the world tomorrow.

Footnotes

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Pharmacokinetics of Local Anesthetics in Fascial Plane Blocks: Clinical Implications and Safety Considerations-A Narrative Review

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Abstract

Fascial plane blocks (FPBs) are increasingly used in modern regional anaesthesia and differ from conventional nerve blocks by delivering local anesthetic (LA) into interfascial compartments. This approach results in distinct pharmacokinetics with clinically relevant systemic absorption. Pharmacokinetic behavior in FPBs is determined by interactions among patient-related factors, drug properties, adjuvant use, and fascial plane characteristics. High-volume injections, tissue vascularity, and injection technique influence peak plasma concentration and time to peak concentration. Patient variables, such as advanced age, pregnancy, obesity, malnutrition, and organ dysfunction, further increase variability and the risk of toxicity. Epinephrine may reduce the absorption rate and improve safety, whereas dexamethasone and dexmedetomidine mainly prolong analgesia through pharmacodynamic effects. Because systemic absorption is inherent to FPBs, LA systemic toxicity remains a key concern. Individualized dosing, appropriate drug selection, and close monitoring are essential for safe and effective clinical practice.

Keywords: Fascial plane blocks, local anesthetics, adjuvants, local anesthetic systemic toxicity, pharmacokinetics, regional anaesthesia

Main Points

- Fascial plane blocks (FPBs) exhibit distinct pharmacokinetics characterized by high-volume interfascial spread and clinically relevant systemic absorption, making peak plasma concentration and time to peak critical determinants of safety.
- Pharmacokinetic variability is driven by the interplay between patient factors, drug properties, adjuvants, and fascial plane anatomy, necessitating individualized dosing strategies.
- Systemic exposure after FPBs may approach or exceed toxicity thresholds even within conventional dose limits, highlighting the persistent risk of local anesthetic systemic toxicity.
- Rational selection of drugs and adjuvants, combined with vigilant monitoring, is essential for optimizing analgesic efficacy while maintaining pharmacokinetic safety.

Introduction

Fascial plane blocks (FPBs) involve the injection of local anesthetic (LA) into potential interfascial compartments rather than around a discrete peripheral nerve. The ability of deep fascial layers to form expandable interfascial spaces provides the anatomical basis for these techniques and facilitates the spread of injectate over relatively large tissue planes.[1,2] Although ultrasound guidance enables visualization of fascial separation and injectate spread, visible distribution does not necessarily

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predict sensory nerve coverage. Effective analgesia is thought to depend, at least in part, on adequate sensory nerve coverage within the surgical field.[3]

Injectate spread within fascial planes is dynamic and may extend beyond the initial ultrasound image over time, potentially increasing sensory nerve coverage.[1] This property may underlie the volume-dependent nature of FPBs, whereby increasing injectate volume increases sensory nerve coverage and thereby contributes to variability in clinical effects.[4] However, volume dependence also introduces variability, contributing to inconsistencies in dermatomal sensory mapping and clinical effects.

Pharmacokinetically, interfascial injections differ from traditional nerve blocks by distributing LA over extended tissue planes rather than confining it within a discrete compartment. This pattern facilitates systemic absorption, as demonstrated by measurable plasma concentrations following truncal FPBs.[5] Variability in peak plasma concentration (C_{max}) and time-to-peak concentration (T_{max}) across techniques suggests that anatomical plane characteristics and injection variables significantly influence systemic exposure.[5] Since systemic toxicity is closely related to circulating LA concentrations, understanding these determinants is important for safe clinical practice.[6]

With the rapid expansion of FPBs in modern regional anaesthesia, their clinical performance is increasingly linked to pharmacokinetic determinants, including absorption, plasma concentration profiles, duration of action, and safety margins.[7] This review synthesizes current evidence on patient-related characteristics, LA properties, adjuvant use, and fascial plane anatomy as key determinants of pharmacokinetic variability in FPBs and provides a structured, clinically applicable framework to optimize analgesic efficacy while minimizing systemic exposure and the risk of LAST.

Methods of the Search Strategy

This narrative review was informed by literature searches conducted in March 2026 using MEDLINE/PubMed, Embase, the Cochrane Central Register of Controlled Trials, Google Scholar, and Scopus. To ensure that the review reflected the most recent evidence, the literature search was updated prior to finalizing the manuscript to include publications available up to May 2026. Search strategies included combinations of the terms "fascial plane block," "interfascial plane block", "pharmacokinetics," "plasma concentration," "serum concentration," "peak plasma," "local anesthetic," "lidocaine," "bupivacaine," "levobupivacaine," "liposomal bupivacaine," "prilocaine," "ropivacaine," "adjuvant," "epinephrine," "dexmedetomidine," "dexamethasone," "magnesium sulfate," "opioid," "local anesthetic systemic toxicity," "erector spinae plane block," "ESP block," "ESPB," "rectus sheath block," "transversus abdominis plane block," "TAP block," "quadratus lumborum block," "QL block," "interpectoral plane block," "pectoserratus plane block," "PECS block," "serratus anterior plane block," "SAP block," "parasternal intercostal plane block," "PIP block," and "fascia iliaca compartment block." Priority was given to human pharmacokinetic studies, systematic reviews, experimental studies, and clinically relevant investigations.

In accordance with the recommendations of the RULE-AP framework,[8] large language models were used during manuscript preparation to support medical English translation, grammar refinement, and figure generation. All scientific content, interpretations, critical appraisals, and final editorial decisions were performed and verified by the authors.

Patient-related Factors

In FPBs, pharmacokinetics is influenced not only by the dose and physicochemical properties of the LA but also by patient-specific determinants that modulate absorption, distribution, metabolism, and elimination. The vascularity of the injected plane, total injectate volume, and protein binding characteristics of the drug interact with the patient's physiological reserve and organ function to determine systemic exposure. Because FPBs often require relatively high volumes to achieve adequate distribution, systemic absorption becomes clinically relevant, thereby highlighting the importance of patient-related variability.[9]

Age is a major determinant of pharmacokinetic variability. Although reduced hepatic clearance and altered distribution in elderly patients are well recognized in general LA pharmacology, FPB-specific pharmacokinetic data in frail populations remain limited and are largely extrapolated from peripheral nerve and neuraxial block literature; among the few FPB-specific datasets, a pharmacokinetic study of fascia iliaca compartment block (FICB) (levobupivacaine 75 mg) in patients aged ≥80 years with hip fracture reported slow systemic absorption with all plasma concentrations remaining below the toxic threshold, suggesting that this technique is well tolerated in elderly patients despite the large injectate volume required.[10] In addition, sarcopenia reduces the buffering capacity of skeletal muscle, which normally serves as a reservoir for circulating drugs. As muscle mass declines, redistribution toward toxicity-sensitive organs such as the brain and myocardium may occur more rapidly. Although some evidence supports a more conservative dosing approach in frail elderly patients, with practical dose reductions of approximately 10-20% suggested in the literature, FPB-specific dosing algorithms remain insufficiently validated. Accordingly, such reductions should be interpreted cautiously and individualized according to patient characteristics, procedural factors, and anticipated systemic exposure.[11]

In pediatric populations, pharmacokinetics varies significantly with developmental stage. Neonates and infants, particularly those younger than 6 months, have reduced plasma protein concentrations, including α1-acid glycoprotein (AAG) and albumin, which result in a higher unbound fraction of LAs. In addition, immature hepatic metabolism leads to reduced clearance and a prolonged elimination half-life. These factors collectively narrow the safety margin for systemic toxicity compared with adults.[12] Clinical studies confirm that systemic absorption after FPBs is relevant in children: levobupivacaine administered via transversus abdominis plane (TAP) block reaches C_{max} values within approximately 20 minutes, with considerable interindividual variability, whereas ropivacaine concentrations following erector spinae plane block (ESPB) have, in some cases, exceeded neurotoxic thresholds defined in adults.[13,14] As children mature, pharmacokinetic parameters become more predictable; however, systemic exposure remains clinically significant.

The influence of biological sex on FPB pharmacokinetics is less well defined. Although FPB-specific evidence is limited, a recent volunteer study demonstrated that women had higher systemic exposure to ropivacaine despite similar block characteristics.[15] However, this finding should be interpreted with caution. In that study, male participants were substantially heavier than female participants (median weights 80.0 vs. 62.5 kg), and both groups received an identical fixed dose of ropivacaine. Therefore, the higher exposure in women may partly reflect dosing relative to body weight rather than biological sex per se. Notably, the authors also attributed the difference to higher CYP1A2-mediated clearance in men. In contrast, other studies evaluating interfascial techniques such as ESPB and pectointercostal FPB have not identified a consistent relationship between pharmacokinetic parameters and demographic variables.[16] Overall, sex alone appears to have limited clinical relevance, whereas associated factors, such as pregnancy, body composition, and comorbidity burden, are more important determinants.

Body composition plays a critical role in pharmacokinetics, whereas body mass index (BMI) alone is insufficient to guide dosing. In obese patients, total body weight increases disproportionately relative to lean body mass, and pharmacokinetic parameters such as volume of distribution and clearance do not increase linearly. Increased cardiac output and tissue perfusion may accelerate systemic absorption, while elevated AAG levels associated with chronic inflammation may partially buffer the unbound drug fraction.[17] However, dosing based solely on total body weight, particularly in high-volume FPBs, may result in increased C_{max} values and systemic exposure.[18] Therefore, lean body weight, ideal body weight, or adjusted body weight provide a more appropriate basis for dosing. Recommendations regarding dosing adjustments in obesity are largely extrapolated from broader regional anaesthesia and pharmacokinetic literature, as FPB-specific evidence remains limited. Conversely, in underweight or catabolic patients, reduced muscle and fat reserves, impaired protein binding, and decreased clearance increase susceptibility to systemic toxicity.[11] Thus, pharmacokinetics in FPBs is better explained by body composition and physiological reserve than by BMI alone.

Comorbid conditions, particularly hepatic, renal, and cardiac diseases, significantly influence pharmacokinetics. Amide LAs depend primarily on hepatic metabolism; therefore, their clearance may be reduced in advanced liver disease or conditions associated with decreased hepatic blood flow. Although dose adjustment may not be mandatory for single injections, a more conservative approach is warranted in the presence of repeated dosing, continuous infusions, or combined organ dysfunction. FPB-specific data support this approach: in patients undergoing major hepatectomy, high-dose bilateral TAP block has been associated with ropivacaine concentrations approaching toxic thresholds that are proportional to the extent of liver resection.[19] Renal disease presents a more complex scenario. In severe renal failure, hyperdynamic circulation may lead to earlier C_{max} values, while increased AAG may partially reduce the unbound fraction. However, uremia and metabolic acidosis impair protein binding and increase toxicity risk, narrowing the safety margin.[20] In cardiac disease, conduction abnormalities increase vulnerability to cardiotoxic effects, and reduced cardiac output limits hepatic and renal perfusion, further impairing drug elimination.

Pregnancy is one of the most significant patient-related risk factors. Much of the current understanding regarding pregnancy-related alterations in LA pharmacokinetics is extrapolated from neuraxial and peripheral nerve block literature rather than from FPB-specific investigations. Reduced concentrations of albumin and AAG increase the unbound fraction of LAs, while increased cardiac output and tissue perfusion enhance systemic absorption. Studies have demonstrated that the unbound fraction of bupivacaine increases progressively during pregnancy, particularly at term, thereby increasing the proportion of the drug within the toxic concentration range.[21] Consequently, conservative dosing and vigilant monitoring are recommended for pregnant patients, particularly when high-volume interfascial blocks are performed.

Malnutrition, although poorly studied in FPBs, has clear pharmacokinetic implications. Altered body composition, reduced protein synthesis, and impaired organ function affect drug distribution and clearance. Low muscle mass and hypoproteinemia reduce buffering capacity and increase the variability of the unbound fraction.[22] Although AAG is

the primary binding protein for amide LAs, malnutrition is often associated with multiple physiological impairments, including reduced hepatic and renal function; this supports the use of lower doses and closer monitoring in these patients.

Clinically, patient-related factors determine key pharmacokinetic outcomes: the magnitude of systemic absorption, C_{max}, unbound fraction, and elimination rate. Accordingly, individualized dosing strategies are essential in high-risk populations, including frail elderly patients, pregnant individuals, underweight or catabolic patients, and those with significant hepatic, renal, or cardiac disease. In conditions such as pregnancy, hypoalbuminemia, or renal dysfunction, reduced protein binding may increase the free fraction of circulating LA despite apparently acceptable total plasma concentrations. Furthermore, even apparently safe total plasma concentrations may be associated with systemic toxicity when they are accompanied by an increased free fraction of the LA, by acidosis, or by reduced protein binding. In such cases, conservative dosing, careful concentration-volume balance, fractionated injection, and close monitoring should be standard practice to minimize the risk of LAST. It should be acknowledged, however, that many of these recommendations are extrapolated from broader regional anaesthesia and LA pharmacology, as FPB-specific evidence for individualized dosing in high-risk populations remains limited.

Local Anaesthetic-related Factors

The pharmacokinetic behavior of LAs in FPBs is largely determined by the interplay between drug-specific physicochemical properties and high-volume interfascial injection techniques.[9] Given the marked variability in systemic absorption across different anatomical planes, intrinsic characteristics such as lipid solubility, protein binding, and metabolic profile play a central role in influencing both analgesic efficacy and toxicity risk. Accordingly, a clear understanding of drug-specific pharmacokinetics is essential for the safe and effective use of FPBs, in which systemic exposure following a bolus injection is typically characterized by C_{max} and T_{max}.[9]

However, it should be emphasized that most clinical pharmacokinetic studies in FPBs report total plasma concentrations, whereas the free (unbound) fraction, which represents the portion available to interact with target tissues, correlates more directly with the risk of systemic toxicity.[9] Commonly cited toxic plasma thresholds should therefore be interpreted with caution: the clinical likelihood of LAST is shaped not only by total plasma concentration but also by the free drug fraction, arterial versus venous sampling site, acid-base status, patient comorbidity, and individual susceptibility.[11] A total concentration that appears acceptable by conventional standards may still produce toxicity when protein binding is diminished, the free fraction is elevated, or systemic acidosis is present.[9]

Lidocaine

Beyond its LA effect, lidocaine has analgesic, anti-hyperalgesic, and anti-inflammatory properties that make it a versatile agent.[23] Approximately 90% of the drug is metabolized in the liver; the elimination half-life is approximately 96 minutes.[23,24] Because lidocaine causes vasodilation, it is often absorbed rapidly from tissues; therefore, a vasoconstrictor is commonly added in clinical practice.[23] Kato et al.[25] measured serum lidocaine after bilateral TAP blocks with 400 mg total dose and found a mean C_{max} of 3.6±0.7 μg mL^{-1} at 30 minutes with individual peaks ranging from 2.7 to 5.5 μg mL^{-1}. Absorption from ESP blocks is notably faster, with T_{max} values of 5-6 minutes.[26] With continuous bilateral ESP catheters in pediatric cardiac surgery patients, Caruso et al.[27] found mean peak lidocaine concentrations of 1.82 μg mL^{-1}, well within the safe range. SAP catheter concentrations were approximately 43.5% higher than ESP values, likely due to differences in the administered dose.[28] Although early toxicity signs are typically described at concentrations above 5 μg mL^{-1}, and frank convulsions at concentrations above 10 μg mL^{-1}, these reference values were largely derived from controlled intravenous studies and should therefore be applied to FPB settings with appropriate caution.[24]

Bupivacaine

Bupivacaine's prolonged action reflects its high lipophilicity (partition coefficient of 27.5), its pKa of 8.1, and extensive protein binding of 95-96%.[24,29] Reported toxicity thresholds, derived largely from volunteer infusion studies, are approximately 2.1 μg mL^{-1} for total venous concentrations and 4.0 μg mL^{-1} for arterial concentrations; these values should not be regarded as absolute, given the substantial influence of free fraction, sampling site, and individual susceptibility.[9,30] Notably, clinical toxicity has been documented even at doses below 2 mg kg^{-1}.[9]

Levobupivacaine

Levobupivacaine is the S(−)-enantiomer of bupivacaine, developed to retain anesthetic potency while reducing cardiac and neurological toxicity.[9,31] In FPBs, it is typically used at a concentration of 0.125-0.25%.[9] Bardsley et al.[30] reported that the maximum tolerated venous concentration was 2.62 μg mL^{-1} for levobupivacaine, compared with 2.25 μg mL^{-1} for bupivacaine, a small but clinically relevant difference. In ESP blocks using 2 mg kg^{-1} levobupivacaine, Shigeta et al.[32] measured a C_{max} of 1.24 μg mL^{-1} and a T_{max} of 6 minutes; epinephrine reduced the C_{max} by approximately half. Onishi et al.[33] reported a median C_{max} of 553 ng/mL following levobupivacaine TAP block, approximately one-fifth of the commonly cited toxic threshold. Within the limits of currently available evidence, doses up to 2.5 mg kg^{-1} appear to be safe for FPBs.[9]

Liposomal Bupivacaine

Liposomal bupivacaine employs DepoFoam® technology, in which the drug is enclosed within multivesicular liposomes with a honeycomb-like internal structure that enables sustained release.[34] This produces a characteristic bimodal plasma profile: an initial peak within the first hour, arising from the approximately 3% of free bupivacaine outside the liposomes, and a second peak at 12-36 hours as the encapsulated drug is gradually released.[35] In volunteer studies, a fourfold-higher dose of liposomal bupivacaine produced nearly the same C_{max} as plain bupivacaine (0.87 vs. 0.83 μg mL^{-1}), while the terminal half-life was almost tenfold longer than that of plain bupivacaine.[34] Importantly, the formulation should not be mixed with other LAs or come into contact with antiseptics such as chlorhexidine, since they disrupt the lipid membrane, causing rapid, uncontrolled drug release.[34] At least 20 minutes should elapse between the injection of a different LA and the administration of liposomal bupivacaine.[34]

Prilocaine

Prilocaine exhibits the weakest vasodilatory effect among amide LAs, permitting effective use without a vasoconstrictor.[23] The combination of rapid clearance, low peak concentrations, and limited vasodilation makes prilocaine an appealing candidate, at least in theory, for high-volume FPBs, although direct pharmacokinetic data in FPB settings remain limited.[36]

Ropivacaine

Ropivacaine was the first long-acting LA marketed as a pure S(−)-enantiomer, and its lower lipophilicity provides a wider safety margin for both CNS and cardiovascular toxicity than bupivacaine.[31,37] It also shows relative motor sparing, with smaller Aδ and C fibers being blocked more readily than large motor fibers.[37] Approximately 94% of circulating ropivacaine is protein-bound to AAG, and it is hepatically metabolized by CYP1A2 and CYP3A4, with approximately 86% of metabolites excreted renally.[37]

In FPB studies, ropivacaine is usually prepared at concentrations of 0.25-0.5% in volumes of 20-40 mL.[9] When doses approach 3 mg kg^{-1} in TAP blocks, mean total venous concentrations reach 1.8-2.0 μg mL^{-1}, and some patients exceed the commonly cited toxicity threshold of 2.2 μg mL^{-1}; however, free concentrations were not consistently measured in these studies.[9] Toju et al.[38] reported a mean arterial C_{max} of 1.87±0.78 μg mL^{-1} after subcostal TAP at 3 mg kg^{-1}. PECS blocks appear relatively concerning: Versyck et al.[39] observed that half of their 20 patients had free ropivacaine concentrations in the potentially toxic range at 2.5 mg kg^{-1}, a finding that is particularly informative because the unbound fraction was directly quantified. In a population pharmacokinetic analysis of continuous ESP blocks, Schwenk et al.[40] found that 5 of 15 patients reached plasma concentrations approaching reported toxic thresholds despite standard dosing; their model predicted that halving the initial bolus from 150 mg to 75 mg would substantially reduce this risk. Clinicians should also be aware that CYP1A2 inhibitors, such as fluvoxamine, can elevate ropivacaine levels and may necessitate a dose adjustment.[37] Because FPBs are frequently performed under general anaesthesia, which can mask the early CNS signs of toxicity, close hemodynamic monitoring for at least 30-60 minutes after injection and immediate availability of lipid emulsion for rescue remain important safety measures.[38,41]

Overall, LA pharmacokinetics in FPBs reflect a complex interplay among drug properties, injection-site vascularity, total dose, and patient factors.[5,9,42] Although the literature continues to grow, one consistent observation is that plasma concentrations may approach or exceed commonly cited toxic thresholds even when conventional weight-based dose limits are respected, particularly with bilateral or high-volume techniques.[9,42] In clinical practice, this argues for a more conservative approach to high-volume bilateral truncal FPBs, particularly in frail elderly patients, parturients, and those with hepatic dysfunction or hypoalbuminemia. Using lower concentrations at adequate volumes may reduce systemic exposure while preserving interfascial spread.[9,11] Current dosing recommendations and agent-specific safety considerations relevant to FPBs are summarized in Table 1.[9,11,23-26,30,32,34-37,39,40,43,44] These values should be interpreted with caution. Reported toxic plasma thresholds predominantly reflect total venous concentrations derived from heterogeneous studies, including controlled volunteer infusions, and may not directly translate to clinical FPB practice, where free drug fraction, sampling methodology, acid-base status, and patient comorbidities all influence individual risk. Although current evidence supports cautious dose reduction in vulnerable populations (e.g., the elderly, parturients, and patients with hepatic dysfunction or hypoalbuminemia), precise FPB-specific dosing algorithms remain insufficiently validated. Population pharmacokinetic modeling, such as the ropivacaine model developed by Schwenk et al.,[40] offers a promising path toward more individualized, site-specific dosing. Moving forward, prospective studies with serial plasma sampling across different block types and patient populations, ideally including measurement of free drug fractions, will be needed to replace empirical dose ceilings with genuinely evidence-based guidelines.[26,42]

Adjuvant-related Factors

In FPBs, adjuvants are commonly used to enhance analgesic efficacy and prolong block duration. From a mechanistic perspective, adjuvants can be broadly classified into two categories: (i) agents that modify the pharmacokinetics of LAs and (ii) agents that primarily enhance analgesia through pharmacodynamic mechanisms without substantially

Table 1. Suggested Dose Considerations and Agent-Specific Pharmacokinetic Features for Local Anesthetics used in FPBs

Agent	MRD plain (mg kg^{-1})	MRD+Epi (mg kg^{-1})	FPB-specific considerations
Lidocaine	5 (350 mg)	7 (500 mg)	Rapid absorption from ESP (T_{max} 5-6 min); bilateral TAP C_{max} can reach 5.5 μg mL^{-1}; early toxicity signs reported above 5 μg/mL; vasoconstrictor often added in clinical practice
Bupivacaine	2 (175 mg)	3 (225 mg)	LAST reported at doses <2 mg kg^{-1}; narrowest seizure-to-cardiac-arrest margin; reported venous toxicity threshold ~2.1-2.25 μg mL^{-1}; consider avoiding continuous infusions where feasible (51% of infusions exceeded MRD)
Levo-bupivacaine	2 (200 mg)	3 (225 mg)	≤2.5 mg kg^{-1} appears safe for FPBs; epinephrine halves C_{max} in ESP block; reported maximum tolerated venous concentration 2.62 μg mL^{-1}; less cardiotoxic than racemic bupivacaine
Ropivacaine	3 (200 mg)	3 (250 mg)	Suggested limits of ≤2 mg kg^{-1} without epinephrine and ≤2.5 mg kg^{-1} with epinephrine for FPBs; reported venous toxicity threshold ~2.2 μg mL^{-1}; 50% of patients had free ropivacaine concentrations in the potentially toxic range in PECS blocks at 2.5 mg kg^{-1}; caution with CYP1A2 inhibitors; motor-sparing at low concentrations
Prilocaine	6 (400 mg)	8 (600 mg)	Fastest clearance (2.84 L min^{-1}); no vasoconstrictor needed; theoretical advantage for high-volume FPBs; dose-dependent methemoglobinemia risk (contraindicated in sickle cell disease); limited FPB-specific PK data
Liposomal bupivacaine	266 mg max*	-	Bimodal PK profile (peaks at ~1 h and 12-36 h); do not mix with other LAs or antiseptics; wait ≥20 min after conventional LA injection; ~4× dose produces similar C_{max} as plain bupivacaine

These values should be interpreted cautiously, as most recommendations are derived from narrative reviews and heterogeneous pharmacokinetic data rather than formal dose-finding studies. MRD, maximum recommended dose; Epi, epinephrine; FPB, fascial plane block; ESP, erector spinae plane; TAP, transversus abdominis plane; PECS, pectoral nerves; PK, pharmacokinetic; LA, local anesthetic; LAST, local anesthetic systemic toxicity;

C_{max}, peak plasma concentration. *Not weight-based; absolute dose limit. Traditional MRD values adapted from El-Boghdadly et al.[11] and Rosenberg et al.[44]; FPB-specific recommendations from Bailey et al.[9]

altering LA pharmacokinetics. Pharmacodynamic effects primarily involve modulation of nociceptive transmission, inflammatory signaling, and neuronal excitability, whereas pharmacokinetic effects involve alterations in LA absorption, systemic uptake, tissue distribution, or plasma concentration profiles. Importantly, several adjuvants likely exert combined effects through both pathways, and the relative contribution of each mechanism remains incompletely defined (Table 2).[1,45-47] This distinction is particularly relevant because FPBs differ fundamentally from conventional peripheral nerve blocks. In FPBs, drugs are injected into relatively large interfascial compartments rather than directly adjacent to a discrete nerve. Consequently, injected solutions may undergo substantial redistribution within fascial planes, diffusion into adjacent muscular compartments, and variable vascular absorption depending on the anatomical characteristics of the block. These factors significantly influence systemic drug exposure and complicate the interpretation of whether observed prolongation of analgesia is attributable to local peripheral mechanisms, systemic effects, or a combination of both.

Epinephrine: Modulation of Absorption Kinetics

Epinephrine is the most established pharmacokinetic adjuvant in regional anaesthesia. Its primary mechanism is local vasoconstriction, which reduces vascular uptake and modifies the systemic absorption profile of LAs. However, in FPBs, the magnitude of this effect is highly dependent on the anatomical characteristics of the injected fascial plane, including vascularity, compartment size, and diffusion dynamics.[1,48]

Across truncal FPBs, the most consistent pharmacokinetic effect of epinephrine is prolongation of T_{max}, indicating a slower absorption rate. In contrast, its effect on C_{max} is less predictable and appears to be block-specific. For example, in TAP blocks, epinephrine reliably delays T_{max} but does not consistently reduce C_{max}, likely because the relatively large, compliant fascial compartment facilitates widespread distribution.[48,49] Conversely, in more confined spaces such as the rectus sheath, epinephrine may reduce both T_{max} and C_{max}, reflecting a more pronounced limitation of systemic uptake.[50]

These findings highlight that the pharmacokinetic behavior of epinephrine in FPBs is not uniform but depends on the interaction between vasoconstriction and fascial plane characteristics. Clinically, epinephrine should therefore be considered primarily as a safety-enhancing agent that delays systemic absorption rather than a reliable means of reducing overall systemic exposure or consistently prolonging analgesia.[48-50] Its use may be particularly valuable in high-volume truncal blocks, where large LA doses increase the risk of systemic toxicity.

Table 2. Pharmacokinetic Effects of Adjuvants in Fascial Plane Blocks

Adjuvant	Principal mechanism in FPBs	Effect on LA absorption kinetics	Expected effect on T_{max}	Expected effect on C_{max}	Evidence consistency/ certainty	Practical clinical interpretation
Epinephrine	Local vasoconstriction	Decreases absorption rate	↑ Often prolonged	↓ Variable; may be unchanged in some planes and reduced in others	Moderate consistency; effects on C_{max} and analgesic duration remain block-dependent	Primarily considered when modulation of systemic absorption and widening of the PK safety margin are desired rather than direct analgesic enhancement
Dexmedetomidine	Local antinociceptive effect+systemic α_2-mediated action after absorption	Variable effect on LA absorption; not consistently demonstrated across all planes	Variable	Variable	Moderate but heterogeneous evidence; systemic absorption likely contributes to clinical effects	May be considered when prolonged analgesia is desired, although caution is required in hemodynamically vulnerable patients
Dexamethasone	Anti-inflammatory and antinociceptive action	Minimal direct effect on LA absorption	Usually no major direct PK effect	Usually no major direct PK effect	Moderate consistency for analgesic prolongation, although FPB-specific PK mechanisms remain insufficiently characterized	Reasonable option for prolonging analgesia without prominent α_2-mediated hemodynamic effects
Magnesium sulfate	NMDA receptor antagonism	Minimal direct effect on LA absorption	Usually unchanged	Usually unchanged	Limited-to-moderate evidence with substantial interstudy heterogeneity	Primarily a pharmacodynamic adjuvant rather than a PK modifier
Tramadol	Peripheral and systemic analgesic contribution	No consistent major effect on LA PK	Usually unchanged	Usually unchanged	Limited and heterogeneous evidence	May be considered when α_2 agonists are undesirable, but systemic adverse effects should be considered
Nalbuphine/ opioid-derived adjuvants	Peripheral opioid receptor effect + systemic contribution	No consistent major effect on LA PK	Usually unchanged	Usually unchanged	Limited FPB-specific evidence	Potential utility remains uncertain because peripheral and systemic contributions are difficult to distinguish

C_{max}, peak plasma concentration; FPB, fascial plane block; LA, local anesthetic; NMDA, N-methyl-D-aspartate; PK, pharmacokinetic; T_{max}, time-to-peak concentration

Dexmedetomidine: Dual Local and Systemic Effects

Dexmedetomidine (DEX) is one of the most extensively studied adjuvants in FPBs and exhibits both pharmacodynamic and pharmacokinetic interactions. Evidence indicates that DEX undergoes clinically relevant systemic absorption when administered in fascial planes, with measurable plasma concentrations following TAP block.[46] In addition, numerous clinical studies report sedation, bradycardia, hypotension, and opioid-sparing effects consistent with systemic α2-adrenergic receptor activation.[45-47,51]

In ESPB and TAP block studies, DEX has been associated with a prolonged duration of analgesia and a delayed requirement for rescue analgesics. Although these effects are frequently attributed to local peripheral mechanisms, the observation of dose-dependent systemic effects, including sedation and hemodynamic changes, suggests that systemic absorption may also contribute to its clinical profile.[45-47,51] Accordingly, the analgesic effects of DEX in FPBs likely reflect a combination of peripheral modulation of nociceptive transmission and systemic pharmacodynamic effects following vascular uptake, although the relative contribution of each mechanism remains incompletely understood.

The potential of DEX to reduce LA absorption via local vasoconstriction has been proposed, but pharmacokinetic evidence supporting this effect in FPBs remains inconsistent.[1,45,52] Consequently, the prolongation of analgesia observed with DEX is more plausibly explained by pharmacodynamic mechanisms than by substantial modification of LA pharmacokinetics.[1,45]

Current clinical evidence suggests that DEX may be an effective adjuvant in selected FPBs. In the TAP block, randomized controlled trials demonstrate prolonged analgesia and reduced opioid consumption, while in the ESPB, both RCTs and meta-analyses show delayed time to first rescue analgesia and decreased opioid requirements.[45-47,51]

Dose-dependent adverse effects are clinically relevant. Lower doses (e.g., 0.5 μg/kg) provide analgesic benefits with

a more favorable hemodynamic profile, whereas higher doses (e.g., 1 μg/kg) prolong analgesia further but increase the incidence of bradycardia and hypotension.[47,53] Given its systemic absorption, caution is required in hemodynamically unstable or vulnerable patients.

The prolongation of analgesia observed with DEX likely reflects a combination of peripheral and systemic pharmacodynamic effects, whereas its influence on LA absorption remains inconsistent across studies.[45-47,51] Although local vasoconstrictive effects have been proposed, current pharmacokinetic evidence does not consistently demonstrate substantial reductions in systemic LA exposure.

Dexamethasone: Pharmacodynamic Enhancement

Dexamethasone is among the most commonly used adjuvants in regional anaesthesia and has been associated with prolonged analgesia in multiple studies. Its mechanism in FPBs is primarily pharmacodynamic, involving anti-inflammatory effects, reduced nociceptor sensitization, and attenuation of rebound pain.[45,54]

Unlike epinephrine, dexamethasone does not significantly reduce LA absorption through vasoconstriction. Instead, its benefits appear to result from modulation of the inflammatory milieu and peripheral nociceptive pathways. Clinical studies and meta-analyses have demonstrated prolonged analgesia and reduced opioid consumption when dexamethasone is added to TAP or ESP blocks.[55,56]

Combination strategies, particularly the combination of dexamethasone and DEX, have recently attracted increasing interest in FPBs because several studies have reported prolonged analgesia and improved postoperative recovery profiles compared with single-adjuvant techniques.[55-57] Some investigations have also suggested potential modulation of perioperative stress and inflammatory responses with these combinations.[56,57] However, the currently available evidence remains limited by substantial heterogeneity in study design, block type, adjuvant dosing, and outcome assessment. In addition, the relative contributions of peripheral pharmacodynamic mechanisms and systemic absorption remain insufficiently defined. Although additive or synergistic interactions are biologically plausible, the pharmacokinetic consequences of combined adjuvant administration within interfascial compartments have not yet been adequately characterized. Therefore, combination adjuvant strategies should be interpreted cautiously until larger FPB-specific pharmacokinetic and pharmacodynamic studies become available.

Magnesium Sulfate: NMDA-mediated Modulation

Magnesium sulfate ($MgSO_4$) acts primarily through NMDA receptor antagonism, reducing central sensitization and nociceptive transmission. In FPBs, its role appears to be predominantly pharmacodynamic, as it does not consistently alter LA pharmacokinetics or systemic absorption.[58,59]

Clinical evidence, particularly from TAP block studies, suggests that $MgSO_4$ can prolong analgesia and reduce postoperative opioid consumption.[58] However, its efficacy is less consistent than that of α_2 agonists or corticosteroids, and results vary across block types and study designs.[60,61] In ESPB, its effects may be present but are often less pronounced than those observed with DEX.[60,61]

Magnesium generally has a favorable safety profile, but systemic absorption may occur after high-volume FPBs. Excessive exposure can theoretically lead to hypotension, sedation, or neuromuscular weakness, particularly in patients with renal dysfunction or impaired magnesium homeostasis.[60-62] Thus, while $MgSO_4$ may be a useful alternative adjuvant, its role remains less well-defined.

Opioid-derived Adjuvants: Peripheral vs. Systemic Effects

Opioid-derived adjuvants, including buprenorphine, tramadol, and nalbuphine, have been investigated in regional anaesthesia for their potential to prolong analgesia via peripheral opioid receptor activation. However, in FPBs, it is often difficult to distinguish local receptor-mediated effects from those resulting from systemic absorption.[63]

Given the relatively large volumes used in FPBs and the variable vascularity of fascial planes, systemic uptake of these agents may be substantial, leading to effects similar to those of intravenous administration.[1,5,16] Clinical studies comparing tramadol and DEX in the TAP block demonstrate differences not only in analgesic efficacy but also in adverse-effect profiles, including sedation and nausea, which are more likely attributable to systemic exposure.[64] Similarly, combination regimens such as nalbuphine with DEX in ESPB highlight the increasing interest in multimodal adjuvant strategies.[65]

From a pharmacokinetic perspective, the systemic effects of opioid-derived adjuvants may limit their advantage as purely peripheral agents. Adverse effects such as sedation and postoperative nausea and vomiting are likely driven by systemic concentrations, reinforcing the need for cautious dosing and patient selection.[63-65]

Synthesis: Efficacy versus Pharmacokinetic Safety

The literature on FPBs reflects considerable heterogeneity in both efficacy and mechanisms. While some reviews emphasize their effectiveness within multimodal analgesia, others highlight variability in clinical outcomes.[66-69] This divergence is largely attributable to the inherent variability of FPBs, which depend on fascial plane anatomy, injectate spread, and systemic absorption dynamics.[1,16,52]

Accordingly, adjuvant selection should not be based solely on the expectation of prolonged analgesia. Instead, it should incorporate an assessment of pharmacokinetic safety, particularly in high-volume truncal blocks where systemic exposure may be substantial. The key question is whether a given adjuvant will enhance analgesia without narrowing the safety margin by increasing systemic exposure or potentiating adverse effects.[6,16]

Clinical Approach to Adjuvant Selection

A rational approach to adjuvant use in FPBs should consider three principal factors: the characteristics of the fascial plane, the desired duration of analgesia, and patient-specific risk factors. First, the anatomical plane determines the absorption kinetics. Blocks associated with rapid systemic uptake require greater emphasis on safety, including conservative LA dosing and consideration of epinephrine to modulate absorption.[16,39] Although current evidence supports cautious dose reduction in vulnerable populations, precise FPB-specific dosing algorithms remain insufficiently validated. Pharmacokinetic studies in different FPBs demonstrate substantial variability in systemic exposure depending on block type and patient characteristics.[10,18]

In practical terms, a risk-stratified approach may be preferable to fixed dosing strategies. Lower initial LA doses, incremental injection techniques, and consideration of vasoconstrictive adjuvants such as epinephrine may be reasonable in patients at increased risk of systemic toxicity, including elderly individuals, patients with reduced hepatic or renal reserve, patients at extremes of body weight, or patients with conditions associated with altered protein binding.[10,17-21] However, these recommendations are primarily extrapolated from broader regional anaesthesia principles, as validated FPB-specific dosing frameworks remain limited. Second, the desired duration of analgesia should guide adjuvant selection. For shorter procedures, optimization of LA dose and volume may be sufficient. For prolonged analgesia, a single well-established adjuvant—most commonly dexamethasone or DEX—may be preferred over multiple agents.[45,47,51,53,57] Third, patient-related risk factors must be integrated into decision-making. Patients prone to hemodynamic instability may not tolerate DEX well, while those with diabetes may experience systemic corticosteroid effects. Magnesium should be used cautiously in patients with renal impairment.[58,60,62]

Fascial Plane-related Factors

Peripheral nerve blocks and FPBs differ fundamentally in their pharmacokinetic behavior. In conventional nerve blocks, LA is deposited adjacent to a defined neural structure, resulting in relatively predictable spread and absorption. In contrast, FPBs involve the injection of larger volumes into interfascial compartments, where drug distribution and systemic uptake depend on fascial architecture, tissue vascularity, and dynamic fluid behavior within the plane.[1,52]

Fascia consists of a collagen-rich matrix embedded in a hydrated environment containing glycosaminoglycans, adipocytes, and fibroblasts. While the dense collagen network restricts macroscopic fluid flow, it permits diffusion of small molecules such as LAs through microscopic channels. Following injection, the LA distributes along the fascial plane, diffuses into adjacent tissues, and is absorbed into the systemic circulation. The relative contribution of these pathways varies according to the anatomical location and local perfusion. Because FPBs require larger injectate volumes, systemic absorption may be greater than that observed with traditional nerve blocks.[1,52]

Beyond anatomical and physiological determinants, the pharmacokinetic profile of an FPB is also strongly influenced by operator-dependent factors. Because ultrasound-guided FPBs rely on accurate identification of the correct interfascial plane and on real-time visualization of needle-tip position during injection, even subtle differences in technique (needle-tip depth), injection pressure, the pattern of hydrodissection, and unintended intramuscular or subcutaneous deposition can alter the surface area of fascia exposed to LA, the rate of capillary absorption, and ultimately the systemic concentration profile.[3,66] *In vivo* observations and microdialysis measurements have shown that interstitial and plasma concentrations may vary substantially even when identical doses are injected by experienced practitioners, underscoring the inherent variability of these techniques.[1]

The TAP block is one of the most extensively studied FPBs and illustrates key pharmacokinetic principles. In this technique, LA is injected between the internal oblique and transversus abdominis muscles, targeting thoracolumbar nerve branches. This plane is relatively well vascularized by intercostal and deep circumflex iliac vessels, which contribute to systemic uptake.[70] C_{max} values typically occur within 20-60 minutes, with reported ropivacaine concentrations ranging from approximately 0.4 to 1.6 μg mL^{-1}, depending on dose and technique.[50,71] Although these levels generally remain below toxicity thresholds, the available evidence suggests that bilateral blocks and continuous infusions may lead to higher systemic exposure. In obstetric patients, bilateral TAP blocks have been associated with plasma concentrations approaching toxic levels, and significant interindividual variability has been observed during continuous infusions.[71,72] These findings support individualized dosing strategies in high-volume FPBs.

The rectus sheath block (RSB), another abdominal wall technique, exhibits a similar pharmacokinetic profile, albeit with delayed absorption. When performed with comparable volumes and concentrations, RSB yields C_{max} values similar to those of the TAP block but with a longer T_{max}, likely

reflecting differences in compartment characteristics and vascularity.[73]

Quadratus lumborum block (QLB) targets the fascial compartments surrounding the quadratus lumborum muscle and the thoracolumbar fascia. Although several approaches exist, pharmacokinetic data suggest that C_{max} values generally remain below toxic thresholds.[74] The addition of epinephrine has been shown to reduce systemic absorption and prolong analgesia, further illustrating the interaction between pharmacokinetics and fascial plane characteristics.[75]

Thoracic FPBs are often performed in highly vascular regions, resulting in relatively rapid systemic absorption. The ESP block, located adjacent to the dorsal branches of intercostal and lumbar arteries, demonstrates rapid uptake, with T_{max} values frequently occurring within 5-10 minutes.[32] Despite this rapid absorption, reported C_{max} values of levobupivacaine typically remain below toxic thresholds, usually around 1-1.5 μg mL^{-1}.[10,50] This pattern suggests that rapid uptake does not necessarily translate into toxic exposure, but underscores the importance of considering both the rate and the extent of absorption.

A recent systematic review of pharmacokinetic studies of single-injection ESP block identified nine eligible studies with amide LAs and confirmed that a short T_{max} is a near-universal feature of the technique: in most studies, the peak concentration coincided with the earliest sampling time point, and pharmacokinetic modelling estimated T_{max} as early as 1 minute after injection.[76] The same review reported that eight patients in two studies exceeded total LA toxicity thresholds, although in most cases this was driven by methodological choices (venous rather than arterial sampling, or the use of conservative threshold definitions). More importantly, only two of the included studies measured free (unbound) plasma concentrations: in four pediatric patients receiving 1.5 mg kg^{-1} ropivacaine, the peak unbound arterial concentration exceeded the central nervous system toxicity threshold of 0.6 μg mL^{-1} as defined by Knudsen et al.[77] even though total concentrations remained below accepted limits; however, this finding is based on only four paediatric patients in a pilot pharmacokinetic study judged at unclear risk of bias, and should therefore be interpreted as hypothesis-generating rather than definitive. In adults, the median free bupivacaine concentrations were approximately 20-fold lower than reported toxicity thresholds.[76]

Similarly, interpectoral and pectoserratus plane blocks, performed in the pectoral region, are associated with rapid systemic uptake due to the dense vascular network supplied by thoracoacromial, lateral thoracic, and intercostal arteries. C_{max} values are generally reached within 10-30 minutes, although total systemic exposure typically remains within safe limits.[39,78]

The serratus anterior plane (SAP) block further illustrates the influence of vascularity and dose on pharmacokinetics. Performed in a highly vascular region, the SAP block demonstrates relatively rapid absorption, with C_{max} values typically occurring within 10-20 minutes and ranging from 1.5 to 2.0 mg/L, depending on dose and concentration.[79,80] In pediatric cardiac surgery, plasma concentrations around 2.1 mg/L have been reported without signs of systemic toxicity.[81]

The deep parasternal intercostal plane (PIP) block generally results in lower systemic exposure despite bilateral administration. Mean peak bupivacaine concentrations have been reported around 0.6 μg mL^{-1} following doses up to 2.5 mg kg^{-1}. However, two patients had concentrations >2.0 μg mL^{-1} within 15 minutes of the block. The injection site is located close to the internal mammary artery.[82]

Taken together, these data indicate that FPBs fall along a spectrum of systemic absorption, which has direct implications for monitoring and dosing. At the higher-absorption end lie the thoracic and chest-wall techniques: the ESP block shows the most rapid uptake, with T_{max} frequently occurring within the first few minutes and modelled peaks estimated as early as one minute, while the SAP and interpectoral/pectoserratus blocks similarly reach C_{max} within 10-30 minutes, reflecting the dense vascularity of these regions. At the lower-absorption end are the abdominal wall blocks (TAP, rectus sheath, and QLB), in which C_{max} typically occurs later (approximately 20-60 minutes for the TAP block and later still for the RSB), and peak concentrations at equivalent doses tend to be lower.[50,71,73,74] However, a rapid T_{max} does not necessarily imply a higher C_{max}; for example, after ESP blocks, rapid uptake is usually accompanied by peak concentrations below accepted thresholds. In addition, the extent of absorption still matters at the tails of the distribution, as illustrated by the PIP block, in which mean exposure is low yet individual patients exceeded 2.0 μg mL^{-1} within 15 minutes,[82] likely reflecting proximity to the internal mammary artery.

Clinically, this spectrum translates into a graded approach to monitoring and dose selection. Thoracic blocks with higher absorption warrant vigilance in the early post-injection period and the use of the lowest effective concentration, together with consideration of epinephrine in high-volume single-injection techniques; the slower-absorbing abdominal wall blocks provide a somewhat wider temporal margin but still require caution when performed bilaterally or at high volume. Because the highest plasma concentrations after slower-absorbing or continuous techniques may occur well beyond the intraoperative period, the duration of monitoring should be extended accordingly.

The FICB is performed to reach the nerves of the lumbar plexus distally with a single injection.[83] FICB demonstrates

that systemic exposure may vary substantially depending on technique, patient population, and dosing strategy. Studies of early FICB using landmark techniques in pediatric patients, employing 0.7 mL/kg of 0.375% or 0.5% ropivacaine reported peak ropivacaine concentrations as high as 4.3-5.6 μg mL^{-1}, raising concerns about systemic toxicity.[84] In a more recent study, none of the patients had total or free ropivacaine levels above the toxic concentration after suprainguinal FICB with 40-mL of 0.5% ropivacaine.[85] These findings highlight the importance of technique optimization and dose adjustment, particularly in vulnerable populations.

An additional determinant of pharmacokinetic variability in FPBs is the heterogeneity of drug distribution within fascial compartments. Microdialysis studies have shown that interstitial LA concentrations may vary significantly within the same plane, even across small distances.[86] This uneven distribution implies heterogeneous neural exposure to effective drug concentrations, contributing to variability in analgesic efficacy and systemic absorption.

The pharmacokinetics of continuous catheter infusions warrant separate consideration. A review of TAP and paravertebral catheters found that manufacturer-recommended dosing limits were exceeded in 28% of ropivacaine infusions and 51% of bupivacaine infusions, with LAST occurring in 0.48% and 0.37% of patients, respectively.[87] These data suggest that, for continuous catheter techniques, the cumulative 24-hour dose may be a more clinically relevant determinant of toxicity risk than the size of any single bolus.[26] The main risk factors identified were a high 24-hour cumulative dose, bilateral catheters, cardiac surgery, use of cytochrome P-450 inhibitors, and hypoalbuminemia.[87,88] Continuous infusions also tend to produce higher plasma concentrations than programmed intermittent boluses at equivalent total doses,[42] and there is very little pharmacokinetic data available for infusions running longer than 20 hours.[26] Unlike single-injection FPBs, continuous interfascial infusions introduce an additional risk of delayed accumulation and a progressive rise in plasma concentration over several days, particularly when bilateral catheters are used or clearance is impaired.[26] In bilateral SAP catheters with programmed intermittent bolus delivery, Chen and Tsui[28] found that lidocaine plasma concentrations peaked around days 2-3 at a mean concentration of approximately 2.6 μg mL^{-1}, with considerable variability between patients (SD 32-44%), highlighting the importance of ongoing monitoring during prolonged infusions.

