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OPIOID-FREE AND OPIOID-SPARING ANESTHESIA IN MODERN PERIOPERATIVE CARE — BENEFITS, LIMITATIONS, AND CLINICAL APPLICATIONS

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ABSTRACT

Opioid-free anesthesia (OFA) and opioid-sparing anesthesia (OSA) have emerged from two converging developments in perioperative medicine: first, the need to reduce opioid-related adverse drug events such as postoperative nausea and vomiting (PONV), respiratory depression, ileus, sedation, and possibly persistent postoperative use; and second, the maturation of enhanced recovery pathways built around multimodal, function-oriented analgesia. In contemporary evidence, however, strict elimination of intraoperative opioids has not shown universal superiority over well-conducted opioid-based anesthesia (OBA) for postoperative pain control or 24-hour opioid consumption. The most reproducible benefit of OFA is lower PONV in selected settings, whereas the most important safety signal is regimen-dependent bradycardia and hemodynamic instability, especially in dexmedetomidine-heavy protocols. By contrast, broader OSA strategies, particularly when built on acetaminophen, NSAIDs, regional anesthesia, judicious total intravenous anesthesia (TIVA), and selected adjuvants such as ketamine or lidocaine, are aligned with ERAS and other major perioperative guidance and have the strongest overall clinical support.

This narrative review examines definitions, mechanisms, pharmacology, protocols, clinical outcomes, limitations, and practical applications of OFA and OSA in modern perioperative care.

Conclusion: contemporary perioperative practice is better supported by individualized opioid stewardship and multimodal opioid-sparing care than by a dogmatic “zero-opioid” rule. OFA remains a reasonable option in selected phenotypes and procedures, but current evidence does not justify its routine use as a default replacement for all opioid-inclusive techniques.

KEYWORDS

Opioid-Free Anesthesia, Opioid-Sparing Anesthesia, Multimodal Analgesia, Dexmedetomidine, Ketamine, Lidocaine, Regional Anesthesia, ERAS

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1. Introduction

For decades, perioperative opioids have been a cornerstone of anesthetic and analgesic practice because of their reliable antinociceptive effects (Ferry et al., 2026). Their limitations are equally well established. Society and guideline documents now emphasize that opioid-centered care may worsen PONV risk, bowel dysfunction, sedation, respiratory compromise, discharge prescribing burden, and long-term opioid-related harm, while also distracting teams from recovery-oriented goals such as effective coughing, mobilization, sleep, oral intake, and discharge readiness (Gan et al., 2020; Hyland et al., 2021).

In recent years, perioperative medicine has shifted from a purely pain-intensity-based model toward a broader recovery-oriented approach. Contemporary enhanced recovery after surgery protocols emphasize that effective analgesia should support early mobilization, deep breathing and coughing, adequate sleep, oral intake, gastrointestinal recovery, patient participation in rehabilitation, and timely discharge (Cheung et al., 2022; Hyland et al., 2021). From this perspective, the goal of postoperative pain management is not only to reduce numerical pain scores, but also to improve functional outcomes and minimize treatment-related harm. Opioid-centered analgesia may conflict with these objectives when adverse effects limit ambulation, impair respiratory function, worsen nausea, delay bowel recovery, or increase postoperative fatigue (Hyland et al., 2021; Tan et al., 2015).

Another important concern is the relationship between perioperative opioid exposure and longer-term opioid-related harm. Surgical procedures are recognized as a potential point of new opioid exposure, and postoperative prescribing may contribute to persistent opioid use in some patients (Howard et al., 2023; Hyland et al., 2021). Although the risk varies depending on the type of surgery, patient characteristics, preoperative opioid status, psychological factors, and prescribing practices, this issue has increased interest in strategies that reduce unnecessary opioid administration. Importantly, opioid reduction does not imply undertreatment of pain. Rather, it requires the use of evidence-based multimodal analgesia that targets different mechanisms of

nociception, inflammation, central sensitization, and sympathetic activation (Chou et al., 2016; Hyland et al., 2021).

These concerns have led to growing interest in opioid-sparing and opioid-free anesthesia. Opioid-sparing anesthesia aims to reduce, but not necessarily eliminate, perioperative opioid exposure by combining non-opioid systemic analgesics, regional anesthesia techniques, local anesthetic infiltration, and non-pharmacological strategies (Ghai et al., 2022; Hyland et al., 2021). Opioid-free anesthesia, in contrast, seeks to avoid intraoperative opioids entirely, usually through the use of agents such as ketamine, dexmedetomidine, lidocaine, magnesium sulfate, non-steroidal anti-inflammatory drugs, acetaminophen, gabapentinoids in selected patients, and regional or neuraxial blocks (Ghai et al., 2022). Both approaches are based on the principle that surgical pain is multifactorial and should therefore be managed through multiple complementary pathways rather than by reliance on a single drug class (Ghai et al., 2022; Majerić Kogler et al., 2023).

2. Methodology

This study was conducted as a narrative review using a structured, thesis-oriented search strategy. Due to the absence of a precisely defined target population in the initial research question, the analysis was limited primarily to adult patients undergoing elective non-cardiac surgery. Studies involving pediatric, obstetric, cardiac, transplant, trauma, and exclusively intensive care unit (ICU) sedation populations were excluded, except where they provided relevant mechanistic insights, addressed key safety concerns, or represented widely cited, practice-defining evidence. Eligible study designs included randomized controlled trials, systematic reviews, meta-analyses, network meta-analyses, clinical guidelines, consensus statements, high-quality observational studies, and selected case series where higher-level evidence was unavailable. English-language publications were preferentially included, while editorials and narrative opinion papers were used only for contextual interpretation and were not considered primary sources of evidence. The literature search was conducted using PubMed/MEDLINE, Embase, and the Cochrane Library, supplemented by targeted searches of major anesthesiology journals and official publications from guideline-developing organizations. The primary time frame covered January 2016 to May 2026, with selective inclusion of earlier seminal studies and guidelines that remain central to current clinical practice, particularly in relation to perioperative ketamine, intravenous lidocaine, total intravenous anesthesia (TIVA), and foundational perioperative pain management strategies. In the final synthesis, priority was given to PubMed-indexed studies, Cochrane reviews, society guidelines, and accessible full-text articles and abstracts. When multiple sources addressed similar research questions, preference was given to higher levels of evidence, including formal clinical guidelines