A pragmatic, risk-stratified approach is useful when translating these pharmacokinetic data into clinical practice. FPBs can be stratified by their expected systemic absorption profile: thoracic blocks typically produce a rapid Tmax and should be regarded as higher absorption techniques, whereas TAP, RSB, and QLB show slower absorption and lower peak concentrations at equivalent doses.[42] Patient-level risk should be assessed. On this basis, the following principles, rather than fixed algorithms, may be suggested: (i) calculate the total LA dose on a weight-adjusted basis, using ideal body weight in cases of obesity; (ii) apply a downward adjustment of approximately 25-30% in identified high-risk patients and in any bilateral or continuous technique; (iii) prefer the lowest effective concentration over the lowest effective volume when reducing dose, in order to preserve spread; and (iv) consider the addition of epinephrine in high-volume single-injection thoracic FPBs. These suggestions are presented as expert-opinion recommendations rather than validated dosing algorithms, which remain an unmet need.

Explicit monitoring after high-volume FPBs is warranted because the highest plasma concentrations may not coincide with the operating-room phase. After single-injection bilateral or high-volume FPBs, continuation of standard ASA monitoring is recommended throughout the block and for at least 30-60 minutes thereafter in a monitored environment, with immediate availability of resuscitation equipment and 20% lipid emulsion in accordance with current LAST management guidelines.[11,89] For continuous interfascial infusions, monitoring should extend beyond the immediate postoperative period, and ward staff should be educated to recognize early symptoms of LAST.

Despite growing clinical use, pharmacokinetic data for many FPBs remain limited. In particular, few studies report unbound (free) plasma concentrations, which are more directly associated with systemic toxicity than total drug levels. Furthermore, variability in study design, sampling protocols, and patient characteristics complicates comparisons across techniques. Future research should focus on standardized pharmacokinetic methodologies, the routine reporting of unbound drug concentrations, and improved characterization of dose-concentration relationships across different fascial planes, with the goal of developing prospectively validated, FPB-specific dosing and monitoring frameworks.

Heterogeneity in the Literature

Interpretation of the current pharmacokinetic literature on FPBs is substantially limited by heterogeneity in study methodology, block techniques, dosing strategies, sampling protocols, and analytical reporting standards.[5,9,37,42] As a result, direct comparisons between studies are often difficult and may lead to overinterpretation of apparent differences in systemic absorption or toxicity risk.

One of the major sources of heterogeneity relates to variability in LA dosing and injection volume. Studies investigating TAP, ESPB, SAP, and QLB frequently use

different concentrations, total doses, and bilateral versus unilateral injection strategies, all of which may substantially influence reported plasma concentrations.[5,9,13,14,16,25,38,40,48,49,75] For example, some TAP block studies reported peak plasma ropivacaine concentrations approaching potentially toxic thresholds, whereas others reported substantially lower systemic exposure despite using similar techniques.[5,9,13,25,38] However, these findings are not directly comparable because the studies differed considerably in total dose administered, injection volume, patient body habitus, and timing of blood sampling.

Similarly, variability in pharmacokinetic sampling methodology represents another important limitation. Reported C_{max} and T_{max} values may be highly dependent on plasma-sampling frequency and duration.[9,42] Studies employing sparse sampling protocols may fail to identify true peak concentrations, particularly in FPBs, where systemic absorption may continue over prolonged periods because of the large interfascial surface area.[5,9,26] Consequently, differences in reported C_{max} values between studies may reflect methodological variation rather than true pharmacokinetic differences.

Additional heterogeneity arises from inconsistencies in reporting total versus free plasma LA concentrations. Some studies report only total plasma concentrations, whereas others additionally measure unbound (free) fractions, which may correlate more closely with systemic toxicity risk.[6,9,11,37,44] Variability in assay methodology and reporting standards therefore complicates interpretation of toxic thresholds and limits the ability to establish universally applicable pharmacokinetic safety margins across FPBs.[6,9,12,42]

Comparisons between different FPBs are similarly challenging. Apparent differences in systemic absorption between TAP, ESPB, PECS, SAP, and QL blocks may reflect not only anatomical differences in fascial plane vascularity but also substantial methodological heterogeneity among studies.[1-3,52,66,67,90] Factors such as needle approach, exact injectate location, spread pattern, patient positioning, ultrasound guidance technique, and operator experience may influence systemic uptake and clinical outcomes.[1-3,52,66,67,90] Furthermore, the anatomical continuity of some fascial planes may facilitate unpredictable injectate spread, thereby increasing variability in both pharmacokinetic and analgesic findings.[1,52,90]

Continuous catheter studies introduce an additional layer of complexity. Continuous infusion protocols vary considerably in background infusion rate, intermittent bolus strategy, cumulative LA dose, and infusion duration.[27,28] These differences substantially influence systemic exposure and make cross-study comparisons particularly difficult. In addition, accumulation kinetics during prolonged interfascial infusion remain poorly characterized in many FPBs.[26-28]

Substantial heterogeneity also exists in patient populations included in current studies. Age, body composition, hepatic function, renal function, pregnancy status, and perioperative hemodynamic conditions may all influence LA disposition and systemic absorption.[12,15,17-22,42] For instance, elderly patients and individuals with reduced plasma protein binding capacity may exhibit altered pharmacokinetics and increased susceptibility to systemic toxicity despite similar administered doses.[10,17,22]

The same limitations apply to studies investigating adjuvants. Considerable variability exists in adjuvant dosing, combinations, timing of administration, and outcome definitions. In DEX studies, some investigators evaluate fixed doses, whereas others use weight-based dosing regimens, complicating the interpretation of dose-response relationships and systemic effects.[45-47,51,53,57] Likewise, studies examining dexamethasone, $MgSO_4$, ketamine, or combination adjuvant strategies differ substantially in methodology, which makes pooled interpretation difficult.[45,54-62]

Importantly, many studies focus primarily on analgesic outcomes without an integrated pharmacokinetic analysis. Consequently, prolonged analgesia is often interpreted as evidence of local interfascial mechanisms, despite limited assessment of systemic drug exposure. This distinction is particularly relevant for adjuvants such as DEX, clonidine, opioid-derived agents, $MgSO_4$, and ketamine, in which clinically relevant systemic absorption may contribute significantly to observed analgesic effects.[45-47,51,53-65]

Taken together, the current FPB literature should be interpreted cautiously. Although existing studies provide valuable insights into interfascial analgesia and adjuvant use, substantial methodological heterogeneity limits definitive conclusions regarding comparative pharmacokinetics, toxicity thresholds, and mechanistic interpretations. Future investigations would benefit from standardized reporting of block technique, LA dosing, plasma sampling protocols, free versus total drug concentrations, and clinically relevant pharmacokinetic-pharmacodynamic correlations.

Local Anaesthetic Systemic Toxicity

LAST is a serious complication of regional anaesthesia and is recognized in the European Resuscitation Council 2025 guidelines as a "special circumstance" due to its distinct pathophysiology and management.[91] The American Society of Regional Anesthesia and Pain Medicine defines LAST as systemic toxicity resulting from elevated plasma concentrations of LAs, caused by inadvertent intravascular injection or significant systemic absorption, leading to CNS and/or cardiovascular dysfunction.[6]

The clinical presentation of LAST is variable and may involve neurological, cardiovascular, or combined manifestations. Traditional descriptions suggest an initial phase of CNS excitation—such as perioral numbness, tinnitus, agitation, or seizures—followed by CNS depression and subsequent cardiovascular compromise. However, systematic analysis of published cases demonstrates that this sequence is not universal.[92] Contemporary review literature also notes that, with the increasing use of truncal and interfascial techniques, atypical and delayed toxicity patterns are increasingly being recognised, and early neurological warning signs may be masked in sedated or anaesthetised patients.[93]

In FPBs, the risk of LAST is closely linked to pharmacokinetic characteristics. While ultrasound guidance reduces the likelihood of intravascular injection, it does not eliminate the risk of toxicity.[6,93] Pharmacokinetic studies demonstrate that high-volume interfascial injections can result in measurable systemic absorption, with plasma concentrations in some cases approaching toxic thresholds.[5] Therefore, LAST in FPBs may arise not only from direct intravascular injection but also from significant systemic uptake.

Macfarlane et al.[93] noted that a growing proportion of LAST reports now arise from fascial-plane and field blocks, with delayed-onset presentations becoming increasingly common, partly because ultrasound guidance reduces but does not eliminate inadvertent intravascular injection, and partly because early neurological warning signs may be masked in sedated or anaesthetised patients. Pharmacokinetic studies demonstrate that plasma concentrations, in some patients, approach or exceed established toxicity thresholds, even in the absence of overt clinical symptoms.[5,6]

Reported cases of LAST associated with TAP blocks illustrate the risks inherent in high-volume bilateral techniques. Griffiths et al.[71] documented symptomatic neurotoxicity in postpartum patients receiving bilateral ropivacaine TAP blocks (2.5 mg kg^{-1}) after caesarean section, with peak plasma ropivacaine concentrations of 2.2-3.8 μg mL^{-1} within 60 minutes; neurological symptoms resolved spontaneously without intravenous lipid emulsion (ILE). Boleyn et al.[89] reported LAST-induced cardiac arrest following bilateral TAP block with liposomal bupivacaine in a 68-year-old man undergoing open sigmoidectomy, successfully treated with advanced cardiac life support and 20% ILE. Regarding asymptomatic threshold exceedances, Hessian et al.[72] found that four of 20 patients exceeded the accepted threshold for total ropivacaine concentration (3.4 mg/L) during 72-hour bilateral TAP infusions without neurological symptoms, highlighting the dissociation between total plasma concentration and clinical toxicity. Torup et al.[94] similarly demonstrated that bilateral TAP blocks with 20 mL of 0.5% ropivacaine per side (total 200 mg) produced potentially toxic peak total concentrations (above 2.2 μg mL^{-1}) in six of 18 patients (33%); one patient experienced a 33% drop in mean arterial pressure, although none showed overt LAST. In a patient with cardiac, respiratory, and renal dysfunction, Ishida et al.[95] documented peak total ropivacaine concentrations of 2.5 μg mL^{-1} at 15 minutes following bilateral TAP blocks with only 1.8 mg kg^{-1}, a potentially neurotoxic level despite a conventionally low dose; the patient became drowsy but recovered without intervention.

ESPB-related LAST cases span both adult and neonatal populations and encompass single-injection and continuous catheter techniques. Yawata et al.[96] described neurological LAST (dizziness, speech disturbance, and loss of consciousness) within minutes following 30 mL of 0.5% levobupivacaine (150 mg, 2.6 mg kg^{-1}) for lumbar spinal surgery in a 58 kg patient; symptoms resolved with supportive care without ILE. Crowe and Mislovič[97] reported the first neonatal LAST case following ESPB: a 6-day-old, 4.0 kg neonate developed acute cardiovascular compromise (falling oxygen saturation, hypotension) within minutes of receiving 1 mg kg^{-1} levobupivacaine for laparotomy, successfully treated with epinephrine and ILE 1.5 mL/kg. In continuous-catheter settings, Smith et al.[98] described delayed-onset LAST from an ESPB lidocaine catheter in a post-cardiac surgery patient, in whom toxicity manifested several days postoperatively due to impaired hepatic lidocaine clearance secondary to liver shock from worsening pulmonary hypertension; this illustrates that organ dysfunction can convert a standard infusion rate into a toxic cumulative dose.

Pharmacokinetic studies further demonstrate that subclinical threshold exceedances are not rare in FPB practice. In a systematic review of TAP block and RSB pharmacokinetics, Rahiri et al.[5] found that mean C_{max} values were generally below accepted toxicity thresholds but that individual patients exceeded these limits in several studies, particularly with high-volume bilateral techniques. In a systematic review of single-injection ESPB pharmacokinetics, De Cassai et al.[76] reported that eight patients across two studies exceeded total LA toxicity thresholds. Importantly, in the two studies that measured free (unbound) plasma concentrations, paediatric patients receiving 1.5 mg kg^{-1} ropivacaine had peak unbound arterial concentrations exceeding the CNS toxicity threshold of 0.6 mg/L, even when total concentrations remained within conventional limits, whereas adult free bupivacaine concentrations remained well below toxic levels.[14] Bailey et al.[9] synthesised pharmacokinetic data across multiple FPB types and concluded that while mean plasma concentrations of ropivacaine, levobupivacaine, and bupivacaine typically remain below established thresholds, a consistent minority of patients exceed accepted toxicity levels without overt LAST symptoms; risk is substantially amplified by fixed-volume dosing, higher LA concentrations, bilateral or continuous

infusions, and patient comorbidities such as pregnancy, extremes of age, and hepatic or cardiac disease. Collectively, these data confirm that total plasma concentration alone is an insufficient safety surrogate: patients with reduced protein binding or impaired clearance may have a clinically relevant free drug fraction substantially higher than their total concentration would suggest.

Management requires immediate, structured intervention (Table 3). Current guidelines recommend cessation of LA administration, airway management with optimization of oxygenation and ventilation, and prompt seizure control.[6,91] Correction of hypoxia and acidosis is essential, as both exacerbate toxicity.[6] In cases of cardiovascular instability or cardiac arrest, advanced life support should be initiated, recognizing LAST as a toxin-mediated condition.[91] ILE therapy is a cornerstone of treatment for severe toxicity.[6,91]

ILE is believed to reverse severe LAST through complementary pharmacokinetic and pharmacodynamic mechanisms rather than through a single "lipid sink" effect.[99-102] The most widely accepted framework is the dynamic lipid shuttle, whereby an expanded intravascular lipid phase partitions highly lipophilic LAs away from toxicity-sensitive organs such as the heart and brain, lowers their freely available concentration at these target sites, and promotes their redistribution through the circulation to the liver, skeletal muscle, and adipose tissue for subsequent storage, metabolism, and detoxification.[99,100,102] In parallel, ILE appears to exert direct cardiocirculatory effects by enhancing both inotropy and lusitropy, thereby improving myocardial contractile and relaxation performance, supplying fatty-acid substrate for ATP generation, restoring intracellular calcium homeostasis, attenuating mitochondrial dysfunction and permeability transition pore opening, and partially counteracting toxic LA induced vasoplegia and conduction abnormalities through modulation of nitric oxide-dependent vasorelaxant signaling and, at least in part, sodium-channel dysfunction.[99-101,103] At the vascular and electrophysiologic levels, ILE may also partially reverse LA-induced vasodilatory responses, plausibly through modulation of nitric oxide-dependent vasorelaxant signaling, and attenuate ion-channel dysfunction, particularly sodium-channel blockade, thereby contributing to restoration of vascular tone, improvement in conduction stability, and earlier hemodynamic stabilization.[99-101,103]

Conclusion

FPBs represent a paradigm shift in regional anaesthesia, characterized by variable and often significant systemic absorption due to high-volume interfascial injection. Pharmacokinetic variability appears to be shaped by patient-, drug-, fascial plane-, technical-, and adjuvant-related factors, each influencing C_{max}, T_{max}, and ultimately toxicity risk (Table 4). In particular, advanced age, impaired protein binding, highly vascular interfascial planes, bilateral or continuous techniques, and higher total doses may increase systemic exposure and susceptibility to LAST. Interpretation of the current pharmacokinetic literature is further complicated by substantial heterogeneity in study design, including differences in LA dose, concentration,

Table 3. Structured Management Approach to Local Anaesthetic Systemic Toxicity

Clinical stage	Recommended management	Dose/monitoring
Initial response	Immediately stop local anaesthetic administration. Call for help. Obtain LAST rescue kit. Consider cardiopulmonary bypass team. Consider early lipid emulsion therapy.	—
Lipid emulsion therapy (20%)-adults >70 kg	Administer intravenous lipid emulsion.	Bolus 100 mL over 2-3 min, followed by infusion 250 mL over 15-20 min. If instability persists, repeat bolus and double infusion rate.
Lipid emulsion therapy (20%)-<70 kg	Administer intravenous lipid emulsion.	Bolus 1.5 mL kg^{-1} over 2-3 min, followed by infusion 0.25 mL kg^{-1} min^{-1}. Consider infusion pump if <40 kg. Repeat bolus if instability persists. Maximum cumulative dose 12 mL kg^{-1}.
Seizure management	Ensure airway protection. Administer benzodiazepine (e.g., lorazepam 0.1 mg kg^{-1} IV, midazolam 0.05-0.1 mg kg^{-1} IV). If only propofol available, use small incremental doses (e.g., 20 mg).	Avoid large doses in cardiovascular instability.
Cardiovascular instability (arrhythmia / hypotension)	LAST resuscitation differs from standard ALS. Use reduced-dose epinephrine. Avoid additional local anaesthetics, vasopressin, beta-blockers, and calcium channel blockers.	Start epinephrine ≤1 μg kg^{-1}.
Post-stabilisation monitoring	Continue lipid infusion for at least 15 min after haemodynamic stability.	Observe ≥2 h after seizure; 4-6 h after cardiovascular instability; longer after cardiac arrest.

ALS, advanced life support; LAST, local anaesthetic systemic toxicity; IV, intravenous

Table 4. Determinants of Pharmacokinetics in Fascial Plane Blocks

Factor category	Specific factor	Mechanism affecting pharmacokinetics	Effect on C_{max}	Effect on T_{max}	Clinical implications in FPBs
Patient-related factors	Age (elderly)	↓ Hepatic/renal perfusion, ↓ clearance, ↓ muscle reservoir	↑	↔/↑	Accumulation risk, dose reduction (≈10-20%)
	Pediatrics (especially <6 months)	↓ Protein binding, immature metabolism	↑ (free fraction ↑)	↑	Narrow safety margin, cautious dosing
	Pregnancy	↓ Albumin and AAG, ↑ cardiac output	↑ (free fraction ↑)	↓	Increased systemic absorption, toxicity risk
	Body composition (obesity)	↑ Cardiac output, altered distribution	↑ (if TBW-based dosing)	↓	Dose based on lean/adjusted weight
	Low body mass/ malnutrition	↓ Protein binding, ↓ tissue buffering	↑	↔	Higher free drug fraction, toxicity risk
	Hepatic disease	↓ Metabolism of amide LAs	↑ (with repeated dosing)	↔	Accumulation, cautious use in infusions
	Renal disease	Altered protein binding, acidosis	↑ (free fraction ↑)	↓	Increased toxicity susceptibility
	Cardiac disease	↓ Perfusion → ↓ clearance	↑	↔	Increased cardiotoxic risk
LA-related factors	Lipid solubility	↑ Tissue penetration, slower redistribution	↑	↑	Prolonged effect, higher toxicity risk (e.g., bupivacaine)
	Protein binding (AAG)	↓ Free fraction when high	↓ (free fraction)	↔	Higher binding=longer duration, safer profile
	Metabolic pathway	Hepatic vs. extrahepatic metabolism	↑ (if impaired metabolism)	↔	Drug-specific accumulation risk
Adjuvant-related factors	Epinephrine	Vasoconstriction → ↓ vascular uptake	↓ (variable)	↑	Reduces the risk of systemic toxicity
	Dexmedetomidine	Systemic absorption + α_2 effect	Variable	Variable	Prolonged analgesia, HD effects
	Dexamethasone	Anti-inflammatory (PD effect)	↔	↔	Prolonged analgesia
	Magnesium	NMDA antagonism	↔	↔	Prolonged analgesia, PD contribution
	Opioid-derived adjuvants	Systemic absorption	↔	↔	Effects often systemic rather than local
Fascial plane-related factors	Vascularity of plane	Determines systemic uptake rate	↑ in highly vascular planes	↓	Faster absorption (e.g., ESP, PECS)
	Plane compliance/ volume	Larger space → wider distribution	↑ (dose-dependent)	↑	High-volume techniques increase systemic exposure and toxicity risk
	Bilateral blocks	Increased total dose	↑	↔	Higher systemic exposure
	Continuous infusion	Drug accumulation over time	↑ progressively	↔	Increased LAST risk
	Injection technique (bolus vs. infusion)	Alters absorption kinetics	↑ (continuous infusion)	↔	Intermittent bolus may be safer
Technical factors	Total dose (mg)	Primary determinant of systemic exposure	↑	↔	Most critical predictor of toxicity
	Volume vs. concentration	Volume affects spread, dose affects C_{max}	↑ (with total dose)	↑ (volume-dependent)	Balance required for efficacy vs. safety
	Injection rate	Faster injection → higher peak levels	↑	↓	Fractionated injection recommended

AAG, alpha-1-acid glycoprotein; ESP, erector spinae plane; FPB, fascial plane block; HD, hemodynamic; LA, local anesthetic; LAST, local anesthetic systemic toxicity; PD, pharmacodynamic; PECS, pectoral; TBW, total body weight; C_{max}, peak plasma concentration; T_{max}, time to peak plasma concentration; NMDA, N-methyl-D-aspartate

sampling intervals, assay methodology, patient populations, and reporting of total versus free plasma concentrations. Therefore, a patient-centered approach that integrates dose optimization, appropriate adjuvant selection, and vigilant monitoring is essential. Detailed clinical guidance on the pharmacokinetics and safety of FPBs is presented in Supplementary Material 1. Future research should focus on standardized pharmacokinetic models and harmonized reporting strategies to enable more precise, evidence-based dosing recommendations in FPBs.

Footnotes

Authorship Contributions: Concept – M.Z., O.K.; Design – M.Z., E.N.Z., O.K.; Data Collection or Processing – M.Z., H.U.Y., O.G., A.A., E.N.Z., C.T., E.Ş.Ö.S., O.K.; Analysis or Interpretation - M.Z., H.U.Y., O.G., A.A., E.N.Z., C.T., E.Ş.Ö.S., O.K.; Literature Review - M.Z., H.U.Y., O.G., A.A., E.N.Z., C.T., E.Ş.Ö.S., O.K.; Writing - H.U.Y., O.G., A.A., E.N.Z., C.T., E.Ş.Ö.S., O.K.

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Anaesthesiologists Under Strain: Burnout and Its Associated Factors in a Conflict-affected Context, a Cross-sectional Study

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Abstract

Objective: Anaesthesiologists are particularly vulnerable to burnout due to extended working hours, high-pressure situations, limited patient interactions, multiple responsibilities, and inherent tensions in relationships with surgeons and administrators. The study aimed to explore burnout levels and the factors associated with them among anaesthesiologists in a conflict-affected setting.

Methods: A cross-sectional study was carried out between May 2024 and August 2025 using a voluntary, anonymous, and electronic survey. The Copenhagen Burnout Inventory, demographics, and practice environment questions were included. Statistical analyses were conducted to identify factors associated with personal, work-related, and client-related burnout. A significance threshold of 0.05 was applied.

Results: Among the 82 anaesthesiologists, 57% experienced personal burnout, 51% experienced work-related burnout, and 28% experienced client-related burnout. Positive and significant associations were observed between working longer hours and personal burnout (adjusted β [95% confidence interval (CI)]=15.6 (0.88; 30.3); *P*=0.04) and work-related burnout [adjusted ß (95% CI)=17.7 (3.68; 31.7); *P*=0.01], as well as between covering five or more night shifts per month and client-related burnout [adjusted ß (95% CI)=15.3 (3.86; 26.7); *P*=0.009].

Conclusion: The findings reveal concerning levels of burnout among anaesthesiologists in conflict-affected regions, which is particularly important given the ongoing regional conflict and limited conflict-specific data, and highlight the potential role of modifiable predictors and associated factors. Targeted interventions are essential to support anaesthesiologists' well-being and ensure the effective functioning of healthcare institutions in such settings. Future studies with larger, randomly selected samples are warranted to further explore this issue.

Keywords: Anaesthesiologists, client-related burnout, conflict-affected region, personal burnout, work-related burnout

Main Points

- High levels of burnout were observed among anaesthesiologists, with personal and work-related burnout affecting more than half of participants, and client-related burnout affecting over one-quarter of participants.
- Workload-related factors were independently associated with burnout, with longer working hours associated with increased personal and work-related burnout, and frequent night shifts (≥5 per month) with higher client-related burnout.
- The findings underscore the cumulative psychological burden of practicing in a conflict-affected setting, where prolonged instability may exacerbate occupational stress.
- Interventions targeting modifiable work conditions are warranted to mitigate burnout and support anaesthesiologists' well-being; further research using larger, randomized samples is also warranted.

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Introduction

The demanding requirements and excessive levels of stress among healthcare professionals, especially physicians, often place a strain on their mental and physical wellbeing, making them more vulnerable to burnout.[1] Anaesthesiologists are particularly susceptible to burnout due to prolonged working hours, high-pressure environments, and frequent exposure to critical situations.[2-4] Additionally, multiple responsibilities, including clinical, academic, research, and administrative duties, coupled with limited patient interaction and insufficient compensation, can further exacerbate burnout.[5,6] The inherent tension in relationships with surgeons and interventionalists can compound the psychological strain experienced by anaesthesiologists.[5,7]

Burnout is a condition of persistent physical and psychological fatigue resulting from chronic stress, often affecting personal, work, and client-related areas.[8] Burnout can compromise patient care by causing delayed decisions, impaired judgment, poor communication, and inadequate record-keeping, all of which increase the risk of adverse events.[9] Previous research indicated that 34% of medical school faculty suffered from emotional exhaustion, 66.3% from depersonalization, and 92.4% from reduced personal accomplishment, while 30.5% exhibited high burnout in all dimensions.[10] A systematic review conducted among anaesthesiologists found a prevalence ranging from 10 to 41% of high-risk of burnout, and up to 59% of at least moderate risk.[2] While the exact prevalence of burnout among anaesthesiologists remains hard to determine in low- and middle-income countries (LMICs) due to methodological limitations, studies suggest that a significant proportion may be affected.[11-13] Factors positively associated with burnout were long working hours, working as a younger practice, and having children; while no associations were observed with gender or marital status.[2] Moreover, anaesthesiologists in LMICs face additional challenges that contribute to burnout. Heavy workloads, resource shortages, and low income can take a toll on LMICs anaesthesiologists' physical and mental well-being, in addition to their personal life outcomes.[13-15]

Lebanon has experienced unprecedented crises since 2019, encompassing the coronavirus disease-19 pandemic with its mental health repercussions, the economic meltdown including sharp currency devaluation and banking sector deterioration, and the aftermath of the 2020 Beirut Port explosion. These crises have resulted in soaring inflation, scarcities of essential goods, and an exodus of skilled labor, including healthcare professionals. Political corruption and historical conflicts have compounded the strain on the economy, deepening unemployment and poverty amid persistent social unrest.[16-18] Moreover, in late 2024, bombings in Beirut and other regions further heightened stress among Lebanese healthcare workers.[19] In 2025, burnout levels among Lebanese residents and fellows were assessed using the Maslach Burnout Inventory (MBI), revealing that 58% of participants experienced high levels of emotional exhaustion, 28% demonstrated high depersonalization, and 50% noted low personal accomplishment.[20] Among anaesthesiology residents, 71% reported personal burnout, 68% reported work-related burnout, and 36% experienced client-related burnout.[19] Additionally, earlier data from 2020 showed that 19% of surveyed physicians experienced high burnout levels.[21] While these studies confirm that burnout is prevalent among healthcare professionals in Lebanon, they predominantly include participants from mixed specialties or focus on trainees, and do not capture the specific occupational exposures and stressors unique to attending anaesthesiologists. Furthermore, existing literature has largely examined burnout in stable or single-crisis settings, without accounting for the compounded and prolonged impact of overlapping economic collapse, workforce migration, and active conflict.

Anaesthesiologists represent a particularly relevant group to study in this context, as their role extends beyond routine perioperative care to include critical care management, emergency response, and involvement in mass casualty incidents, responsibilities that are amplified in conflict-affected and resource-constrained environments.[22] Despite this, there remains a lack of specialty-specific evidence assessing burnout and its determinants among anaesthesiologists practicing under such compounded stressors. Therefore, this study addresses a critical gap by providing a specialty-specific evaluation of burnout among anaesthesiologists practicing within a context characterized by overlapping crises, workforce depletion, and heightened clinical demands. By examining both individual and system-level determinants, this work offers a more comprehensive perspective on burnout compared to prior studies.

Thus, this study aimed to investigate the level of burnout. Specifically, it aimed to (1) assess burnout using a validated multidimensional tool, 2) identify occupation- and context-specific factors associated with burnout, including workload and work-environment variables and 3) generate context-informed recommendations that may be transferable to other conflict-affected or resource-limited settings.

Methods

Study Design

A cross-sectional study was conducted among anaesthesiologists practicing in Lebanon between May 2024 and August 2025. Anaesthesiology was selected because of its high exposure to occupational stressors, critical care workload, and perioperative decision-making demands,

which make it a high-risk specialty for burnout. In the Lebanese context, this specialty is particularly affected by post-crisis health-system strain and workforce migration, which have increased workload pressures and staffing shortages, making this population particularly relevant for burnout assessment.

Sample Size Calculation

In 2024, the Lebanese Society of Anaesthesiologists database included approximately 400 anaesthesiologists. In Lebanon, a prior study on physician burnout indicated that 90.1% met the established criteria.[21] Based on calculations using Epi Info software, a minimum of 78 participants was required to ensure a 90% confidence interval, and a 5% margin of error for the expected burnout prevalence estimate. A total of 82 anaesthesiologists participated in the study; the final sample represents approximately 20.5% of the known anaesthesiology workforce in Lebanon. However, because recruitment was conducted using snowball sampling, the number of individuals who received or viewed the survey invitation could not be determined, and a formal response rate could not be calculated.

Data Collection, Patient Consent and Ethical Approval

A web-based questionnaire in English was developed using Google Forms and pilot-tested with five anaesthesiologists. The final version was distributed to participants through a snowball sampling approach. At the beginning of the survey, the study's objectives and scope were clearly explained, and participants were informed that their participation was voluntary, anonymous, and confidential. The informed consent procedure required participants to click the survey link, which directed them to a consent page. To access the survey, participants had to click "yes" to indicate their consent, while selecting "no" terminated the survey (Patient Consent Form). The study was conducted online and was granted exemption by the Lebanese American University Institutional Review Board (IRB tracking number: LAU.SOM.VA2.21/May/2024; date: 21 May 2024; IRB Notice of Exemption). This online approach was particularly appropriate given the post-crisis context in Lebanon, where geographic dispersion of physicians, time constraints due to increased clinical burden, and migration-related workforce instability limited the feasibility of in-person data collection.

Measurement Tools

The questionnaire was divided into 2 sections: 1) demographic and practice-related questions and personal and occupational risk factors for burnout; and 2) burnout, determined using the Copenhagen Burnout Inventory (CBI).

Description of the CBI

The CBI is a validated instrument comprising three parts: personal burnout, work-related burnout, and client-related burnout. Personal burnout items assess general fatigue and exhaustion, while work-related burnout items assess perceived burnout related to their job among individuals in paid employment. Client-related burnout items measure burnout associated with working with clients (referred to as patients in this study). The CBI consists of 19 items, with 6, 7, and 6 questions addressing personal, work-related, and client-related burnout, respectively. Responses are recorded on a five-point Likert scale and scored from 0 (never, almost never, or to a very low degree) to 100 (always or to a very high degree). Although the CBI authors did not specify cut-off scores, several studies have categorized burnout using a threshold of <50 versus ≥ 50[21,23] and ≥ 75 reflecting high burnout levels.[24-26]

Statistical Analysis

The CBI subscales were computed, and descriptive statistics were used to summarize participants' characteristics and subscale scores. Continuous variables were reported as mean ± standard deviation (SD) or median with interquartile range, as appropriate, while categorical variables were expressed as percentages. Internal consistency of the CBI subscales was assessed using Cronbach's alpha, and correlations among subscales were examined. The normality of quantitative variables was examined using the Shapiro-Wilk test and visually assessed using histograms.

For bivariate analyses, Student's t-test was used to compare means between two groups, and ANOVA was used to compare means across three or more groups after verifying homogeneity of variances with Levene's test. For subgroups with fewer than 30 participants or with non-normally distributed continuous variables, non-parametric tests such as the Kruskal-Wallis test were employed. Pearson correlation coefficients were used to test associations between continuous variables when assumptions of normality and linearity were satisfied.

Multivariable linear regression analyses were conducted to assess associations between the CBI subscales and potential confounders after verifying the assumptions of normality (of dependent variables or residuals), homoscedasticity, linearity, and the absence of multicollinearity. Three separate regression models were fitted, with personal, work-related, and client-related burnout as dependent variables. Variables with a $P < 0.2$ in the bivariate analysis were included as covariates (e.g., weekly working hours). Regression coefficients (β) and 95% confidence intervals (CIs) were reported to quantify these associations. Statistical significance was set at $\alpha=0.05$. All analyses were performed using IBM SPSS Statistics version 29 (IBM Corp., Armonk, NY, USA).

Results

Participants' Characteristics

This study included 82 anaesthesiologists, whose mean age was 48 years. Around half were female, and 81% were married or in a relationship. Moreover, 45% were exercising, and 67% were non-smokers. Around half reported experiencing chronic diseases, and 22% reported mental health problems (Table 1).

The Practice Environment

The majority (65%) were affiliated with a university hospital, and 51% had over 16 years of experience. In addition, 59% worked over 40 hours per week, and 61% covered 5 or more night shifts each month (Table 1). Additional variables related to the perceived work environment, including staffing shortages and support systems, are presented in Supplementary Figure 1 (Participants' concerns).

Burnout Across the CBI Subscales

Cronbach's alpha for the CBI subscales was 0.90 for personal burnout, 0.90 for work-related burnout, and 0.67 for client-related burnout, indicating acceptable to excellent internal consistency. In addition, the proportion of burnout was found to be 57.3% (95% CI=45.9%-68.2%), 51.2% (95% CI=39.9%-62.4%) and 28% (95% CI=18.7%-39.1%) for personal (mean ± SD=51.6±20.1), work-related (mean ± SD=49.7±21.5) and client-related burnout (mean ± SD=35.5±16.3) respectively. High burnout levels (score ≥75) were observed for personal [17.1% (95% CI=8.5%-24.4%)], and work-related burnout [14.6% (7.3%-22%)]. A strong positive correlation was observed between personal and work-related burnout; moderate positive correlations were observed between personal and client-related burnout and between work-related and client-related burnout (Table 2).

Factors Associated with CBI Subscales

Personal Burnout

The bivariate analysis showed that anaesthesiologists who experienced personal burnout were younger and less physically active. Moreover, they tended to report more mental health problems, to have fewer years of experience, and to work longer hours, particularly those working 50 hours per week or more. They also covered more night shifts (specifically more than 5 per month) and took fewer vacation days (Table 3). In the multivariable analysis, and after adjusting for covariates, working ≥50 hours in a week was significantly associated with a 15.6-point higher personal burnout compared to working fewer than or equal to 40 hours (95% CI=0.88, 30.3; *P*=0.04) (Table 4).

Work-related Burnout

Anaesthesiologists who experienced work-related burnout were younger, more likely to be smokers and to report mental health problems. Moreover, they were mostly affiliated with community hospitals, tended to have fewer years of experience, and worked longer hours; this was especially true for those working 50 hours per week or more. They also covered more night shifts, specifically 5 per month or more, and took fewer vacation days (Table 3). In the multivariable analysis, working ≥50 hours in a week was significantly associated with a 17.7-point higher work-related burnout compared to working fewer than or equal to 40 hours (95% CI=3.68, 31.7; *P*=0.01) (Table 4).

Table 1. Participants' Socio-Demographic Characteristics and Working Environment (n = 82)

		n (%)
Gender	Female	43 (52%)
	Male	39 (48%)
Age; mean ± SD		48.2±11.8
Minimum-maximum		28-83
Relationship status	Single/not in a relationship	16 (19%)
	Married or in a relationship	66 (81%)
Smoking status	Non-smokers	55 (67%)
	Smokers	20 (24%)
	Ex-smokers	7 (9%)
Physical activity	No or occasionally	45 (55%)
	1 to 2 times per week	29 (35%)
	3 times or more per week	8 (10%)
Chronic diseases[#]	Yes %	42 (51%)
Mental health problems[#]	Yes %	18 (22%)
Primary practice environment	University hospital/ academic	53 (65%)
	Private practice	24 (29%)
	Community hospital	5 (6%)
Years experience[*]	0 to 5	15 (18%)
	6 to 15	25 (31%)
	16 or more	42 (51%)
Working hours per week	≤40	10 (12%)
	41 to 50	24 (29%)
	>50	48 (59%)
Night shifts per month	0	11 (13%)
	1 to 4	21 (26%)
	5 or more	50 (61%)
Number of days' vacation per year	≤14	16 (20%)
	15 to 21	24 (29%)
	22 to 30	42 (51%)

[#]As diagnosed by a physician; [*]After last year anaesthesia training (including fellowship); SD, standard deviation; all results are presented as n (%) unless otherwise specified

Table 2. CBI Burnout Dimensions or Subscales			
	Personal	**Work-related**	**Client-related**
Mean ± SD	51.6±20.1	49.7±21.5	35.5±16.3
Minimum-maximum	0-100	0-100	0-71
Correlation among CBI burnout subscales			
	Personal	**Work-related**	**Client-related**
Personal burnout		r=0.85 ***P* < 0.001**	r=0.47 ***P* < 0.001**
Work-related burnout			r=0.49 ***P* < 0.001**
Values in bold indicate statistical significance at $P < 0.05$, r, pearson correlation coefficient; *P*, *P* value			

Table 3. Bivariate Associations with CBI Burnout Subscales							
		Personal		**Work-related**		**Client-related**	
		(Mean ± SD) or r	***P***	**(Mean ± SD) or r**	***P***	**(Mean ± SD) or r**	***P***
Gender	Female	50.1±21.4	0.5	47.4±21.5	0.3	35.6±16	0.9
	Male	53.2±18.6		52.3±21.4		35.4±16.8	
Age		-0.43	**<0.001**	-0.47	**<0.001**	-0.26	**0.02**
Relationship status	Not in a relationship	52.1±17.5	0.9	48±20.7	0.7	33.3±15.1	0.6
	Married/In a relationship	51.5±20.8		51.2±21.8		36±16.6	
Smoking status	Non-smokers	48.3±19.3	0.054	46.4±19.9	**0.01**	33.7±14.8	0.2
	Smokers	60.8±20.1		61.6±21.6		42.1±20.5	
	Ex-smokers	51.2±20.4		42.3±23		30.9±8.28	
Physical activity	No or occasionally	54.5±20.2	**0.04**	53.6±22.2	0.1	37.4±16.9	0.2
	1 to 2 times per week	51.4±17.6		47.2±16.9		35.3±15.3	
	3 times or more per week	35.4±22.2		37.5±28.5		25.5±14	
Chronic diseases	Yes	52.4±20.8	0.7	50±22.5	0.9	35.7±17.7	0.9
	No	50.7±19.5		49.5±20.6		35.3±14.9	
MH problems	Yes	61.1±18.7	**0.02**	64.3±18.2	**<0.001**	37.7±16.4	0.5
	No	48.9±19.7		45.6±20.6		34.9±16.3	
Main practice type	University hospital	49.6±17.4	0.08	49.2±19.8	**0.047**	34.8±17.3	0.2
	Private	53.3±25.7		48.2±26.1		34.5±13.4	
	Community hospital	64.2±11.6		62.9±9.7		47.5±16	
Years Experience#	0 to 5	66.1±12.7	**<0.001**	64.8±16.4	**<0.001**	39.2±14.2	0.2
	6 to 15	55±22.9		55±22		38.5±17.4	
	16 or more	44.3±17.2		41.2±19		32.4±16	
Working hours per week	≤40	36.3±16.2	**<0.001**	32.5±16.9	**<0.001**	27.1±11.2	**0.007**
	41 to 50	41.8±17.9		38.1±19		29.9±13.3	
	>50	59.6±17.9		59.2±18.4		40.1±17.1	
Night shifts per month	zero	37.5±18	**<0.001**	30.8±18.5	**<0.001**	22.3±12.7	**<0.001**
	1 to 4	41.1±17.9		36.7±19.9		27.8±15.6	
	5 or more	59.1±16.9		59.4±16.8		41.7±14.2	

Table 3. Continued

		Personal		Work-related		Client-related	
		(Mean ± SD) or r	*P*	(Mean ± SD) or r	*P*	(Mean ± SD) or r	*P*
Days vacation per year	≤14	63± 21.8	**0.009**	60.7±18.8	**0.009**	38±13	0.7
	15 to 21	54.2±19		54±22.7		36.3±16.1	
	22 to 30	45.7±18.1		43.1±19.7		34.1±17.6	

#After last year anaesthesia training (including fellowship), values in bold indicate statistical significance at $P < 0.05$; SD, standard deviation; *P*, *P* value; CBI, Copenhagen Burnout Inventory; MH, mental health

Table 4. Multivariable Models for Each CBI Burnout Subscale

1st regression. Personal burnout		**Adjusted β (95% CI)**	***P***
Age		-0.13 (-0.84; 0.59)	0.7
Smoking status	Non-smokers	Reference	
	Smokers	2.79 (-6.97; 12.6)	0.6
	Ex-smokers	0.97 (-14.4; 16.3)	0.9
Physical activity	No or occasionally	Reference	
	1 to 2 times per week	-3.14 (-11.8; 5.46)	0.4
	3 times or more per week	-12.4 (-25.7; 0.89)	0.06
MH problems	Yes	-1.98 (-12.5; 8.50)	0.7
	No	Reference	
Main practice type	University hospital	Reference	
	Private	0.68 (-9.62; 10.9)	0.9
	Community hospital	0.18 (-17.4; 17.4)	0.9
Years experience#	0 to 5	Reference	
	6 to 15	-8.12 (-21.1; 4.82)	0.2
	16 or more	-10 (-29.7; 9.67)	0.3
Working hours per week	≤40	Reference	
	41 to 50	5.01 (-8.85; 18.9)	0.5
	>50	15.6 (0.88; 30.3)	**0.04**
Night shifts per month	0	Reference	
	1 to 4	-5.96 (-20.3; 8.38)	0.4
	5 or more	4.19 (-10.3; 18.7)	0.6
Days vacation per year	≤14	Reference	
	15 to 21	-2.89 (-15.5; 9.66)	0.6
	22 to 30	-10.6 (-22.9; 1.59)	0.08
2nd regression. Work-related burnout		**Adjusted ß (95% CI)**	***P***
Age		-0.24 (-0.92; 0.44)	0.5
Smoking status	Non-smokers	Reference	
	Smokers	1.40 (-7.92; 10.7)	0.8
Physical activity	Ex-smokers	-8.08 (-22.8; 6.61)	0.3
	No or occasionally	Reference	
	1 to 2 times per week	-7.49 (-15.7; 0.73)	0.07
	3 times or more per week	-6.56 (-19.2; 6.12)	0.3

Table 4. Continued			
		Adjusted ß (95% CI)	***P***
MH problems	Yes	4.96 (-5.05; 15)	0.3
	No	Reference	
Main practice type	University hospital	Reference	
	Private	-4.51 (-14.4; 5.33)	0.4
	Community hospital	-2.61 (-19.3; 14)	0.8
Years Experience#	0 to 5	Reference	
	6 to 15	-3.76 (-16.1; 8.6)	0.5
	16 or more	-4.08 (-22.9; 14.7)	0.7
Working hours per week	≤40	Reference	
	41 to 50	4.95 (-8.29; 18.2)	0.5
	>50	17.7 (3.68; 31.7)	**0.01**
Night shifts per month	zero	Reference	
	1 to 4	-4.41 (-18.1; 9.29)	0.5
	5 or more	9.45 (-4.41; 23.3)	0.2
Days vacation per year	≤14	Reference	
	15 to 21	0.38 (-11.6; 12.4)	0.9
	22 to 30	-9.76 (-21.4; 1.93)	0.1
3rd regression. Client-related burnout		**Adjusted ß (95% CI)**	***P***
Age		-0.04 (-0.35; 0.26)	0.8
Working hours per week	≤40	Reference	
	41 to 50	-1.05 (-12.8; 10.8)	0.9
	>50	5.59 (-6.47; 17.6)	0.4
Night shifts per month	zero	Reference	
	1 to 4	2.65 (-9.48; 14.8)	0.7
	5 or more	15.3 (3.86; 26.7)	**0.009**

#After last year anaesthesia training (including fellowship), values in bold indicate statistical significance at $P < 0.05$; CI, confidence interval; *P*, *P* value; CBI, Copenhagen Burnout Inventory; MH, Mental health

Client-related Burnout

Anaesthesiologists experiencing client-related burnout were more likely to be younger, have longer working hours, and cover more night shifts, specifically if they worked 5 or more night shifts per month (Table 3). In the multivariable analysis, covering 5 or more night shifts per month was significantly associated with a 15.3-point higher client-related burnout score compared with not covering night shifts (95% CI=3.86, 26.7; *P*=0.009) (Table 4). These findings inform the practical considerations outlined in Table 5.

Discussion

This study, among the first to examine burnout among attending anaesthesiologists in Lebanon, a conflict-affected region, within the context of ongoing economic and political crises and regional conflict, found high burnout levels, with personal and work-related burnout affecting over half of participants and client-related burnout affecting over one quarter. Longer working hours and frequent night shifts (≥5/month) were significantly associated with higher burnout across these domains.

Burnout among anaesthesiologists appears more widespread than reported in other countries. A 2021 study conducted in the United States and using the MBI, reported that 13.8% met the criteria for burnout, while 59.2% were at high-risk for burnout.[27] Another 2023 study conducted among French anaesthesiologists and using CBI reported lower proportions with 24% experiencing burnout.[5] A 2017 systematic review indicated that 10-41% of anaesthesiologists are at high-risk of burnout, with up to 59% experiencing at least moderate risk. In addition, burnout among anaesthesiologists has been reported as prevalent in LMICs, with proportions reaching

51.3% among anaesthesiologists in Zambia and 62.2% for emotional exhaustion among those in Egypt.[13,15] While previous studies report varying rates of burnout among anaesthesiologists, influenced by study design, location, and collective stressors,[28] our findings suggest a comparatively higher burden of burnout within a conflict-affected and economically strained setting, thereby extending existing evidence by contextualizing burnout within compounded crises rather than isolated occupational stressors.

In addition, a 2020 study assessing burnout among physicians in Lebanon and using CBI reported that 90% of participants were experiencing burnout, with high levels observed in 19.1% of them.[21] Unlike previous work, our study focuses specifically on anaesthesiologists and provides a specialty-specific perspective with more homogeneous exposures, allowing a clearer identification of profession-related drivers of burnout. However, there is consistency in the ranking of dimensions: personal burnout ranked first in both studies. This consistency reinforces the relevance of personal-level stress even across heterogeneous and specialty-specific samples. As the conflict persists, burnout among anaesthesiologists may worsen, threatening both physician well-being and the quality, safety, and sustainability of healthcare in fragile settings.

This study found that working more than 50 hours per week was positively associated with work-related and personal burnout, consistent with previous reports. Actually, long working hours were significantly associated with a poor mental health, chronic stress and a higher incidence of burnout.[29-31] Long working hours may increase job demands, such as night calls and irregular schedules, leading to physical and mental fatigue and leaving fewer opportunities for rest, particularly when these demands are imposed and accompanied by a reduced sense of autonomy. Those extended working hours might impair the body's ability to restore energy and often require sustained attention, cause decision-making fatigue, and lead to errors, further exacerbating burnout. Besides, they may restrict time for family, social activities, and recovery, leading to dissatisfaction.[32,33] Importantly, this study raises the possibility that the observed extended working hours are partly linked to the ongoing emigration of physicians from Lebanon, a structural factor that is driven by the economic crisis and is rarely quantified in burnout research. The outflow of trained professionals has increased workload among those remaining, requiring longer shifts and expanded responsibilities.[34] This highlights how workforce depletion may act as a system-level driver of burnout, distinguishing our findings from studies conducted in more stable healthcare systems.

On the other hand, long working hours were not associated with client-related burnout. This finding provides a nuanced, specialty-specific insight, as patient interaction might not be the primary driver of burnout among anaesthesiologists. Unlike other specialties that involve prolonged direct patient interactions, such as oncology or psychiatry, anaesthesiologists' patient contact is intense but limited. In fact, stress is more likely driven by technical demands, long operating room hours, and on-call duties rather than emotional strain from patient interactions.[2,3]

In addition, taking more than 5 night shifts per month was associated with client-related burnout. Previous reports showed that the odds of burnout increased by 3 to 9 percent for every additional night on call per week.[1] In our context, this association might be further compounded by workforce shortages due to physician migration, which increases the frequency of night duties among remaining staff.[35] Night shifts disrupt the circadian rhythms, leading to sleep deprivation, and eventually compromising attention and emotional regulation.[36,37] Our findings suggest that under such strained conditions, even brief patient interactions may become more psychologically demanding, particularly when staffing is reduced during night hours.[38]

Additionally, younger age and fewer years of professional experience were significantly associated with higher levels of personal and work-related burnout. However, these associations did not reach statistical significance in the multivariable models. Previous studies reported that younger anaesthesiologists, particularly those early in their careers, are more vulnerable to burnout.[2,39] Anaesthesiologists with fewer years of experience may have limited autonomy or may feel uncertain about independently managing difficult situations, such as airway difficulties or cardiac arrest. In conflict-affected countries, this challenge is amplified, as early-career anaesthesiologists may be required to assume responsibilities in crisis or resource-limited environments without sufficient preparation or mentorship, an aspect that remains underexplored in the literature.[4] This may also reflect a "surviving effect", as described by Downey et al.,[40] where those who remain in the profession develop coping strategies over time. Thus, those remaining may appear less impacted by stress compared to younger or newer anaesthesiologists.[2,40] This study included a relatively small number of anaesthesiologists with fewer years of experience, which may explain why working hours emerged as a stronger predictor of burnout, whereas age and years of experience were not significant in the regression model.

No significant association was found between gender and burnout, consistent with prior systematic reviews reporting mixed findings.[2] This supports the interpretation that structural and workplace-related factors may outweigh individual characteristics in determining burnout in high-stress and crisis.[41] In the Lebanese context, socio-cultural dynamics, economic instability, and the stigma surrounding mental health likely affect male and female anaesthesiologists similarly. Furthermore, strong female leadership and

visibility within Lebanese anaesthesiology may foster a supportive professional environment, potentially reducing gender-related disparities in burnout.[16] Collectively, these observations indicate that while gender may play a role in burnout at a global level, in conflict-affected settings, working conditions may be more decisive in shaping burnout among anaesthesiologists.

Moreover, this study found no association between physical activity among anaesthesiologists and burnout levels in the regression analysis. This finding contrasts with previous studies reporting that physically active healthcare workers are at lower risk of burnout.[42] The mechanisms of this association may be explained by the release of endorphins, improved sleep quality, and enhanced overall physical health, which collectively promote mental well-being and reduce burnout risk.[42] Our findings indicate that in high-burden environments, occupational stressors such as workload intensity and staffing shortages may overshadow individual-level protective behaviors. We believe that, among anaesthesiologists, working hours, night shifts, and workload intensity are the main drivers of burnout. These occupational demands may outweigh the potential protective effects of physical activity, making the association statistically insignificant. Moreover, physical activity was self-reported; data on the type of activity were not collected, which may affect its observed association with burnout.

Practical Implications

By integrating both occupational and structural determinants of burnout, this study provides a more comprehensive framework for intervention compared to prior research. The authors propose multi-level strategies targeting policy-makers, institutions, and individuals to mitigate burnout.[43]

Table 5. Practical Implications for Reducing Burnout Among Anaesthesiologists in Conflict-affected Settings

Level	Key interventions	Expected impact
Policy	Enforce working-hour limits (e.g., 48h/week as in EU directive)[44] Develop national wellness and retention policies	Reduced chronic fatigue Alignment with international safety standards
Organizational	Ensure protected rest periods consecutive and consecutive night shifts, adapted to staffing shortages in resource-limited settings. Use flexible staffing models to address physician emigration, including workload redistribution and surge capacity planning. Improve fair recognition and compensation[45] to support retention amid economic and workforce migration pressures Provide leadership training[9,46] focused on crisis management and supporting staff under prolonged system strain	Lower workload-driven stress Improved morale, equity, and resilience
Individual	Promote autonomy, teamwork, and open communication Encourage early detection and help-seeking for burnout [45] Provide accessible mental health support Encourage healthy lifestyle measures (physical activity, sleep hygiene, Mediterranean diet)[41]	Enhanced job satisfaction Prevention of burnout progression
Disaster preparedness	Conduct regular disaster-preparedness training tailored to conflict-affected and resource-limited settings. Implement simulation-based crisis management exercises reflecting mass casualty and prolonged crisis scenarios. Establish structured institutional support systems for healthcare workers during mass casualty or conflict events and sustained conflict conditions, including surge capacity and psychological support	Greater resilience in crisis Improved patient safety as well as quality of care

Study Limitations

This study is among the first to assess burnout levels in attending anaesthesiologists in the context of Lebanon's ongoing economic and political crises and regional conflict. Its primary strength is its context-specific contribution, which captures the combined effects of workforce migration, systemic instability, and high clinical demand, factors that are rarely examined together in the existing literature. These findings may have broader implications for anaesthesiologists working in other conflict-affected or resource-constrained settings, where overlapping crises amplify professional stress and burnout. Importantly, the study did not include conflict-specific variables (e.g., displacement or direct exposure to mass casualty events), because all participants were indirectly exposed to a shared conflict-affected healthcare environment, which limited the ability to examine heterogeneity in individual conflict exposure. The non-random snowball sampling method and relatively small sample size may have introduced selection bias and may not fully represent the broader population of anaesthesiologists. Participants who were more professionally connected, more engaged in professional networks, or more motivated to participate because of personal experiences with burnout may have been overrepresented. Consequently, the burnout estimates should be interpreted with caution, as levels may have been overestimated or underestimated, and overestimation is plausible if individuals experiencing greater burnout were more likely to respond. Although the study achieved the minimum sample size required under the predefined assumptions and a 90% confidence level, a larger sample would have been required had the more conventional 95% confidence level been used. Therefore, the relatively small sample size may have reduced the precision of some estimates and limited the statistical power to detect smaller associations, warranting cautious interpretation of the findings. Therefore, the findings may not be fully generalizable to all anaesthesiologists practicing in Lebanon. Moreover, because snowball sampling was used, the total number of anaesthesiologists who received the survey is unknown, and a true response rate cannot be calculated. Although 82 participants represented about 20.5% of the estimated workforce, this does not constitute a response rate. Selection bias may exist, as participants could differ from non-participants, limiting generalizability. The cross-sectional design precludes the establishment of causal relationships, and the reliance on self-reported data may have introduced information bias. This potential bias was likely mitigated by the use of validated instruments, such as the CBI. Although relevant covariates were included in the analyses, the possibility of residual confounding from unmeasured variables cannot be excluded. Although analyses were conducted on the predefined CBI subscales and were guided by a priori hypotheses, the possibility of type I error due to multiple comparisons cannot be excluded. Therefore, findings, particularly those with borderline statistical significance, should be interpreted with caution.

Conclusion

This study highlights concerning levels of burnout among anaesthesiologists, particularly in the context of an ongoing and intensifying regional conflict. However, it adds value by situating these findings within the current Lebanese context of compounded systemic strain, including prolonged economic instability, workforce depletion, and escalating regional conflict. In this setting, anaesthesiologists work under increasingly constrained conditions, which may exacerbate established risk factors for burnout. Nevertheless, the key predictors and associated factors identified appear to be modifiable. Implementing targeted interventions to reduce occupational stress, such as enforcing a maximum 48-hour workweek, limiting consecutive night shifts, promoting access to mental health support, and encouraging self-care practices, may be essential for safeguarding anaesthesiologists' well-being and maintaining the effective functioning of healthcare institutions in fragile settings. Future research should incorporate randomly selected samples and longitudinal designs to monitor burnout trends over time in crisis-affected health systems. Additionally, interventional studies are warranted to evaluate the effectiveness of institutional support measures, wellness programs, and preparedness training initiatives.

Ethics

Ethics Committee Approval: The study was conducted online and was granted exemption by the Lebanese American University Institutional Review Board (IRB tracking number: LAU.SOM.VA2.21/May/2024; date: 21 May 2024).

Informed Consent: Participants were informed that their participation in the study was voluntary, and they were assured that their responses would remain anonymous and confidential. Informed consent was obtained from all of the participants before completing the questionnaire.

Footnotes

Authorship Contributions: Concept – V.Y.K., Z.A., H.B.; Design - V.Y.K., Z.A.; Data Collection or Processing - V.Y.K., Z.A.; Analysis or Interpretation – Z.A.; Literature Search – Z.A.; Writing – V.Y.K., Z.A., G.A., C.S., S.S., R.A.N., S.E., J.A.N., C.G., M.B., H.B.

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Original Article
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Impact of Structured Preoperative Counseling on Anaesthesia Preference in Elective Cesarean Delivery: A Prospective Study

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Abstract

Objective: To assess changes in anaesthesia preference before and after structured preoperative counseling and to identify factors associated with anaesthesia preference among women scheduled for elective cesarean delivery.

Methods: This prospective, single-center, single-arm, pre-post observational study included 200 pregnant women classified as the American Society of Anesthesiologists physical status II. Data were collected using a structured questionnaire assessing demographic characteristics, obstetric history, previous anaesthesia experience, level of knowledge, and anaesthesia preference, both before and after counseling. Statistical analyses were performed using SPSS version 22.0, and a *P* value < 0.05 was considered statistically significant.

Results: At baseline, 53% of patients preferred spinal anaesthesia and 47% preferred general anaesthesia. Following counseling, the preference for spinal anaesthesia increased to 88.5% ($P < 0.001$). Increasing age was associated with a decreased likelihood of choosing spinal anaesthesia [odds ratio (OR)=0.94, 95% confidence interval (CI): 0.89-0.99], whereas higher education (OR=1.78, 95% CI: 1.05-3.02), prior knowledge (OR=1.65, 95% CI: 1.02-2.68), and previous spinal anaesthesia experience (OR=2.95, 95% CI: 1.65-5.28) were identified as independent predictors of spinal anaesthesia preference. No significant association was found between smoking and anaesthesia preference, or between comorbidities and anaesthesia preference. The postoperative satisfaction rate with the anaesthesia was 91.5%.

Conclusion: Following structured preoperative counseling, the preference for neuraxial anaesthesia increased among women scheduled for elective cesarean delivery. These findings suggest that standardized patient education may be a useful component of preoperative anaesthesia assessment.

Keywords: Cesarean delivery, spinal anaesthesia, general anaesthesia, patient preference, patient education, decision making

Main Points

- Anaesthesia preference for elective cesarean delivery was associated with patient-related factors, including education level, prior knowledge, and experience with spinal anaesthesia.
- Preference for neuraxial (spinal) anaesthesia increased following structured preoperative counseling.
- Fear-related concerns, such as paralysis and intraoperative pain, play a major role in the choice of general anaesthesia.
- Higher educational level and prior knowledge of anaesthesia are associated with increased preference for spinal anaesthesia.
- Structured preoperative information may support patient-centered discussions during preoperative anaesthesia assessment.

Introduction

Cesarean delivery is one of the most commonly performed surgical procedures worldwide, and anaesthesia management plays a critical role in both maternal and neonatal outcomes. While neuraxial anaesthesia is currently recommended as the preferred approach for cesarean delivery, general anaesthesia is still used in certain situations depending on clinical conditions, urgency, maternal comorbidities, and patient preference.[1,2] Neuraxial anaesthesia offers several advantages, including

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improved postoperative analgesia, preservation of maternal awareness, and a lower risk of neonatal depression.[3,4]

The choice of anaesthesia technique in cesarean delivery is influenced not only by clinical requirements but also by its impact on maternal and neonatal outcomes. Although neuraxial techniques are generally associated with better neonatal outcomes, general anaesthesia remains essential in emergency situations due to its rapid applicability.[5,6] In addition, some studies suggest that general anaesthesia may be associated with adverse psychological outcomes, including postpartum depression.[7] In high-risk obstetric conditions such as placenta previa and placenta accreta spectrum, the choice of anaesthesia becomes more complex and requires an individualized approach.[8,9]

With the increasing emphasis on patient-centered care, patients' knowledge, expectations, and anxiety levels have been recognized as key determinants of anaesthesia preference. Previous studies have shown that appropriate preoperative information can reduce anxiety and increase the preference for neuraxial anaesthesia.[10] However, patients' and healthcare providers' priorities may differ, which can influence decision-making processes.[11,12] In particular, misconceptions and fear-related concerns remain important factors driving the preference for general anaesthesia.[13] These concerns may include fear of paralysis, intraoperative pain, awareness, back pain, and post-dural puncture headache; structured counseling may help address these misconceptions more systematically than routine, unstructured preoperative information.

Although previous studies have shown that preoperative education may influence anaesthesia preference, most have focused on comparing different educational methods or evaluating anxiety reduction. Evidence regarding the integration of standardized, structured face-to-face counseling into routine anaesthesiology practice and its association with changes in anaesthesia preference remains limited. Furthermore, studies evaluating both pre- and post-counseling anaesthesia preferences, together with patient-related factors influencing these preferences, are scarce. Therefore, this study aimed to assess changes in anaesthesia preference before and after structured preoperative counseling and to identify factors associated with anaesthesia preference among women scheduled for elective cesarean delivery.

Methods

This prospective, single-center, single-arm, pre-post observational study was conducted in pregnant women scheduled for elective cesarean delivery. The study was designed to evaluate changes in anaesthesia preference before and after (Supplementary Material 1) structured preoperative counseling. Due to the absence of a control group, the study design allowed the assessment of changes in preference following counseling, but did not allow causal inference regarding the effect of counseling.

The study was approved by the Niğde Ömer Halisdemir University, Non-Interventional Clinical Research Ethics Committee (approval no.: 2022/32, date: April 23, 2022) and conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants.

The sample size calculation was based on an anticipated absolute increase of 20% in spinal anaesthesia preference following preoperative counseling. This conservative effect size was selected based on the findings of Karataş et al.,[10] who reported an increase in spinal anaesthesia preference from 36% before preoperative information to 73% after educational intervention among women scheduled for elective cesarean delivery. To avoid overestimating the expected effect and to ensure an adequate sample size, a more conservative absolute increase of 20% was used for the power analysis. To achieve 80% power with a significance level of $\alpha = 0.05$, a minimum of 185 participants was required. Accounting for a 10% anticipated dropout rate due to incomplete data or emergency status, 200 pregnant women were included in the study.

Pregnant women aged 18 years or older, classified as American Society of Anesthesiologists physical status II and scheduled for elective cesarean delivery, who agreed to participate and were able to complete the study questionnaire, were eligible for inclusion. Patients undergoing emergency cesarean delivery, those who declined to participate, those unable to complete the questionnaire, and those with incomplete data were excluded.

Data were collected using a standardized questionnaire assessing demographic variables, obstetric history, prior anaesthesia experiences, anaesthesia preferences, reasons for preference, and patient satisfaction. The questionnaire used in the study is provided as Supplementary Material 2. Participants self-administered a questionnaire specifically developed by the investigators for this study. No formal validation study was performed. Patients' initial anaesthesia preferences (spinal or general) were recorded. Subsequently, all participants received a standardized 15-minute face-to-face preoperative counseling session from an experienced anaesthesiologist. This session included information on the technical aspects of spinal and general anaesthesia, on their clinical advantages and potential risks, and targeted clarification of common misconceptions such as the risk of paralysis or intraoperative awareness. The counseling was delivered using a structured verbal format with predefined key components to ensure consistency across participants. All sessions were conducted by the same experienced anaesthesiologist, and no written materials or visual aids were used.

The counseling session was conducted according to a predefined, structured counseling form developed by the investigators. The counseling covered available anaesthesia options for cesarean delivery, the procedure and characteristics of spinal anaesthesia, advantages and disadvantages of spinal and general anaesthesia, common concerns and misconceptions (including paralysis, intraoperative pain, awareness, back pain, and post-dural puncture headache), maternal-infant interaction, early breastfeeding, and postoperative pain management strategies. Patients were encouraged to ask questions throughout the session. To ensure consistency, all counseling sessions were delivered by the same experienced anaesthesiologist using the same structured framework.

Following this structured session, anaesthesia preferences were reassessed to evaluate changes resulting from counseling. The primary outcome was the change in anaesthesia preference, while secondary outcomes included patient satisfaction and specific reasons for anaesthesia choice. A change in anaesthesia preference was defined as a shift in the participant's preferred anaesthesia technique (spinal or general anaesthesia) between the pre-counseling and post-counseling assessments. Patient satisfaction was assessed at 24 hours postoperatively using a binary (yes/no) question about satisfaction with the anaesthesia received. No validated satisfaction scale was used. Data on the anaesthesia technique administered and any conversions from spinal to general anaesthesia were also recorded in the anaesthesia records.

Statistical Analysis

Statistical analyses were performed using SPSS version 22.0 (IBM Corp., Armonk, NY, USA). Normality of the data distribution was assessed using appropriate tests. Continuous variables were expressed as mean ± standard deviation or median (minimum-maximum), depending on data distribution. Categorical variables were presented as numbers and percentages. Group comparisons were performed using the chi-square test or Fisher's exact test for categorical variables and the Student's t-test or Mann-Whitney U test for continuous variables, as appropriate. The McNemar test was used to evaluate changes in anaesthesia preference before and after counseling.

Multivariable logistic regression analysis was performed to identify factors independently associated with baseline preference for spinal anaesthesia. The dependent variable was the initial anaesthesia preference (spinal anaesthesia vs. general anaesthesia). Variables demonstrating statistical significance in univariate analyses, together with clinically relevant variables, were entered into the multivariable logistic regression model. Education level was categorized as higher (high school or university) or lower (no schooling or primary school). Collinearity diagnostics were performed using variance inflation factor (VIF) analysis, and no evidence of multicollinearity was identified (all VIF values <2). A P value < 0.05 was considered statistically significant.

Results

A total of 200 pregnant women were included in the study. The demographic and obstetric characteristics of the participants are presented in Table 1.

Overall, anaesthesia preferences are summarized in Table 2. At baseline, 106 women (53.0%) preferred spinal anaesthesia and 94 (47.0%) preferred general anaesthesia. Following structured preoperative counseling, the number of women preferring spinal anaesthesia increased to 177 (88.5%), while those preferring general anaesthesia decreased to 23 (11.5%). Specifically, 82 women (87.2%) changed their preference from general to spinal anaesthesia, whereas 11 women (10.4%) changed from spinal to general anaesthesia

Table 1. Demographic and Obstetric Characteristics (n = 200)

Variable	Value
Age (years)	27.4±3.9
Height (cm)	162.1±5.1
Weight (kg)	68.7±8.8
Gestational age (weeks)	38.0±0.8
Gravida	2.3±1.0
Parity	1.1±0.8
Comorbidity (yes)	17.0% (n = 34)
Smoking (yes)	13.0% (n = 26)
Education-no schooling	9.0% (n = 18)
Education-primary school	36.5% (n = 73)
Education-high school	32.5% (n = 65)
Education-university	22.0% (n = 44)
Occupation-housewife	61.0% (n = 122)
Occupation-working	39.0% (n = 78)
Prior information (yes)	48.0% (n = 96)

Table 2. Changes in Anaesthesia Preference before and after Structured Preoperative Counseling (n = 200)

Initial preference	Post-counseling spinal	Post-counseling general	Total
Spinal	95	11	106
General	82	12	94
Total	177	23	200

McNemar test: $P < 0.001$. Values represent anaesthesia preference before and after counseling, not the final anaesthesia technique administered

(McNemar test, $P < 0.001$). The preferred anaesthesia technique after counseling was initially attempted in all participants. Spinal anaesthesia was initiated in 177 patients and general anaesthesia in 23 patients. Among patients in whom spinal anaesthesia was initiated, 4 required conversion to general anaesthesia. Therefore, the final anaesthesia techniques used were spinal anaesthesia in 173 patients and general anaesthesia in 27 patients. Overall concordance between the post-counseling preference and the final anaesthesia technique received was 98.0%. Patient satisfaction was assessed 24 hours postoperatively using a binary yes/no question regarding satisfaction with the anaesthesia received. Overall, 183 patients (91.5%) reported satisfaction with the anaesthesia received. Among the 4 patients who required conversion from spinal to general anaesthesia, 3 were satisfied with the anaesthesia received. The participant flow and anaesthesia preferences before and after counseling are illustrated in Figure 1.

Patients who initially preferred spinal anaesthesia were significantly younger than those who preferred general anaesthesia. In addition, a higher level of education, prior information about anaesthesia, and previous experience with spinal anaesthesia were significantly associated with preference for spinal anaesthesia. No significant differences were observed between the groups in terms of gravida, parity, gestational age, smoking status, or comorbidities (Table 3).

The reasons for anaesthesia preference differed between the groups. The desire to see the baby immediately (45%) and early breastfeeding (38%) were the most frequently reported reasons for preferring spinal anaesthesia, whereas fear-related concerns—particularly fear of paralysis (44%), pain, and post-procedural headache—were more common among patients who preferred general anaesthesia.

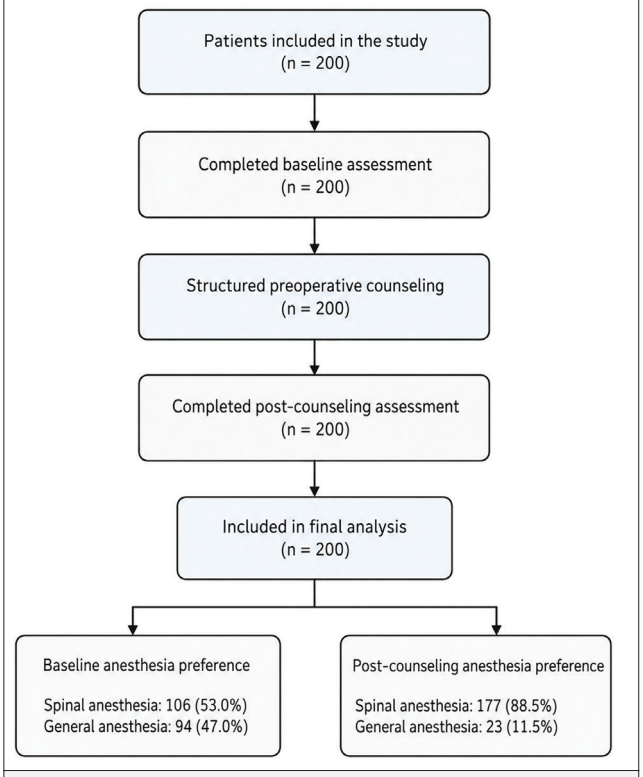


Figure 1. Participant flow diagram illustrating patient inclusion, completion of baseline and post-counseling assessments, structured preoperative counseling, and anaesthesia preference before and after counseling.

In multivariable logistic regression analysis, increasing age was associated with a decreased likelihood of choosing spinal anaesthesia. In contrast, higher educational level, prior information about anaesthesia, and previous experience with spinal anaesthesia were independently associated with an increased preference for spinal anaesthesia. Smoking status and comorbidities were not significantly associated with anaesthesia preference (Table 4).

Table 3. Comparison of Patients According to Initial Anaesthesia Preference

Variable	Spinal (n = 106)	General (n = 94)	*P* value	Effect size
Age (years)	26.8±3.7	28.1±4.0	0.018	0.34 (Cohen's d)
Gravida	2.2±0.9	2.4±1.1	0.210	0.20 (Cohen's d)
Parity	1.0±0.7	1.2±0.9	0.095	0.25 (Cohen's d)
Gestational age (weeks)	38.0±0.8	38.1±0.7	0.410	0.13 (Cohen's d)
Higher education (%)	61.3%	46.8%	0.040	0.15 (ϕ)
Prior information (%)	55%	40%	0.041	0.15 (ϕ)
Previous spinal anaesthesia (%)	48%	22%	0.001	0.27 (ϕ)
Smoking (%)	10%	17%	0.120	0.10 (ϕ)
Comorbidity (%)	15%	19%	0.350	0.05 (ϕ)

Data are presented as mean ± standard deviation or percentage. Continuous variables were compared using Student's t-test or the Mann-Whitney U test, as appropriate. Categorical variables were compared using the chi-square test or Fisher's exact test. Effect sizes are presented as Cohen's d for continuous variables and the phi coefficient (ϕ) for categorical variables

Table 4. Multivariable Logistic Regression Analysis for Factors Associated with Spinal Anaesthesia Preference

Variable	OR	95% CI	*P* value
Age	0.94	0.89-0.99	0.021
Higher education	1.78	1.05-3.02	0.032
Prior information	1.65	1.02-2.68	0.041
Previous spinal anaesthesia	2.95	1.65-5.28	0.001
Smoking	0.72	0.38-1.35	0.310
Comorbidity	0.81	0.42-1.58	0.540

OR, odds ratio; CI, confidence interval

Discussion

In this study, the factors influencing anaesthesia preference in pregnant women scheduled for elective cesarean delivery were evaluated from multiple perspectives. Our findings demonstrate that anaesthesia preference is influenced not only by clinical necessity but also by patient-related factors, including education level, prior knowledge, and experience with spinal anaesthesia. These findings highlight the importance of patient-centered approaches in anaesthesia decision-making.

Neuraxial anaesthesia is widely recommended as the standard approach for cesarean delivery due to its well-established benefits for both maternal and neonatal outcomes.[1,2] Despite these advantages, nearly half of the participants in our study initially preferred general anaesthesia, indicating a discrepancy between clinical recommendations and patient perceptions. This finding is consistent with previous studies emphasizing the role of patient knowledge and perception in shaping anaesthesia choice.[10]

One of the key findings of this study is the substantial increase in the preference for spinal anaesthesia following structured preoperative counseling. This finding indicates that anaesthesia preferences may change following structured preoperative counseling. However, due to the observational pre-post design and the absence of a control group, the observed change cannot be attributed solely to the counseling intervention. Previous studies have similarly reported that appropriate preoperative information reduces anxiety and increases the preference for neuraxial anaesthesia.[10] The magnitude of change observed in our study appears higher than that reported in previous studies, which may be attributable to differences in baseline patient knowledge and the structured counseling provided. In addition, the post-counseling preferred anaesthesia technique was initially attempted for all participants, and concordance between post-counseling preference and the final anaesthesia technique was high. However, the concordance finding should be interpreted with caution because the study was not designed to evaluate validated patient-centered outcomes or the detailed reasons for conversion.

The analysis of the reasons for anaesthesia preference indicates that patient decisions are strongly influenced by perceptual and emotional factors. While the desire to see the baby immediately and to initiate early breastfeeding were the main drivers of preference for spinal anaesthesia, fear-related concerns were more prominent among patients preferring general anaesthesia. In particular, fears such as paralysis, intraoperative pain, and headache appear to play a decisive role, although they are not always supported by clinical evidence.[13] These findings underline the importance of addressing misconceptions and providing accurate, targeted information during preoperative counseling.

Multivariable analysis demonstrated that a higher level of education, prior knowledge about anaesthesia, and previous experience with spinal anaesthesia were independent predictors of preference for spinal anaesthesia. These results suggest that health literacy and prior exposure play a critical role in shaping patient choices.[10,11] In contrast, older age was associated with a lower likelihood of preferring spinal anaesthesia, which may reflect greater anxiety or more established beliefs among older patients.

No significant association was found among smoking, comorbidities, and anaesthesia preference. Although these factors are clinically relevant to obstetric outcomes, their limited influence on choice of anaesthesia suggests that cognitive and experiential factors may play a more decisive role in this context.

Study Limitations

This study has several limitations. First, it was conducted at a single center using a single-arm, pre-post observational design without a control group; therefore, causal relationships between counseling and changes in anaesthesia preference cannot be established. Second, having all counseling sessions delivered by the same anaesthesiologist may have introduced interviewer bias, physician authority bias, and social desirability bias. Third, the questionnaire used in the study was not a formally validated instrument. Fourth, patient satisfaction was assessed using a simple binary question rather than a validated satisfaction scale. Because of the small number of patients requiring conversion from spinal to general anaesthesia and the binary nature of the satisfaction assessment, no formal subgroup statistical comparison of satisfaction by conversion status was performed. Although the actual anaesthesia technique administered and any conversions from spinal to general anaesthesia were recorded, detailed clinical reasons for conversion and validated patient-centered outcomes, such as decisional conflict, anxiety reduction, and quality of

decision-making, were not evaluated. These limitations should be considered when interpreting the findings.

Conclusion

Anaesthesia preference during elective cesarean delivery was associated with patient-related factors, including educational level, prior knowledge of anaesthesia, and prior experience with spinal anaesthesia. Preference for neuraxial anaesthesia increased following structured preoperative counseling. In addition, higher education level, prior information about anaesthesia, and previous spinal anaesthesia experience were independently associated with a greater likelihood of preferring spinal anaesthesia. These findings suggest that standardized patient education may be a useful component of routine preoperative anaesthesia assessment.

Ethics

Ethics Committee Approval: The study was approved by the Niğde Ömer Halisdemir University, Non-Interventional Clinical Research Ethics Committee (approval no.: 2022/32, date: April 23, 2022) and conducted in accordance with the Declaration of Helsinki.

Informed Consent: Written informed consent was obtained from all participants.

Footnotes

Authorship Contributions: Surgical and Medical Practices - S.K., O.A.; Concept - S.K., B.Ç.; Design - S.K., B.Ç.; Data Collection and/or Processing - S.K., O.A.; Analysis and/or Interpretation - S.K., B.Ç.; Literature Review - S.K., O.A.; Writing - S.K., B.Ç.

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Supplementary Material 2: https://d2v96fxpocvxx.cloudfront.net/72b4fafb-5db4-4d61-bedf-c8100360bb15/content-images/83b7bc5a-1312-4cd6-8afd-0555cbb05367.pdf

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Trends in the Use of Neuraxial vs. General Anaesthesia for Transurethral Resection of the Prostate

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Abstract

Objective: Historically, neuraxial anaesthesia (NA) was preferred for transurethral resection of the prostate (TURP) to allow monitoring for TURP syndrome, but modern surgical techniques have largely eliminated this risk. We aimed to characterise trends in anaesthesia utilisation for TURP over a 15-year period and to identify patient factors associated with anaesthetic technique selection.

Methods: We performed a retrospective cohort study of patients undergoing primary TURP using the ACS-NSQIP database (2009-2023). Multivariable logistic regression identified predictors of the use of general anaesthesia (GA) versus NA. Subgroup analyses examined trends by patient health status and age.

Results: Of 73,214 patients identified, GA utilisation increased significantly from 69.9% in 2009 to 88.8% in 2023 ($P < 0.001$). In multivariable analysis, each successive year was associated with a 15% increase in the odds of receiving GA [odds ratio (OR) 1.15, 95% confidence interval (CI) 1.14-1.15]. Black patients (OR 1.65, 95% CI 1.47-1.87) had higher odds of GA than White patients, and Hispanic patients (OR 1.51, 95% CI 1.38-1.64) had higher odds of GA than non-Hispanic patients. Conversely, older age, chronic obstructive pulmonary disease (OR 0.77, 95% CI 0.71-0.84), and diabetes (OR 0.88, 95% CI 0.84-0.93) were associated with decreased GA use. The shift towards GA was significantly more pronounced among medically complex patients (American Society of Anesthesiologists 3-4) than among less medically complex patients (P=0.005).

Conclusion: The anaesthetic management of TURP has evolved over the last 15 years, and GA has further solidified its status as the dominant modality. This evolution likely reflects the diminished risk of TURP syndrome, allowing practice to be driven by airway control and efficiency rather than by historical safety constraints.

Keywords: General anaesthesia, spinal block, transurethral resection of prostate, prostatic hyperplasia, aged

Main Points

- The gap in usage between general and neuraxial anaesthesia has widened significantly.
- General anaesthesia has solidified its status as the primary choice for transurethral resection of the prostate.
- Neuraxial anaesthesia has become an infrequent choice for transurethral resection of the prostate.
- Chronic obstructive pulmonary disease and diabetes remain key drivers in the choice of neuraxial anaesthesia.

Introduction

Benign prostatic hyperplasia (BPH) is one of the most common clinical diagnoses in ageing men, with a prevalence that increases dramatically with age, affecting approximately 50% of men over 50 and over 80% of men over 70.[1] The clinical significance of BPH stems from its role as the leading cause of lower urinary tract symptoms (LUTS), which can profoundly impair quality of life.[1] For decades, transurethral resection of the prostate (TURP) has been the surgical gold standard for treating moderate-to-severe LUTS secondary to BPH, and it remains the benchmark against which newer invasive treatments are measured.[2-5]

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The choice of anaesthesia for TURP, almost exclusively general anaesthesia (GA) or neuraxial anaesthesia (NA), has historically been influenced by the risks inherent in conventional monopolar TURP (M-TURP). M-TURP necessitates the use of a hypotonic irrigation fluid, which, upon absorption, can lead to TURP syndrome. This rare but potentially fatal complication is characterised by hypervolemia and dilutional hypo-osmolality.[6] The early neurological symptoms of TURP syndrome are masked by GA, which led to a long-standing clinical preference for spinal anaesthesia to allow for intraoperative monitoring of the patient's mental status.[7,8]

However, the widespread adoption of modern bipolar and laser-based surgical techniques has fundamentally altered this risk-benefit calculation. By enabling the use of isotonic saline as the irrigation fluid, these newer technologies have virtually eliminated the risk of the severe dilutional hypo-osmolality that defines TURP syndrome.[6] This technological evolution has profound implications for anaesthetic practice, as the primary safety imperative that once heavily favoured NA has been significantly diminished. With this historical constraint lifted, factors such as guaranteed patient immobility and absolute control over ventilation may now weigh more heavily in the decision-making process, potentially favouring the use of GA.

The anaesthetic management of TURP has been explored in the NSQIP database, with prior studies comparing clinical outcomes between different anaesthetic techniques.[9,10] Some of this work has also reported the aggregate utilisation rates for each anaesthetic modality across multi-year study windows.[10,11] Other research has presented anaesthesia data as a secondary characteristic in analyses of surgical trends, but without a dedicated analysis of how anaesthetic practice itself has evolved.[11] However, no published study has conducted a dedicated longitudinal analysis of year-over-year trends in anaesthesia utilisation for TURP. This distinction is important because an aggregate rate fails to show the direction of change in practice patterns over time. As a result, a contemporary analysis of how national practice patterns have evolved remains a critical gap in knowledge. This study aims to fill that gap by describing these trends over the 15-year period from 2009 to 2023.

Methods

Study Design and Data Source

We performed a retrospective cohort study using the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database. The NSQIP is a large, multicenter, outcomes-based registry that collects data on preoperative risk factors, intraoperative variables, and 30-day postoperative outcomes from hospitals participating in the ACS-NSQIP.

Ethics Committee

This study was approved by the Institutional Review Board at Baylor College of Medicine (approval no: H-58079, date: 14.10.2025). The requirement for informed consent was waived due to the retrospective nature of the study and the use of de-identified data.

Study Population

We queried the NSQIP database to identify all adult patients (≥18 years of age) who underwent a primary TURP, identified by current procedural terminology code 52601, between January 1, 2009, and December 31, 2023. We excluded patients with an American Society of Anesthesiologists (ASA) physical status classification of 5, those classified as emergent or with preoperative sepsis. To create a cohort focused on benign disease, patients with a postoperative diagnosis of prostate cancer [identified using International Classification of Diseases (ICD)-9 code 185 and ICD-10 code C61] or with disseminated cancer flagged in the NSQIP registry were excluded (Figure 1).

Study Variables

The primary variable of interest was the type of anaesthesia administered, as recorded in the ANESTHES variable. We categorised this variable into two groups for comparison: GA and NA, with the NA group encompassing cases recorded as "spinal", "epidural", or "regional". To create a clear comparison between these two primary techniques, the small number of cases performed under monitored anaesthesia care (MAC) or local anaesthesia were excluded from the final analysis.

Additional patient and procedural variables were collected to describe the study cohorts and to serve as covariates in multivariable models. These included patient demographics [age, race, Hispanic ethnicity, body mass index (BMI) category], preoperative comorbidities [ASA class, diabetes mellitus, hypertension requiring medication, congestive heart failure, chronic obstructive pulmonary disease (COPD), smoking status, dialysis dependence], and the year of surgery. All variables were used to perform a descriptive comparison between the two anaesthetic groups (Table 1). The multivariable model described in the statistical analysis section (Table 2) retained year of surgery, age, race, Hispanic ethnicity, ASA class, diabetes mellitus, hypertension, congestive heart failure, COPD, dialysis dependence, and BMI category. These covariates were pre-specified based on documented or biologically plausible relevance to anaesthetic technique selection.

Statistical Analysis

All statistical analyses were performed using R statistical software (version 4.3.1, R Foundation for Statistical Computing). A two-sided *P* value of < 0.05 was considered statistically significant.

First, a longitudinal trend analysis was performed to assess the primary objective. The proportion of TURPs performed under GA versus NA was calculated for each calendar year from 2009 to 2023, and a line graph was generated to visualise this trend (Figure 2). The year of surgery was modelled as a continuous variable throughout the analysis. The statistical significance of the temporal trend reported in the trends in anaesthesia utilisation section was assessed using the coefficient for year of surgery from an unadjusted logistic regression model with anaesthesia type (GA vs. NA) as the outcome; this unadjusted association was then re-examined in a model adjusted for the covariates listed above, with the adjusted estimate reported separately in the predictors of anaesthesia choice section (Table 2).

Second, a descriptive analysis was performed to compare the baseline characteristics of the two anaesthetic groups. Categorical variables were compared using the chi-square test; continuous variables were compared using the Student's t-test. To assess clinically meaningful imbalances between groups, the standardised mean difference was calculated for each variable.

Third, to identify factors independently associated with the choice of anaesthesia, a multivariable logistic regression model was constructed. The outcome was receipt of GA (vs. NA), and the model included year of surgery, patient demographics, and key comorbidities as predictors.

Finally, to explore whether the trend in anaesthesia utilisation differed across patient populations, a subgroup analysis was performed. The cohort was stratified by both patient health status (ASA class 1-2 vs. 3-4) and age (<70 vs. ≥70 years). The longitudinal trend analysis was then repeated for each subgroup. To formally test for a difference in trends between the groups, an interaction term between the year of surgery

Table 1. Demographics for Patients Receiving General Anaesthesia versus Neuraxial During Their Procedure (2009-2023)

n	General anaesthesia	Neuraxial anaesthesia	*P* value	SMD
	59193	14021		
Age [mean (SD)]	70.32 (9.08)	72.55 (8.58)	<0.001	0.252
BMI category (%)			<0.001	0.146
Normal	14481 (24.5)	3964 (28.3)		
Obese	19267 (32.5)	3928 (28.0)		
Overweight	24289 (41.0)	5639 (40.2)		
Underweight	1156 (2.0)	490 (3.5)		
Race (%)			<0.001	0.802
Asian	2080 (3.5)	478 (3.4)		
Black	4648 (7.9)	323 (2.3)		
Other/unknown	12648 (21.4)	7982 (56.9)		
White	39817 (67.3)	5238 (37.4)		
Hispanic	5308 (9.0)	703 (5.0)	<0.001	0.156
ASA class (%)			<0.001	0.126
1-No disturb	1323 (2.2)	542 (3.9)		
2-Mild disturb	25399 (42.9)	5902 (42.1)		
3-Severe disturb	29937 (50.6)	6738 (48.1)		
4-Life threat	2534 (4.3)	839 (6.0)		
Diabetes mellitus (%)	13194 (22.3)	3259 (23.2)	0.015	0.023
Hypertension requiring medication (%)	35736 (60.4)	8272 (59.0)	0.003	0.028
Congestive heart failure (%)	1281 (2.2)	221 (1.6)	<0.001	0.043
COPD (%)	3219 (5.4)	1002 (7.1)	<0.001	0.070
Smoking history (%)	6259 (10.6)	1441 (10.3)	0.311	0.010
Dialysis (%)	319 (0.5)	66 (0.5)	0.348	0.010

SD, standard deviation; BMI, body mass index; ASA, American Society of Anesthesiologists; COPD, chronic obstructive pulmonary disease; SMD, standardised mean difference

Table 2. Multivariable Analysis of Factors Predicting Receipt of General Anaesthesia over Neuraxial Anaesthesia for TURP

	Odds ratio	*P* value	95% CI lower	95% CI upper
Year of operation	1.15	<0.001	1.14	1.15
Age	0.98	<0.001	0.97	0.98
Race-Asian	0.52	<0.001	0.47	0.58
Race-Black	1.65	<0.001	1.47	1.87
Race-other/unknown	0.19	<0.001	0.18	0.19
Hispanic	1.51	<0.001	1.38	1.64
ASA class 2	1.18	0.004	1.05	1.33
ASA class 3	1.21	0.002	1.07	1.36
ASA class 4	0.97	0.665	0.83	1.12
Diabetes mellitus	0.88	<0.001	0.84	0.93
Hypertension requiring medication	1.01	0.659	0.97	1.06
Congestive heart failure	1.18	0.045	1.01	1.40
COPD	0.77	<0.001	0.71	0.84
Dialysis	1.12	0.445	0.84	1.53
BMI category-obese	1.11	<0.001	1.05	1.18
BMI category-overweight	1.08	0.003	1.03	1.14
BMI category-underweight	0.87	0.032	0.77	0.99

Reference categories: White race, non-Hispanic ethnicity, ASA class 1, normal BMI, and absence of each comorbidity. Year of operation and age were modelled as continuous variables (OR per one-year increase). Model based on complete-case analysis (n = 71,890); 1,324 patients with missing age were excluded
BMI, body mass index; CI, confidence interval; COPD, chronic obstructive pulmonary disease; ASA, American Society of Anesthesiologists; TURP, transurethral resection of the prostate; OR, odds ratio

and the subgroup variable was added to the multivariable logistic regression model. All multivariable models were constructed using a complete-case analysis; the extent of missing data and the number of patients excluded on this basis are reported in the patient characteristics section.

Results

Patient Characteristics

After applying the inclusion and exclusion criteria, a final cohort of 73,214 patients who underwent TURP between 2009 and 2023 was identified. Of these, 59,193 (80.8%) received GA and 14,021 (19.2%) received NA. The study flow diagram (Figure 1) shows the number of patients excluded at each step: 13 for ASA class 5; 1,264 for emergent cases; 318 for preoperative sepsis; 1,575 for disseminated cancer; 5,321 for prostate cancer (ICD-9 185/ICD-10 C61); 2,665 for MAC or local anaesthesia; and 214 for missing/uninterpretable ASA class, yielding the final analytic cohort of 73,214 patients. Among the covariates included in the multivariable model, only age had missing values (1,324 patients; 1.81%); all other covariates were complete. A total of 1,324 patients were excluded on a complete-case basis, leaving 71,890 patients in the final multivariable regression model (Table 2).

The baseline characteristics of the two groups differed significantly (Table 1). Patients who received NA on average were older than those who received GA (mean ages 72.55 and 70.32 years, $P < 0.001$). The NA cohort also had a higher burden of comorbidities, notably a greater proportion of ASA class 4 patients (6.0% vs. 4.3%, $P < 0.001$) and a higher prevalence of COPD (7.1% vs. 5.4%, $P < 0.001$). Conversely, congestive heart failure was more prevalent in the GA cohort (2.2% vs. 1.6%, $P < 0.001$).

Trends in Anaesthesia Utilisation

Over the 15-year study period, a significant and sustained trend toward increased use of GA and a corresponding decrease in use of NA for TURP procedures was observed (Figure 2). The proportion of TURPs performed under GA increased from 69.9% in 2009 to 88.8% in 2023. Conversely, the proportion of procedures performed under NA decreased from 30.1% in 2009 to 11.2% in 2023. This trend was statistically significant over time ($P < 0.001$).

Predictors of Anaesthesia Choice

The multivariable logistic regression analysis identified several independent predictors of receiving GA over NA (Table 2). After controlling for other factors, each successive year of surgery was associated with a 15% increase in the odds of receiving GA (OR 1.15, 95% CI 1.14-1.15). Older

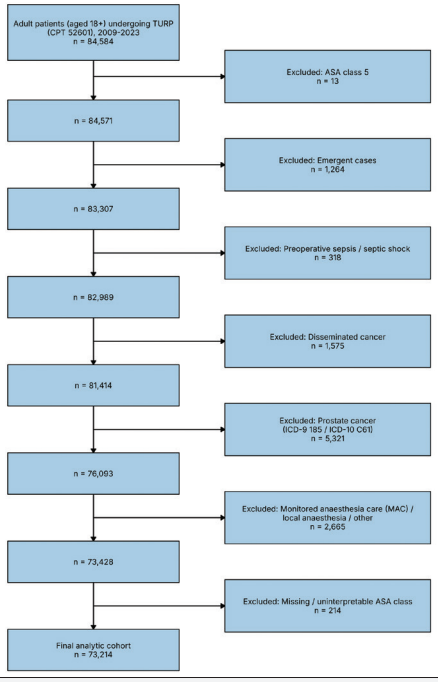


Figure 1. Study cohort selection flow diagram.

Flow diagram illustrating the sequential application of inclusion and exclusion criteria used to derive the final study cohort from the ACS-NSQIP database (2009-2023).

ACS-NSQIP, American College of Surgeons National Surgical Quality Improvement Program; ASA, American Society of Anesthesiologists; TURP, transurethral resection of the prostate; CPT, current procedural terminology; ICD, International Classification of Diseases.

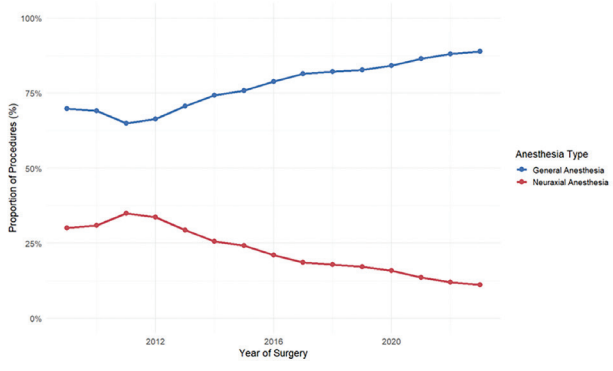


Figure 2. Trends in type of anaesthesia for transurethral resection of the prostate (TURP) (2009-2023). The line graph illustrates the annual proportion of TURP procedures performed under general anaesthesia (blue line) versus neuraxial anaesthesia (red line) within the ACS-NSQIP database. Over the 15-year study period of 2009-2023, there was a significant increase in the use of general anaesthesia with a concurrent decline in neuraxial anaesthesia.

ACS-NSQIP, American College of Surgeons National Surgical Quality Improvement Program.

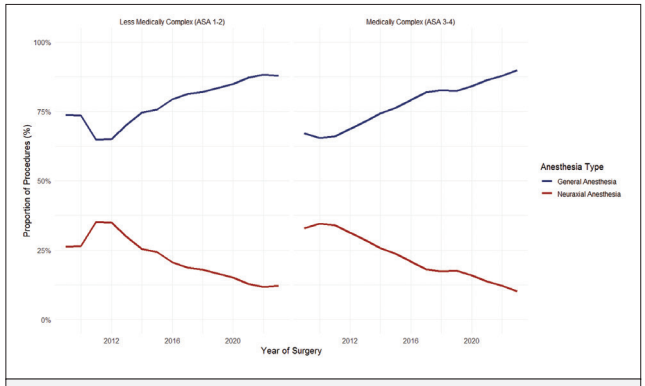


Figure 3. Trends in type of anaesthesia by patient health status. The figure displays the longitudinal trends in anaesthesia choice for healthier patients (ASA class 1-2, left panel) and medically complex patients (ASA class 3-4, right panel). The blue line represents general anaesthesia, and the red line represents neuraxial anaesthesia.

ASA, American Society of Anesthesiologists.

age was associated with decreased odds of receiving GA (OR 0.98 per year, 95% CI 0.97-0.98).

Compared with White patients, Black patients had significantly higher odds of receiving GA (OR 1.65, 95% CI 1.47-1.87), as did Hispanic patients compared with non-Hispanic patients (OR 1.51, 95% CI 1.38-1.64). ASA class was non-linearly associated with anaesthetic choice. Compared with ASA class 1 patients, patients classified as ASA class 2 and ASA class 3 had higher odds of receiving GA (OR 1.18 and 1.21, respectively), whereas the odds for ASA class 4 patients did not differ significantly from those for ASA class 1 patients (OR 0.97, 95% CI 0.83-1.12). Conversely, patients with a history of COPD (OR 0.77, 95% CI 0.71-0.84) or diabetes (OR 0.88, 95% CI 0.84-0.93) had significantly lower odds of receiving GA.

Subgroup Analysis of Anaesthesia Trends

A subgroup analysis was performed to determine whether the trend in anaesthesia utilisation differed by patient health status or age. The trend towards increased GA use differed significantly between patients with lower ASA scores (ASA 1-2) and those with higher ASA scores (ASA 3-4) (Figure 3). Although ASA class 4 patients were proportionally more common in the NA group (Table 1), the trend of increasing GA utilisation over the 15-year period was significantly more pronounced in this group than in less medically complex patients (*P* value for interaction =0.005). In contrast, the trend was consistent across both younger (<70 years) and older (≥70 years) patient populations (Figure 4), with no statistically significant difference observed between the two groups (*P* value for interaction =0.991). Both subgroup analyses (Figures 3 and 4) were restricted to the 71,890 patients with non-missing age data. The primary trend analysis (Figure 2) and Table 1 remain unaffected because they do not depend on this exclusion.

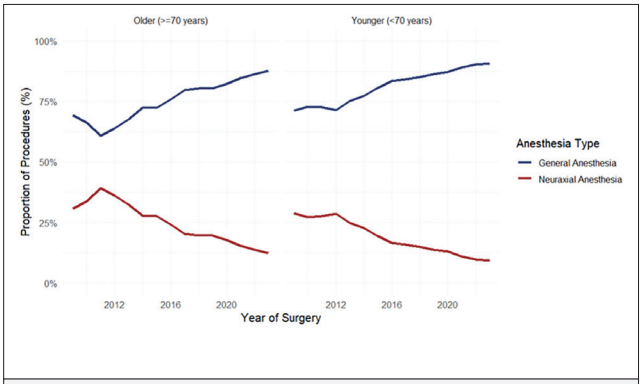


Figure 4. Trends in type of anaesthesia by patient age group. The figure displays longitudinal trends in anaesthesia choice for older patients (≥70 years, left panel) and younger patients (<70 years, right panel). The blue line indicates general anaesthesia, and the red line indicates neuraxial anaesthesia.

Discussion

In this large, multi-institutional study of over 73,000 patients, we found a profound and sustained shift in anaesthetic practice for TURP between 2009 and 2023. The data clearly show that GA has become the dominant modality, increasing from just over two-thirds of cases in 2009 to nearly 90% in the modern era. This trend toward GA remained highly significant even after adjusting for a wide range of patient demographics and comorbidities.

While several factors may contribute to this trend, one plausible and clinically coherent contributor is the procedural innovation, which has transformed TURP over time. The NSQIP database does not capture the specific surgical technology used in each case; therefore, this interpretation should be regarded as a likely explanation rather than a finding directly supported by our data. Historically, the risk of the rare but potentially fatal TURP syndrome made NA the preferred technique, as it allowed for the intraoperative monitoring of a patient's mental status to detect early signs of hypo-osmolality.[7,8] However, the widespread adoption of bipolar and laser-based technologies, which permit the use of isotonic saline for irrigation, has virtually eliminated this risk. The neutralisation of the primary safety concern that once favoured NA has liberated the choice of anaesthetic, allowing other factors, such as procedural efficiency, guaranteed patient immobility, and absolute airway control, to potentially favour the use of GA.

Interestingly, our analysis reveals that while a national trend towards GA exists, nuanced clinical judgement remains a critical component of anaesthetic choice. Compared with those receiving GA, patients selected for NA were, on average, slightly older and more likely to have comorbidities, such as COPD and diabetes mellitus. Prior studies indicate that spinal anaesthesia may decrease morbidity in patients with COPD, which may underlie anaesthesiologists' preference for NA in this population.[12] Additionally, another study that utilised the NSQIP database found that NA offered a statistically significant advantage in 30-day outcomes.[9] These findings demonstrate that clinicians may be selectively using NA for a population they perceive to be at higher risk.

Our subgroup analysis reveals that the shift towards GA is not uniform. The trend towards GA was significantly more pronounced in medically complex patients (ASA 3-4), which represents an evolution in the anaesthetic management of this higher-risk cohort. In contrast, the trend towards GA has progressed similarly across age groups, with no statistically significant difference in the rate of change between younger and older patients. These findings suggest that the factors influencing this national trend are more closely related to patient health status than to age.

Prior research using the NSQIP database has analysed anaesthesia trends in other surgical specialties, providing valuable context for our findings. In oncologic breast surgery, a 15-year analysis found a significant trend towards increased GA use for lumpectomy procedures, mirroring the shift we observed in TURP.[13] However, this pattern is not consistent with orthopaedic procedures. For hip fracture repair, the opposite trend was observed between 2007 and 2017, with a notable increase in the use of spinal anaesthesia.[14] Moreover, for total hip and knee arthroplasty, the utilisation of spinal anaesthesia was found to be largely unchanged between 2011 and 2018, despite being considered a grossly underutilised gold standard.[15] These contrasting trajectories suggest that procedural evolution, patient characteristics, and established clinical pathways unique to each field are the primary drivers of anaesthetic selection.

Study Limitations

This study has multiple limitations inherent in its retrospective design, which used a large administrative database. The NSQIP database does not contain information on the specific surgical technology used (e.g., monopolar, bipolar, laser); therefore, we cannot directly attribute the observed trend to the adoption of newer technologies. Additionally, we lack data on surgeon or patient preferences, operating room scheduling pressures, or the specific reasons behind each anaesthetic choice. As with any observational analysis, residual confounding from unmeasured factors such as institutional practice patterns or individual anaesthetist preference cannot be excluded and may partly account for the associations observed. The number of hospitals contributing to the NSQIP database grew substantially over the study period. Therefore, the cohort from the initial study period may be less representative of national practice patterns compared to the cohort from more recent years.[16]

Conclusion

In conclusion, the anaesthetic landscape for TURP has been fundamentally reshaped over the last 15 years. The practice has moved away from a choice dictated by the risk of a single, now-rare complication and toward a choice influenced by a modern balance among patient factors, procedural demands, and demographic patterns. This study documents a paradigm shift in anaesthetic practice for TURP that mirrors the broader technological transformation of the procedure.

Ethics

Ethics Committee Approval: This study was approved by the Institutional Review Board at Baylor College of Medicine (approval no: H-58079, date: 14.10.2025).

Informed Consent: The requirement for informed consent was waived due to the retrospective nature of the study and the use of de-identified data.

Footnotes

Authorship Contributions: Surgical and Medical Practices - R.G., A.K.; Concept - R.G., V.P., E.B., N.P., A.K.; Design - R.G., A.K.; Data Collection or Processing - R.G., V.P., E.B.; Analysis or Interpretation - R.G., V.P., N.P., A.K.; Literature Search - R.G., V.P., E.B., N.P., A.K.; Writing - R.G., V.P., E.B., N.P., A.K.

Declaration of Interests: The authors declare no conflict of interests.

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Original Article

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Early Postoperative Nausea and Vomiting in Routine Clinical Practice: A Retrospective Observational Study of Associated Perioperative Factors and Prophylactic Practices

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Abstract

Objective: Postoperative nausea and vomiting (PONV) remains a common complication in the post-anaesthesia care unit (PACU) and negatively affects patient comfort and satisfaction. In routine clinical practice, identifying perioperative factors associated with early PONV may help optimize preventive strategies and guide anesthetic management. This study primarily aimed to evaluate PONV during the first postoperative hour and associated perioperative factors, and secondarily to describe PONV at later postoperative time points and antiemetic practices.

Methods: This retrospective observational study evaluated adult patients who underwent elective surgery under general or regional anaesthesia from January to December 2021. After applying eligibility and complete-case criteria, 584 ASA I-III patients were included. Demographic characteristics, anesthetic techniques, surgical features, Apfel risk factors, antiemetic prophylaxis, rescue antiemetic use, and binary PONV data at postoperative hours 1, 6, 12, and 24 were assessed.

Results: PONV occurred in 128 patients (22%) during the first postoperative hour and decreased at later postoperative time points. In univariate analyses, first-hour PONV was associated with general anaesthesia, inhalational anesthetic use, perioperative opioid use, female sex, non-smoking status, and perioperative medication-related variables ($P < 0.05$). The adjusted analysis suggested that early PONV in routine clinical practice reflects an overlapping, multifactorial pattern rather than the effect of a single dominant perioperative factor.

Conclusion: First-hour PONV remained a clinically relevant problem in routine perioperative care despite the common use of prophylactic antiemetics. These findings highlight the importance of careful early postoperative monitoring and individualized risk-based preventive strategies in daily anaesthesia practice.

Keywords: Postoperative nausea and vomiting, antiemetic prophylaxis, Apfel risk score, opioid use, total intravenous anaesthesia (TIVA), inhalation anaesthesia

Main Points

- First-hour postoperative nausea and vomiting (PONV) remained a clinically relevant problem during routine perioperative care but decreased at later postoperative time points.
- Early PONV was associated with overlapping patient-related, anesthetic-related, and medication-related variables, supporting its multifactorial nature in daily clinical practice.
- These findings highlight the importance of careful early postoperative monitoring, standardized risk assessment, and individualized preventive strategies.

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Introduction

Postoperative nausea and vomiting (PONV) occurs in approximately 20-30% of all surgical patients and in 70-80% of those with specific risk factors.[1] PONV may result in patient dissatisfaction, serious clinical complications, and economic losses. Patients undergoing surgery have described PONV as a worse experience than postoperative pain.[2] PONV can cause clinically significant complications such as wound dehiscence, esophageal rupture, pneumothorax, and delayed discharge from the post-anaesthesia care unit (PACU).[3]

Guidelines state that the incidence of PONV can be reduced to 40% or lower through the use of antiemetics.[4] Most guidelines advocate the use of risk-based PONV scoring systems, such as the Apfel score, which recommend antiemetic strategies based on stratified risk levels.[5-7]

Although randomized controlled trials have demonstrated the effectiveness of risk-based PONV scoring systems, their implementation in daily perioperative care remains variable. As a result, the incidence of early PONV and the prophylactic and therapeutic approaches currently used in routine practice are not always clearly characterized. A better description of current practice may help identify perioperative factors associated with early PONV and clarify where preventive strategies may be further optimized. In recent years, multimodal approaches to PONV prevention have gained popularity. Enhanced Recovery After Surgery protocols combine both pharmacological and non-pharmacological methods.[4,8] Strategies include avoiding emetogenic agents, such as inhalation anesthetics, and using propofol for anaesthesia induction and maintenance. Shortened preoperative fasting, preoperative carbohydrate loading, and adequate hydration have also been shown to be beneficial. The use of regional anaesthesia techniques—such as epidural analgesia or transversus abdominis plane blocks—can reduce postoperative opioid requirements and subsequently lower PONV incidence.[4,8] NSAIDs are also recommended as opioid-sparing agents. Combining two or more antiemetics has been shown to enhance efficacy. Dexamethasone has also been proven to reduce the prevalence of PONV.[8]

Effective PONV management should include risk assessment, application of preventive strategies, determination of appropriate antiemetic dose and timing, and establishment of a rescue treatment algorithm tailored to each patient.[4,8]

Accordingly, the primary objective of this study was to evaluate PONV during the first hour and perioperative factors associated with its occurrence in routine clinical practice. The secondary objectives were to describe PONV at postoperative hours 6, 12, and 24 and to characterize prophylactic and rescue antiemetic practices used in the study population.

Methods

This retrospective observational study, using routinely recorded clinical data, was conducted at the Department of Anesthesiology and Reanimation of Süleyman Demirel University Faculty of Medicine following approval by the Clinical Research Ethics Committee of Süleyman Demirel University (decision no: 34, date: 26.01.2022).

Between January and December 2021, a total of 4,500 patients underwent surgery under general or regional anaesthesia at our institution. Because this was a retrospective chart review, 1,000 records with accessible archived anaesthesia forms and hospital information system data were reviewed based on availability. Patients younger than 18 years of age, those undergoing emergency surgery, and those classified as American Society of Anesthesiologists (ASA) physical status IV or V were excluded. A complete-case analytical approach was applied, and records with missing data required for Apfel risk assessment, anaesthesia characteristics, perioperative medication use, or postoperative PONV follow-up were excluded. Of the 1,000 records reviewed, 416 were excluded because they did not meet the eligibility criteria or had incomplete perioperative or postoperative follow-up data. The final analysis included 584 patients who met the study criteria and had complete and verifiable datasets. Because the reasons for exclusion were not recorded as mutually exclusive categories during retrospective screening, the exact number of patients excluded for each criterion could not be reliably reconstructed. The patient selection process is summarized in Figure 1.

Patient medical files were retrieved from the hospital archive and the hospital information system using protocol numbers obtained from operating room records. The following data were collected on standardized case report forms: demographic characteristics, medical history, presence of PONV risk factors according to the Apfel scoring system, surgical characteristics, anaesthesia-related variables (type of anaesthesia, anesthetic agents used, duration of anaesthesia), perioperative medication use, postoperative analgesic requirements, and occurrence of nausea and vomiting at postoperative hours 1, 6, 12, and 24. When nausea or vomiting was observed, the antiemetic treatments administered were also recorded. Preoperative fasting duration and type of surgery were extracted from the medical records and evaluated as perioperative variables. Time to postoperative oral intake was not consistently available in the retrospective records; therefore, it could not be included in the analysis.

For the purposes of this study, PONV was defined as the presence of nausea, vomiting, or both, as documented in postoperative follow-up records. PONV was evaluated at postoperative hours 1, 6, 12, and 24. The primary outcome was PONV during the first postoperative hour. Secondary

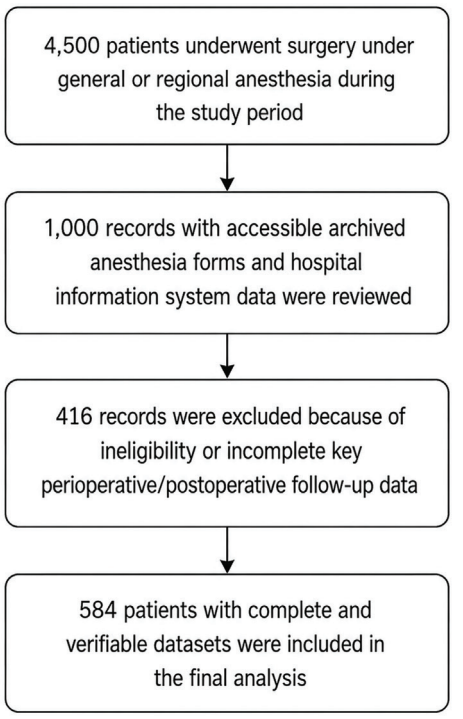


Figure 1. Patient flow diagram

outcomes included PONV at postoperative hours 6, 12, and 24 and use of rescue antiemetic treatment. No validated severity grading scale for nausea or vomiting was available in the retrospective records; therefore, PONV was analyzed as a binary outcome at each postoperative time point.

Personal data were anonymized, and all patient information was stored digitally without disclosure of individual identities. Written informed consent, obtained at hospital admission, referred to anaesthesia and routine clinical care. Because this was a retrospective chart review study using anonymized data, study-specific informed consent was not obtained. The retrospective use of anonymized patient data was approved by the Clinical Research Ethics Committee of Süleyman Demirel University.

Statistical Analysis

Statistical analyses were performed using the Statistical Package for Social Sciences (SPSS) version 26 (SPSS Inc., Chicago, IL, USA). Qualitative variables were expressed as numbers and percentages, while quantitative variables were presented as mean ± standard deviation. The Kolmogorov-Smirnov and Shapiro-Wilk tests were used to assess the normality of the distribution of continuous variables.

For comparisons between two independent groups, the Student's t-test was used for normally distributed variables and the chi-square test was used for categorical variables. Time-dependent changes in postoperative assessments 1, 6, 12, and 24 hours were evaluated using repeated-measures analysis of variance.

Associations between PONV and perioperative variables were first evaluated using univariate analyses at each postoperative time point. To address potential confounding, a multivariable logistic regression analysis was performed for first-hour PONV, the primary outcome. Variables considered clinically relevant were selected for adjusted analysis and entered into the model, including sex (female), smoking status (non-smoking), perioperative opioid use, type of anaesthesia (inhalational or total intravenous), and antiemetic prophylaxis regimen. The antiemetic prophylaxis regimen was entered as a categorical variable, with no antiemetic prophylaxis as the reference category. Because antiemetic agents were administered in overlapping combinations in routine clinical practice, prophylaxis was modeled as mutually exclusive regimens rather than as separate drug variables. Rare or overlapping prophylaxis regimens were retained as a separate category because individual rare combinations had very small cell counts. The Apfel risk score was not included in the same model as its individual components to avoid collinearity. Adjusted odds ratios (ORs) with 95% confidence intervals (CIs) were reported. A P value of <0.05 was considered statistically significant.

Results

During the study period, 4,500 patients underwent surgery under general or regional anaesthesia at our institution. As shown in Figure 1, 1,000 records with archived and accessible anaesthesia forms and hospital information system data were reviewed. After applying eligibility and complete-case criteria, 416 records were excluded, leaving 584 patients with complete and verifiable datasets for the final analysis.

The demographic characteristics, ASA physical status classifications, and perioperative features of the study population are summarized in Table 1. The distribution of surgical procedures is presented in Table 2. According to the surgical risk classification, 286 patients were categorized as low-risk, 263 as medium-risk, and 35 as high-risk (Table 1). General anaesthesia was administered to 461 patients, while 123 underwent surgery under regional anaesthesia (Table 1). Inhalational anesthetic agents were used in the majority of patients, whereas total intravenous anaesthesia (TIVA) was applied in a small proportion of cases (Table 3).

The distribution of PONV risk factors according to the Apfel scoring system is shown in Table 3. Overall, 358 patients had an Apfel risk score of 2 or higher (Table 3). Preoperative fasting duration and characteristics of perioperative oxygen administration are presented in Table 3. Preoperative carbohydrate loading was performed in a limited number of patients.

Table 1. Baseline Demographic and Perioperative Characteristics of the Study Population

Parameter	Mean ± SD	
Age (years)	49.40±17.812	
Height (cm)	168.56±10.658	
Weight (kg)	76.55±14.692	
Duration of surgery (min)	117.05±70.863	
Duration of anaesthesia (min)	133.36±74.250	
Total blood loss (mL)	168.37±315.58	
Total fluid given (mL)	1757.55±1198.72	
ASA	**Frequency (n)**	**Percentage (%)**
I	114	19.5
II	403	69
III	67	11.4
Type of anaesthesia		
General anaesthesia	461	78.9
Regional anaesthesia	123	21.1
Surgical risk level		
Low-risk	286	49.0
Medium-risk	263	45.0
High-risk	35	6.0
Total	584	100.0

Values are presented as mean ± SD or n (%). n, number of patients; ASA, American Society of Anesthesiologists; SD, standard deviation

Table 2. Surgical Characteristics of the Study Population

Type of Surgery	Frequency (n)	Percentage (%)
Tonsillectomy	1	0.2
Rhinoplasty	23	3.9
Septoplasty	13	2.2
Tympanoplasty	5	0.9
Endoscopic sinus surgery	5	0.9
Ophthalmologic surgeries	8	1.4
Other head and neck surgeries	45	7.7
Abdominal-laparoscopic-lower	71	12.2
Abdominal-laparoscopic-upper	28	4.8
Abdominal-non-laparoscopic-lower	165	28.3
Abdominal-non-laparoscopic-upper	53	9.1
Thoracic-laparoscopic	6	1.0
Thoracic-non-laparoscopic	13	2.2
Extremity surgeries	118	20.2
Other surgeries	30	5.1
Total	584	100.0

Values are presented as n (%). n, number of patients

The distribution of mutually exclusive antiemetic prophylaxis regimens is summarized in Table 4. Overall, 467 patients received at least one prophylactic antiemetic regimen, while 117 patients did not receive antiemetic prophylaxis.

The incidence of PONV and the use of rescue antiemetics at different postoperative time points are shown in Table 5. The incidence of PONV was highest during the first postoperative hour, affecting 128 patients (22.0%), and decreased at subsequent postoperative time points, with 47 patients at 6 hours, 14 patients at 12 hours, and 7 patients at 24 hours (Table 5).

Because first-hour PONV was the primary outcome, perioperative factors associated with this early recovery period were examined in detail. Univariate analyses showed that first-hour PONV was related to patient-related factors, anesthetic technique, and perioperative medication exposures rather than to a single variable (Table 6). This pattern was consistent with the highest PONV incidence

Table 3. Baseline PONV Risk Factors and Anaesthesia-Related Exposures

Anesthetic agent (yes/no)	Frequency (n)	Percentage (%)
Inhalation anaesthesia	428/156	(73.3/26.7)
Nitrous oxide	1/583	(0.2/99.8)
TIVA	26/558	(4.5/95.5)
Female/male	295/289	(50.5/49.5)
History of motion sickness (yes/no)	12/572	(2.1/97.9)
Non-smoker (yes/no)	333/251	(57.0/43.0)
Perioperative opioid use (yes/no)	331/253	(56.7/43.3)
Apfel risk score		
0	62	10.6
1	164	28.1
2	258	44.2
3	98	16.8
4	2	0.3
Fasting duration (hours)		
8	87	14.9
10	333	57.0
11	5	0.8
12	102	17.5
13	15	2.6
14	33	5.7
15	3	0.5
16	6	1.0
Total	584	100.0

Values are presented as n (%). n, number of patients; TIVA, total intravenous anaesthesia; PONV, postoperative nausea and vomiting

observed during the first postoperative hour and decreasing thereafter.

In the multivariable logistic regression analysis, perioperative opioid use remained significantly associated with first-hour PONV after adjustment for clinically relevant variables and antiemetic prophylaxis regimens (adjusted OR: 0.58, 95% CI: 0.38-0.89, *P*=0.013). Female sex, non-smoking status, general anaesthesia, inhalational anaesthesia, TIVA, and antiemetic prophylaxis regimens were not independently associated with first-hour PONV in the adjusted model. The inverse association observed for perioperative opioid use should be interpreted cautiously because opioid administration was not standardized and may reflect clinical selection in this retrospective cohort (Table 7).

Clinical and perioperative characteristics of patients who experienced PONV during the first postoperative hour are summarized in Panel B of Table 6. These descriptive findings provide additional context for the early PONV subgroup, while adjusted associations are presented separately in Table 7.

Table 4. Mutually Exclusive Antiemetic Prophylaxis Regimens Used in the Study Population

Regimen	Frequency (n)	Percentage (%)
No antiemetic prophylaxis	117	20.0
Ondansetron 4 mg only	147	25.2
Metoclopramide 20 mg only	163	27.9
Ondansetron+dexamethasone	134	22.9
Rare or overlapping prophylaxis regimens	23	3.9
Total	584	100.0

Values are presented as n (%). Rare or overlapping prophylaxis regimens included ondansetron+metoclopramide, ondansetron+metoclopramide+dexamethasone, ondansetron+scopolamine+dexamethasone, dexamethasone only, and metoclopramide+dexamethasone. n, number of patients

Table 5. Incidence of Postoperative Nausea and Vomiting and Rescue Antiemetic use by Postoperative Time Point

	PONV (yes/no)	Ondansetron/metoclopramide
Postop 1st hour	128/456	48/77
Postop 6th hour	47/537	14/28
Postop 12th hour	14/570	7/4
Postop 24th hour	7/577	3/2

Values are presented as n. Rescue antiemetic values indicate recorded ondansetron and metoclopramide administration at each time point and may not equal the total number of patients with documented PONV. PONV, postoperative nausea and vomiting; Postop, postoperative

Table 6. PONV-Associated Factors by Postoperative Time Point and Characteristics of Patients with Early PONV

Panel A. PONV-associated factors by postoperative time point

Variable	1st hour	6th hour	12th hour	24th hour
Type of surgery	0.157	0.020	0.889	0.034
Type of anaesthesia	0.001	0.146	0.174	0.169
ASA classification	0.466	0.813	0.888	0.773
Surgical size	0.501	0.004	0.586	0.346
Blood product use	0.408	0.041	0.624	0.917
Female gender	0.023	0.012	0.034	0.266
Motion sickness history	0.794	0.001	<0.001	0.700
Non-smoker	0.015	0.712	0.270	0.123
Perioperative opioid use	0.011	<0.001	0.560	0.751
Risk score	0.430	0.188	<0.001	0.062

Table 6. Continued

Panel A. PONV-associated factors by postoperative time point				
Inhalation anaesthesia	0.021	0.222	0.441	0.108
TIVA	0.037	0.032	0.414	0.566
Fasting duration	0.367	0.205	0.730	0.998
High FiO_2	0.374	0.780	0.696	0.915
NSAID use	<0.001	<0.001	0.624	0.032
Ondansetron use	0.001	0.019	0.681	0.294
Metoclopramide use	0.981	0.440	0.832	0.135
Dexamethasone use	0.024	0.907	0.121	0.516

Panel B. Characteristics of patients with PONV during the first postoperative hour	
Demographic data of patients with nausea and vomiting in 1 hour	**Value (mean ± SD)**
Age (years)	44.43±18.31
Height (cm)	168.33±8.57
Weight (kg)	76.39±15.15
Duration of surgery (min)	134.53±80.89
Duration of anaesthesia (min)	151.80±82.67
Total blood loss (mL)	173.63±286.55
Total fluid administered (mL)	1944.53±1293.93
Gender (F/M) (%)	76/52 (59.4/40.6)
ASA I/II/III (n) (%)	28/90/10 (21.9/70.3/7.8)
Type of anaesthesia (general/regional)	114 (89.1)/14(10.9)
Surgery type (laparoscopic/non-laparoscopic)	18 (14.1)/110 (85.9)
Surgical risk (low/medium/high)	59 (46.1)/63 (49.2)/6 (4.7)
RBC Transfusion (yes/no) (%)	4 (3.1)/122 (96.8)
Motion sickness history (yes/no) (%)	3 (2.3)/125 (97.7)
Non-Smoker (yes/no) (%)	85 (66.4)/43 (33.6)
Perioperative opioid use (yes/no) (%)	58 (45.3)/70 (54.7)
Ondansetron (%)	83 (64.8)
Metoclopramide (%)	40 (31.3)
Dexamethasone (%)	22 (17.2)

Panel A values are presented as *P* values. Panel B values are presented as mean ± SD or n (%). n, number of patients; F/M, female/male; ASA, American Society of Anesthesiologists; TIVA, total intravenous anaesthesia; FiO_2, fraction of inspired oxygen; NSAID, non-steroidal anti-inflammatory drug; PONV, postoperative nausea and vomiting; RBC, red blood cell; SD, standard deviation

Table 7. Multivariable Logistic Regression Analysis for First-Hour PONV

Variable	**Adjusted OR (95% CI)**	***P* value**
Female sex	1.28 (0.82-1.99)	0.272
Non-smoking status	1.38 (0.88-2.15)	0.158
Perioperative opioid use	0.58 (0.38-0.89)	0.013
General anaesthesia	1.62 (0.57-4.61)	0.366
Inhalational anaesthesia	1.36 (0.50-3.71)	0.551
Total intravenous anaesthesia	2.55 (0.83-7.85)	0.102

Table 7. Continued

Variable	Adjusted OR (95% CI)	*P* value
Metoclopramide-only prophylaxis	1.09 (0.41-2.89)	0.861
Ondansetron-only prophylaxis	2.05 (0.78-5.37)	0.146
Ondansetron+dexamethasone prophylaxis	0.84 (0.30-2.36)	0.743
Rare or overlapping prophylaxis regimens	1.77 (0.49-6.41)	0.385

Values are presented as adjusted odds ratios (ORs), 95% confidence intervals (CIs), and *P* values. The dependent variable was first-hour postoperative nausea and vomiting. No antiemetic prophylaxis was used as the reference category for antiemetic prophylaxis regimen variables. For binary variables, the reference categories were male sex, smoking status, no perioperative opioid use, regional anaesthesia, no inhalational anaesthesia, and no TIVA. PONV, postoperative nausea and vomiting; TIVA, total intravenous anaesthesia

Discussion

PONV remains a common complication following anaesthesia and adversely affects patient comfort and satisfaction. In some patients, PONV may lead to clinically significant consequences, particularly in those who cannot tolerate increases in heart rate, blood pressure, intrathoracic pressure, or central venous pressure. Previous studies have reported PONV incidences of up to 80% in high-risk populations and approximately 20-30% in the general surgical population.[1,4] In the present study, the incidence of nausea and vomiting during the first postoperative hour was 22%, which is consistent with rates reported in the literature. This finding suggests that early PONV remains a clinically relevant problem under routine perioperative conditions despite the widespread use of preventive strategies.

The incidence of PONV decreased progressively after the first postoperative hour, with lower rates observed at the 6th, 12th, and 24th postoperative hours. This temporal pattern may reflect the decreasing emetogenic effect of anesthetic agents after early recovery, the administration of rescue antiemetics to symptomatic patients, and the stabilization of postoperative pain and analgesic requirements over time. Therefore, the first postoperative hour appears to represent a clinically important period for detecting early PONV and evaluating immediate prophylactic effectiveness in the PACU setting.

An important component of PONV management is identifying patients who are more likely to experience this complication. Numerous patient-related, surgical, and anesthetic factors have been associated with an increased risk of PONV. Patient-related factors such as female sex, non-smoking status, a history of motion sickness, and perioperative opioid use have been consistently reported, whereas the influence of surgical type and extent remains variable across studies.[4-6,9,10]

In the present study, first-hour PONV was associated with several patient-related, anesthetic-related, and medication-related factors in univariate analyses. However, after adjustment for clinically relevant variables, including antiemetic prophylaxis regimens, female sex, non-smoking status, general anaesthesia, inhalational anaesthesia, TIVA were not independently associated with first-hour PONV. Although perioperative opioid use remained statistically associated with first-hour PONV in the adjusted model, the inverse association should be interpreted cautiously, because opioid administration was not standardized and may reflect clinical selection rather than a causal or protective effect.

Perioperative opioid administration is a well-recognized contributor to PONV, and opioid-sparing analgesic strategies form an important component of multimodal perioperative care.[11,12] In the present study, perioperative opioid use remained statistically associated with first-hour PONV in the adjusted model; however, the inverse direction of this association should not be interpreted as a protective effect. Because opioid type, dose, timing, pain intensity, and rescue analgesic requirements were not standardized in the retrospective records, this finding may reflect clinical selection or unmeasured confounding. Therefore, detailed prospective studies are needed to clarify the relationship between opioid exposure and early PONV.

Risk stratification tools, such as the Apfel scoring system, are widely used to estimate the likelihood of PONV and guide prophylactic strategies.[5] In the present study, a substantial proportion of patients had Apfel risk scores of two or higher, indicating a moderate-to-high baseline risk. Although the overall incidence of early PONV was relatively modest, the observed associations between Apfel-related factors and PONV are in line with previous literature.[5,6]

The type and extent of surgery have been variably associated with PONV in prior studies. While certain procedures, such as laparoscopic and gynecologic surgeries, have been described as higher risk, evidence remains inconsistent.[4,6] In the present study, no strong association was observed between surgical type or extent and early PONV, suggesting that anesthetic and patient-related factors may play a more prominent role in this setting.

Dexamethasone and 5-HT$_3$ receptor antagonists are commonly used antiemetic agents with established efficacy

in PONV prophylaxis.[4,13-15] Combination antiemetic therapy has been shown to provide greater protection than single-agent prophylaxis.[4,8,13,14] In the adjusted model, antiemetic prophylaxis regimens were evaluated as mutually exclusive categories; however, none of the prophylaxis regimens was independently associated with first-hour PONV. Because prophylaxis was not randomized and was likely influenced by baseline risk and clinician preference, these findings should be interpreted as descriptive associations rather than direct evidence of prophylactic efficacy.

The main contribution of this study is its description of early PONV and antiemetic practice patterns in an unselected real-world surgical cohort rather than in a protocol-driven trial population. By evaluating PONV at multiple postoperative time points and combining univariate findings with an adjusted analysis of first-hour PONV, the study provides insight into how established risk factors and routine prophylactic practices manifest in daily anaesthesia care. These findings may help identify areas where standardized risk assessment, documentation of antiemetic timing, and opioid-sparing strategies could be improved in prospective studies.

Overall, the findings of this study reflect real-life perioperative practice and highlight the multifactorial nature of PONV. Given the retrospective design and the presence of potential confounding factors, the results should be interpreted as associative rather than causal. Nevertheless, these observations may help inform preventive strategies and reinforce the importance of individualized PONV management.[4,6]

Study Limitations

This study has several limitations that should be considered when interpreting the findings. First, its retrospective design inherently limits control over data completeness and the standardization of variables. A complete-case analytical approach was applied, and patients with missing data in key perioperative variables or postoperative follow-up were excluded. As a result, selection bias cannot be fully excluded, and the analyzed cohort may not entirely represent the source population. In addition, the 1,000 reviewed records were selected based on record availability rather than random sampling, which should be considered when interpreting the external validity of the findings.

Second, although a multivariable logistic regression analysis, including clinically relevant variables and antiemetic prophylaxis regimens, was performed for first-hour PONV, the retrospective design and the routinely recorded nature of the data limited the ability to control for all potential confounders. Antiemetic prophylaxis was not randomized and may have been influenced by baseline PONV risk, clinician preference, and intraoperative clinical decisions. In addition, important exposure details, including antiemetic timing, opioid type, opioid dose and timing, pain intensity, rescue analgesic requirements, and standardized severity grading of nausea or vomiting, were not consistently available. Therefore, the adjusted results, particularly those related to opioid use and prophylaxis regimens, should be interpreted as exploratory and associative rather than causal or predictive.

Third, the study reflects real-world clinical practice at a single center, which may limit the generalizability of its results to other institutions with different patient populations or perioperative management protocols. Additionally, the small number of patients receiving TIVA limited the interpretability of findings related to anesthetic maintenance techniques; these results should not be interpreted as evidence against the established antiemetic advantages of propofol-based anaesthesia.

Despite these limitations, the study provides valuable insight into the incidence of early PONV and associated perioperative factors in routine anaesthesia practice.

Conclusion

This retrospective observational study showed that first-hour PONV remained a clinically relevant problem in routine perioperative care despite the common use of prophylactic antiemetics. Early PONV was associated with overlapping patient-related, anesthetic-related, and medication-related factors, supporting its multifactorial nature in daily anaesthesia practice. After adjustment, many of the observed associations were attenuated, emphasizing the need for cautious interpretation of retrospective real-world data. These findings highlight the importance of careful early postoperative monitoring, standardized risk assessment, and individualized risk-based preventive strategies.

Ethics

Ethics Committee Approval: This study was approved by the Süleyman Demirel University Clinical Research Ethics Committee (decision no: 34, date: 26.01.2022).

Informed Consent: Written informed consent, obtained at hospital admission, referred to anaesthesia and routine clinical care. Because this was a retrospective chart review study using anonymized data, study-specific informed consent was not obtained.

Footnotes

Authorship Contributions: Surgical and Medical Practices – O.B.; Concept – F.A.S.; Design – O.B., F.A.S.; Data Collection or Processing – M.S.Ö., G.İ.; Analysis or Interpretation – M.S.Ö., G.İ., P.K.; Literature Search – M.S.Ö., P.K.; Writing – O.B., F.A.S.

Declaration of Interests: The authors declare no conflict of interests.

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Original Article
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Comparison of Postoperative Analgesic Efficacy Between Opioid-free Anaesthesia Using Intravenous Magnesium, Lidocaine, and Erector Spinae Plane Block, and Opioid-based Anaesthesia in Laparoscopic Abdominal Surgeries: A Randomised Controlled Trial

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Abstract

Objective: Opioid-based anaesthesia is a standard practice in laparoscopic surgeries. However, it is associated with adverse effects that can limit its use. To address these issues, opioid-free anaesthesia has been introduced as an alternative. This study aims to compare the analgesic efficacy of opioid-free anaesthesia, incorporating magnesium, lidocaine, and an erector spinae plane block (ESPB), with traditional opioid-based anaesthesia during laparoscopic procedures.

Methods: Seventy patients aged 18-60 years undergoing laparoscopic surgery were randomly divided into two groups of 35 each. Opioid-free group received opioid-free anaesthesia, which included an intravenous (IV) bolus of 2 g magnesium, a continuous lidocaine infusion at 1.5 mg kg^{-1} hr^{-1}, and a bilateral ESPB with 25 mL of 0.25% bupivacaine. Opioid-based group received opioid-based anaesthesia with an IV dose of 2 µg kg^{-1} fentanyl. Postoperative pain and the need for rescue analgesia were assessed for 24 h. Perioperative haemodynamic parameters were recorded, and the incidence of postoperative complications, including sedation, nausea, vomiting, and shivering, was monitored for 24 h.

Results: Pain scores were significantly lower in the opioid-free group compared to the opioid-based group at 0 h ($P < 0.001$), 2 h ($P < 0.001$), and 4 h ($P=0.005$) postoperatively. The opioid-based group required rescue analgesia more frequently ($P < 0.001$). Additionally, the incidence of postoperative complications was significantly lower in the opioid-free group than in the opioid-based group ($P < 0.001$). Haemodynamic parameters were similar between the two groups.

Conclusion: Opioid-free anaesthesia provides superior postoperative analgesia and reduces the incidence of postoperative complications compared with opioid-based anaesthesia for laparoscopic surgery.

Keywords: Fentanyl, lidocaine, magnesium, opioid, pain, regional anaesthesia

Main Points

- Opioid-free anaesthesia provides better postoperative analgesia than opioid-based anaesthesia.
- The requirement for rescue analgesia is lower in the opioid-free group than in the opioid-based group.
- The incidence of postoperative complications was lower in the opioid-free group.

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Introduction

Laparoscopic procedures are widely preferred for their minimally invasive approach, which leads to reduced postoperative pain and faster recovery compared to open surgery. However, the early postoperative period may still involve pain owing to tissue injury. Peritoneal irritation from pneumoperitoneum and residual blood can also cause considerable discomfort.[1] These surgeries are typically performed under general anaesthesia, with opioids used to blunt the intubation response and manage perioperative pain. Despite their sympatholytic benefits, opioids are associated with adverse effects such as sedation, respiratory depression, vomiting, dependence, and tolerance.[2] To address these concerns, opioid-free anaesthesia has recently become a popular approach to perioperative pain management.[3] The erector spinae plane block (ESPB) achieves analgesia by blocking the ventral and dorsal rami of thoracic spinal nerves.[4] Lidocaine and magnesium are also used for managing perioperative pain. We hypothesised that opioid-free anaesthesia, incorporating magnesium, lidocaine, and ESPB, would provide superior postoperative analgesia compared to opioid-based anaesthesia. The primary objective of this study was to assess the time to first postoperative rescue analgesia as a measure of analgesic efficacy. Secondary objectives included monitoring perioperative hemodynamic parameters and postoperative complications such as sedation, nausea, vomiting, and shivering.

Current literature on the use of the ESPB as part of opioid-free anaesthesia in laparoscopic surgeries is limited. This study aims to promote the broader adoption of ESPB in these procedures. In this context, we conducted the study to evaluate the analgesic efficacy of opioid-free anaesthesia, including intravenous (IV) magnesium, lidocaine, and ESPB, compared with opioid-based anaesthesia with fentanyl during laparoscopic surgery.

Methods

This prospective, randomised, controlled trial was performed at a tertiary care hospital and enrolled 70 patients aged 18-60 years with American Society of Anesthesiologists (ASA) physical status I-II who were undergoing laparoscopic cholecystectomy or appendectomy. The study commenced after receiving approval from the Aarupadai Veedu Medical College & Hospital Institutional Human Ethical Committee (approval no: AV/IHEC/2022/061, date: 18.08.2022) and after being registered with the Clinical Trial Registry of India (CTRI/2022/10/046738).

The study period spanned from November 2022 to May 2024. Patients were excluded if they had coagulation abnormalities, infections at the regional block site, hypersensitivity to the administered drugs, a body mass index >35 kg m^{-2}, or if they were undergoing emergency surgeries.

After obtaining informed written consent, preoperative assessments were performed and baseline vital signs were recorded for all 70 patients. Patients were randomly allocated to two groups (n = 35 each) using a computer-generated randomisation sequence created by an independent statistician, and group allocation was concealed using sealed opaque envelopes. The opioid-free group received IV lidocaine and magnesium, whereas the opioid-based group received IV lidocaine and fentanyl.

Alprazolam 0.25 mg and pantoprazole 40 mg were administered orally as premedication the night before surgery. Standard ASA fasting guidelines were adhered to before the procedure. In the preoperative area, an IV cannula was inserted, and IV fluids were started. Upon arrival in the operating room, standard ASA monitors were attached, including electrocardiogram, pulse oximetry, and non-invasive blood pressure monitoring. The patients were pre-oxygenated with 100% oxygen for 3 min. Premedication was administered to both groups with IV midazolam 0.05 mg kg^{-1}, glycopyrrolate 0.01 mg kg^{-1}, and ondansetron 0.1 mg kg^{-1}.

Opioid-free group patients received an IV bolus of lidocaine 1.5 mg kg^{-1} and magnesium 2 g before induction. Opioid-based group patients received an IV bolus of lidocaine 1.5 mg kg^{-1} and fentanyl 2 µg kg^{-1} before induction.

In both groups, patients were induced with propofol 2 mg kg^{-1} IV, and succinylcholine 2 mg kg^{-1} IV was administered to facilitate intubation. After intubation, a loading dose of cisatracurium 0.2 mg kg^{-1} IV was given to maintain muscle relaxation. In the opioid-free group, a lidocaine infusion at a rate of 1.5 mg kg^{-1} hr^{-1} was started after intubation, and an ESPB was performed at the T6 level bilaterally with 25 mL of 0.25% bupivacaine while the patient was positioned laterally. Anaesthesia was maintained with a mixture of 50% nitrous oxide, 50% oxygen, and 1% isoflurane to achieve a Minimum alveolar concentration of 1. Cisatracurium 0.03 mg kg^{-1} IV was administered every 30 min in both groups. In both groups, intraoperative haemodynamic parameters, including heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP), were monitored and recorded at eight time points: baseline, after intubation, before pneumoperitoneum, and at 10, 30, and 60 min after pneumoperitoneum, as well as after carbon dioxide (CO_2) deflation and after extubation. If HR or MAP increased by more than 20% from baseline, the opioid-free group received an Esmolol 10 mg IV bolus, while the opioid-based group was administered fentanyl 0.5 µg kg^{-1}. In the opioid-free group, the lidocaine infusion was discontinued at the beginning of skin suturing. Both groups received neostigmine 0.05 mg kg^{-1} IV and glycopyrrolate

0.01 mg kg^{-1} IV for reversal of neuromuscular blockade. After extubation, patients were transferred to the recovery room for observation and were provided with oxygen support via a face mask. Upon arrival in the recovery room, pain and sedation level were assessed using the Visual Analogue Scale (VAS) and the Ramsay Sedation Scale, respectively. Assessments were then repeated at 2, 4, 6, 12, and 24 h postoperatively. Patients with a VAS score of 5 or higher received 1 g paracetamol IV as rescue analgesia. Postoperative complications such as nausea, vomiting, and shivering were monitored and treated as needed for 24 h.

Statistical Analysis

The sample size was calculated a priori for the primary outcome (postoperative VAS score) based on data from a previously published study by Ragupathy et al.,[5] which evaluated postoperative pain using the VAS in patients undergoing laparoscopic surgeries. A clinically meaningful mean difference of 2 VAS units and a standard deviation of 2.3 VAS units were assumed. With a two-sided significance level (α) of 0.05 and a power (1-β) of 80%, the minimum required sample size was 66 participants (33 per group). To account for potential dropouts (anticipated 6-10%), the sample size was increased and rounded up to 35 participants per group, resulting in a total of 70 participants.

Statistical analyses were performed using the Statistical Package for the Social Sciences, version 23.0 (IBM Corp., Armonk, NY, USA). Continuous data were expressed as mean ± standard deviation and compared using the independent samples t-test. Categorical data were presented as counts (percentages) and compared using the chi-square test or Fisher's exact test, as appropriate. All tests were two-sided, and a P value <0.05 was considered statistically significant.

Results

A total of 83 patients were evaluated for the study, with 13 excluded for not meeting eligibility criteria. The remaining 70 patients were randomly assigned to two groups of 35 each. All participants completed the study (Figure 1). Demographic and patient characteristics were similar across groups (Table 1).

Figure 2 shows the distribution of VAS scores at various postoperative time intervals for each group. VAS scores were significantly higher in the opioid-based group at 0 h (P < 0.001), 2 h (P < 0.001), and 4 h (P=0.005).

The requirement for rescue analgesia was significantly higher in the opioid-based group than in the opioid-free group (P <

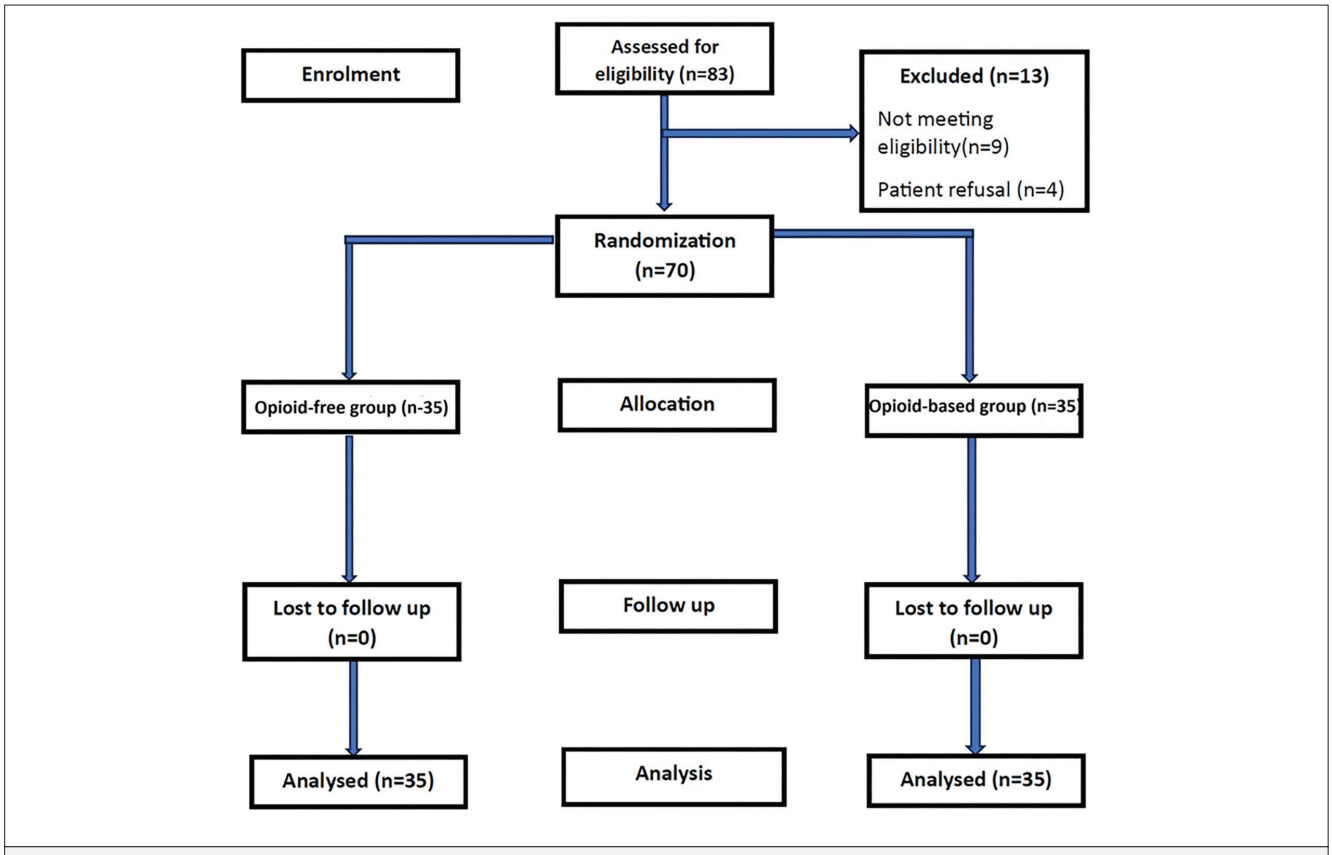


Figure 1. Consort flowchart.

Table 1. Comparison of Demographic and Clinical Characteristics Among the 2 Groups

	Opioid-free group	Opioid-based group	*P* value
Age (years), mean ± SD	40.32±13.642	37.63±11.184	0.370
Gender, n (%)			0.454
Male	21 (60.0)	24 (68.6)	
Female	14 (40.0)	11 (31.4)	
BMI (kg m^{-2}), mean ± SD	23.16±1.842	23.42±2.301	0.603
ASA class, n (%)			0.445
Class I	25 (71.4)	22 (62.9)	
Class II	10 (28.6)	13 (37.1)	
Surgical procedure, n (%)			0.337
Laparoscopic appendectomy	14 (40)	18 (51.4)	
Laparoscopic cholecystectomy	21 (60)	17 (48.6)	
Duration of surgery, n (%)			0.858
Less than 60 minutes	13 (37.2)	11 (31.4)	
60 to 120 minutes	18 (51.4)	19 (54.3)	
More than 120 minutes	4 (11.4)	5 (14.3)	

BMI, body mass index; ASA, American Society of Anesthesiologists physical status; SD, standard deviation

0.001) (Table 2). However, time to first rescue analgesia did not differ significantly between groups (*P*=0.401) (Table 2).

Mean HR values at different time points were comparable between the two groups, with no statistically significant differences (all $P > 0.05$) (Table 3).

Similarly, baseline SBP, DBP, and MAP were comparable between the groups, with no significant differences observed after intubation or before CO_2 insufflation (Table 4). However, at 10 and 30 minutes after CO_2 insufflation, SBP, DBP, and MAP were significantly higher in the opioid-based group compared to the opioid-free group (all $P < 0.05$). No statistically significant differences were observed at 60 minutes after CO_2 insufflation, after CO_2 deflation, or after extubation (all $P > 0.05$) (Table 4).

This study found that sedation levels were significantly higher in the opioid-based group compared to the opioid-free group at 2 h (*P*=0.018) and 4 h (*P*=0.031) postoperatively (Figure 3).

Postoperative nausea (*P*=0.074), vomiting (*P*=0.555), and shivering (*P*=0.314) did not differ significantly between the two groups. However, the overall incidence of complications was significantly higher in the opioid-based group than in the opioid-free group (*P*=0.021) (Figure 4).

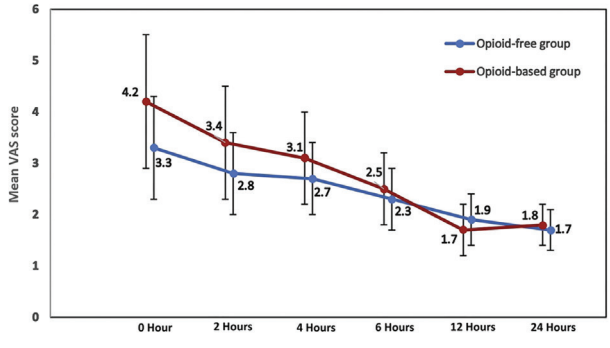


Figure 2. Postoperative mean VAS score at various time points among the 2 groups. Error bars represent standard deviation.

VAS, visual analogue scale.

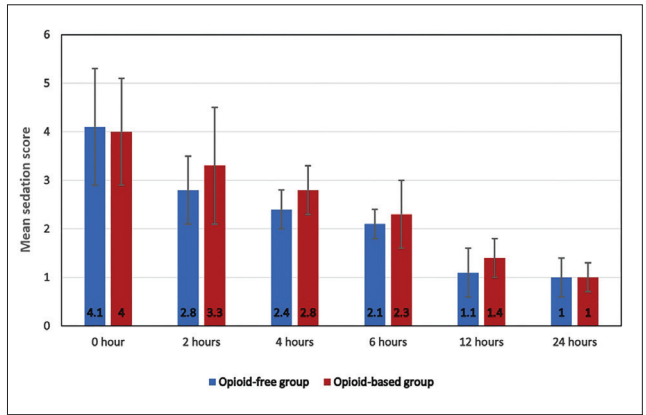


Figure 3. Mean Ramsay Sedation Scale at various time points among the 2 groups. Error bars represent standard deviation.

Table 2. Distribution of Need for Rescue Analgesia and Time Taken for the First Dose of Rescue Analgesia Among the 2 Groups

Need for rescue analgesia	Opioid-free group n (%)	Opioid-based group n (%)	Total n (%)	*P* value
Yes	17 (48.6)	32 (91.4)	49 (70.0)	<0.001*
No	18 (51.4)	3 (8.6)	21 (30.0)	
Total	35 (100)	35 (100)	70 (100)	
Time taken for the first dose of rescue analgesia	**Opioid-free group n**	**Opioid-based group n**	**Total n**	***P* value**
Less than 6 hours	12	27	39	0.401
6-12 hours	4	3	7	
More than 12 hours	1	2	3	
Total	17	32	49	

*: Statistical significance

Table 3. Comparison of Heart Rate Between the Two Groups at Different Intraoperative Time Points

Heart rate	Opioid-free group Mean ± SD	Opioid-based group Mean ± SD	*P* value
Baseline	86.1±4.8	87.5±5.2	0.245
After intubation	87.3±5.9	86.4±6.4	0.541
Before CO_2 insufflation	85.4±7.5	84.3±7.2	0.532
10 mins after CO_2 insufflation	86.6±7.3	86.5±6.6	0.953
30 mins after CO_2 insufflation	85.3±7.5	85.2±7.6	0.957
60 mins after CO_2 insufflation	85.7±8.0	85.6±6.1	0.954
After CO_2 deflation	84.3±7.5	84.2±7.6	0.957
After extubation	82.7±8.3	83.6±6.5	0.614

CO_2, carbon dioxide, SD, standard deviation

Table 4. Comparison of Systolic Blood Pressure, Diastolic Blood Pressure, and Mean Arterial Pressure Between the Two Groups at Different Intraoperative Time Points

Time point	SBP opioid-free group Mean ± SD	SBP opioid-based group Mean ± SD	SBP *P* value	DBP opioid-free group Mean ± SD	DBP opioid-based group Mean ± SD	DBP *P* value	MAP opioid-free group Mean ± SD	MAP opioid-based group Mean ± SD	MAP *P* value
Baseline	113.2±6.6	113.0±3.4	0.874	72.5±5.3	73.3±2.7	0.428	69.2±4.4	67.7±3.2	0.107
After intubation	114.8±5.1	114.3±9.1	0.778	71.8±6.9	72.0±1.4	0.867	68.4±5.4	66.3±3.9	0.067
Before CO_2 insufflation	112.3±6.7	112.1±3.7	0.878	73.9±4.1	72.3±3.9	0.098	68.3±5.8	66.6±3.5	0.165
10 mins after CO_2 insufflation	115.7±8.4	111.3±7.8	0.025*	74.1±5.4	71.0±2.9	0.005*	70.3±5.4	67.4±3.4	0.012*
30 mins after CO_2 insufflation	115.8±6.8	112.3±3.2	0.008*	75.2±4.2	72.1±2.1	<0.001*	69.3±5.1	67.2±2.9	0.037*
60 mins after CO_2 insufflation	114.3±5.6	112.8±8.7	0.395	74.6±4.3	74.1±2.8	0.546	69.0±4.7	68.0±2.0	0.250
After CO_2 deflation	112.3±6.3	111.3±3.4	0.412	74.3±3.3	73.0±2.6	0.072	67.8±5.7	66.8±2.4	0.361
After extubation	114.3±6.2	114.5±2.3	0.859	74.1±5.4	74.0±3.4	0.926	68.3±5.5	67.5±2.0	0.409

*: Statistical significance

SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; CO_2, carbon dioxide

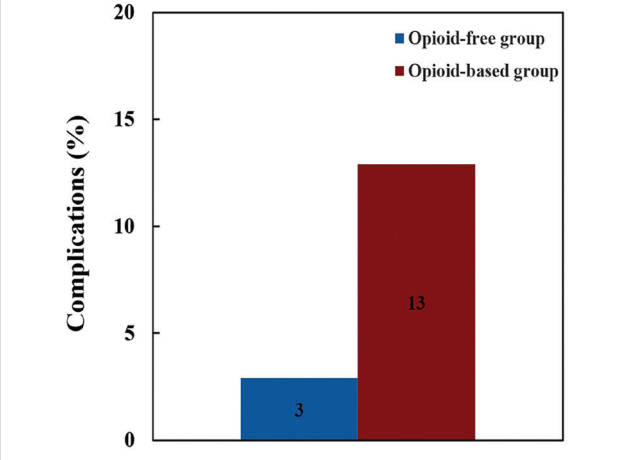


Figure 4. Distribution of overall complications among the 2 groups.

Discussion

In this study, we compared the analgesic efficacy of opioid-free anaesthesia with that of opioid-based anaesthesia during laparoscopic surgeries. Our findings showed that patients in the opioid-free group reported lower pain scores than those in the opioid-based group.

Laparoscopic procedures are preferred for their advantages, such as shorter hospital stays and fewer complications; however, managing immediate postoperative pain remains challenging. Pain after laparoscopic procedures can be substantial for up to 6 h postoperatively.[1] Traditionally, opioids have been used for pain management during these surgeries despite their associated side effects. In response, opioid-free anaesthesia has emerged as an effective alternative that employs a combination of medications, peripheral nerve blocks, and neuraxial analgesia to achieve comparable pain relief and reduce opioid-related complications.[6]

Lidocaine offers several benefits in the perioperative setting, including suppression of the intubation response, reduction of pain, reduction in postoperative nausea and vomiting, and shortening of the duration of ileus.[7,8] Its analgesic effects are multifaceted, involving the inhibition of sodium, potassium, and calcium channels, Gαq-coupled protein receptors, N-methyl-D-aspartic acid (NMDA) receptors, and 5-hydroxytryptamine 3 receptors.[9] Magnesium is also used perioperatively to manage pain, acting through both competitive and non-competitive antagonism of NMDA receptors at hippocampal presynaptic calcium channels, thus preventing central sensitisation.[10] In the ESPB, local anaesthetics are administered into the deep fascia of the erector spinae muscle at the level of the transverse process to block the dorsal rami of the spinal nerves. Additionally, these anaesthetics diffuse into the paravertebral space, providing further pain relief.[4,11]

This study found that the opioid-based group had higher VAS scores at 2 and 4 h postoperatively compared to the opioid-free group. Consequently, the opioid-based group required rescue analgesia more frequently during the first 6 h postoperatively. The lower VAS scores in the opioid-free group can be attributed to the extended analgesic effects of the ESPB and to the administration of lidocaine and magnesium.[12] This finding is consistent with a meta-analysis by Koo et al.,[13] which reviewed eight randomised controlled trials assessing the postoperative analgesic efficacy of the ESPB in patients undergoing laparoscopic cholecystectomy. The analysis concluded that the ESPB effectively reduces pain scores for up to 12 h postoperatively in this patient group.[13]

Aronsohn et al.[14] assessed the analgesic efficacy of opioid-free versus opioid-based anaesthesia, with the opioid-free group receiving dexmedetomidine, ketamine, and lignocaine. They found that median pain scores were similar during both the initial 6 h post-surgery and the subsequent 6-24 h.[14] Based on these findings, we conclude that the extended postoperative pain relief observed in the opioid-free group is mainly attributable to the ESPB rather than to lignocaine and magnesium.

The mean SBP, DBP, and MAP were similar from baseline until CO_2 inflation. However, these values were considerably higher in the opioid-based group at both 10 and 30 min after pneumoperitoneum. This disparity may be attributed to the superior analgesic efficacy and sympatholytic effects of the ESPB, lidocaine, and magnesium used in the opioid-free group, compared with those of fentanyl. This observation is consistent with the study by Elshafie et al.,[12] which compared opioid-free anaesthesia involving the ESPB, dexmedetomidine, magnesium, and lidocaine, with opioid-based anaesthesia during hepatic resection. They found that the block group had significantly lower intraoperative blood pressure than the opioid-based group.[12]

The postoperative Ramsay sedation score was higher in the opioid-based group at both 2 and 4 h than in the opioid-free group, likely owing to the pronounced sedative effects of fentanyl. This result contrasts with a study by Choi et al.,[15] which evaluated recovery quality between opioid-free (dexmedetomidine and lidocaine) and opioid-based (remifentanil) anaesthesia following gynaecological laparoscopy. They found no significant difference in sedation levels between the groups.[15] Another study by Massoth et al.,[16] which compared opioid-free and opioid-based anaesthesia after gynaecological surgery, reported higher sedation levels in the opioid-free group, which received dexmedetomidine and esketamine compared with the group receiving sufentanil. The variation in findings may be attributed to the shorter duration of action of remifentanil and sufentanil.

The incidence of postoperative nausea, vomiting, and shivering was similar between the two groups. However, when individual complications were combined, the opioid-based group showed a significantly higher overall incidence of complications than the opioid-free group. This indicates that while the frequencies of individual complications did not differ considerably, the opioid-based group experienced a higher total number of complications. This finding is consistent with the study by Toleska and Dimitrovski[17] which compared opioid-free and opioid-based anaesthesia during laparoscopic cholecystectomy and found that the opioid-based group had a higher rate of postoperative complications. However, the small sample size and the focus on only two types of laparoscopic surgery limited the generalizability of these results to other laparoscopic procedures.

Conclusion

Opioid-free anaesthesia provides superior perioperative analgesia and reduces the incidence of postoperative complications compared to opioid-based anaesthesia in laparoscopic surgeries. We recommend using the ESPB in combination with lidocaine and magnesium to provide effective analgesia during these procedures.

Ethics

Ethics Committee Approval: Approval from the Aarupadai Veedu Medical College & Hospital Institutional Human Ethical Committee (approval no: AV/IHEC/2022/061, date: 18.08.2022) and after being registered with the Clinical Trial Registry of India (CTRI/2022/10/046738).

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

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Footnotes

Authorship Contributions: Surgical and Medical Practices - J.V.J., E.V.; Concept - J.V.J., P.J.; Design - E.V., P.J.; Data Collection and/or Processing - J.V.J.; Analysis and/or Interpretation - E.V., P.J.; Literature Review - J.V.J., E.V.; Writing - J.V.J.

Declaration of Interests: The authors declare no conflicts of interest.

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Microscopic Evaluation of Crystallization Dynamics in 0.25% Levobupivacaine Mixed with Common Regional Anaesthesia Adjuvants: An *in vitro* Compatibility Study

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Abstract

Objective: To investigate the crystallization dynamics of 0.25% levobupivacaine when combined with common regional anaesthesia adjuvants.

Methods: This *in vitro* study examined mixtures of 0.25% levobupivacaine with dexamethasone (20:1), 25% magnesium sulfate (20:1.5), dexmedetomidine (20:1), 8.4% sodium bicarbonate (10:1), and adrenaline (1:100,000). The study protocol was an *in vitro* investigation. Since no human or animal subjects were involved, the study was exempt from formal ethics committee approval. An institutional waiver was obtained from the Ministry of Health of the Republic of Uzbekistan Research Administration of the Republican Scientific Emergency Medical Centre (ref no: 03-05/119, date: 15.01.2026). All mixtures were incubated at 37 °C and examined under light microscopy (40× magnification) immediately, at 15 minutes, and at 1 hour. Crystallization onset, crystal count, and crystal size were quantified. For accurate dimensional analysis, a stage micrometer was used to calibrate the digital imaging software, and a calibrated scale bar was superimposed on each micrograph. Statistical analyses were performed using IBM SPSS Statistics for Windows, version 30.0 (IBM Corp., Armonk, NY, USA). Overall changes across the three matched assessment times were evaluated using the Friedman test. Significant omnibus results were followed by paired Wilcoxon signed-rank tests with Holm adjustment for multiple comparisons. All tests were two-sided, and a P value <0.05 was considered statistically significant.

Results: Solutions containing sodium bicarbonate and dexamethasone demonstrated the earliest onset of crystallization. Sodium bicarbonate (10:1) produced immediate and massive precipitation. Levobupivacaine-dexamethasone mixtures showed progressive crystallization, with particle counts exceeding 100 per field for particles larger than 10 µm within 60 minutes. Adrenaline, magnesium sulfate, and dexmedetomidine showed significantly lower crystal densities than those of alkaline mixtures.

Conclusion: Based on the present *in vitro* findings, adding either 8.4% sodium bicarbonate or dexamethasone to 0.25% levobupivacaine produced rapid, substantial crystallization, suggesting a physicochemical incompatibility under the tested conditions. These findings suggest that direct admixture of these agents with levobupivacaine in the same syringe should be approached with caution pending confirmation in clinical studies.

Keywords: Adjuvants, anaesthesia, crystallization, drug incompatibility, levobupivacaine, pharmaceutic

Main Points

- Sodium bicarbonate (8.4%) results in immediate, extensive crystallization when mixed with 0.25% levobupivacaine.
- Dexamethasone induces time-dependent crystal formation, with crystals exceeding 10 µm within 60 minutes.
- Adrenaline, magnesium sulfate, and dexmedetomidine exhibit little evidence of crystallization, indicating high physical stability.
- *In vitro* microscopic analysis is an essential pre-clinical tool for screening drug-drug incompatibilities.

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Introduction

In contemporary regional anaesthesia practice, clinicians increasingly rely on intermediate-long-acting local anesthetics, such as bupivacaine, ropivacaine, and liposomal formulations. Among these, levobupivacaine - the S-enantiomer of bupivacaine - is often the clinician's first choice, primarily due to its more favorable safety profile regarding cardiovascular and neurological toxicity.[1] Despite their effectiveness, a clinical challenge remains: the relatively brief duration of action of these agents. To address this, pharmacological additives known as adjuvants are integrated into anaesthesia protocols to accelerate the onset of action, extend the analgesic effect, and mitigate systemic risks.[2] Adjuvants are now recognized as pivotal elements in multimodal analgesia strategies. Current clinical literature supports the use of various substances, including adrenaline, dexmedetomidine, magnesium sulfate, sodium bicarbonate ($NaHCO_3$), clonidine, and dexamethasone, to optimize nerve blocks.[3] For instance, Abanoub M et al.[4] demonstrated that incorporating dexamethasone into a transversus abdominis plane block for emergency laparotomy significantly decreased postoperative opioid requirements compared to using local anesthetics alone (P=0.05). Similarly, research by Zeng et al.[5] on 312 patients indicated that combining both dexamethasone and dexmedetomidine as adjuvants provided a longer analgesic window than using either agent individually. Furthermore, a meta-analysis encompassing 21 randomized trials confirmed that magnesium sulfate as an additive markedly prolonged block duration and improved pain scores on the visual analogue scale (VAS) (mean difference =114.35 minutes; 95% confidence interval: 89.31-139.88) and reduced pain intensity on VAS (mean difference =-1.54 points; 95% confidence interval: -2.56 to -0.53).[6] Despite these clinical benefits, the physicochemical interactions between these adjuvants and local anesthetics —specifically the risk of crystallization—remain under-researched. Local anesthetics are weak bases; both bupivacaine and levobupivacaine have a pKa of 8.1 and limited solubility in water. When combined with substances that alter the local pH, such as the weakly basic corticosteroid dexamethasone, these anesthetics may precipitate as crystalline forms. This crystallization is primarily driven by the transition of the anesthetic into its non-ionized state in an alkaline milieu. Microscopic studies have revealed that mixing dexamethasone with local anesthetics can result in the formation of numerous crystals of varying sizes. Therefore, a thorough evaluation of the crystallization potential is mandatory before implementing these adjuvant combinations in spinal, epidural, or peripheral nerve blocks to ensure patient safety. The objective of this study was to investigate the effects of various adjuvants on the crystallization processes of 0.25% levobupivacaine.

Methods

This study was an in vitro investigation. Since no human or animal subjects were involved, the study was exempt from formal ethics committee approval. An institutional waiver was obtained from the Ministry of Health of the Republic of Uzbekistan Research Administration of the Republican Scientific Emergency Medical Centre (reference no. 03-05/119, dated January 15, 2026). Informed consent was not applicable because no human participants were involved.

The study utilized levobupivacaine (trade name "Sofanest", 0.25%, 20 mL, SP LLC "Jurabek Laboratories", Uzbekistan), dexamethasone (4 mg dexamethasone sodium phosphate, "Radiks" LLC), adrenaline (FSUE "Moscow Endocrine Plant"), magnesium sulfate (SP LLC "Jurabek Laboratories", Uzbekistan), and dexmedetomidine (EVER Pharma, Germany) as adjuvants. All the preparations were heated in a water bath at 37°C prior to mixing. Crystallization of adjuvants mixed with the local anesthetic was observed using a Primo Star light microscope (ZEISS, Germany).

A 20 mL solution of 0.25% levobupivacaine, heated to 37 °C, was mixed with dexamethasone solution at a 20:1 ratio, magnesium sulfate solution at a 20:1.5 ratio, dexmedetomidine solution at a 20:1 ratio, and adrenaline solution diluted to 1:100,000 at an equivalent ratio to levobupivacaine. These selected ratios represent the minimum clinically used doses of adjuvants added to local anesthetics. Additionally, $NaHCO_3$ (8.4%) was tested at a 10:1 ratio. All microscopic preparations were maintained at a physiological temperature of 37 °C on a heated stage during the primary microscopic examinations at 15 minutes and 1 hour to ensure clinical relevance.

Prepared solutions (1 drop each) were placed on a glass slide, covered with a coverslip, and examined under a light microscope at 40× magnification. To simulate *in vivo* conditions and prevent artifactual crystallization caused by sample dehydration or low-temperature exposure over time, the microscopic preparations were maintained at a constant temperature of 37 °C using a thermal stage during the observation periods (15 minutes and 1 hour post-preparation). The mixtures were immediately transferred to slides for microscopic evaluation. Crystallization rates and the shape, number and size of formed crystals were quantified using advanced digital image analysis. To ensure the reliability and reproducibility of the data, multiple AI-based models (including OpenAI ChatGPT-4o, xAI Grok-3, Anthropic Claude 3.5, and Google Gemini 1.5 Pro) were employed to cross-verify the microscopic measurements. The final grade of crystallization (GoC) was determined via a "majority consensus" protocol (agreement of at least 3 models). In cases of split results, a senior investigator, blinded

to the adjuvant type, performed the final assessment. Crystal size, shape, and count were quantified using a validated 0-5 point grading scale (Table 1).[7]

Microscopic images were captured using a Primo Star light microscope (ZEISS, Germany) equipped with a 40× objective lens. For accurate dimensional analysis, a stage micrometer was used to calibrate the digital imaging software. A 20-µm scale bar was superimposed on each micrograph to provide a consistent visual reference for crystal size and density across all time points.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, version 30.0 (IBM Corp., Armonk, NY, USA). For each adjuvant combination, 15 independently prepared replicates were evaluated; each replicate was assessed immediately after preparation and at 15 and 60 minutes. The independently prepared replicate mixture was considered the experimental unit. Continuous variables are presented as mean ± standard deviation, and the ordinal GoC score is reported as an ordinal score. Overall changes across the three matched assessment times were evaluated using the Friedman test. When the omnibus test was statistically significant, paired post-hoc comparisons were performed using Wilcoxon signed-rank tests with Holm adjustment for multiple comparisons. When crystal size could not be measured immediately because no crystals were detected, the 15- and 60-minute measurements were compared using the Wilcoxon signed-rank test. Outcomes that remained constant across all assessment times were not statistically tested, and crystal appearance and morphology were assessed descriptively. All tests were two-sided, and a *P* value <0.05 was considered statistically significant.

Table 1. Crystallization Grading Scale (Adapted From)[7]

Grade	Description
0	No crystals observed
1	1 crystal in 1 field of view, size >10 µm
2	2-10 crystals in 1 field of view, size >10 µm
3	>10 crystals (but <100) in 1 field of view, size >10 µm or 1 crystal, size >50 µm
4	>100 crystals in 1 field of view, size >10 µm or 1 crystal, size >50-<100 µm
5	>100 crystals in 1 field of view, size >10 µm and >1 crystal, size >50 µm and 1 crystal, size >100 µm

Results

Levobupivacaine, an isomer of bupivacaine, is associated with a lower incidence of cardiotoxicity and neurotoxicity than bupivacaine. It has a pKa of 8.1 and a pH range of 4-6.5 and is prepared in an acidic environment to ensure its water solubility. The addition of agents that shift the pH of the solution toward alkalinity accelerates the crystallization of levobupivacaine.

Microscopic observation revealed that crystallization had commenced in the 20:1 mixture of 0.25% levobupivacaine and dexamethasone upon preparation. The number, size, and degree of crystallization of the formed crystals were highest compared with those in preparations in which other adjuvants were added to an equivalent dose of levobupivacaine (Figure 1).

In the first field of view (A), crystallization was observed to have commenced immediately after preparation, as revealed by microscopic examination. The second field of view (B) shows the crystallization process 15 minutes after preparation, while the third field of view (C) shows the

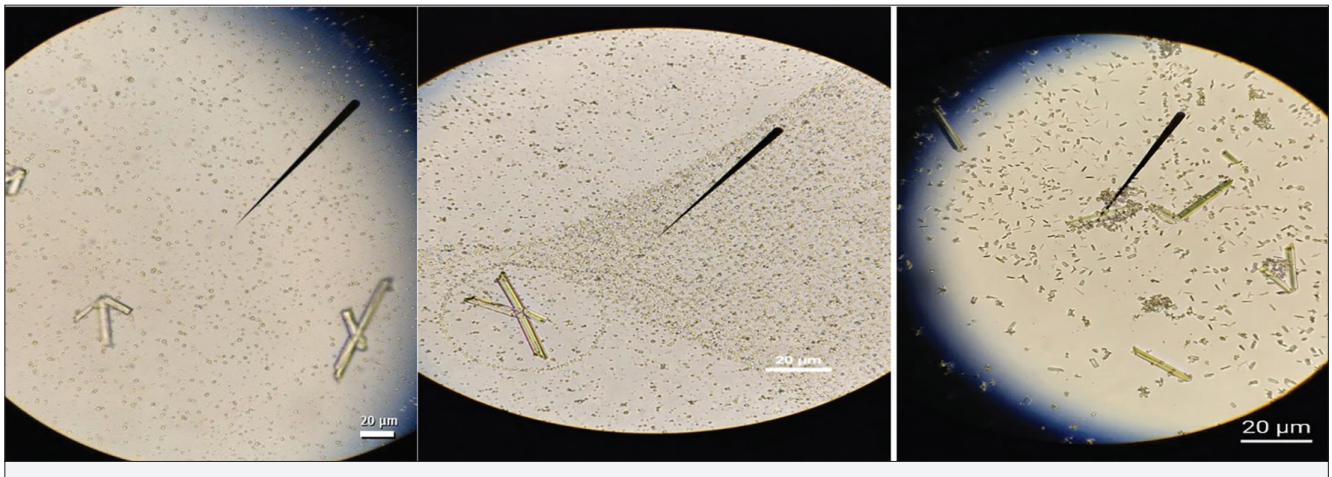


Figure 1. Microscopic appearance of crystals in 0.25% levobupivacaine and dexamethasone solution at a 20:1 ratio. A) Microscopic appearance of crystals immediately upon preparation; B) Microscopic appearance of crystals 15 minutes after preparation; C) Microscopic appearance of crystals 1 hour after preparation.

microscopic analysis 1 hour after preparation. Quantitative parameters of the formed crystals, including the total count, mean size, average surface area, and GoC, were assessed using digital image processing. To ensure high analytical precision, multiple large language models with vision capabilities, OpenAI ChatGPT (GPT-4o), xAI Grok-3, Anthropic Claude 3.5 Sonnet, and Google Gemini 1.5 Pro, were used for independent analyses. The final data points presented in Table 2 represent the consensus results obtained through cross-verification and inter-model agreement.

Microscopic analysis demonstrated that in a 20:1 mixture of levobupivacaine and dexamethasone, the number of crystals, their length, and the degree of crystallization increased over time. This is attributable to the alkaline environment created by dexamethasone upon mixing and the subsequent decrease in temperature. In contrast, magnesium sulfate solution, which is weakly acidic, exhibited a delayed onset of crystallization compared to dexamethasone when added to levobupivacaine, and the formed crystals were significantly smaller (Figure 2A-C). Crystal analysis revealed the following results (Table 3).

Adrenaline, being chemically a weak base, undergoes rapid oxidation and dehydration in neutral or alkaline environments. To prevent this and ensure molecular stability, sodium bisulfite is added to maintain the pH between 2.2 and 5.0. Consequently, when adrenaline is added to levobupivacaine, the crystallization process occurs slowly. Microscopic examination immediately after preparation

Table 2. Analysis of Crystallization Process in 0.25% Levobupivacaine and Dexamethasone Solution at a 20:1 ratio at Respective Time Points

Parameters	Immediately upon preparation	15 minutes after preparation	1 hour after preparation	*P* value
Crystal appearance, shape	Small rod-shaped, clustered	Rod-shaped, clusters enlarged	Fully dispersed, rod- and plate-shaped	
Number of crystals in field of view (n)	340±42 (n = 15)	630±56 (n = 15)	1275±89 (n = 15)	<0.001
Mean crystal size (µm)	9.1±1.2	12.3±1.5	17.4±2.1	<0.001
Degree of crystallization (GoC score)	4 (n = 15)	4 (n = 15)	4 (n = 15)	

Note: Values for crystal count and crystal size are presented as mean ± standard deviation. The reported *P* values are omnibus *P* values from the Friedman test across the three matched assessment times. Significant omnibus results were followed by paired Wilcoxon signed-rank tests with Holm adjustment for multiple comparisons. The GoC score remained constant across all assessment times and was not statistically tested. Crystal morphology was assessed descriptively

GoC, grade of crystallization

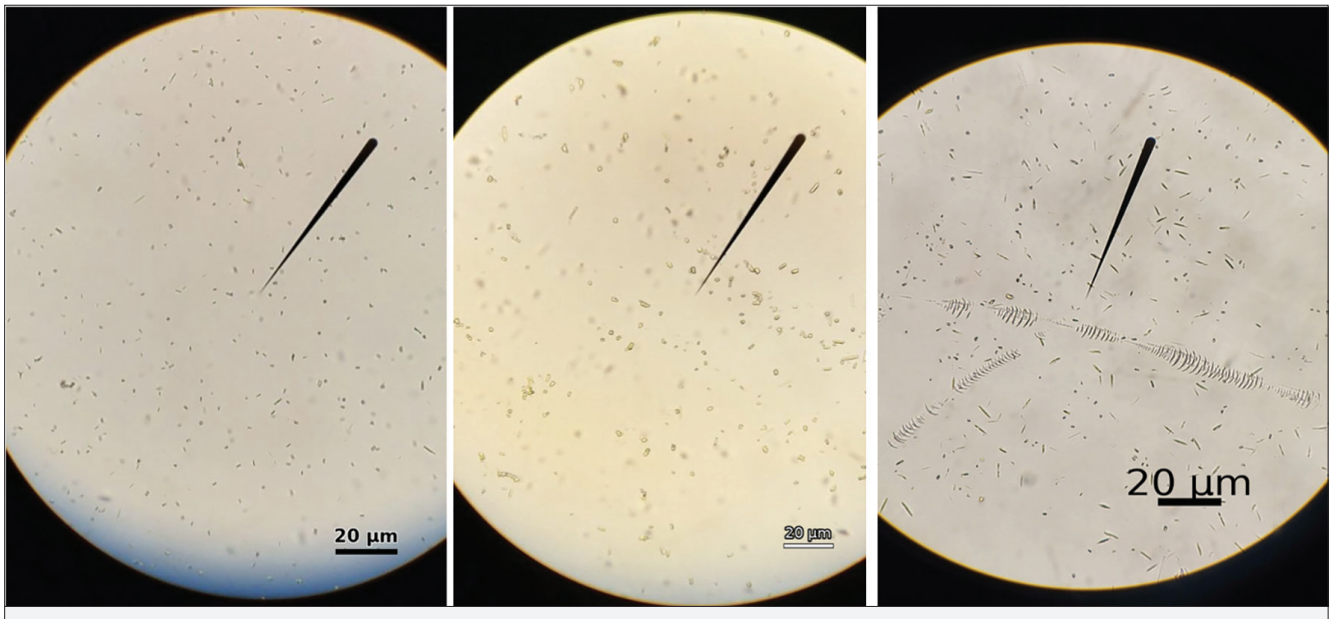


Figure 2. Microscopic appearance of crystals in 0.25% levobupivacaine and 25% magnesium sulfate solution at a 20:1.5 ratio. A) Microscopic appearance of crystals immediately upon preparation; B) Microscopic appearance of crystals 15 minutes after preparation; C) Microscopic appearance of crystals 1 hour after preparation.

revealed no visible crystals. After the preparation was cooled to room temperature and examined 15 minutes later, crystallization was observed to have commenced at the peripheral edges of the preparation (Figure 3, Table 4).

Dexmedetomidine exhibits high solubility with a pKa of 7.1 and pH range of 4.5-7.0. When the sample was mixed with levobupivacaine at a 20:1 ratio and examined by microscopy, the crystallization process proceeded slowly, and the formed crystals were small (Figure 4, Table 5).

As with adrenaline, no crystallization elements were observed in dexmedetomidine when mixed with levobupivacaine at 37 °C. When the preparations were re-prepared at room temperature and examined by microscopy, fine granules (up to 10 per field of view) were identified (Table 5).

In levobupivacaine-dexmedetomidine solutions, the crystallization process was extremely slow, with the passage of time and decreases in temperature having minimal impact on crystal formation. Granule size remained <10 µm for 1 hour. The literature reports the use of $NaHCO_3$ as an adjuvant. Analysis of its crystallization in the presence of local anesthetics (ropivacaine, bupivacaine) revealed extensive crystallization attributable to its basic nature (GoC score =5). However, insufficient data exist regarding its effect on levobupivacaine crystallization. Therefore, we investigated the degree of crystallization at room temperature of a 10:1 levobupivacaine: $NaHCO_3$ solution (recommended adjuvant dose in the literature). Immediately upon mixing, a cloudy precipitate formed (Figure 5).

Microscopic examination of the solution revealed numerous large crystals (50-100 µm) that had aggregated to form substantial precipitates (Figure 6).

Table 3. Analysis of Crystallization Process in 0.25% Levobupivacaine and Magnesium Sulfate Solution at A 20:1.5 Ratio at Respective Time Points

Parameters	Immediately upon preparation	15 minutes after preparation	1 hour after preparation	*P* value
Crystal appearance, shape	Rare small crystals, scattered	Fine rod-shaped, minimal clustering	Small polyhedral crystals, dispersed	
Number of crystals in field of view (n)	45±12 (n = 15)	82±18 (n = 15)	156±24 (n = 15)	<0.001
Mean crystal size (µm)	6.2±0.8	7.8±1.0	9.5±1.3	<0.001
Degree of crystallization (GoC score)	1 (n = 15)	2 (n = 15)	2 (n = 15)	<0.01

Note: Values for crystal count and crystal size are presented as mean ± standard deviation. The reported *P* values are omnibus *P* values from the Friedman test across the three matched assessment times. Significant omnibus results were followed by paired Wilcoxon signed-rank tests with Holm adjustment for multiple comparisons. Crystal morphology was assessed descriptively

GoC, grade of crystallization

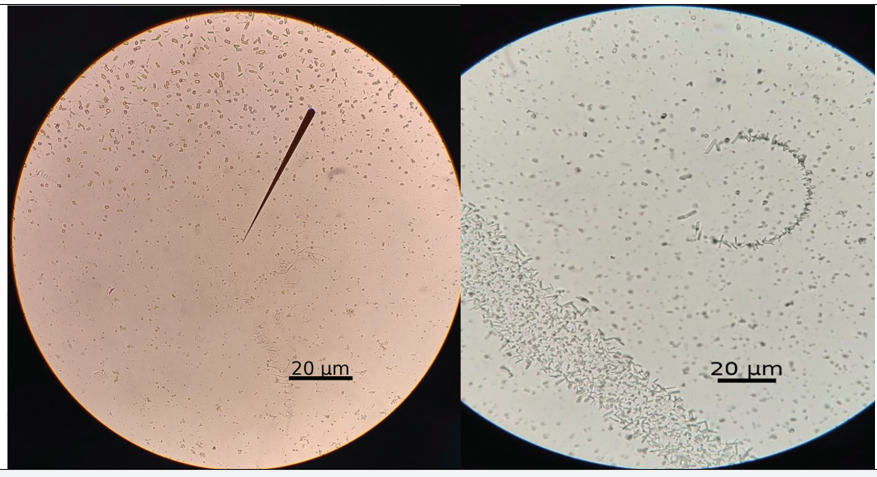


Figure 3. Microscopic appearance of crystals in 0.25% levobupivacaine mixed with adrenaline solution diluted to 1:100,000 ratio. A) Microscopic appearance of crystals 15 minutes after preparation; B) Microscopic appearance of crystals 1 hour after preparation.

Table 4. Analysis of Crystallization Process in 0.25% Levobupivacaine Mixed with Adrenaline Solution Diluted To 1:100,000 Ratio at Respective Time Points

Parameters	Immediately upon preparation	15 minutes after preparation	1 hour after preparation	*P* value
Crystal appearance, shape	No crystals visible	Fine needle-like at periphery	Needle- and irregular-shaped, peripheral	
Number of crystals in field of view (n)	0±0 (n = 15)	28±9 (n = 15)	67±15 (n = 15)	<0.001
Mean crystal size (µm)	N/A	5.4±0.7	7.2±1.0	<0.001
Degree of crystallization (GoC score)	0 (n = 15)	1 (n = 15)	2 (n = 15)	<0.001

Note: Values for crystal count and crystal size are presented as mean ± standard deviation. Overall temporal differences in crystal count and GoC score were evaluated using the Friedman test, followed by paired Wilcoxon signed-rank tests with Holm adjustment when the omnibus test was significant. Crystal size was compared between 15 and 60 minutes using the Wilcoxon signed-rank test because no crystals were detected immediately after preparation. Crystal morphology was assessed descriptively

GoC, grade of crystallization

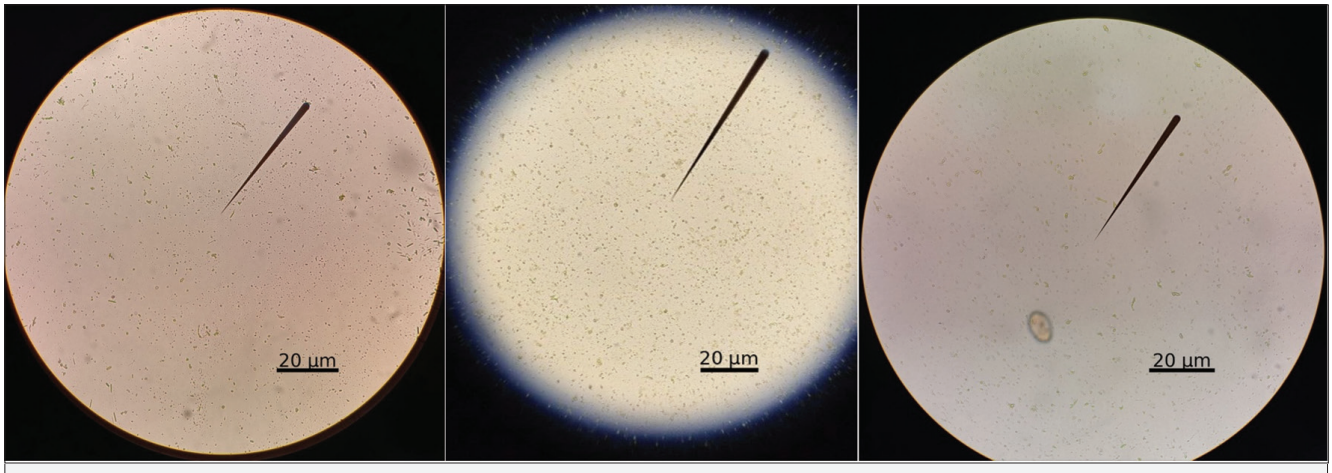


Figure 4. Microscopic appearance of crystals in 0.25% levobupivacaine mixed with dexmedetomidine at a 20:1 ratio. A) Microscopic appearance of crystals immediately upon preparation. B) Microscopic appearance of crystals 15 minutes after preparation; C) Microscopic appearance of crystals 1 hour after preparation.

Table 5. Microscopic Analysis of Crystallization Process in 0.25% Levobupivacaine Mixed with Dexmedetomidine at A 20:1 Ratio

Parameters	Immediately upon preparation (37 °C)	15 minutes after preparation (RT)	1 hour after preparation (RT)	*P* value
Crystal/granule appearance, shape	No crystals/granules visible	Fine granules, scattered	Fine granules, minimal aggregation	
Number of crystals/granules in field of view (n)	0±0 (n = 15)	8±3 (n = 15)	12±4 (n = 15)	<0.001
Mean crystal/granule size (µm)	N/A	3.2±0.5	4.1±0.6	<0.001
Degree of crystallization (GoC score)	0 (n = 15)	1 (n = 15)	1 (n = 15)	<0.01

Note: Values for crystal/granule count and size are presented as mean ± standard deviation. Overall temporal differences in crystal/granule count and GoC score were evaluated using the Friedman test, followed by paired Wilcoxon signed-rank tests with Holm adjustment when the omnibus test was significant. Crystal/granule size was compared between 15 and 60 minutes using the Wilcoxon signed-rank test because no crystals or granules were detected immediately after preparation. Morphology was assessed descriptively. Minimal crystallization compared to other adjuvants ($P < 0.001$); RT, room temperature (~22 °C)

GoC, grade of crystallization

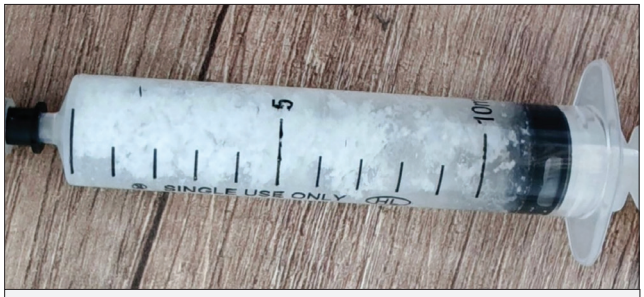


Figure 5. Precipitate formed upon mixing levobupivacaine with $NaHCO_3$ at a 10:1 ratio.

$NaHCO_3$, sodium bicarbonate.

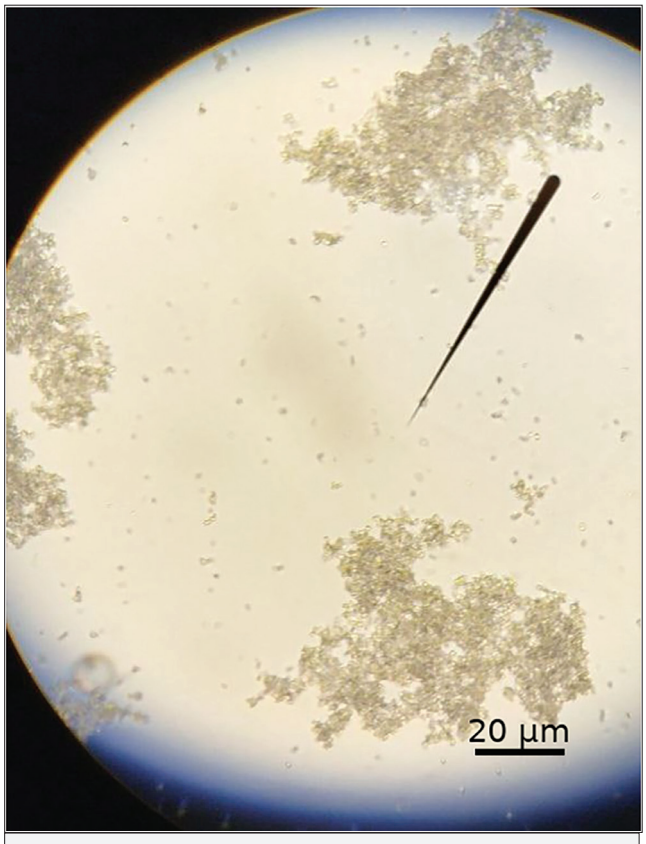


Figure 6. Microscopic appearance of the crystallization process in levobupivacaine and $NaHCO_3$ solutions at a 10:1 ratio (immediately upon preparation).

$NaHCO_3$, sodium bicarbonate.

Discussion

Our study demonstrated that the addition of $NaHCO_3$ and dexamethasone to 0.25% levobupivacaine triggered rapid and substantial crystallization, whereas adrenaline and dexmedetomidine maintained high physical stability. Specifically, $NaHCO_3$ (10:1) produced immediate, substantial precipitation visible to the naked eye (Figure 5), whereas dexamethasone induced time-dependent crystal growth exceeding 10 µm within 60 minutes. These results provide critical evidence regarding the physical stability risks of specific adjuvant-local anesthetic mixtures in regional anaesthesia.

Within the field of anaesthesiology, there is a notable scarcity of scientific literature addressing the physicochemical interactions and crystallization phenomena between local anesthetics and various additives. In particular, comprehensive data regarding the safety and clinical compatibility of integrating adjuvants with levobupivacaine remain inadequate. To date, research on crystallization has predominantly focused on the combinations of bupivacaine, ropivacaine, and lidocaine with agents such as $NaHCO_3$, clonidine, and dexamethasone. In a 2024 doctoral study, Jopua M.A. investigated the crystallization patterns in mixtures of 0.33% ropivacaine and dexamethasone at a 20:2 ratio. Microscopic evaluation immediately following preparation revealed the presence of rod-like crystals with lengths varying between 19 and 70 µm. A subsequent assessment at the 15-minute mark showed a proliferation of these crystals, with their dimensions expanding to 37-108 µm. The researcher highlighted a critical clinical concern: these crystal structures significantly exceed the size of human blood components, such as erythrocytes (7-8 µm), leukocytes (4.5-20 µm), and platelets (2-4 µm). Consequently, the unintentional intravascular administration of such mixtures during regional anaesthesia procedures poses a substantial risk of embolic complications.[7] Our findings with levobupivacaine are consistent with this concern: crystals exceeded 10 µm almost immediately. In a review by Tow et al.,[8] the physical implications of combining dexamethasone with ropivacaine and levobupivacaine were evaluated. The authors noted that mixing these local anesthetics with dexamethasone at a 20:2 ratio resulted in near-instantaneous crystallization. Furthermore, these crystalline structures were found to remain stable and unchanged over a 24-hour observation period.[8]

Dexamethasone has emerged as a widely adopted adjuvant in contemporary regional anaesthesia. Its clinical utility in enhancing the quality and prolonging the duration of nerve blocks, alongside its role in minimizing the systemic toxicity of local anesthetics, is well-supported by a robust body of evidence, including various meta-analyses and systematic reviews.[9] Recent mechanistic evidence also underscores the need for caution when using dexamethasone as an adjuvant. Recent preclinical evidence suggests a need for heightened vigilance regarding the perineural application of dexamethasone. A systematic review by De Cassai et al.[10] indicates that while dexamethasone independently lacks significant neurotoxic potential at therapeutic doses, its interaction with local anesthetics may enhance *in vitro* cytotoxic responses. Furthermore, the authors emphasized that current *in vivo* data—though not definitively linking the combination to long-term nerve damage—are still

constrained by methodological limitations and narrow scope, necessitating careful consideration before routine co-administration.[10] The semiquantitative analysis conducted by Hoerner et al.[11] revealed that mixtures of dexamethasone and local anesthetics, such as mepivacaine, reached the highest crystallization intensity (grade 5 on a 0-5 scale) under microscopic evaluation. Their statistical assessment of the variables influencing this process identified a moderate positive correlation between the duration of the mixture and the degree of crystallization (P=0.57, P=0.0003). In contrast, the correlation between pH variations and the initiation of crystal growth was identified as weak and lacked statistical significance (P=-0.17, $P > 0.05$). This observation, reported in the 2025 study by Hoerner et al.,[11] suggests that the temporal factor (duration of the mixture) may exert a more decisive influence on physical stability than alkalinity across specific local anesthetic-adjuvant combinations. Similar findings have been reported in other studies. When 50 local anesthetic-adjuvant mixtures were examined under microscopy, 26 preparations exhibited a crystallization grade >4, and ropivacaine was found to form more crystals compared to bupivacaine.[12] In a comparative analysis of anesthetic-steroid interactions, Hwang et al.[13] observed distinct crystallization patterns among different agents. Their results indicated that lidocaine-based mixtures remained free of crystal formation. In contrast, combining ropivacaine with betamethasone caused visible precipitates, whereas its mixture with dexamethasone produced fewer crystals ranging from 10 to 100 µm in size. Furthermore, the combination of bupivacaine and betamethasone resulted in the proliferation of numerous micro-crystals, typically measuring up to 10 µm.[13] While Hwang et al.[13] reported specific crystal dimensions for bupivacaine and ropivacaine, our study highlights unique patterns for levobupivacaine, suggesting that the S-enantiomer structure may influence the interaction with adjuvants differently. Investigations into the impact of diverse additives on the stability of bupivacaine and ropivacaine have identified $NaHCO_3$ as the most potent inducer of crystallization. In a semiquantitative microscopic analysis by Hoerner et al.,[14] mixtures containing $NaHCO_3$ exhibited both the highest density and the most substantial dimensions of crystal formations compared to other studied adjuvants. Bhoi et al.[15] conducted a microscopic examination of clinically used ratios of the local anesthetics ropivacaine and lidocaine with the adjuvants dexmedetomidine and dexamethasone to study their effects on crystallization. They observed that dexamethasone at doses of 2, 4, and 8 mg produced crystals of nearly identical size and shape. When dexmedetomidine was added as a second adjuvant to these preparations, an increase in the number of crystals and a reduction in crystal size were noted. According to the conclusions of this study, dexamethasone enhances crystallization starting from a 2 mg dose, and this process is independent of dexamethasone dosage.[15]

The clinical implications of these findings should be interpreted cautiously because the present study was conducted *in vitro* and did not evaluate patient outcomes. Based on these *in vitro* findings, levobupivacaine-sodium bicarbonate and levobupivacaine-dexamethasone mixtures exhibited physicochemical incompatibilities under the tested conditions. These observations suggest that direct admixture in the same syringe warrants caution; however, they do not establish a clinical contraindication to this practice, nor demonstrate the superiority of intravenous over perineural dexamethasone administration. Route-specific recommendations require clinical evidence beyond the scope of this study.

Study Limitations

This study has several limitations that should be acknowledged. First, it was conducted as an *in vitro* laboratory analysis, which may not fully replicate the dynamic physiological conditions present in a clinical setting, such as body temperature, local tissue pH, and blood flow. Second, while microscopic crystallization was observed, the long-term clinical impact of these precipitates on nerve function or systemic safety was not directly evaluated *in vivo*. Further clinical studies are required to correlate these laboratory findings with patient outcomes and potential neurotoxic risks.

Conclusion

Based on the present *in vitro* findings, the addition of $NaHCO_3$ or dexamethasone to 0.25% levobupivacaine substantially influenced crystal formation under the tested conditions. $NaHCO_3$ produced immediate and massive precipitation, whereas the levobupivacaine-dexamethasone mixture showed time-dependent crystal proliferation. These findings suggest that direct admixture of these agents with levobupivacaine in the same syringe may raise physicochemical compatibility concerns. Because routes of administration and clinical outcomes were not compared, no conclusion can be drawn regarding the clinical superiority of intravenous versus perineural administration of dexamethasone.

Ethics

Ethics Committee Approval: Not applicable. This study is an in vitro laboratory investigation and did not involve human subjects or animal experiments.

Informed Consent: Not applicable. This in vitro laboratory study did not involve human participants.

Footnotes

Authorship Contributions: Concept - V.S.; Design - V.S.; Data Collection and/ or/Processing - S.Y.; Analysis and/or/ Interpretation - V.S., I.F.; Literature Review - S.Y., I.F.; Writing - S.Y.

Declaration of Interests: No conflict of interest was declared by the authors.

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Original Article
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Dexmedetomidine versus Subanaesthetic Ketamine for Opioid-sparing Anaesthesia During Lumbar Spine Surgery Under a Standardised Surgical Pleth Index-guided Analgesic Protocol: A Randomised Controlled Trial

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Abstract

Objective: Lumbar spine surgery is associated with significant perioperative pain and increased opioid requirements. Objective nociception-guided opioid administration using the surgical pleth index (SPI) may facilitate individualised intraoperative analgesic titration. Dexmedetomidine and subanaesthetic ketamine are commonly used opioid-sparing adjuvants; however, their effects under SPI-guided analgesia remain inadequately studied.

Methods: In this prospective randomised controlled trial, 50 adult patients undergoing lumbar spine surgery were allocated to 3 groups: dexmedetomidine (Group D), ketamine (Group K), and saline control (Group S). After prone positioning, Group D received a 0.5 μg kg^{-1} dexmedetomidine bolus followed by a 0.2 μg kg^{-1} h infusion; Group K received a 0.5 mg kg^{-1} ketamine bolus followed by a 0.2 mg kg^{-1} h^{-1} infusion; and Group S received saline. Intraoperative fentanyl (0.5 μg kg^{-1}) was administered when SPI exceeded 50, as indicated by Adequacy of Anaesthesia monitoring, allowing objective nociception-guided opioid titration. The primary outcome was intraoperative supplemental fentanyl consumption. Secondary outcomes included extubation time, postoperative pain scores, 24-hour fentanyl consumption, and Quality of Recovery (QoR-15) scores.

Results: Cumulative intraoperative supplemental fentanyl consumption differed among the groups ($P < 0.001$), with lower requirements in Groups D (150±45.9 μg) and K (161.7±35.4 μg) than in Group S (220.5±42.6 μg). In contrast, no difference was observed between Groups D and K. Twenty-four–hour postoperative fentanyl consumption also differed significantly among the groups ($P < 0.001$), with lower consumption in Group D than in Group S, and intermediate consumption in Group K. Extubation time was comparable among the groups. Dexmedetomidine resulted in lower postoperative visual analogue scale scores than saline at all time points; scores also differed between dexmedetomidine and ketamine at 1 hour and between ketamine and saline at 12 hours. QoR-15 scores differed significantly among the groups, with both active treatment groups showing improved recovery compared with the saline group.

Conclusion: Within a standardised SPI-guided analgesic protocol, both dexmedetomidine and subanaesthetic ketamine reduced intraoperative opioid requirements without prolonging extubation time compared with saline during lumbar spine surgery. Dexmedetomidine was associated with lower postoperative opioid consumption and improved postoperative recovery compared with saline. Both interventions demonstrated comparable intraoperative opioid-sparing efficacy.

Keywords: SPI monitoring, adequacy of anaesthesia, dexmedetomidine, ketamine, lumbar spine surgery, opioid-sparing anaesthesia, QoR-15

Main Points

- A standardised surgical pleth index (SPI)-guided analgesic protocol was used to facilitate predefined intraoperative opioid titration and to compare the opioid-sparing effects of dexmedetomidine and ketamine with those of saline.
- Within a standardised SPI-guided analgesic protocol, both dexmedetomidine and ketamine significantly reduced intraoperative opioid requirements compared with saline.
- Dexmedetomidine was associated with lower postoperative opioid consumption and favourable recovery outcomes compared with saline.
- Postoperative pain scores differed significantly among the groups at all assessed time points, with dexmedetomidine demonstrating consistently lower pain scores than saline.

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Introduction

Lumbar spine surgeries are frequently associated with significant postoperative pain due to extensive tissue dissection and muscle retraction required for adequate surgical exposure.[1,2] In addition, many patients present with chronic pain and preoperative opioid use, predisposing them to opioid tolerance and increased perioperative opioid requirements. This escalation in opioid consumption may lead to an increased incidence of opioid-related adverse effects, such as postoperative nausea and vomiting, respiratory depression, sedation, and delayed recovery.[3] To mitigate these challenges, opioid-sparing strategies have been increasingly incorporated into multimodal anaesthesia. Dexmedetomidine and subanaesthetic ketamine are widely used anaesthetic adjuvants with established analgesic properties and the potential to reduce perioperative opioid requirements.[4-7] However, a significant methodological challenge remains: most previous studies evaluating these agents have relied on indirect, subjective parameters-such as changes in heart rate and blood pressure-to guide intraoperative analgesic administration. These parameters may be influenced by several perioperative factors, including anaesthetic depth, intravascular volume status, and surgical stimulation, thereby limiting their reliability as indicators of nociception.[2] The surgical pleth index (SPI) (GE Healthcare, Helsinki, Finland) is a significant methodological advancement, providing an objective tool for monitoring nociception based on photoplethysmographic waveform analysis and reflects the balance between nociception and antinociception during general anaesthesia.[8-10] By utilising SPI, clinicians can move toward a physiologically tailored approach that enables real-time assessment of nociceptive responses and facilitates precise and individualised titration of analgesics, particularly opioids. While the individual efficacy of dexmedetomidine and ketamine is documented, their performance within an objective, SPI-guided titration framework requires further exploration. This study was designed to compare the opioid-sparing effects of dexmedetomidine and subanaesthetic ketamine using a standardised SPI-guided analgesic protocol during lumbar spine surgery. The primary objective was to compare the cumulative intraoperative supplemental fentanyl consumption between the groups. The secondary objectives included comparisons of extubation time, postoperative pain scores, total fentanyl consumption during the first 24 h, and the Quality of Recovery (QoR-15), assessed using the QoR-15 score. We hypothesised that dexmedetomidine and ketamine would reduce intraoperative opioid requirements during SPI-guided analgesic administration, with potential differences in postoperative recovery outcomes between the two agents.

Methods

This prospective randomised controlled trial in adult patients undergoing lumbar spine surgery was conducted after obtaining approval from the Jawaharlal Institute of Postgraduate Medical Education and Research Institute Ethics Committee (approval no: JIP/IEC/2022/09, date: 26.03.2022) and registration with the Clinical Trial Registry of India (CTRI/2023/01/048710). Written informed consent was obtained from all the participants. Fifty patients, aged 18-70 years and of either sex, with American Society of Anesthesiologists physical status I-II were included. Patients with known allergies to study drugs, increased intracranial or intraocular pressure, ischemic heart disease, uncontrolled hypertension, psychiatric illness, seizure disorder, or significant hepatic or renal dysfunction were excluded.

Participants were randomly allocated to 3 groups (Groups D, K, and S) using a computer-generated block randomisation sequence with block sizes of 3 and 6. Randomisation and allocation concealment were achieved using sequentially numbered, opaque, sealed envelopes. Study drugs were prepared by an independent investigator who was not involved in intraoperative management, postoperative assessment, or data analysis. Patients and postoperative outcome assessors remained blinded to treatment allocation. Owing to the nature of the study drug administration, the attending intraoperative anaesthesiologist was aware of group allocation and, therefore, was not blinded. To minimise performance bias, intraoperative fentanyl administration was standardised using a predefined SPI-guided analgesic protocol. Data analysis was performed using coded group allocation.

Upon arrival in the operating room, standard monitoring, including electrocardiography, pulse oximetry, and non-invasive blood pressure monitoring, was instituted, and intravenous access was secured. Entropy sensors were applied prior to induction. Glycopyrrolate (0.2 mg) was administered intravenously, followed by induction of anaesthesia with fentanyl (2 µg kg^{-1}) and propofol (2 mg kg^{-1}). Tracheal intubation was facilitated with vecuronium (0.1 mg kg^{-1}). Anaesthesia was maintained with isoflurane in an oxygen-air mixture. Supplemental vecuronium was administered in 1-mg incremental doses at approximately 40-minute intervals, or earlier if clinical signs of recovery from neuromuscular blockade, such as spontaneous respiratory efforts or patient movement, were observed. The same neuromuscular blockade protocol was followed for all patients throughout the study. Intravenous paracetamol (1 g) was administered prior to the skin incision.

After positioning the patient prone, the study drug was administered as a 10-min loading dose, followed by continuous infusion. Group D received dexmedetomidine (0.5 μg kg^{-1}) as a bolus, followed by a 0.2 μg kg^{-1} h^{-1} infusion. Group K received ketamine 0.5 mg kg^{-1} as a bolus, followed by a 0.2 mg kg^{-1} h^{-1} infusion. Group S received an equivalent volume of 0.9% saline solution. Infusion was continued until muscle closure. Dosing regimens of dexmedetomidine and ketamine were selected based on published studies demonstrating their efficacy as opioid-sparing anaesthetic adjuvants. Given the differing pharmacological mechanisms of these agents, direct dose equivalence was not feasible; therefore, clinically accepted subanaesthetic doses were utilised. The study was designed to evaluate opioid consumption under a standardised SPI-guided analgesic protocol rather than to establish definitive pharmacologic superiority between dexmedetomidine and ketamine.

Adequacy of anaesthesia (AoA) monitoring was performed using a GE Healthcare CARESCAPE B650 monitor (GE Healthcare, Helsinki, Finland), equipped with the E-Entropy module for entropy monitoring and the E-PreSTN module for SPI monitoring. State entropy was maintained between 40 and 60 throughout the surgery by adjusting the inhalational anaesthetic concentration to ensure a standardised anaesthetic depth. The integration of entropy and SPI constitutes AoA monitoring (Figure 1A).

SPI values were continuously monitored intraoperatively as part of the standardised analgesic protocol. Baseline SPI was recorded after induction and before administration of the loading dose of the study drug, while the patient was under stable anaesthesia and prior to surgical incision; stable anaesthesia was defined as the absence of surgical stimulation and stable hemodynamics for at least 2 min. An SPI range of 20-50 was considered acceptable (Figure 1B). If SPI exceeded 50 for more than 1 min, fentanyl at 0.5 μg kg^{-1} was administered intravenously. SPI was reassessed 5 min after each fentanyl bolus, and an additional fentanyl bolus of 0.5 μg kg^{-1} was administered only if SPI remained above 50. Potential confounding factors affecting SPI interpretation, including electrocautery, patient movement, arrhythmias, vasoactive drug administration, abrupt changes in anaesthetic depth, and haemodynamic instability, were identified before clinical intervention. During such events, SPI values were not used to guide fentanyl administration. Opioid titration was deferred until the confounding factor had resolved and a stable SPI signal had been re-established under steady-state anaesthetic and ventilatory conditions. Thus, while dexmedetomidine and ketamine were administered as fixed-dose infusions, opioids were titrated objectively using SPI-based monitoring. The attending anaesthesiologist recorded the SPI values and fentanyl administration as part of routine intraoperative monitoring. Intraoperative fentanyl consumption was defined as the cumulative supplemental fentanyl administered in response to the SPI-guided protocol after induction; the initial fentanyl dose of 2 μg kg^{-1} administered for induction was excluded from this calculation.

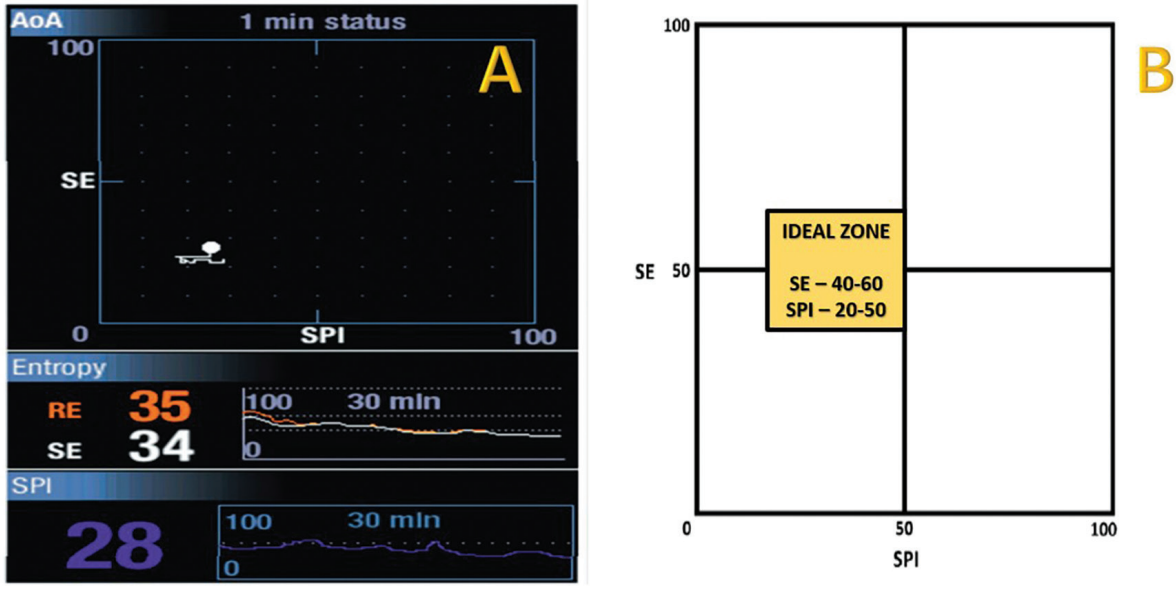


Figure 1. A) Adequacy of Anaesthesia (AoA™) monitoring display showing the integration of state entropy (SE) and surgical pleth index (SPI) during general anaesthesia; B) Schematic representation of the ideal zone in AoA display.

The study drug infusion was discontinued at the end of surgery. Residual neuromuscular blockade was reversed with intravenous neostigmine and glycopyrrolate, in accordance with institutional practice. As objective neuromuscular monitoring was not used, extubation was performed after the fulfilment of standard clinical criteria, including adequate spontaneous ventilation, purposeful motor response, satisfactory airway-protective reflexes, and the ability to obey verbal commands. Extubation time was defined as the interval from the administration of reversal agents to successful extubation. Postoperative analgesia was provided via intravenous patient-controlled delivery of fentanyl (bolus dose 30 µg, lockout interval 10 min, no background infusion, maximum 150 µg/h). All patients received intravenous paracetamol (1 g every 8 h). Postoperative pain intensity was assessed using a visual analogue scale (VAS) at 1, 6, 12, and 24 hours after surgery. The QoR-15 score was assessed at 24 hours using the QoR-15 questionnaire.

The sample size was calculated using OpenEpi software (Version 3.01, Atlanta, GA, USA) based on a previous study by Mitra et al.[2], which reported a mean difference in fentanyl consumption of 14.3 µg (standard deviation 12 µg). A sample size of 15 patients per group was required to achieve a power of 80% at a significance level of 0.05. A total of 50 patients were included to account for potential attrition. Data are presented as the mean ± standard deviation. The sample size was calculated to detect overall differences in opioid consumption between study groups under SPI-guided analgesic administration. It was not specifically powered for a definitive head-to-head comparison between dexmedetomidine and ketamine.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics version 19 (IBM Corp., Armonk, NY, USA). Primary analyses focused on differences in opioid consumption under the standardised SPI-guided analgesic protocol. The normality of the data was assessed using the Shapiro-Wilk test, which confirmed that continuous variables were normally distributed. Continuous variables were expressed as mean ± standard deviation and compared using one-way analysis of variance (ANOVA). When the overall ANOVA was statistically significant, Bonferroni-corrected post-hoc pairwise comparisons were performed to identify between-group differences while controlling the Type I error rate. Categorical variables were expressed as frequencies and percentages and analysed using the chi-square test or Fisher's exact test, as appropriate. A P value <0.05 was considered statistically significant.

Results

Fifty-five patients were assessed for eligibility; 5 were excluded before randomisation because 3 did not meet the inclusion criteria and 2 declined to participate. The remaining 50 patients were randomised into 3 groups, all of whom were included in the final analysis (Figure 2). Baseline demographic characteristics, including age, sex, body mass index, weight, and American Society of Anesthesiologists physical status, were comparable among the groups. Surgical characteristics, including operative duration and distribution of procedure types, were also comparable among the groups (Table 1).

Under the standardised SPI-guided analgesic protocol, cumulative intraoperative supplemental fentanyl consumption differed significantly among the 3 groups (one-way ANOVA, $P < 0.001$). Mean intraoperative supplemental fentanyl consumption was 150±45.9 µg in Group D, 161.7±35.4 µg in Group K, and 220.5±42.6 µg in Group S. Bonferroni-corrected post-hoc analysis demonstrated that intraoperative fentanyl consumption was significantly lower in Group D than in Group S ($P < 0.001$), and in Group K than in Group S ($P < 0.001$). No significant difference was observed between Groups D and K ($P=1.000$) (Table 2).

Total 24-hour postoperative fentanyl consumption also differed significantly among the groups (one-way ANOVA, $P < 0.001$). Mean postoperative fentanyl consumption was 271.3±118.5 µg in Group D, 374.1±80.8 µg in Group K, and 444.1±119.7 µg in Group S. Bonferroni-corrected post-hoc analysis demonstrated significantly lower postoperative fentanyl consumption in Group D than in Group S ($P < 0.001$) and than in Group K ($P=0.026$). In contrast, the difference between Group K and Group S was not statistically significant ($P=0.192$) (Table 2).

Extubation times were comparable among the groups ($P=0.08$) (Table 2). Postoperative VAS scores differed significantly among the groups at all assessed time points. Bonferroni-corrected post-hoc analysis showed that Group D had lower VAS scores than Group S throughout the 24-h postoperative period. Group D also demonstrated lower VAS scores than Group K at 1 h, whereas Group K demonstrated lower VAS scores than Group S at 12 h. No other pairwise differences were statistically significant (Figure 3 and Table 3).

QoR-15, assessed using the QoR-15 questionnaire, differed significantly among the groups (one-way ANOVA, $P < 0.001$). Mean QoR-15 scores were 123±6.9 in Group D, 117±6.8 in Group K, and 109±10.0 in Group S. Bonferroni-corrected post-hoc analyses demonstrated that QoR-15 scores were significantly higher in Group D than in Group S ($P < 0.001$) and in Group K than in Group S ($P=0.017$). In contrast, no significant difference was observed between Groups D and K ($P=0.117$) (Table 2).

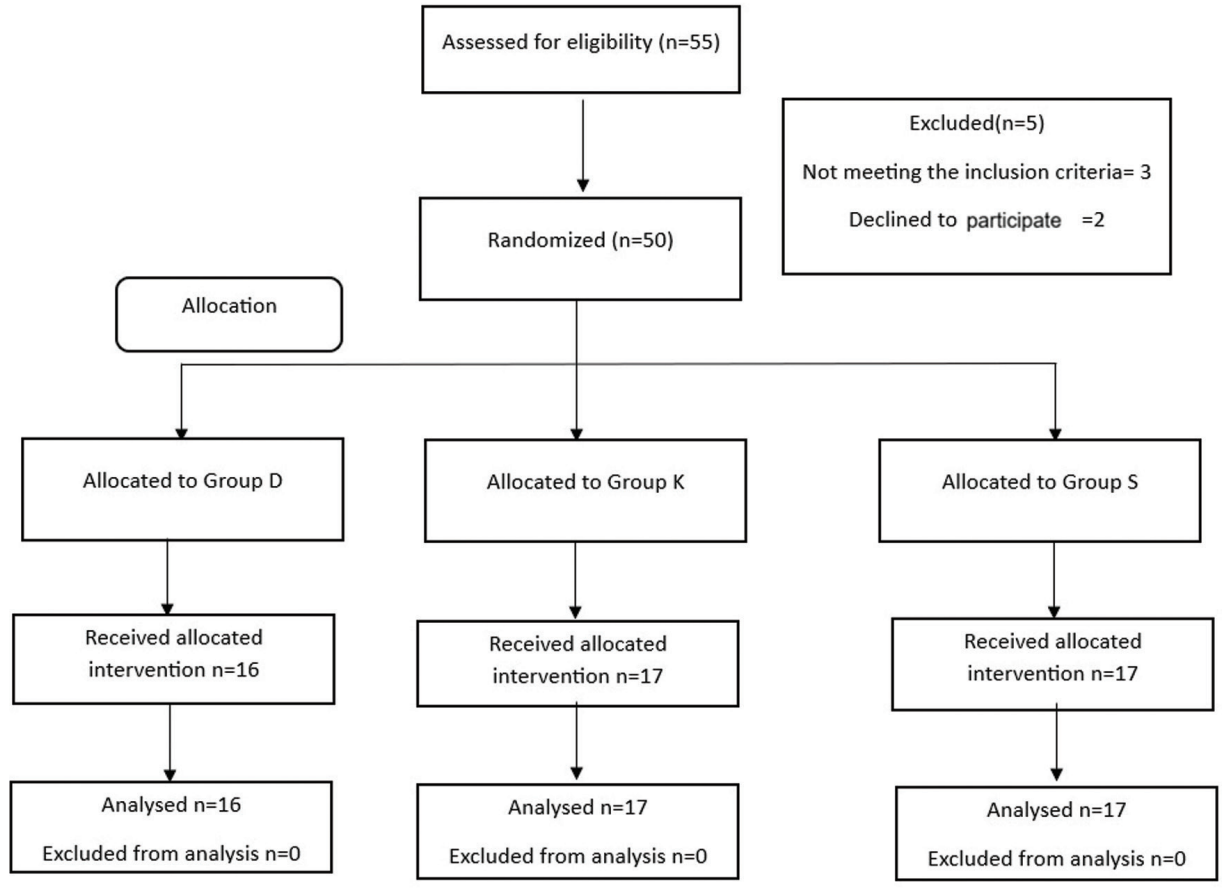


Figure 2. CONSORT diagram.

Table 1. Demographic Parameters of the Study Population

Baseline characteristics		Group D (n = 16)	Group K (n = 17)	Group S (n = 17)	*P* value
Age (years)		45.6±15.78 (37.15-53.97)	41±12.6 (34.52-47.48)	45.6±14.3 (38.26-53.04)	0.56
Gender n (%)	Male	12 (75.0%)	8 (47.1%)	10 (58.8%)	0.28
	Female	4 (25.0%)	9 (52.9%)	7 (41.2%)	
Weight (kg)		64.9±8.41 (60.46-69.42)	62.9±5.2 (60.24-65.64)	66.3±5.62 (63.46-69.24)	0.32
BMI (kg/m^2)		24.6±3.46 (22.85-26.54)	24±1.41 (23.36-24.81)	25.05±2.35 (23.82-26.29)	0.54
ASA n (%)	Class 1	11 (68.8%)	13 (76.5%)	13 (76.5%)	0.99
	Class 2	5 (31.2%)	4 (23.5%)	4 (23.5%)	
Operative duration (min)		282.6±65.5 (247.7-317.4)	280.9±63.7 (248.2-313.7)	277.5±66.1 (243.5-311.5)	0.97
Procedure type n (%)					
Instrumentation (fusion/fixation)		11 (68.8%)	11 (64.7%)	10 (58.8%)	0.97
Discectomy		2 (12.5%)	2 (11.8%)	3 (17.6%)	
Decompression		3 (18.8%)	4 (23.5%)	4 (23.5%)	

Values expressed as mean ± standard deviation (95% CI) and frequency (n). Continuous variables were analysed using one-way ANOVA, and categorical variables were analysed using chi-square or Fisher's exact test

A *P* value <0.05 was considered statistically significant

D, dexmedetomidine; K, ketamine; S, saline; ANOVA, analysis of variance; ASA, American Society of Anesthesiologists; BMI, body mass index; CI, confidence interval

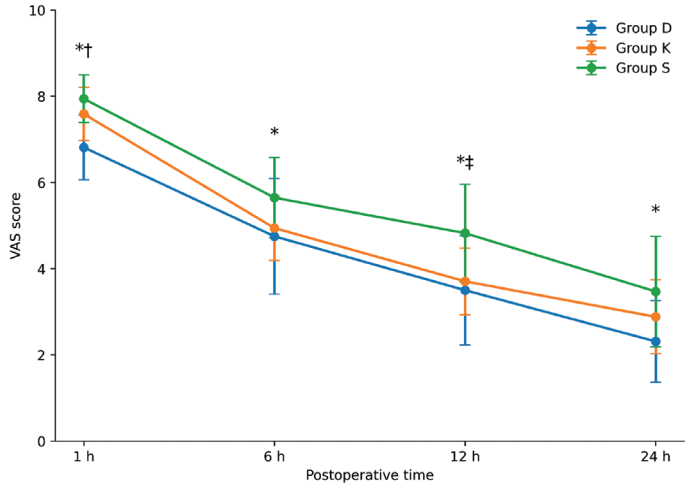


Figure 3. Postoperative visual analogue scale (VAS) scores among the 3 study groups over 24 hours. Data are presented as mean ± standard deviation. *P* < 0.05 for Group D versus Group S; †*P* <0.05 for Group D versus Group K; ‡*P* < 0.05 for Group K versus Group S, based on Bonferroni-corrected post-hoc comparisons.

Group D, dexmedetomidine; Group K, ketamine; Group S, saline.

Table 2. Comparison of Perioperative Fentanyl Requirement, Extubation Time, and QoR-15 Scores Between the 3 Groups

Variable	Group D (n = 16)	Group K (n = 17)	Group S (n = 17)	ANOVA *P* value	Bonferroni-corrected post-hoc *P* values		
					D vs. K	D vs. S	K vs. S
Intraoperative supplemental fentanyl requirement (µg)	150±45.9 (125.55 - 174.45)	161.7±35.4 (143.56-179.96)	220.5±42.6 (198.66 - 242.51)	**<0.001**	1	**<0.001**	**<0.001**
Postoperative fentanyl requirement (µg)	271.3±118.5 (208.1-334.4)	374.1±80.8 (332.58-415.65)	444.1±119.7 (382.55-505.69)	**<0.001**	**0.026**	**<0.001**	0.192
Extubation time (Mins)	10.9±4.1 (8.72-13.03)	8.8±3.1 (7.21-10.44)	8.6±1.9 (7.67-9.63)	0.08	-	-	-
QoR-15 score	123.6±6.9 (119.93-127.32)	117.6±6.8 (114.16-121.13)	109.6±10.1 (104.42-114.76)	**<0.001**	0.117	**<0.001**	**0.017**

Values expressed as mean ± standard deviation (95% CI). Continuous variables were analysed using one-way ANOVA followed by a Bonferroni post-hoc test. A *P* value <0.05 was considered statistically significant

D, dexmedetomidine; K, ketamine; S, saline; ANOVA, analysis of variance; Qor-15, quality of recovery

Table 3. Comparison of Postoperative Visual Analogue Scale Scores Among the 3 Groups Over 24 Hours

Time point	Group D (n = 16)	Group K (n = 17)	Group S (n = 17)	ANOVA *P* value	Bonferroni-corrected post-hoc *P* values		
					D vs. K	D vs. S	K vs. S
1 h	6.81±0.75 (6.41-7.21)	7.59±0.62 (7.27-7.91)	7.94±0.56 (7.66-8.23)	**<0.001**	**0.003**	**<0.001**	0.350
6 h	4.75±1.34 (4.04-5.46)	4.94±0.75 (4.56-5.33)	5.65±0.93 (5.17-6.13)	**0.038**	1.000	**0.048**	0.154
12 h	3.50±1.26 (2.83-4.17)	3.71±0.77 (3.31-4.10)	4.82±1.13 (4.24-5.41)	**0.002**	1.000	**0.003**	**0.012**
24 h	2.31±0.95 (1.81-2.82)	2.88±0.86 (2.44-3.32)	3.47±1.28 (2.81-4.13)	**0.010**	0.374	**0.008**	0.323

Values are expressed as mean ± standard deviation. Overall, intergroup comparisons were performed using one-way ANOVA, followed by Bonferroni-corrected post-hoc pairwise comparisons. A *P* value <0.05 was considered statistically significant.

D, dexmedetomidine; K, ketamine; S, saline; ANOVA, analysis of variance

Discussion

The present study demonstrated that, within a standardised SPI-guided opioid titration protocol, both dexmedetomidine and subanaesthetic ketamine significantly reduced intraoperative supplemental fentanyl requirements compared with saline during elective lumbar spine surgery. Although both active interventions exhibited comparable intraoperative opioid-sparing efficacy, dexmedetomidine was associated with lower postoperative fentanyl consumption and improved QoR-15 compared with saline. The objective of this study was to compare the opioid-sparing effects of dexmedetomidine and ketamine using a standardised SPI-guided analgesic protocol rather than evaluate the effectiveness of SPI monitoring itself.

Both dexmedetomidine and ketamine reduce opioid requirements through distinct pharmacological mechanisms. Dexmedetomidine, a highly selective α_2-adrenergic receptor agonist, produces analgesia by inhibiting norepinephrine release within the locus coeruleus and dorsal horn of the spinal cord, thereby attenuating sympathetic activation and nociceptive transmission.[11] In contrast, ketamine primarily exerts its analgesic effects through N-methyl-D-aspartate (NMDA) receptor antagonism, reducing central sensitisation and limiting opioid-induced hyperalgesia.[12] Despite these differing mechanisms, both agents produced comparable reductions in intraoperative supplemental fentanyl consumption when opioid administration was standardised using a predefined SPI threshold, suggesting that either adjunct can effectively reduce intraoperative opioid requirements during lumbar spine surgery.

An important consideration when interpreting these findings is that SPI is derived from the normalised heartbeat interval and pulse plethysmographic amplitude, both of which may be influenced by autonomic nervous system activity and nociceptive stimulation.[13] As dexmedetomidine and ketamine have differing effects on sympathetic tone, a potential influence on SPI values cannot be entirely excluded. However, the same predefined SPI threshold and opioid titration protocol were applied across all study groups, and potential confounding factors were addressed before fentanyl administration. Therefore, SPI-guided opioid titration provided a standardised approach to comparing the study interventions, although the drugs' autonomic effects on SPI should be considered when interpreting the findings.

Our findings are consistent with those of Andleeb et al.,[14] who reported comparable intraoperative opioid-sparing effects of dexmedetomidine and subanaesthetic ketamine during elective spine surgery using a propofol-fentanyl total intravenous anaesthesia (TIVA) technique. In contrast, Khalil et al.[15] observed significantly lower intraoperative opioid requirements with dexmedetomidine than with ketamine during bariatric surgery. A plausible explanation for this discrepancy lies in differences in anaesthetic technique. Khalil et al.[15] employed propofol-based TIVA, whereas anaesthesia in the present study was maintained with isoflurane. Volatile anaesthetic agents influence peripheral vascular tone and photoplethysmographic waveform characteristics differently from propofol, potentially altering SPI behaviour and subsequent opioid titration.[16] Differences in patient populations, surgical procedures, and infusion regimens may have further contributed to the variation in findings between the 2 studies. Furthermore, unlike bariatric surgery, lumbar spine procedures involve prolonged muscle dissection, tissue retraction, and instrumentation, resulting in sustained nociceptive stimulation throughout surgery. Under these circumstances, standardised SPI-guided opioid titration may reduce variability in opioid administration by providing a predefined physiological target for analgesic supplementation, thereby allowing the opioid-sparing effects of dexmedetomidine and ketamine to be evaluated under similar intraoperative conditions.

Postoperative pain scores progressively decreased in all groups over the 24-h assessment period. Dexmedetomidine was associated with lower VAS scores than saline throughout the postoperative period and showed an additional early difference compared with ketamine at 1 h. This profile may reflect the sustained analgesic and sympatholytic effects of dexmedetomidine that extend into the postoperative period. Ketamine, despite its NMDA-receptor antagonism and antihyperalgesic effects, demonstrated a less consistent postoperative pain profile at the infusion dose used in this study. Mitra et al.[2] similarly reported favourable postoperative analgesic effects of dexmedetomidine compared with ketamine in spine surgery. Nikoubakht et al.[4] reported reduced postoperative pain and opioid requirements with both dexmedetomidine and ketamine compared with control patients undergoing lumbar spine surgery. Differences in postoperative analgesic techniques, including continuous fentanyl infusion with rescue pethidine in their study versus patient-controlled fentanyl analgesia in ours, may account for variations in the observed postoperative pain profiles.

Although intraoperative opioid-sparing efficacy was comparable between dexmedetomidine and ketamine, dexmedetomidine was associated with lower 24-hour postoperative fentanyl consumption. This finding is biologically plausible, as dexmedetomidine provides sustained modulation of both spinal and supraspinal nociceptive pathways while attenuating sympathetic activation throughout the perioperative period.[17] Ketamine primarily reduces central sensitisation and opioid-induced hyperalgesia, but its postoperative analgesic benefit may diminish after discontinuation of the infusion at muscle closure.[18] These pharmacological differences may explain the superior postoperative opioid-sparing effect observed with

dexmedetomidine despite similar cumulative intraoperative supplemental fentanyl requirements.

Extubation times were comparable among the 3 groups despite dexmedetomidine's sedative properties. This observation is consistent with previous reports demonstrating that low-dose dexmedetomidine infusions do not necessarily delay emergence when appropriate neuromuscular reversal and standardised extubation criteria are employed. In the present study, all patients received the same neuromuscular blockade protocol and reversal regimen, and extubation was performed according to predefined clinical criteria, thereby minimising systematic differences between the study groups. Nevertheless, objective neuromuscular monitoring was not employed, and this should be considered when interpreting extubation-related outcomes.

QoR, assessed using the QoR-15 questionnaire, was significantly better in both active intervention groups compared with the saline group, and the highest scores were observed in the dexmedetomidine group. Beyond reducing opioid consumption, dexmedetomidine may improve postoperative recovery through its favourable effects on analgesia, sleep quality, anxiolysis, and opioid-related adverse effects, without causing clinically significant respiratory depression. These findings are consistent with previous studies by Kim et al.[19] and Lee et al.[20] Similarly, the improvement observed with ketamine is in agreement with the findings of Pereira et al.[21] Importantly, the improvement in QoR-15 scores with dexmedetomidine compared with saline exceeded the reported minimal clinically important difference (MCID) of 6-8 points, indicating that the observed benefit was not only statistically significant but also clinically meaningful.[22,23] Although the mean QoR-15 score was 6 points higher with dexmedetomidine than with ketamine, meeting the updated 6-point MCID, this between-group difference should be interpreted cautiously, as the MCID was established primarily to reflect clinically important change at the individual-patient level.[23]

Beyond the immediate perioperative outcomes observed in this study, these findings have potential implications for perioperative analgesic strategies and their broader clinical application. The present findings also have potential implications for enhanced recovery pathways. The use of opioid-sparing adjuvants such as dexmedetomidine or subanaesthetic ketamine within a standardised SPI-guided analgesic protocol may facilitate individualised intraoperative opioid administration while reducing perioperative opioid exposure. Dexmedetomidine was associated with lower postoperative opioid consumption and improved QoR-15, suggesting that it may be a useful adjunct in settings where enhanced postoperative recovery is a priority.

Lumbar spine surgery encompasses procedures that vary in the number of spinal levels operated on, the extent of instrumentation, the degree of muscle dissection, and the duration of tissue retraction, all of which influence the intensity and duration of intraoperative nociceptive stimulation. More extensive procedures may generate greater afferent nociceptive input, resulting in higher analgesic requirements during surgery.[24] Although the overall distributions of procedure types and operative durations were comparable among the study groups, these procedure-specific factors were not quantified and may have contributed to variability in perioperative opioid requirements. Nevertheless, the standardised SPI-guided opioid titration protocol ensured that fentanyl administration followed a predefined criterion uniformly across all study groups, thereby reducing, although not eliminating, the influence of surgical heterogeneity on intraoperative analgesic management.

Although this study was limited to lumbar-spine surgery, the observed opioid-sparing effects of dexmedetomidine and subanaesthetic ketamine may be broadly relevant to other surgical procedures that involve substantial nociceptive stimulation. Previous studies have similarly demonstrated improved intraoperative opioid titration with SPI-guided protocols across diverse surgical populations.[13,25] However, the present study was designed to compare adjunctive analgesic strategies under a standardised SPI-guided protocol, rather than to establish the superiority of SPI-guided analgesia over conventional analgesic management. Further multicentre studies across different surgical populations and anaesthetic techniques are warranted to establish the broader generalizability of these findings.

Study Limitations

This study has certain limitations. First, the sample size was not specifically powered for a definitive head-to-head comparison between dexmedetomidine and ketamine. Second, the attending anaesthesiologist was not blinded to group allocation and was responsible for recording SPI values and administering intraoperative fentanyl. Although predefined SPI thresholds and a fixed fentanyl dosing protocol were used, this may have introduced performance or measurement bias. Third, objective neuromuscular monitoring was not employed, and cumulative supplemental vecuronium doses were not recorded, both of which may have influenced extubation time. Although procedure types and operative durations were comparable, surgical complexity, including the number of levels operated on, the extent of instrumentation, and tissue handling, was not specifically quantified and may have contributed to variability in nociceptive stimulation and perioperative opioid requirements.

In addition, dexmedetomidine and ketamine have distinct pharmacological mechanisms and opposing effects on autonomic tone, with no established dose equivalence

between them. Although the same predefined SPI-guided opioid titration protocol was applied uniformly across all groups, these pharmacological differences should be considered when interpreting comparisons between the active interventions.

Conclusion

Within a standardised SPI-guided analgesic protocol, both dexmedetomidine and subanaesthetic ketamine reduced cumulative intraoperative supplemental opioid requirements without prolonging extubation time compared with saline during lumbar spine surgery. Dexmedetomidine was associated with lower postoperative fentanyl consumption and improved postoperative recovery compared with saline, whereas both active interventions demonstrated comparable intraoperative opioid-sparing efficacy. As SPI-guided opioid titration served as a standardised analgesic protocol throughout the study, these findings reflect the comparative effects of the study interventions rather than the independent clinical effectiveness of SPI-guided analgesia. Further adequately powered studies are warranted to evaluate the role of SPI-guided opioid titration and to compare opioid-sparing adjuncts across different surgical populations.

Ethics

Ethics Committee Approval: This prospective randomised controlled trial in adult patients undergoing lumbar spine surgery was conducted after obtaining approval from the Jawaharlal Institute of Postgraduate Medical Education and Research Institute Ethics Committee (approval no: JIP/IEC/2022/09, date: 26.03.2022) and registration with the Clinical Trial Registry of India (CTRI/2023/01/048710).

Informed Consent: Written informed consent was obtained from all the participants.

Footnotes

Authorship Contributions:

Surgical and Medical Practices - G.A., S.S.; Concept - G.A., S.S., P.U.B.; Design - G.A., S.S., P.U.B.; Data Collection and/ or Processing - G.A., S.S., R.R., P.U.B.; Analysis and/or Interpretation - G.A., S.S., R.R., P.U.B.; Literature Review - G.A., S.S., R.R., P.U.B.; Writing - G.A., S.S., R.R., P.U.B.

Declaration of Interests: No conflict of interest was declared by the authors.

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Medico-legal Knowledge and Awareness Among Anaesthesiology and Reanimation Physicians in Türkiye: A Nationwide Survey

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Abstract

Objective: Anaesthesiologists undertake substantial clinical, organisational, and medico-legal responsibilities throughout perioperative care. This nationwide survey evaluated self-reported and questionnaire-assessed knowledge of professional, organisational, and medico-legal responsibilities among anaesthesiology and reanimation physicians practising in Türkiye.

Methods: This nationwide cross-sectional survey included anaesthesiology and reanimation physicians practising in Türkiye. Participants completed a structured 36-item questionnaire assessing professional duties, legal responsibilities, informed consent, documentation, and the medico-legal framework. A total of 311 physicians participated. Descriptive statistics and exploratory subgroup analyses were performed.

Results: Participants demonstrated excellent awareness of core clinical responsibilities, with 98-99% correctly identifying essential duties such as preoperative assessment, anaesthetic technique selection, and perioperative decision-making. However, important knowledge gaps were identified in the organisational and medico-legal domains. Approximately half of the participants were unaware of responsibilities related to operating theatre management and sterilisation processes, and only 47% correctly recognised responsibility for anaesthesia-related equipment and supplies. Although only 43% reported adequate knowledge of current legal regulations, knowledge assessed by the questionnaire varied considerably across domains. Nearly half of the participants had not previously taken part in structured medico-legal educational activities.

Conclusion: Despite excellent awareness of core clinical responsibilities, important deficiencies were identified in questionnaire-assessed medico-legal knowledge, while self-perceived knowledge of current legal regulations remained limited. Structured medico-legal education should be integrated into residency training and continuing professional development to strengthen professional accountability, documentation practices, physician-patient communication, and safe anaesthesiology practices.

Keywords: Anaesthesiology, duties and authority, informed consent, medical liability, professional responsibility, health knowledge and practice

Main Points

- This nationwide survey demonstrates that anaesthesiology and reanimation physicians in Türkiye have excellent awareness of core clinical responsibilities, but exhibit important deficiencies in organisational and medico-legal responsibilities.
- Knowledge gaps were particularly evident regarding operating room management, sterilisation processes, responsibilities for anaesthesia-related equipment, and legal regulations.
- Participants' self-perceived medico-legal knowledge did not consistently correspond with their questionnaire-assessed knowledge across several medico-legal domains.
- The findings support the integration of structured medico-legal education, documentation standards, and informed consent training into residency curricula and continuing professional development programmes.
- Strengthening medico-legal literacy is essential for promoting professional accountability, effective physician-patient communication, and safe anaesthesiology practice.

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Introduction

Physicians assume substantial clinical, ethical, and legal responsibilities in the delivery of healthcare. Beyond providing medical treatment, they are expected to practise in accordance with professional standards, respect patient autonomy, safeguard confidentiality, and comply with the statutory and regulatory framework governing medical practice. Consequently, medical malpractice and professional liability have become increasingly important challenges in contemporary healthcare systems, with significant implications for both physicians and patients.[1-3] Malpractice claims may arise when clinical practice deviates from accepted standards of care or when legally protected patient rights are compromised.[4-6]

The physician-patient relationship extends beyond clinical care and encompasses ethical as well as legal responsibilities. In many legal systems, including Türkiye, physicians are expected to exercise an appropriate standard of care while fulfilling their obligations regarding informed consent, confidentiality, documentation, and professional accountability.[7,8]

Limited knowledge of professional responsibilities may increase medico-legal risk and negatively affect both physician behavior and patient safety. Despite increasing medico-legal complexity in contemporary healthcare systems, physicians' knowledge of legal responsibilities and regulatory obligations remains variable, and structured medico-legal education is not routinely incorporated into undergraduate or postgraduate medical training in many healthcare settings. Accordingly, strengthening physicians' medico-legal literacy has become increasingly important, not only for mitigating malpractice risk but also for reinforcing professional accountability, improving documentation practices, enhancing physician-patient communication, and supporting patient-centred care. These educational priorities have long been recognised in the medical literature, where greater integration of legal principles into undergraduate and postgraduate medical training has been advocated.[9-13]

Anaesthesiology represents a particularly demanding specialty in which complex clinical decision-making, perioperative risk management, interdisciplinary communication, and high-quality documentation intersect in a high-risk environment. Although remarkable advances in monitoring technologies, patient safety initiatives, and perioperative standards have substantially reduced anaesthesia-related morbidity and mortality over recent decades, medico-legal challenges remain an important aspect of contemporary anaesthesiology practice.[14-16] Medication errors, perioperative adverse events, communication failures, documentation deficiencies, and disputes related to informed consent remain among the leading causes of medico-legal claims in anaesthesiology practice. Accordingly, comprehensive knowledge of professional responsibilities, legal obligations, and applicable regulatory frameworks represents an essential component of contemporary anaesthesiology practice.[17-22]

In Türkiye, physicians' professional and medico-legal responsibilities are governed by a comprehensive legal framework comprising constitutional provisions, statutory legislation, and healthcare-specific regulations. The Constitution of the Republic of Türkiye, the Regulation on the Operation of Inpatient Treatment Institutions, the Fundamental Law on Healthcare Services, the Patient Rights Regulation, the Turkish Penal Code, and the Turkish Code of Obligations define physicians' obligations regarding professional conduct, informed consent, documentation, confidentiality, and legal accountability. Nevertheless, physicians' awareness and understanding of these legal responsibilities may vary considerably according to their education, training, and professional experience. [23-28]

To our knowledge, this is the first nationwide study designed to systematically evaluate professional and medico-legal knowledge and awareness among anaesthesiology and reanimation physicians in Türkiye across multiple domains, including statutory professional duties, institutional responsibilities, informed consent, documentation obligations, and relevant legal regulations. Unlike previous studies that focused solely on malpractice or legal regulations, the present study provides the first multidimensional evaluation of physicians' professional responsibilities and medico-legal awareness. Accordingly, the primary objective of this study was to evaluate both self-reported and questionnaire-assessed medico-legal knowledge among anaesthesiology and reanimation physicians practising in Türkiye and to identify knowledge gaps that may inform future educational strategies and healthcare policy.

Methods

This cross-sectional survey was approved by the Non-Interventional Clinical Research Ethics Committee of Van Yüzüncü Yıl University (decision no: 2023/13-10, date: December 8, 2023) and conducted in accordance with the ethical principles of the Declaration of Helsinki.

Study Population

A nationwide cross-sectional survey was disseminated electronically to anaesthesiology and reanimation physicians actively practising in Türkiye via the Turkish Society of Anaesthesiology and Reanimation (TARD) mailing lists and professional whatsapp groups. Participation was voluntary, anonymous, and uncompensated. The survey employed convenience and snowball sampling through professional networks. Because the exact number of physicians

who received or viewed the questionnaire could not be determined, the response rate could not be calculated.

Questionnaire Development

The questionnaire was specifically designed for the present study by the corresponding author to evaluate anaesthesiology and reanimation physicians' knowledge and awareness of professional responsibilities, medico-legal obligations, informed consent, medical documentation, and the legal framework governing medical practice in Türkiye. Questionnaire development was guided by a comprehensive review of the Turkish medico-legal framework governing medical practice. In addition, current national and international literature in anaesthesiology addressing medical liability, informed consent, documentation, and medico-legal responsibilities was reviewed to ensure comprehensive coverage of the key knowledge domains.

The draft questionnaire was reviewed by senior anaesthesiology and reanimation specialists who have extensive expertise in health law and considerable experience in medico-legal practice. The reviewers evaluated the clarity, relevance, comprehensiveness, and legal accuracy of each questionnaire item. Their recommendations were incorporated into the final version to improve clarity, minimise ambiguity, and ensure legal accuracy.

The questionnaire was designed to assess factual knowledge of the current Turkish medico-legal framework rather than attitudes or latent psychological constructs. For dichotomous and three-option knowledge items (e.g., True/False/I do not know or Yes/No/I do not know), the legally correct response was determined a priori according to the explicit wording and legal definitions contained in the applicable legislation and regulations in force at the time of the study. For multiple-response items, all legally correct options were predefined based on the relevant legislation, and participants' awareness was evaluated based on the number of correctly identified responses. Because the questionnaire assessed factual knowledge of current legislation rather than latent constructs, formal psychometric validation was not performed. No pilot testing was undertaken before nationwide dissemination; this has been acknowledged as a limitation of the study. The complete questionnaire, scoring principles, and response distributions for all 36 survey items are provided in Supplementary Table S1 to ensure transparency and reproducibility. Because question 26 addressed a presumed minimum timeframe of 24 hours for obtaining informed consent, this item was re-examined in light of the applicable legal framework during the revision process. Article 18 of the Turkish Patient Rights Regulation stipulates that, except in emergencies, information should be provided to the patient, and the patient should be allowed a reasonable period for consideration; it does not establish a universally applicable 24-hour minimum timeframe. Therefore, Question 26 was retained in the supplementary questionnaire for transparency but was excluded from the interpretation of questionnaire-assessed factual knowledge.

The survey was created using google forms and distributed electronically to members of the TARD via e-mail. The survey link was also disseminated through professional whatsapp groups comprising anaesthesiology and reanimation physicians practicing in Türkiye. Before accessing the questionnaire, participants were required to confirm their willingness to participate by selecting the statement "I agree to participate," which was accepted as the provision of electronic informed consent.

Survey Instrument

The survey instrument comprised 36 items organised into four predefined domains: (1) demographic characteristics (6 items), (2) duties and professional responsibilities of anaesthesiologists (8 items), (3) legal responsibilities and applicable laws and regulations (6 items), and (4) obligations related to patient information, informed consent, and medical documentation (16 items). The completion time was approximately five minutes. Although the survey was anonymous and direct personal identifiers were not collected, the dataset was reviewed for potential duplicate submissions based on demographic characteristics and response patterns before analysis (Table 1).

Sample Size Calculation

The minimum required sample size was estimated using SurveyMonkey's sample size calculator, assuming a finite population of approximately 11,000 anaesthesiology and reanimation physicians in Türkiye. The calculation was intended to ensure adequate precision for descriptive estimates rather than statistical power for subgroup comparisons. Assuming a 90% confidence level and a 5% margin of error, the minimum required sample size was estimated to be 266 participants. The sample size calculation was performed to provide adequate precision for descriptive estimation of survey responses and was not specifically powered for hypothesis testing or subgroup comparisons. Accordingly, all subgroup analyses should be interpreted as exploratory. A final analysis was conducted on the remaining 311 valid questionnaires.

Statistical Analysis

Statistical analyses were performed using SPSS version 20.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were expressed as mean ± standard deviation for continuous variables and as frequency (n) and percentage (%) for categorical variables. Associations between categorical variables were assessed using Pearson's chi-square test or Fisher's exact test, as appropriate. A two-sided *P* value was considered statistically significant. Subgroup analyses were conducted to explore associations between participant

Table 1. Structure and Content of the Survey Questionnaire

Section 1-Demographic parameters
Age, sex, academic title, type of institution, duration of professional experience in anaesthesiology (years), province of practice
Section 2-Duties and authority of the anaesthesiologist
The anaesthesiologist prepares the daily operating room work schedule. The anaesthesiologist performs the preoperative evaluation and premedication of patients scheduled for surgery.
The anaesthesiologist supervises personnel working in the operating room and postoperative care units, ensures regular and efficient workflow and in-service training, and is responsible to the chief physician within the department.
Depending on the patient's health condition, the anaesthesiologist decides whether surgery may be performed under anaesthesia.
The anaesthesiologist determines the most appropriate position on the operating table and selects the anaesthesia technique; administers the anaesthetic agent or ensures its administration under supervision.
The anaesthesiologist is legally obligated to document the anaesthesia method and perioperative follow-up in the anaesthesia observation (record) form.
The anaesthesiologist assists the operating room supervisor in operating room management and sterilization procedures.
The anaesthesiologist is responsible for the provision, maintenance, preservation, and use of all anaesthesia-related devices, instruments, medications, and medical supplies in the operating room and postoperative care unit.
According to the Regulation on the Operation of Inpatient Treatment Institutions, the anaesthesiologist is responsible for the anaesthesia administered to the patient.
Section 3-Legal responsibilities and applicable laws, regulations, and statutes
I have comprehensive knowledge of the current laws, regulations, and statutes governing the legal responsibilities of anaesthesiologists in professional practice.
Please specify the scientific meeting(s) you have previously attended regarding the professional and legal responsibilities of anaesthesiologists.
Have you ever been subject to a legal complaint or judicial investigation related to healthcare services you provided in your professional practice?
Which laws, statutes, and regulations currently in force define the legal framework of our professional responsibilities? (Multiple selection)
Anaesthesiologists may incur legal liability for intentional or negligent acts arising from healthcare services or scientific research activities. Which of the following acts are classified as criminal offenses under the Turkish Penal Code? (Multiple selection)
I am aware of the disciplinary sanctions that may be imposed following an investigation conducted under Article 657 of the Civil Servants Law and its related Disciplinary Regulations.
Section 4-Information disclosure, informed consent, and medical record-keeping obligations
I understand that information disclosure and informed consent are not the same and that consent must be obtained in written form when legally required.
Informed disclosure: prior to any planned medical intervention, the anaesthesiologist performing the procedure must provide the patient with the necessary information. The primary purpose is to eliminate the patient's lack of knowledge, and the information may be provided verbally or in writing.
Please select the mandatory elements that must be included in the informed disclosure process. (Multiple selection)
The obligation to obtain patient consent is assigned to physicians under the Patient Rights Regulation and the Medical Deontology Regulation.
Informed consent is defined as a person's voluntary and informed acceptance of a medical intervention. No intervention violating bodily integrity or personal rights may be performed without consent.
A reasonable period must be granted for the patient to consider providing consent. What is the minimum required time? (This item was excluded from the interpretation of questionnaire-assessed factual knowledge because the applicable regulation does not establish a universally applicable 24-hour minimum timeframe.)
Consent must be present at the beginning of treatment and remain valid throughout its duration. Except for legal exceptions, consent is not bound to a specific form and may be explicit or implicit, written or verbal.
Consent may be withdrawn after being given. I understand the legal and procedural implications of a patient withdrawing consent and the appropriate course of action in such cases.
In medical malpractice claims, the burden of proof lies with the physician to demonstrate absence of fault.
Please specify the physician's documentation obligations and potential criminal liabilities related to medical records. (Multiple selection)
In anaesthesia monitoring records, any crossed-out or corrected entries must remain legible.
Who holds ownership of medical records, including anaesthesia monitoring forms?
For how many years must anaesthesia records (anaesthesia monitoring forms) be retained at a minimum?
Altering medical records or creating false documentation may constitute the criminal offense of forgery of private or official documents under the law.
Since public-sector physicians have a legal obligation to maintain medical records, failure to do so may constitute a criminal offense under Article 257/2 of the Turkish Penal Code.
I would like to attend a training program on the professional and legal responsibilities of anaesthesiologists.
Abbreviations and Response Formats: Likert-type items were rated on a 5-point scale (1= Strongly disagree, 2= Disagree, 3= Neither agree nor disagree, 4= Agree, 5= Strongly agree). For knowledge-based items, response options were structured as True/False/I do not know or Yes/No/I do not know, as appropriate. Multiple-selection questions allowed participants to select more than one response option where applicable.

characteristics and medico-legal knowledge; however, these analyses were considered exploratory because the study was not specifically powered for comparisons between subgroups. For descriptive analyses, responses to Likert-scale items were summarised according to the five original response categories. Where appropriate, adjacent categories (strongly agree/agree and strongly disagree/disagree) were combined to facilitate interpretation, as specified in the results section. For multiple-response questions, percentages were calculated according to the total number of participants, and respondents were permitted to select more than one option where applicable.

Results

A total of 311 anaesthesiology and reanimation physicians completed the survey. Overall, participants demonstrated excellent awareness of core clinical responsibilities but had substantially lower knowledge across several organisational and medico-legal domains. Associations with professional experience differed across individual questionnaire items.

Participant Characteristics

A total of 311 participants completed the questionnaire. Of these, 59.2% were male and 40.8% were female. Specialist physicians (52.7%) and residents (28.3%) constituted over four-fifths of the study population. Regarding professional experience, 32.2% had 11-20 years, 23.8% had 0-5 years, 27.0% had 6-10 years, and 17.0% had more than 20 years of experience. The largest proportion of participants worked in state university hospitals (38.6%) (Table 2). The complete distribution of responses for all 36 questionnaire items is provided in Supplementary Table S1 to ensure comprehensive reporting and transparency.

Knowledge of Duties and Authority of the Anaesthesiologist

Participants demonstrated consistently high levels of awareness regarding their core clinical responsibilities (Figure 1). Correct response rates ranged from 84% to 99%, with the highest levels observed for preoperative evaluation, operating room scheduling, selection of anaesthetic technique, and perioperative decision-making (98-99%).

Table 2. Demographic and Professional Characteristics of the Participants

Variable	n	%
Gender		
Male	184	59.2
Female	127	40.8
Academic title		
Professor	15	4.8
Associate Professor	19	6.1
Assistant Professor	18	5.8
Lecturer	7	2.3
Specialist Physician	164	52.7
Resident	88	28.3
Professional experience (year)		
0-5	74	23.8
6-10	84	27.0
11-20	100	32.2
>20	53	17.0
Institution type		
State University Hospital	120	38.6
Foundation University Hospital	4	1.3
Training and Research Hospital	59	19.0
Affiliated/Contracted Hospitals	17	5.5
City Hospital	17	5.5
State Hospital	55	17.7
Private Hospital	39	12.5

Nevertheless, important knowledge gaps remained regarding operating theatre management, sterilisation processes, documentation responsibilities, and the management of anaesthesia-related equipment and supplies. Awareness of documentation-related legal responsibilities was also suboptimal, with only 67.2% of participants correctly recognising the legal implications of failing to maintain medical records (Figure 2).

Medico-legal Awareness and Determinants

Medico-legal awareness varied considerably across the domains evaluated (Figure 3). Only 43% of participants self-reported adequate knowledge of current legal regulations (strongly agree and agree) (Figure 3A). Participation in structured medico-legal educational activities remained limited, with 46% of respondents reporting no prior attendance at relevant scientific meetings (Figure 3B). Notably, 40% of anaesthesiologists self-reported prior exposure to legal complaints or judicial investigations (Figure 3C). Encouragingly, a substantial majority (94.9%) expressed a willingness to participate in future training programs. Awareness of disciplinary sanctions under Article 657 of the Civil Servants Law remained high (87%), although some uncertainty persisted (Figure 3D).

To further explore factors associated with medico-legal exposure, chi-square analyses were performed. No statistically significant association was found between gender and exposure to legal complaints (P=0.113). In contrast, a

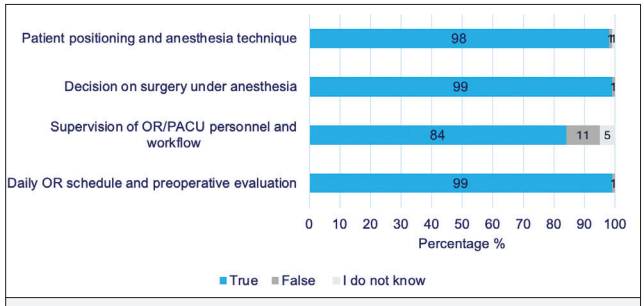


Figure 1. Questionnaire-assessed knowledge of core clinical responsibilities. Data are presented as percentages of responses (True/False/I do not know); n = 311.

OR, operating room; PACU, postanesthesia care unit.

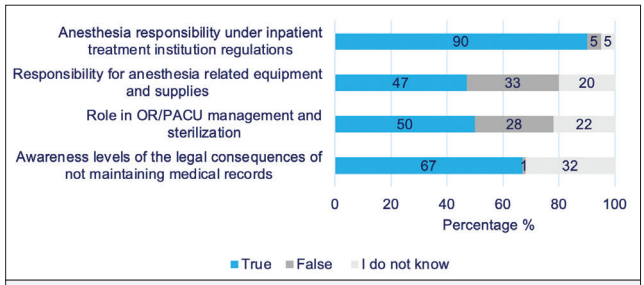


Figure 2. Questionnaire-assessed awareness of organisational responsibilities. Data are presented as percentages of responses (True/False/I do not know); n = 311.

OR, operating room; PACU, postanesthesia care unit.

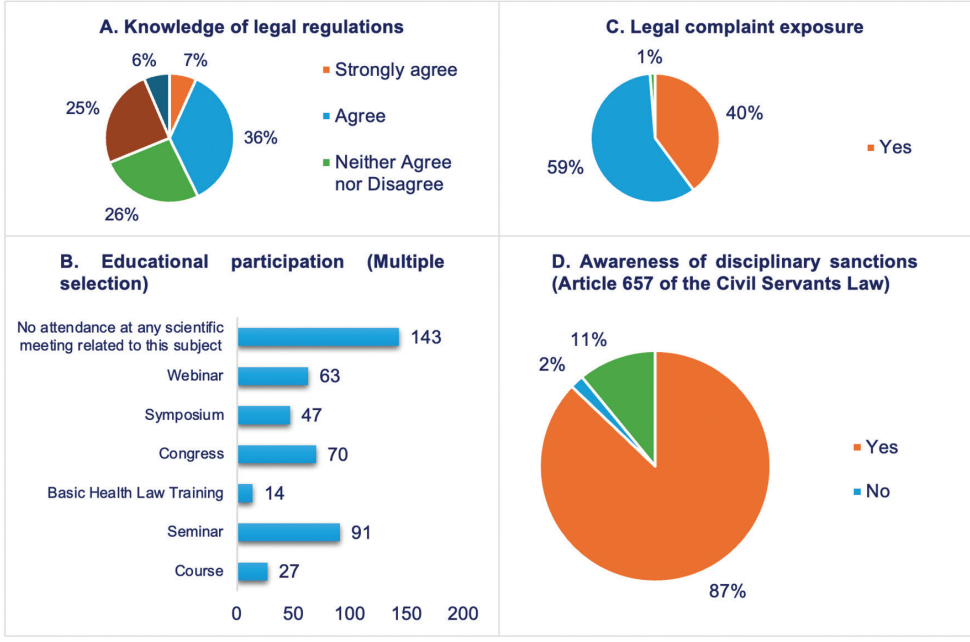


Figure 3. Self-reported medico-legal awareness and prior medico-legal exposure. Data are presented as number or percentages of responses; variability was observed across different domains. (A) Self-reported knowledge of legal regulations. (B) Participation in medico-legal educational activities (Multiple selection). (C) Exposure to legal complaints or judicial investigations. (D) Awareness of disciplinary sanctions under national regulations (n = 311).

significant association was observed between professional experience and exposure to legal complaints ($P < 0.001$), with the likelihood of legal complaints increasing with years of practice. Similarly, academic rank was significantly associated with legal complaint exposure ($P=0.001$), with higher academic rank associated with increased reporting of prior legal complaints. While exposure to legal complaints was independent of gender, its significant association with professional experience likely reflects cumulative medico-legal exposure over time rather than differences in individual risk.

Knowledge of Medico-legal Principles, Documentation, and Legal Framework

Participants demonstrated variable levels of knowledge across different medico-legal domains (Figure 4). Regarding informed disclosure, 84.6% of participants correctly distinguished informed disclosure from informed consent, and 84.2% correctly identified the concept of informed disclosure. Almost all participants (96.8%) correctly defined informed consent. However, knowledge regarding several practical legal principles was considerably lower. Only 39.5% correctly recognised that informed consent remains valid throughout the entire course of treatment, 49.5% correctly identified the patient's right to withdraw consent, and 43.1% correctly recognised the burden of proof in informed consent-related disputes. Knowledge of documentation responsibilities also varied. Most participants recognised that corrections to anaesthesia records must remain legible (88.1%) and nearly all recognised document forgery as a criminal offence (94.9%). However, only 56.6% correctly identified the minimum legal retention period for anaesthesia records, whereas awareness of the legal ownership of medical records was substantially lower. The complete response distribution for all questionnaire items is presented in Supplementary Table S1.

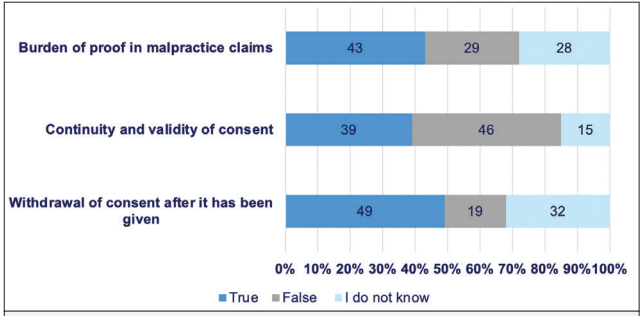


Figure 4. Questionnaire-assessed knowledge of informed consent and related legal principles. Data are presented as percentages of responses (True/False/I do not know); n = 311.

Self-reported knowledge of legal regulations varied significantly by level of professional experience ($P < 0.001$) (Table 3), with more experienced participants reporting higher levels of knowledge.

When participants were asked whether failure to maintain medical records could constitute a criminal offense under article 257/2 of the Turkish Penal Code, 67.2% responded correctly, 32.2% reported no opinion, and 0.6% responded incorrectly. No significant association was observed between this perceived adequacy of knowledge and professional experience ($P =0.092$) (Table 4).

In contrast, awareness of the legal consequences of falsifying or altering medical records was high, with 94.9% of participants responding correctly. This knowledge was significantly associated with professional experience ($P=0.022$); lower levels of experience were associated with higher rates of uncertainty or incorrect responses (Table 5).

Participants also demonstrated marked variability in recognising the statutory framework governing physicians' professional responsibilities (Figure 5). Awareness was relatively high regarding commonly encountered legislation, including the Civil Servants Law (Law No. 657), the Turkish Penal Code, the Regulation on Inpatient Treatment Institutions, the Patient Rights Regulation, and the Medical Deontology Regulation. In contrast, recognition of several other laws defining physicians' professional responsibilities was considerably lower, particularly for the Criminal Procedure Code, the Law on Private Hospitals, the Turkish Code of Obligations, the Military Penal Code, and the Law on the Socialization of Health Services.

Table 3. Self-Reported Knowledge of Legal Regulations According to Professional Experience

Professional experience (years)	Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree	Total	*P* value
0-5	4	16	27	19	8	74	
6-10	3	26	28	21	6	84	
11-20	5	37	21	32	5	100	<0.001$^{\chi^2}$
>20	9	33	5	5	1	53	
Total	21	112	81	77	20	311	

χ^2: Chi-square test; Fisher's exact test when appropriate

Table 4. Awareness of Legal Responsibility for Failure to Maintain Medical Records According to Professional Experience

Professional experience (years)	True (n)	False (n)	I do not know (n)	Total (n)	*P* value
0-5	56	0	18	74	0.092$^{\chi^2}$
6-10	57	0	27	84	
11-20	62	0	38	100	
>20	34	2	17	53	
Total (n)	209	2	100	311	

χ^2: Chi-square test; Fisher's exact test when appropriate

Table 5. Awareness of Legal Consequences of Falsifying Medical Records According to Professional Experience

Professional experience (years)	True (n)	False (n)	I do not know (n)	Total (n)	*P* value
0-5	64	1	9	74	0.022 $^{\chi^2}$
6-10	82	0	2	84	
11-20	98	0	2	100	
>20	51	1	1	53	
Total (n)	295	2	14	311	

χ^2: Chi-square test; Fisher's exact test when appropriate

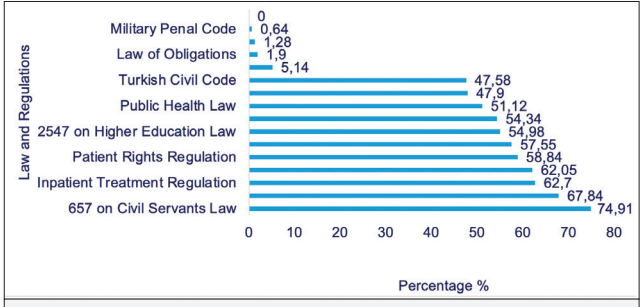


Figure 5. Percentage of participants correctly identifying laws and regulations relevant to physicians' professional responsibilities. Data are presented as the percentage of participants who correctly identified each legal regulation; n = 311.

Discussion

An important finding of the present study was the discrepancy between participants' self-reported medico-legal knowledge and their knowledge, assessed across multiple questionnaire domains. This finding highlights that self-perceived familiarity with medico-legal issues does not necessarily correspond to questionnaire-assessed factual knowledge.

The observed disparity between clinical proficiency and medico-legal awareness is consistent with previous literature indicating that physicians' legal literacy frequently lags behind their technical and clinical expertise. Increasingly complex healthcare systems, expanding patients' rights, and evolving legal frameworks require physicians not only to provide scientifically appropriate care but also to understand the legal and ethical responsibilities that accompany clinical decision-making. Importantly, malpractice risk is influenced not only by technical performance but also by communication, documentation quality, informed consent practices, organisational factors, and system-level processes. Studies evaluating malpractice risk and defensive medicine have similarly demonstrated that legal concerns substantially influence physicians' professional behaviour and clinical decision-making.[9,10,14] The present findings are also consistent with decades of evidence generated by the American Society of Anesthesiologists (ASA) Closed Claims Project. One of the major contributions of the Closed Claims Project has been the demonstration that serious anaesthesia-related injuries are frequently associated not only with technical failures but also with communication problems, documentation deficiencies, errors in clinical judgment, and system-related factors. Importantly, detailed medico-legal analyses have highlighted that understanding professional responsibilities and maintaining high standards of documentation and communication are essential components of safe anesthetic practice and effective risk management. These observations support the interpretation that strengthening medico-legal awareness should be regarded as an integral component of professional competence rather than merely a legal obligation. Anaesthesiology represents a unique context in this regard because perioperative care requires simultaneous responsibility for patient safety, interdisciplinary communication, documentation, equipment management, and rapid decision-making under time-critical conditions. The present findings are particularly relevant because

approximately half of participants demonstrated insufficient awareness of operating room management and sterilisation responsibilities, while fewer than half correctly identified their responsibility for anaesthesia-related equipment and supplies. These findings warrant particular attention because equipment-related failures and organisational deficiencies continue to contribute to anaesthesia-related adverse events and malpractice litigation.[29]

An equally important observation concerns informed consent and physicians' broader professional responsibilities. Consequently, deficiencies in physicians' medico-legal awareness may extend beyond litigation risk and adversely influence physician-patient communication, trust, and the quality of perioperative care.[7]

Documentation represents another cornerstone of contemporary anaesthesiology practice and deserves particular emphasis when interpreting the present findings. Accurate perioperative documentation supports continuity of care, facilitates multidisciplinary communication, enables quality improvement initiatives, and provides an essential legal record in the event of malpractice investigations or judicial review. Comprehensive anaesthesia records are widely recognised as an integral component of safe perioperative practice and professional accountability. Therefore, the relatively limited awareness of documentation-related responsibilities should not be interpreted solely as a legal concern but also as an important quality-of-care issue directly relevant to perioperative patient management.[29-31]

The present findings should also be interpreted in the context of patient safety culture within modern anaesthesiology. The Helsinki Declaration on Patient Safety in Anaesthesiology emphasises that safe perioperative care depends not only on technical competence but also on effective communication, organisational responsibility, education, standardisation of practice, and continuous quality improvement. From this perspective, medico-legal competence should not be viewed merely as protection against litigation but rather as an integral component of patient safety systems. Improving physicians' understanding of informed consent, documentation standards, institutional responsibilities, and professional accountability may, therefore, contribute to safer perioperative care through enhanced communication, transparency, and organisational performance, rather than through legal risk reduction alone.[31]

Our findings are also consistent with recent evidence from Türkiye analyzing closed anaesthesia malpractice claims between 2009 and 2022. That study demonstrated that perioperative mortality, intraoperative complications, delayed diagnosis, communication failures, and allegations of negligence continue to represent substantial medico-legal challenges within anaesthesia practice. Importantly, many of these events involve factors extending beyond technical proficiency alone, highlighting the importance of documentation quality, communication processes, organisational responsibility, and familiarity with applicable legal frameworks. The convergence of national malpractice data and the present survey findings further supports the need to strengthen medico-legal competence among practicing anaesthesiologists.[32]

The educational implications of these findings are considerable. Nearly half of physicians participating in the study self-reported no prior involvement in medico-legal educational activities despite substantial exposure to legal complaints during their professional careers. This observation suggests that existing educational frameworks may inadequately prepare physicians for the legal dimensions of contemporary clinical practice. Rather than relying exclusively on traditional lectures, residency programmes and continuing professional development initiatives may benefit from structured medico-legal curricula incorporating case-based learning, simulation exercises, documentation workshops, informed consent scenarios, interdisciplinary seminars involving legal experts, and periodic micro-learning modules. Professional organisations such as the TARD may play an important role in promoting such educational initiatives at a national level. Importantly, the educational value of closed claims analyses extends beyond litigation itself. By systematically examining rare but severe adverse events, closed claims reviews function as specialty-wide learning opportunities that enhance situational awareness, strengthen professional judgment, and improve physicians' preparedness for uncommon but high-consequence clinical scenarios.

The relatively limited awareness of several key legal statutes, particularly the Turkish Code of Obligations and the Criminal Procedure Code, suggests that physicians are generally more familiar with regulations encountered in daily clinical practice than with broader medico-legal legislation that may nevertheless become highly relevant during judicial proceedings.

Taken together, the present findings suggest that strengthening medico-legal competence should be regarded not merely as a strategy for reducing malpractice litigation but as an essential component of professional accountability, effective communication, high-quality documentation, and safe anaesthesiology practice. Consistent with lessons learned from the ASA Closed Claims Project and the principles of the Declaration of Helsinki, improving medico-legal literacy should be considered an investment in patient safety, professional excellence, and continuous quality improvement.

Study Limitations

This study has several important strengths. To our knowledge, this is among the first nationwide surveys in

Türkiye to systematically examine professional and medico-legal awareness among anaesthesiology and reanimation physicians using a structured questionnaire. The relatively large sample size and inclusion of physicians with varying levels of professional experience provide a broad overview of current awareness levels at the national level. In addition, the multidimensional assessment of medico-legal awareness, including knowledge, education, legal exposure, and disciplinary awareness, allows for a more integrated evaluation of professional preparedness. Nevertheless, the nationwide distribution of the survey through the national professional society enabled participation by physicians working in various institutions and at different career stages, providing valuable insight into current medico-legal knowledge across a broad professional spectrum.

However, certain limitations should be acknowledged. The electronic distribution of the questionnaire through email and whatsapp may have introduced selection bias by preferentially reaching physicians who were more digitally engaged or interested in medico-legal issues. In addition, participation was voluntary, potentially introducing self-selection bias. Because the exact number of physicians who received or opened the survey could not be determined, the response rate could not be calculated. Therefore, although the survey included physicians from across Türkiye, the findings should not be interpreted as a statistically representative sample of all anaesthesiology and reanimation physicians in the country. Second, the cross-sectional design precludes causal inferences regarding the relationship between education, professional experience, and medico-legal awareness. The assessment of knowledge was based on questionnaire responses rather than objective testing; questionnaire responses may not fully reflect actual competency. Another limitation is that the questionnaire was specifically developed for this study and did not undergo formal psychometric validation or pilot testing. Therefore, the findings should be interpreted as reflecting physicians' knowledge of the Turkish medico-legal framework rather than representing a universally validated measure of medico-legal competence. Although subgroup analyses according to professional experience, gender, and academic title were conducted, the sample size calculation was based on descriptive survey estimation methods rather than on statistical power for between-group comparisons. Consequently, subgroup findings should be interpreted as exploratory, particularly for categories with relatively small sample sizes. Although no direct personal identifiers were collected, the dataset was screened for potential duplicate submissions by reviewing demographic characteristics and response patterns before analysis. Future studies evaluating the impact of structured medico-legal training interventions on objective knowledge outcomes are warranted.

Conclusion

Despite high awareness of core clinical responsibilities, participants demonstrated significant deficiencies in questionnaire-assessed knowledge across several medico-legal domains, and self-perceived knowledge of current legal regulations also remained limited. The findings highlight a significant gap between physicians' real-world exposure to legal challenges and their perceived preparedness to navigate the increasingly complex medico-legal environment of contemporary healthcare.

Strengthening medico-legal competence should not be viewed solely as a strategy for reducing malpractice risk, but rather as an essential component of professional accountability, effective physician-patient communication, high-quality documentation, and safe anaesthesiology practice. Integrating structured medico-legal education into residency training and continuing professional development programmes may enhance physicians' legal literacy and preparedness while supporting ethically responsible, evidence-based, and patient-centred clinical decision-making.

Ultimately, improving medico-legal awareness should be regarded as an essential component of professional excellence, patient safety, and high-quality anaesthesiology practice.

Ethics

Ethics Committee Approval: This study was approved by the Non-Interventional Clinical Research Ethics Committee of Van Yüzüncü Yıl University Faculty of Medicine (Approval date: December 8, 2023; Decision No: 2023/13-10) and conducted in accordance with the Declaration of Helsinki.

Informed Consent: Written informed consent was obtained from all enrolled participants.

Previous Presentation

This study was presented as an oral presentation at the 59th National TARK Congress, Antalya, Türkiye, December 4-7, 2025.

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Supplementary Table Links: https://d2v96fxpocvxx.cloudfront.net/66b874bd-7aaa-4f61-9199-52f558d61c0d/documents/2588.xlsx

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Case Report
Regional Anaesthesia

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Turkish Journal of Anaesthesiology & Reanimation

Low-angle Paramedian Approach versus Midline Approach for Remote Access Epidural Blood Patch: A Case Report

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Abstract

While mid-thoracic cerebrospinal fluid leaks (T7-T8) require targeted epidural blood patches, direct thoracic puncture carries a significant risk of spinal cord injury due to the narrow epidural space. To mitigate this risk, a safety-oriented remote-access strategy from the T12-L1 level, with cranial advancement of the catheter, was employed to prevent direct thoracic spinal cord injury. We present a 46-year-old male with a T7-T8 leak in whom a standard midline approach failed due to poor catheter steerability. By adopting a low-angle (<30°) paramedian approach, we achieved precise ipsilateral catheter positioning; this technical modification provides optimized vector alignment and a tangential epidural trajectory for unilateral thoracic leaks. This technical modification may improve maneuverability and safety for unilateral thoracic leaks, compared to standard midline techniques, and appears to facilitate an optimized tangential trajectory in this case.

Keywords: Algology, epidural blood patch, intracranial hypotension, pain, regional anaesthesia

Main Points

- Mid-thoracic cerebrospinal fluid leaks pose high procedural risk due to a narrow epidural space.
- Midline approaches often limit catheter steerability during remote access.
- A low-angle (<30°) paramedian approach aligns with the epidural axis, enabling easier cephalad advancement.
- This technique is an effective alternative for precise targeting in difficult interventions.

Introduction

Spontaneous intracranial hypotension is characterized by reduced cerebrospinal fluid (CSF) volume and can mimic Arnold-Chiari malformation (ACM) through "brain sagging". In post-ACM-surgery patients, low CSF pressure causes downward brainstem displacement, leading to diagnostic confusion and potentially unnecessary re-operation.[1] While the epidural blood patch (EBP) is the gold standard,[2] direct mid-thoracic (T5-T9) needle entry risks spinal cord injury due to narrow epidural anatomy.[3] To mitigate this, a safety-oriented remote-access strategy using the T12-L1 interspace, with cranial advancement of the catheter to the T7-T8 target, is preferred. However, unilateral targeting remains challenging via standard midline approaches. This report documents technical success using a low-angle paramedian approach after failure of the midline technique.

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Case Report

Written informed consent was obtained. A 46-year-old male who underwent posterior fossa decompression for ACM Type-1 in 2021 presented three years postoperatively with progressive orthostatic headache, balance disturbance, and a 40-kg weight loss over 18 months. Physical examination showed hoarseness, horizontal diplopia, mild left-sided clumsiness or latent paresis, wide-based ataxic gait, and a positive left Babinski reflex.

Cranial magnetic resonance imaging demonstrated findings highly suggestive of intracranial hypotension: tonsillar descent to C2, diffuse dural contrast enhancement, narrowed prepontine cistern, and prominent pituitary gland. Dynamic computed tomography myelography identified an active CSF leak at the right T7-T8 neural foramen (Figure 1). Following failure of conservative management, an EBP was planned.

Interventional Procedure

Performed prone under conscious sedation (2 mg midazolam, 50 µg fentanyl) and intermittent fluoroscopy. The T12-L1 interspace was selected for remote entry to avoid thoracic cord injury.

Standard Midline Approach

The epidural space was accessed via a midline interlaminar approach using an 18-gauge, 9-cm Tuohy needle (B. Braun, Melsungen, Germany), confirmed by loss of resistance to saline. A standard 20-gauge polyamide catheter consistently deviated into the left lateral (contralateral) space on anteroposterior (AP) and lateral fluoroscopy and failed to advance past T10. The injection of 2 mL of non-ionic contrast medium (iohexol, 300 mg I/mL) confirmed contralateral spread (Figure 2). A right-sided low-angle paramedian approach was subsequently performed at the same level. The Tuohy needle was inserted at the right paramedian line, forming an angle of less than 30 degrees relative to the skin. This shallow trajectory produced a tangential epidural path parallel to the longitudinal axis of the epidural space. Due to this optimized vector alignment, the catheter was advanced cranially along the ipsilateral dorsal gutter to the target at the T8 level without resistance. Catheter position and strictly unilateral contrast spread were confirmed using AP and lateral fluoroscopic projections (Figure 3). The geometric and vector differences between these two needle trajectories are schematically illustrated in Figure 4.

Following fluoroscopic confirmation and contrast spread, 10 mL of autologous venous blood was injected. Following the injection, the catheter was removed, and the patient was kept on strict supine bed rest for 4 hours and underwent regular neurological assessments. The patient experienced immediate and complete resolution of the orthostatic headache and associated neurological deficits. At the 1-month post-procedural follow-up, the patient remained asymptomatic, with complete restoration to baseline function and no clinical signs of recurrence.

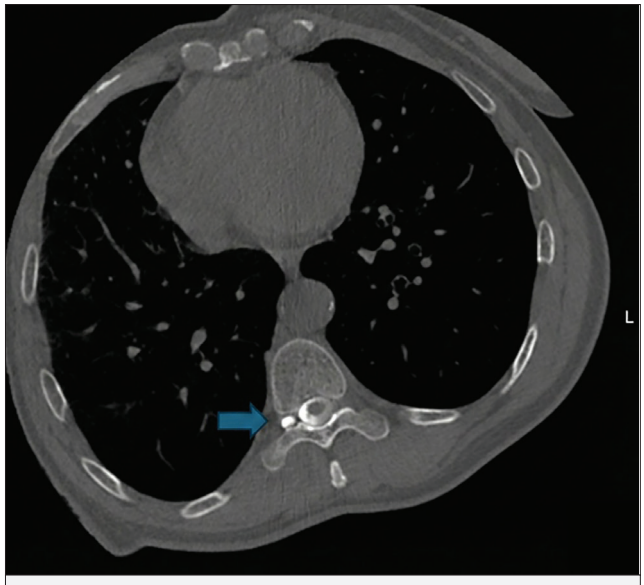


Figure 1. Axial dynamic computed tomography (CT) section showing a cerebrospinal fluid (CSF) leak on the right side of the spinal canal (area indicated by the arrow).

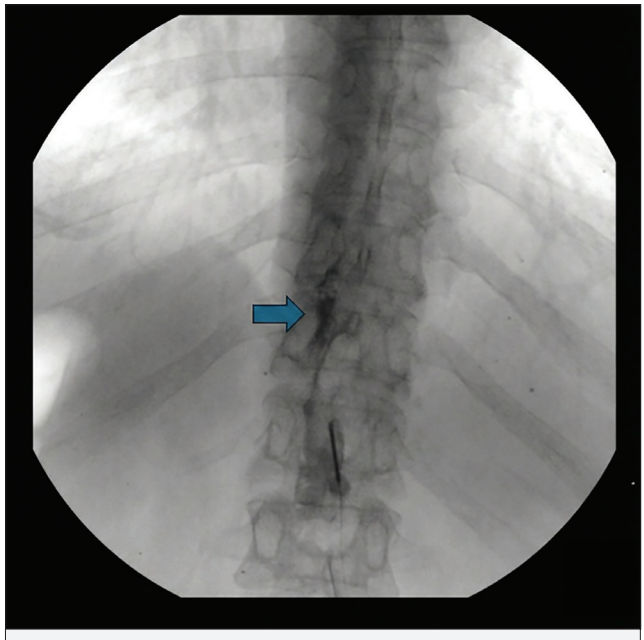


Figure 2. Fluoroscopic view of the standard midline approach. Upon entering the epidural space via the T12-L1 midline, the catheter consistently deviates toward the left side, preventing any corrective steering toward the right-sided target. Epidurography clearly demonstrates a contralateral contrast spread pattern, visually defining the technical failure to achieve targeted unilateral lateralization due to the steep insertion geometry.

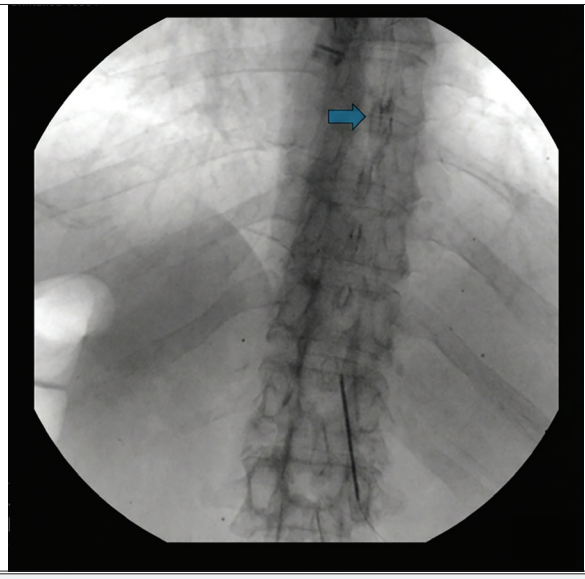


Figure 3. Fluoroscopic view of the low-angle paramedian approach. Utilizing a right-sided oblique entry angle, the catheter advances smoothly through the right epidural space into the dorsal gutter, with the tip precisely positioned at the T8 level. Epidurography demonstrates a strictly ipsilateral contrast spread pattern, confirming highly accurate and successful anatomical targeting of the right-sided thoracic leak.

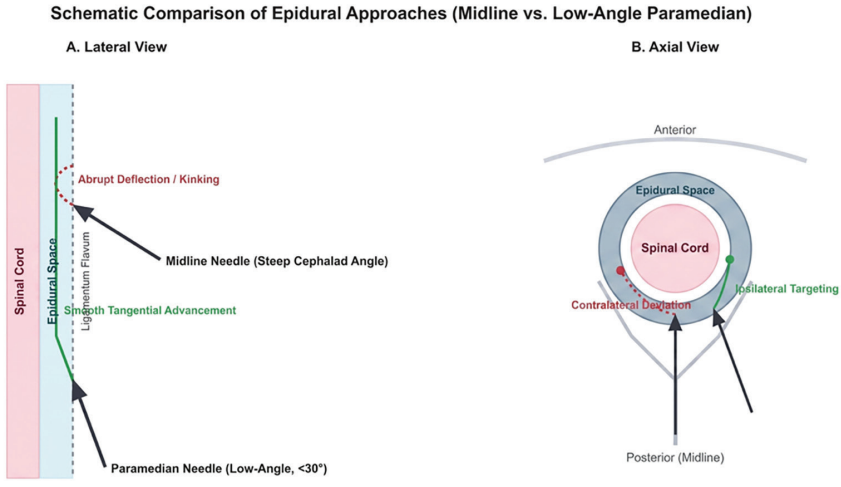


Figure 4. Schematic illustration highlighting the direct relationship between needle tract geometry, catheter behavior, and the resulting contrast distribution patterns. (A) Lateral View: The steep midline approach forces an abrupt deflection of the catheter upon entry, leading to kinking and unpredictable navigation. Conversely, the low-angle (<30°) paramedian approach establishes a tangential trajectory parallel to the longitudinal epidural axis, facilitating smooth, unobstructed cranial advancement. (B) Axial View: The midline approach results in an uncontrolled vector that drives the catheter into the opposite side, producing a contralateral contrast spread pattern. In contrast, the right-sided paramedian approach optimizes the directional vector directly into the right dorsal gutter, achieving the definitive ipsilateral contrast spread pattern that constitutes the central technical success of this technique.

Discussion

The mid-thoracic region is a high-risk zone for interventional procedures due to the narrowness of the epidural space and the anatomical position of the spinal cord.[4] In our case, distinguishing remote-access entry level (T12-L1) from the target thoracic leak level (T7-T8) constitutes a safety-oriented strategy explicitly designed to obviate the need for direct mid-thoracic puncture and thereby reduce the risk of direct injury to the thoracic spinal cord. The most critical technical finding presented in this case is the impact of the insertion angle on the steerability of the epidural catheter. In standard midline approaches, entering the epidural space at a steep vertical angle alters the vector alignment, making

the cephalad advancement of the catheter unpredictable. This steep trajectory may lead to reduced torque control and increase the potential for interactions with epidural fat or connective tissue structures, which can deflect the catheter tip. Furthermore, the specific orientation of the Tuohy needle bevel during a steep entry profile may steer the catheter into an unfavorable pathway from the outset. A clinical study by Ryu et al.[5] demonstrated that approaching the thoracic epidural space at a more horizontal angle significantly increases catheter threading length without coiling, directly illustrating how steeper tracts impede linear advancement. In contrast, the paramedian, shallow-angle entry (<30°) used in spinal cord stimulation implantation ensures parallel alignment with the longitudinal epidural axis, thereby creating a tangential trajectory within the epidural space.[6] This configuration provides an optimized vector alignment, allowing unimpeded insertion of the epidural catheter into the caudal end of the epidural segment, effectively preventing it from impacting the bony lamina above. As a result, this technique increases the likelihood of the catheter remaining on its intended trajectory and significantly reduces the risk of unintended lateral or anterior deviation, venous puncture, and paraesthesia.[7] Furthermore, achieving complete clinical recovery with only 10 mL of autologous blood is a noteworthy aspect of this case. Unlike conventional patches where the injectate spreads diffusely over multiple segments, the blood in this case was deposited locally via the catheter tip and remained directly at the T7-T8 level. Conventional lumbar or non-targeted epidural blood patches frequently require larger injectate volumes, often around 20 mL, to ensure sufficient cranial migration and volume distribution to reach distant mid-thoracic leaks.[2] Our experience suggests that accurate ipsilateral targeting within the dorsal gutter may allow effective treatment using lower blood volumes in selected patients, potentially minimizing the risks of transient post-procedural back pain or excessive intrathecal pressure spikes associated with large-volume injections. Nonetheless, given the single-case nature of this report, these observations must be interpreted with caution. Definitive comparative conclusions regarding the technical superiority or safety profile of this approach cannot be firmly established, and prospective comparative studies are required to validate these potential benefits.

Conclusion

Catheter-guided EBP at T12-L1 appears to be a viable approach to reduce complications from mid-thoracic CSF leaks. While midline steering is often limited for unilateral targets, a low-angle paramedian approach appeared to facilitate safe catheter advancement and improve maneuverability, enabling effective access to the targeted side.

Ethics

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

Footnotes

Authorship Contributions: Concept - A.P., C.E., M.U.; Design - A.P., C.E., B.Ö., M.U.; Data Collection and/or Processing - A.P.; Analysis and/or/Interpretation - A.P., C.E., M.U.; Literature Review - A.P., M.U.; Writing - A.P., M.U.

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Case Report
Cardiovascular and Thoracic Anaesthesia

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Hybrid Airway Management for Neuromonitoring-guided Selective Phrenic Nerve Surgery in Intractable Hiccups: A Case Report

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Abstract

Intractable hiccups are rare but debilitating, and may cause sleep disturbances, nutritional impairment, exhaustion, and a severe deterioration in quality of life. When pharmacological and interventional treatments fail, selected surgical procedures targeting the phrenic nerve may be considered. We report the anaesthetic management of a 32-year-old woman with idiopathic intractable hiccups who underwent right-sided selective phrenic nerve surgery guided by thoracoscopic neuromonitoring. Because thoracoscopic exposure and intraoperative neuromonitoring were required simultaneously, a hybrid airway strategy combining an electromyography endotracheal tube with a bronchial blocker was used. The patient was positioned in the left lateral decubitus position, and the bronchial blocker was placed in the right main bronchus under fiberoptic bronchoscopic guidance. One-lung ventilation was maintained for 35 minutes with FiO_2 of 0.70 to 0.80, tidal volume of 5-6 mL kg^{-1}, respiratory rate of 18 min^{-1}, and PEEP of 5 cmH_2O; the arterial blood gas analysis at 25 minutes showed pH 7.38, $PaCO_2$ 41 mmHg, and PaO_2 92 mmHg. Sugammadex was administered intraoperatively to restore diaphragmatic motor responses required for branch-specific neuromonitoring. The medial and anterolateral branches of the right phrenic nerve exhibited abnormal electrophysiological responses and were treated with selective bipolar ablation and clipping. Postoperatively, the patient remained on room air, reported no intraoperative recall, and showed no clinically relevant diaphragmatic dysfunction on clinical and functional assessment. This case illustrates that established anaesthetic techniques can be carefully adapted to meet the competing requirements of lung isolation, anaesthetic depth control, and neuromonitoring in selected patients undergoing phrenic nerve surgery for intractable hiccups.

Keywords: Intractable hiccups, phrenic nerve, intraoperative neuromonitoring, one-lung ventilation, electromyography endotracheal tube, bronchial blocker, sugammadex

Main Points

- We report the anaesthetic management of a patient undergoing a phrenic nerve procedure for intractable hiccups using intraoperative electromyography (EMG) monitoring.
- An EMG endotracheal tube was utilized to ensure reliable neuromonitoring while maintaining secure airway control.
- A bronchial blocker was mandatorily employed to achieve lung isolation without compromising EMG signal integrity.
- This case demonstrates that a hybrid airway strategy combining an EMG tube and bronchial blocker may be feasible in complex procedures requiring simultaneous lung isolation and neuromonitoring.

Introduction

Hiccups are involuntary, repetitive contractions of the diaphragm and intercostal muscles followed by abrupt glottic closure. Although most episodes are benign and self-limiting, persistent or intractable hiccups may cause sleep deprivation, nutritional impairment, exhaustion, psychological distress, and marked deterioration in quality of life. Intractable hiccups are generally defined as lasting longer than two months despite appropriate treatment.[1]

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The hiccup reflex arc involves afferent pathways through the vagus, phrenic, and sympathetic nerves, central processing within the brainstem and cervical spinal cord, and efferent motor output mainly through the phrenic nerve to the diaphragm. Because this pathway is complex, etiological evaluation should include central nervous system, thoracic, and abdominal causes, as well as metabolic, pharmacological, and psychogenic causes. Pharmacological therapy is generally considered the first-line treatment and may include chlorpromazine, baclofen, gabapentin, metoclopramide, proton pump inhibitors, and other agents selected according to the suspected etiology.[2] However, some patients remain refractory despite multimodal therapy.

Invasive interventions, including phrenic nerve block or surgical interruption, have been described in carefully selected refractory cases. However, proximal phrenic nerve interruption may cause ipsilateral diaphragmatic paralysis and reduced ventilatory reserve. In contrast, selective distal phrenic nerve procedures aim to target pathological branches while avoiding complete proximal phrenic nerve interruption.[3] Such procedures require precise intraoperative localization of the relevant branch and, therefore, introduce specific anaesthetic challenges: maintaining lung isolation for thoracoscopic exposure, preserving or restoring neuromuscular transmission for phrenic nerve monitoring, avoiding intraoperative awareness during neuromuscular recovery, and maintaining oxygenation during one-lung ventilation.

This report describes the anaesthetic management of a patient undergoing right-sided thoracoscopic neuromonitoring-guided selective phrenic nerve surgery for idiopathic intractable hiccups. The educational focus is on adapting established anaesthetic tools—an electromyography (EMG) endotracheal tube, a bronchial blocker, total intravenous anaesthesia, bispectral index (BIS) monitoring, and intraoperative reversal of neuromuscular blockade—to meet the competing requirements of lung isolation and phrenic nerve neuromonitoring.

Case Report

A 32-year-old woman presented with continuous hiccups lasting six months. The symptoms occurred at approximately 48 episodes per minute, causing severe sleep disturbance, nutritional impairment, exhaustion, and a marked deterioration in quality of life. A comprehensive etiological work-up was performed to exclude secondary causes of persistent hiccups. Neurological, thoracic, abdominal, gastrointestinal, metabolic, biochemical, and radiological evaluations did not reveal any identifiable organic cause. Therefore, the hiccups were considered idiopathic after exclusion of secondary etiologies.

The patient had previously received multiple pharmacological treatment protocols, including proton pump inhibitors, metoclopramide, antispasmodics, muscle relaxants, anxiolytics, chlorpromazine infusion, and baclofen. Despite these multimodal pharmacological treatments, the symptoms persisted. She also underwent consecutive right- and left-sided selective phrenic nerve blocks performed by the pain medicine unit for diagnostic and therapeutic purposes; however, these interventions did not provide sustained symptomatic improvement.

Dynamic fluoroscopic and ultrasonographic examinations demonstrated a pathological, asymmetric, paradoxical movement of the right hemidiaphragm, discordant with the left hemidiaphragm. Based on the failure of pharmacological and interventional treatments and the dynamic imaging findings, the right hemidiaphragm was considered the predominant pathological side, and right-sided thoracoscopic neuromonitoring-guided selective phrenic nerve surgery was planned.

The procedure was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from the patient for the surgical procedure and for publication of this case report and accompanying images.

Preoperative anaesthetic evaluation revealed American Society of Anesthesiologists I status and Mallampati class I. Because intraoperative phrenic nerve neuromonitoring and thoracoscopic exposure were required simultaneously, a hybrid airway strategy was planned. A conventional double-lumen tube was avoided because it would not have provided the same compatibility with the planned neuromonitoring configuration. Therefore, an EMG endotracheal tube, combined with a bronchial blocker, was selected.

Standard monitoring, invasive arterial blood pressure monitoring, BIS monitoring, and neuromuscular monitoring were applied. Anaesthesia was induced with propofol 3 mg kg^{-1}, fentanyl 1 μg kg^{-1}, and rocuronium 0.6 mg kg^{-1}. After adequate hypnotic depth was achieved, with a BIS value of approximately 45, the patient was intubated with a 7.5-mm EMG endotracheal tube. The patient was then positioned in the left lateral decubitus position with the right hemithorax up.

Anaesthesia was maintained using total intravenous techniques. Propofol was administered at 6-14 mg kg^{-1} h^{-1} and titrated to maintain BIS values between 40 and 60. Remifentanil was maintained at a constant rate of 0.2 μg kg^{-1} min^{-1} throughout the procedure. This anaesthetic strategy was selected to avoid interference with neuromonitoring and to maintain adequate hypnotic depth during periods of neuromuscular recovery.

Under fiberoptic bronchoscopic guidance, a 7-Fr bronchial blocker was advanced through the EMG endotracheal tube into the right main bronchus (Figure 1). The correct blocker position was confirmed bronchoscopically both after placement and after final positioning. One-lung ventilation was initiated with FiO_2 0.70-0.80, tidal volume of 5-6 mL kg^{-1} (approximately 350 mL), respiratory rate of 18 min^{-1}, and PEEP of 5 cmH_2O. Peripheral oxygen saturation remained between 95% and 100% during one-lung ventilation. One-lung ventilation lasted 35 minutes. An arterial blood gas analysis obtained at the 25th minute of one-lung ventilation showed a pH of 7.38, a $PaCO_2$ of 41 mmHg, and a PaO_2 of 92 mmHg.

The most critical phase of anaesthetic management was the restoration of neuromuscular transmission before selective ablation and clipping, since diaphragmatic motor responses were required to identify the pathological distal branches of the phrenic nerve. Sugammadex 2 mg kg^{-1} was administered intraoperatively, 25 minutes after the induction dose of rocuronium. Although neuromuscular monitoring equipment was available, no documented train-of-four (TOF) or post-tetanic count (PTC) values prior to sugammadex administration could be retrieved on retrospective review. The purpose of reversal at this stage was not emergence or extubation but the restoration of sufficient diaphragmatic motor activity for intraoperative neuromonitoring.

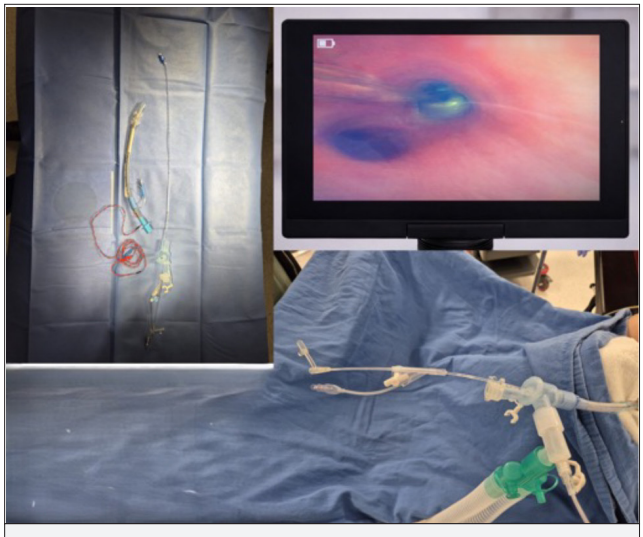


Figure 1. Hybrid airway setup for right-sided thoracoscopic neuromonitoring-guided selective phrenic nerve surgery. The image demonstrates the configuration of an electromyographic endotracheal tube and a 7-Fr bronchial blocker, together with confirmation of bronchial blocker placement in the right main bronchus by fiberoptic bronchoscopy. This setup enabled right lung isolation for thoracoscopic exposure while maintaining compatibility with the intraoperative neuromonitoring strategy.

During neuromuscular recovery after sugammadex administration, BIS values transiently increased to above 60 and were accompanied by mild increases in heart rate and arterial blood pressure. No gross patient movement was observed apart from the expected diaphragmatic contractions required for phrenic nerve monitoring. The propofol infusion was therefore increased by 2 mg kg^{-1} h^{-1}, after which the BIS values were maintained within the target range of 40-60.

Intraoperative neuromonitoring was performed after careful dissection of the right phrenic nerve around the pericardium and exposure of its distal branching pattern near the diaphragmatic entry point. Four distal branches extending posteriorly, medially, anterolaterally, and laterally were identified. Spontaneous diaphragmatic electrical activity was recorded using conductive strip electrodes placed on the diaphragm. Additional conductive strip electrodes were then positioned along the intramuscular course of each distal phrenic nerve branch. Motor evoked potentials were elicited by primary motor cortex stimulation, and branch-specific responses were compared. The medial and anterolateral branches of the right phrenic nerve demonstrated markedly reduced amplitudes and delayed conduction compared with those of the posterior and lateral branches. These findings, together with the abnormal right hemidiaphragmatic movement observed during dynamic preoperative assessment, guided selective bipolar ablation and clipping of the medial and anterolateral branches.

After ablation and clipping, repeat assessment showed the disappearance of the pathological, hiccup-like diaphragmatic contractions. No additional neuromuscular blocking agent was administered after sugammadex because continued assessment of diaphragmatic motor responses was required during selective ablation, clipping, and the final confirmation phase of the procedure. The bronchial blocker was deflated, bilateral ventilation was restored, and recruitment maneuvers were performed. The total durations of surgery and anaesthesia were 115 and 155 minutes, respectively (Table 1).

At the end of the procedure, anaesthetic infusions were discontinued. Extubation was performed after the return of protective airway reflexes and the achievement of adequate clinical recovery. Complete resolution of hiccups was observed immediately after extubation. During postoperative evaluation, the patient was specifically questioned about intraoperative awareness and recall. She did not report recall, pain, choking sensation, distressing intraoperative experience, or awareness during surgery.

Postoperative recovery was uneventful. The patient was managed on room air and did not require supplemental oxygen or admission to intensive care. No clinical signs of respiratory compromise were observed. Early postoperative

Table 1. Summary of Perioperative Management and Key Outcomes

Domain	Key details
Preoperative status	Six-month idiopathic intractable hiccups refractory to multimodal pharmacological treatment and bilateral selective phrenic nerve blocks; no organic cause identified after comprehensive evaluation.
Side selection	Dynamic fluoroscopic and ultrasonographic assessment showed pathological asymmetric paradoxical movement of the right hemidiaphragm.
Airway and positioning	Left lateral decubitus position with the right hemithorax up; 7.5-mm electromyography endotracheal tube and 7-Fr bronchial blocker placed in the right main bronchus under fiberoptic bronchoscopy.
One-lung ventilation	Duration 35 minutes; FiO_2 0.70 to 0.80, tidal volume 5-6 mL kg^{-1}, respiratory rate 18 min-1, PEEP 5 cmH_2O, SpO_2 95-100%; ABG at 25 minutes: pH 7.38, $PaCO_2$ 41 mmHg, PaO_2 92 mmHg.
Neuromonitoring and reversal	Sugammadex 2 mg kg-1 was administered 25 minutes after rocuronium to restore diaphragmatic motor responses; medial and anterolateral branches showed reduced amplitude and delayed conduction.
Surgical intervention	Neuromonitoring-guided selective bipolar ablation and clipping of the medial and anterolateral branches of the right phrenic nerve; pathological hiccup-like contractions disappeared after treatment.
Outcome	Surgery 115 minutes, anaesthesia 155 minutes; no supplemental oxygen or ICU admission; no intraoperative recall; no clinically relevant postoperative diaphragmatic dysfunction; no recurrence at two months.

ICU, intensive care unit; ABG, arterial blood gas

and pre-discharge chest radiographs did not show elevation of the right hemidiaphragm. Additional postoperative assessment included diaphragmatic ultrasonography, fluoroscopic sniff testing, pulmonary function testing, and clinical respiratory evaluation, none of which demonstrated clinically relevant diaphragmatic dysfunction. The patient was discharged on postoperative day seven. At the two-month follow-up, no recurrence of hiccups was reported.

Discussion

This case illustrates the anaesthetic challenges encountered during right-sided thoracoscopic selective phrenic nerve surgery guided by neuromonitoring for idiopathic intractable hiccups. The main difficulty was not a single component of the anaesthetic technique, but rather the need to integrate several competing requirements: right lung isolation for thoracoscopic exposure, preservation of a neuromonitoring-compatible airway, restoration of diaphragmatic motor responses for phrenic nerve branch mapping, maintenance of adequate anaesthetic depth during neuromuscular recovery, and prevention of perioperative respiratory compromise. Therefore, the educational value of this case lies in the careful adaptation of established anaesthetic techniques to a rare surgical indication rather than in the introduction of an entirely new anaesthetic method.

Intractable hiccups may severely impair sleep, nutrition, physical endurance, and quality of life.[1,2] In the present case, the diagnosis was considered idiopathic only after a comprehensive etiological evaluation failed to identify an organic cause. Neurological, thoracic, abdominal, gastrointestinal, metabolic, biochemical, and radiological assessments did not reveal a secondary etiology. The patient also failed to respond to multimodal pharmacological therapy and bilateral diagnostic and therapeutic selective phrenic nerve blocks. Dynamic fluoroscopic and ultrasonographic examinations demonstrated a pathological, asymmetric, paradoxical movement of the right hemidiaphragm, discordant with the left hemidiaphragm. These findings support the selection of the right side for thoracoscopic selective phrenic nerve surgery.

The surgical approach was based on a recently described thoracoscopic neuroprotective phrenotomy technique for idiopathic incurable chronic hiccups.[3] In this patient, intraoperative neuromonitoring was essential for identifying the pathological distal branches of the right phrenic nerve. After careful dissection around the pericardium, four distal branches of the right phrenic nerve were identified near the diaphragmatic entry point: posterior, medial, anterolateral, and lateral. Diaphragmatic electrical activity was recorded using conductive strip electrodes placed on the diaphragmatic muscle and along the intramuscular course of each distal branch. Motor evoked potentials were elicited by primary motor cortex stimulation, and branch-specific responses were compared. The medial and anterolateral branches demonstrated reduced amplitude and delayed conduction compared with the posterior and lateral branches. These findings, together with the abnormal right hemidiaphragmatic movement observed preoperatively, guided selective bipolar ablation and clipping of the medial and anterolateral branches. Repeat assessment after ablation and clipping showed the disappearance of the pathological hiccup-like diaphragmatic contractions.

Clarifying the neuromonitoring method is important because the role of the electromyographic endotracheal tube should not be misinterpreted. In this case, diaphragmatic electrical activity was recorded from conductive strip electrodes rather than from the endotracheal tube itself. The electromyographic endotracheal tube was used as part of a neuromonitoring-

compatible airway strategy, thereby avoiding the need for a conventional double-lumen tube, which would have been less suitable for the planned monitoring configuration. This distinction is clinically relevant because the monitoring endpoint was not limited to visual assessment of diaphragmatic movement; it involved branch-specific electrophysiological comparison and confirmation of the functional effect of ablation.

The airway strategy also required careful planning. A conventional double-lumen tube would have provided reliable lung isolation but would not have allowed the same neuromonitoring-compatible configuration. Therefore, an electromyographic endotracheal tube was combined with a bronchial blocker. Similar combinations of an EMG endotracheal tube and bronchial blocker have been described for thoracic procedures requiring recurrent laryngeal nerve monitoring.[4] In the present case, this established concept was adapted for right-sided thoracoscopic selective phrenic nerve surgery. The bronchial blocker was advanced into the right main bronchus under fiberoptic bronchoscopic guidance, enabling right lung isolation while maintaining the airway setup required for neuromonitoring.

The available oxygenation and ventilation data support the feasibility of this hybrid airway approach in this patient. One-lung ventilation lasted 35 minutes and was performed with FiO_2 of 0.70-0.80, tidal volume of 5-6 mL kg^{-1}, respiratory rate of 18 min^{-1}, and PEEP of 5 cmH_2O. Peripheral oxygen saturation remained between 95% and 100%. Arterial blood gas analysis obtained at the 25th minute of one-lung ventilation showed pH 7.38, $PaCO_2$ 41 mmHg, and PaO_2 92 mmHg. These findings indicate that adequate gas exchange was maintained during right lung isolation. However, additional respiratory mechanics data, such as peak airway pressure and plateau pressure, were not available for retrospective reporting.

Neuromuscular management was another critical aspect of this case. Rocuronium was required for induction, tracheal intubation, and initial airway manipulation. However, persistent neuromuscular blockade would have prevented reliable assessment of diaphragmatic motor responses during mapping of phrenic nerve branches. Previous physiological studies have shown that recovery from neuromuscular blockade may differ among the diaphragm, laryngeal muscles, and peripheral muscles.[5] In this case, sugammadex 2 mg kg^{-1} was administered 25 minutes after the induction dose of rocuronium and before selective ablation and clipping. The purpose of reversal was not the emergence from anaesthesia, but the restoration of sufficient diaphragmatic motor activity for intraoperative neuromonitoring. No additional neuromuscular blocking agent was administered after administration of sugammadex, because continued assessment of diaphragmatic responses was required until the selective procedure was completed.

Nevertheless, this aspect of management has an important limitation. Sugammadex dosing should ideally be guided by quantitative neuromuscular monitoring. Although neuromuscular monitoring equipment was available, no documented TOF or PTC value before sugammadex administration could be retrieved retrospectively. This limitation has been explicitly acknowledged because the absence of an objective, documented neuromuscular measurement reduces reproducibility and limits generalizability. Future cases using this strategy should include quantitative neuromuscular monitoring and report TOF or PTC values before and after reversal.

The reversal phase required particular vigilance, because restoration of neuromuscular transmission during ongoing surgery may increase the risk of patient movement and intraoperative awareness if hypnotic depth is insufficient. Le Guen et al.[6] reported that sugammadex administration during propofol and remifentanil anaesthesia may be associated with increases in BIS values suggestive of arousal. In the present case, BIS values transiently exceeded 60 after sugammadex administration and were accompanied by mild increases in heart rate and arterial blood pressure. No gross patient movement was observed apart from the expected diaphragmatic contractions required for neuromonitoring. The propofol infusion was increased by 2 mg kg^{-1} h^{-1}, after which BIS values were maintained within the target range of 40-60. During postoperative evaluation, the patient was specifically questioned about intraoperative awareness and recall, and did not report pain, choking sensation, distressing intraoperative experiences, or any awareness or recall of events during surgery. However, a formal, structured awareness questionnaire was not used, which is a limitation.

The postoperative findings support the absence of clinically relevant diaphragmatic dysfunction after the selective procedure, although they should not be overinterpreted. The patient remained on room air and did not require supplemental oxygen or intensive care admission. No clinical signs of respiratory compromise were observed. Early postoperative and pre-discharge chest radiographs showed no elevation of the right hemidiaphragm. Additional postoperative evaluation, including diaphragmatic ultrasonography, fluoroscopic sniff testing, pulmonary function testing, and clinical respiratory assessment, did not demonstrate clinically relevant diaphragmatic dysfunction. This postoperative course contrasts with the potential risk of diaphragmatic paralysis after more proximal interruption of the phrenic nerve. A previous case report described phrenic nerve clipping for intractable hiccups after stroke,[7] but the present case differs by emphasizing branch-specific

neuromonitoring, selective distal treatment, and the anaesthetic strategy required to support this approach.

This report has several limitations. First, it represents a single case and cannot establish the safety or efficacy of this strategy. Second, no documented TOF or PTC values were available before sugammadex administration. Third, although the patient was specifically questioned postoperatively and denied awareness or recall, a formal structured awareness questionnaire was not used. Fourth, although postoperative clinical, radiographic, ultrasonographic, fluoroscopic, and pulmonary function assessments did not demonstrate clinically relevant diaphragmatic dysfunction, the detailed quantitative diaphragmatic excursion and pulmonary function values were not presented. Finally, some respiratory mechanics data during one-lung ventilation, including peak and plateau airway pressures, were not available. Despite these limitations, this case provides a practical example of how established anaesthetic techniques may be integrated for a rare procedure requiring simultaneous lung isolation, anaesthetic depth control, neuromuscular recovery, and phrenic nerve neuromonitoring.

Conclusion

Right-sided thoracoscopic selective phrenic nerve surgery for intractable hiccups requires careful coordination of lung isolation, anaesthetic depth, neuromuscular management, and intraoperative neuromonitoring. In this case, a hybrid airway strategy using an EMG endotracheal tube and a bronchial blocker, combined with total intravenous anaesthesia, BIS monitoring, and procedural sugammadex-mediated recovery of diaphragmatic motor responses, enabled neuromonitoring-guided selective ablation and clipping of pathological distal phrenic nerve branches. The patient had immediate resolution of hiccups and no clinically relevant postoperative diaphragmatic dysfunction. This single case suggests that established anaesthetic techniques can be adapted for selected patients undergoing this rare procedure; however, future reports should include quantitative neuromuscular monitoring, structured awareness assessment, and detailed postoperative diaphragmatic function measurements.

Ethics

Informed Consent: Written informed consent was obtained from the patient for publication of this case report and accompanying images. The patient was informed that personal identifying information would not be disclosed.

Footnotes

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Case Report
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One-lung Ventilation for Neonatal Pneumonectomy in a Hydropic Premature Infant: Fiberoptic-guided Left Mainstem Intubation

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Abstract

Congenital cystic adenomatoid malformation (CCAM) is a rare lung anomaly that can cause severe respiratory distress and hydrops fetalis. One-lung ventilation (OLV) in neonates poses extreme anatomical challenges due to the lack of appropriately sized double-lumen tubes or bronchial blockers. A male neonate (2500 g, 30 weeks' gestation) presented with hydrops fetalis and a massive right-sided thoracic CCAM. Due to progressive respiratory failure and hemodynamic instability, an emergency right pneumonectomy was scheduled on postnatal day 3. To achieve OLV, a 3.5-mm cuffed endotracheal tube (with the cuff left deflated) was advanced into the left main bronchus under fiberoptic bronchoscopy (FOB) guidance. Removal of the tube adaptor facilitated rapid, pragmatic placement while minimizing interruptions to ventilation during apneic oxygenation. Pressure-controlled lung-protective ventilation was maintained. Transient desaturation episodes during mediastinal manipulation were successfully managed. The 3-hour procedure was completed without intraoperative complications. In premature neonates in whom commercial lung-isolation devices are impractical, FOB-guided selective mainstem bronchial intubation is a rapid, feasible, and effective strategy for OLV. Individualized airway planning and FOB guidance are instrumental in ensuring accurate placement and maintaining oxygenation.

Keywords: One-lung ventilation, hydrops fetalis, neonatal anaesthesia, fiberoptic bronchoscopy, left mainstem intubation

Main Points

- In low-birth-weight premature neonates in whom commercial bronchial blockers or double-lumen tubes cannot be deployed, selective mainstem bronchial intubation is a highly effective and definitive rescue strategy for lung isolation.
- Modifying the selective intubation technique by removing the endotracheal tube adapter allows rapid fiberoptic bronchoscopy-guided placement, thereby reducing ventilation interruptions during apneic oxygenation.
- A tailored lung-protective ventilation strategy using low peak inspiratory pressures makes major thoracic procedures—such as a right pneumonectomy for massive congenital cystic adenomatoid malformation complicated by hydrops fetalis—hemodynamically feasible and safe even in fragile neonates.

Introduction

Congenital cystic adenomatoid malformation (CCAM) is a rare developmental anomaly of the lung characterized by the overgrowth of terminal bronchioles. CCAM is characterized by cystic structures that can lead to severe respiratory distress, mediastinal shift, and cardiovascular collapse in the neonatal period. In severe cases, these masses increase intrathoracic pressure, thereby impeding venous return and triggering the development of hydrops fetalis starting from the fetal period.[1,2]

Indications for one-lung ventilation (OLV) in neonatal surgery include the resection of lesions such as CCAM, congenital lobar emphysema, and bronchopulmonary sequestration, or the management of intractable pulmonary hemorrhage.[1]

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However, the application of OLV in neonates poses profound anatomical and physiological challenges. These primarily include the rapid onset of hypoxia within seconds—driven by a low functional residual capacity—and an elevated risk of mucosal edema due to a narrow airway caliber, compounded by the fact that adult double-lumen tubes (DLT) are disproportionately large for the neonatal trachea.[1,3] Since DLT cannot be utilized in the pediatric and infant age groups, fiberoptic bronchoscopy (FOB)-guided selective bronchial intubation or bronchial blocker (BB) applications are employed to achieve lung isolation in neonates.[3,4]

The aim of this case report is to share our successful management of a neonatal patient undergoing pneumonectomy for CCAM-induced hydrops fetalis, in which OLV was effectively provided via FOB-guided left mainstem bronchial intubation.

Case Presentation

A male neonate weighing 2500 g was delivered by emergency cesarean section at 30 weeks of gestation because of hydrops fetalis and a massive right-sided thoracic lesion diagnosed antenatally. Apgar scores were 4 and 7 at 1 and 5 minutes, respectively. The infant was intubated immediately after birth with a 2.5-mm uncuffed endotracheal tube and transferred to the neonatal intensive care unit. Initial arterial blood gas (ABG) analysis revealed severe respiratory acidosis (pH 6.96, $PaCO_2$:108 mmHg, PaO_2:56 mmHg). On postnatal day 3, progressive respiratory failure and hemodynamic instability prompted emergency surgical intervention.

Preoperative examination demonstrated generalized edema and ascites consistent with hydrops fetalis. Oxygen saturation was 89%, and heart rate was 105 beats/min. ABG analysis showed pH 7.20, $PaCO_2$:61 mmHg, and PaO_2:36 mmHg despite mechanical ventilation.

Written informed consent was obtained from the patient's legal guardians prior to the procedure. Standard monitoring was applied in the operating room, and vascular access was obtained through an umbilical venous catheter. Induction and maintenance of anaesthesia were achieved with sevoflurane. Because commercially available DLT and BB are unsuitable for neonatal airways, a selective left mainstem intubation was planned.

To accommodate the FOB, the initial 2.5-mm uncuffed endotracheal tube was exchanged for a 3.5-mm cuffed endotracheal tube, the smallest tube diameter that allows internal passage of the pediatric bronchoscope. The cuffed tube was selected to achieve complete lung isolation based on its structural fit, with the cuff intentionally left deflated throughout the procedure to prevent mucosal injury. The 3.5-mm tube was advanced into the left main bronchus under fiberoptic guidance. By removing the tube adaptor, the procedure offered a pragmatic, time-efficient alternative, thereby minimizing ventilation interruptions during apneic oxygenation. To minimize the risk of airway injury, the cuff remained completely deflated throughout the procedure, bronchoscopic guidance was used to avoid repeated airway manipulations, and the tube position was carefully confirmed after patient positioning. No clinical evidence of airway injury was observed (Figure 1).

Pressure-controlled ventilation was maintained throughout the procedure using a lung-protective strategy. Ventilation parameters were adjusted to keep peak inspiratory pressures below 20 cm H_2O with a positive end-expiratory pressure of 5 cm H_2O and a respiratory rate of 35-40 breaths/min. A strategy of mild permissive hypercapnia was adopted, targeting an arterial $PaCO_2$ below approximately 60 mmHg while maintaining an arterial pH above 7.25. The inspired oxygen fraction (FiO_2) was adjusted according to continuous pulse oximetry and ABG analysis to maintain adequate oxygenation throughout OLV. During right pneumonectomy, transient desaturation episodes related to mediastinal manipulation were successfully managed by increasing inspired oxygen concentration and temporarily interrupting surgical traction. The procedure lasted approximately three hours and was completed without intraoperative complications; the non-functioning cystic lung tissue was successfully removed by pneumonectomy (Figure 2). The patient was transferred to the neonatal intensive care unit while intubated.

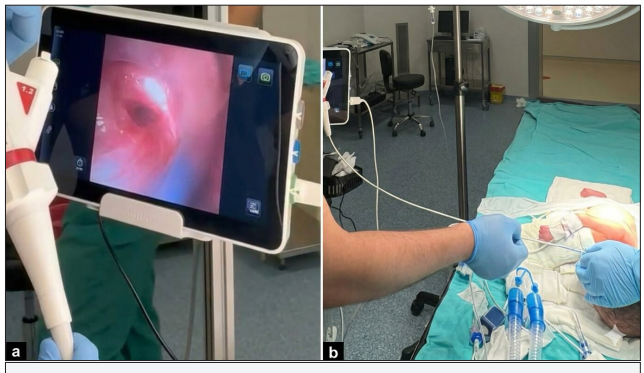


Figure 1. Fiberoptic-guided selective left mainstem bronchus intubation. a) Intraoperative bronchoscopic view confirming the correct positioning and patency within the left main bronchus. b) Clinical procedure in the operating room demonstrating the controlled advancement of the ultra-thin fiberoptic scope through the small-caliber endotracheal tube (with the tube adaptor removed) to achieve lung isolation.

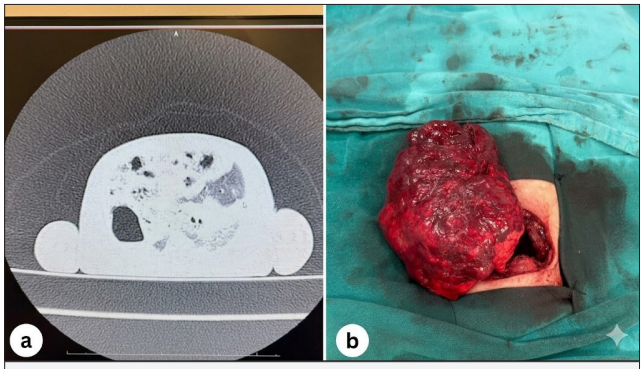


Figure 2. Preoperative imaging and macroscopic view of the resected specimen. a) Axial chest computed tomography scan demonstrating a massive right-sided congenital cystic adenomatoid malformation causing significant mediastinal shift, b) postoperative macroscopic view of the completely excised cystic right lung specimen following the formal pneumonectomy procedure.

Discussion

Neonatal OLV can theoretically be achieved using either BB or selective mainstem bronchial intubation. Although BB are widely utilized in thoracic surgeries in older pediatric patients, their application in extremely low birth weight neonates is severely constrained by technical difficulties with placement, unstable positioning, and the inherent risk of partial or complete airway obstruction. Furthermore, the small internal diameter of neonatal endotracheal tubes significantly restricts device manipulation, which increases procedural complexity and escalates the likelihood of ventilation interruption.[1,3,4]

Although upsizing the endotracheal tube in a premature neonate may increase the risk of airway complications, including mucosal ischemia, vocal cord injury, post-extubation edema, and subglottic stenosis, accurate fiberoptic-guided placement was considered essential to achieve reliable lung isolation during emergency pneumonectomy.[1,5] In the absence of appropriately sized BBs or DLT, selective mainstem intubation was the only technically feasible option for this patient's airway.

Selective mainstem intubation using a single-lumen endotracheal tube is not without limitations, as excessive advancement may obstruct the upper lobe bronchus or result in inadequate lung isolation. However, fiberoptic bronchoscopic guidance allows precise tube placement beyond the carina while preserving upper lobe ventilation and facilitates immediate confirmation and repositioning after patient positioning or surgical manipulation.[3] Consequently, this technique may represent a reliable strategy for lung isolation in extremely premature neonates, in whom BB placement is technically challenging. Therefore, the choice of lung-isolation technique should be individualized according to patient size, airway anatomy, available equipment, and surgical requirements.[1,2,4]

Conclusion

This case suggests that selective left mainstem bronchial intubation may provide an effective means of achieving lung isolation in selected premature neonates undergoing thoracic surgery when BBs or other dedicated lung-isolation devices are impractical. FOB guidance facilitated accurate tube placement while allowing continued ventilation or apneic oxygenation during airway manipulation. These factors may have contributed to a shorter, more efficient lung-isolation procedure. Careful patient selection and individualized airway planning remain essential for the successful management of complex neonatal thoracic cases.

Ethics

Informed Consent: Written informed consent was obtained from the patient's legal guardians prior to the procedure.

Footnotes

Authorship Contributions: Surgical and Medical Practices - Z.B., B.G.E., N.Y.; Concept - Z.B., B.G.E.; Design - B.G.E., N.Y.; Data Collection and/or Processing - Z.B., B.G.E.; Literature Search - Z.B., B.G.E., N.Y.; Writing - Z.B., B.G.E., N.Y.

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Letter to the Editor

Perioperative Care

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Additional Insights Into the Analgesia Management of a High-risk Postoperative Setting

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Keywords

Cardiovascular and thoracic anaesthesia, intensive care, pain, perioperative care, pharmacology, regional anaesthesia

To the Editor,

Akın et al.[1] are sincerely commended on formulating an effective analgesia management plan centered around the use of interfascial plane blocks in their high-risk patient who had undergone concomitant liver transplant and coronary artery bypass grafting (CABG) surgery in a single surgical setting. Meanwhile, the combination of pecto-intercostal fascial plane block (PIFB) and modified thoracoabdominal nerve block via perichondrial approach aided the postoperative stabilization and successful extubation of the index patient; however, other important factors warrant elaboration.[1]

To begin with, Akın et al.[1] employed a total of 80 mL of 0.125% bupivacaine for administering the interfascial blocks where no rescue analgesia was interestingly required amidst satisfactory pain scores for the entire duration of 24 h, despite the absence of an added adjuvant to the local anaesthetic (LA) mixture. While duly acknowledging the authors' caution not to exceed the maximum safe dose for the corresponding LA, we note that the choice of LA agent deserves attention.[1,2] Notably, the literature suggests that ropivacaine is less cardiotoxic than bupivacaine, even at equipotent doses.[2] The former becomes more important in the context of a CABG patient when pre-operative and post-operative left ventricular ejection fraction data are missing.[1] The predisposition to postoperative rhythm disturbances should not be overlooked, particularly in high-risk postoperative settings.[1,2] Secondly, a Delphi consensus led by "American Society of Regional Anesthesia and Pain Medicine" and the "European Society of Regional Anaesthesia and Pain Therapy" recommends employing anatomically descriptive nomenclature in regional analgesia.[3-5] It is recommended that PIFB be referred to as the superficial parasternal intercostal plane block for standardized academic and clinical communication.[3,4] Finally, given the pivotal role of multimodal analgesia in assisting enhanced recovery after surgery, the formal account of the quality of recovery scores alongside the 24 h pain scores would have added incremental objective value to the index case presentation.[1,5]

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Letter to the Editor
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Authors' Reply to "Additional Insights into the Analgesia Management of a High-risk Postoperative Setting"

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Analgesia management, high-risk patient, intensive care unit, interfascial plane blocks, M-TAPA block, pecto-intercostal fascial block

To the Editor,

We would like to thank the authors for their interest in, and constructive feedback on, our case report describing a combination of fascial plane blocks—the modified thoracoabdominal nerve block via the perichondrial approach and the pectointercostal fascial block—which we performed as part of multidisciplinary postoperative care in the intensive care unit (ICU) for a patient who underwent simultaneous liver transplant and coronary artery bypass grafting.[1] Detailed explanations and our responses to the authors' criticisms are provided below.

First, we address the authors' concerns and criticisms regarding the selection and dosage of local anaesthetic (LA). A total of 80 mL of 0.125% bupivacaine was administered to our patient for the combined block, without adjuvants. As is well known, bupivacaine is already a long-acting LA; it should come as no surprise that its effect lasts for 24 hours, and examples of this situation can be found in a careful review of the literature.[2-6] Since the effect of fascial plane blocks is volume-dependent, the duration of action extends as the administered volume increases.[7,8] When used at highly diluted concentrations, such as 0.125%, bupivacaine is known to provide effective analgesia without the absolute need for adjuvants. For instance, a recent randomized controlled study by Singh et al.[3] demonstrated that bilateral pecto-intercostal fascial plane blocks utilizing exclusively 0.125% bupivacaine eliminated the need for rescue analgesia and provided highly effective pain control in cardiac surgery patients. Furthermore, comparative studies by Ahmed et al.[9] and Akgul et al.[10] evaluating bupivacaine concentrations in fascial plane blocks for major orthopedic surgeries demonstrated that 0.125% bupivacaine effectively maintained low postoperative pain scores (< 4) across a 24- to 48-hour period. While higher concentrations (such as 0.25% and 0.5%) were associated with statistically superior pain scores in these studies, the clinical difference was marginal. Importantly, Akgul et al.[10] highlighted that higher concentrations resulted in a significantly higher incidence of motor block (e.g., 100% quadriceps weakness with 0.5% bupivacaine versus 8.7% with 0.125% bupivacaine), underscoring the clinical advantage of using a 0.125% concentration to achieve a balance between effective analgesia and minimizing motor or systemic side effects. Given that we administered a high volume (80 mL) of 0.125% bupivacaine, the outcome is consistent with the literature, which reports that this regimen provides effective, prolonged, and safe analgesia in our high-risk patient. Adjuvants are used to extend the duration of the analgesic effect of LA agents, such as bupivacaine, beyond 24 hours.

Furthermore, the total dose of bupivacaine administered at this concentration and volume (80 mL of 0.125% bupivacaine) was 100 mg in our case. For a 75-kg patient, this dose is approximately 1.33 mg kg^{-1}. According to standard pharmacological guidelines, the recommended maximum dose for bupivacaine is 2-2.5 mg kg^{-1} without epinephrine, and up to 3 mg kg^{-1} when

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combined with epinephrine.[11-13] For our 75-kg patient, the administered dose of approximately 1.33 mg kg^{-1} is well below these established toxic thresholds. We agree that ropivacaine has a safer cardiotoxic profile than bupivacaine, provided that toxic dose limits are not exceeded. We found examples in the literature showing that bupivacaine is frequently used as a LA agent in patients undergoing cardiac surgery.[3-6] In addition, the risk of LA systemic toxicity depends not only on total dose but also on patient-related factors and systemic absorption from the injection site. We emphasize that bupivacaine, when used at a very low concentration of 0.125%, is safe even in patients undergoing high-risk cardiac surgery and provides effective analgesia for 24 hours.

Second, we agree with the authors' emphasis on standardization and nomenclature of fascial plane blocks. The term "superficial parasternal intercostal plane block," as agreed upon in the American Society of Regional Anesthesia and Pain Medicine and European Society of Regional Anaesthesia and Pain Therapy Delphi consensus, is important for establishing a common language and facilitating academic communication regarding fascial plane blocks.[14] However, in daily practice, clinicians often use the terminology to which they are accustomed and reflect this usage in the literature. As De Cassai et al.[15] also noted in the journey toward standardizing the nomenclature of interfascial plane blocks, "there is still much to do." In their literature review, De Cassai et al.[15] noted that for pectoral blocks, the older terms "PECS I and II" are still in use rather than the newer terms ("interpectoral" and "pecto-serratus"). If we conduct a quick and careful literature review, we can see that the term "Pecto-intercostal fascial plane block (PIFPB)," which anatomically and clearly denotes the targeted fascial plane, remains more widely used in many studies.[3-6,16-18] Therefore, our choice of terminology is consistent with the current literature.

Finally, we agree with the comment that the Quality of Recovery (QoR) scoring system is valuable for evaluating postoperative analgesia from multiple perspectives. However, our case report describes a patient who underwent simultaneous liver transplantation and coronary artery bypass surgery, which lasted 12 hours, and was mechanically ventilated in the ICU during the postoperative period. In such a critically important and cognitively demanding scenario, these measures—ensuring the patient's hemodynamic stability, a decrease in the numeric rating scale score, and successful extubation one hour after block administration—rather than the numerous questions required for QoR scoring, are more practical and concrete indicators of recovery and analgesic success in clinical practice.

We believe that fascial plane blocks performed under ultrasound guidance in ICUs are reliable and effective rescue analgesic methods for such high-risk patients. We would like to thank the authors once again for their valuable scientific contributions.

Footnotes

Authorship Contributions: Surgical and Medical Practices - B.Ç., A.N.A., D.K., I.A.G., Ö.B., C.E.; Concept - B.Ç., A.N.A., D.K., I.A.G., Ö.B., C.E.; Design - B.Ç., A.N.A., D.K., I.A.G., Ö.B., C.E.; Data Collection or Processing - B.Ç., A.N.A., D.K., Ö.B., C.E.; Analysis or Interpretation - B.Ç., A.N.A., D.K., Ö.B., C.E.; Literature Search - B.Ç., A.N.A., I.A.G., Ö.B.; Writing - B.Ç., A.N.A.

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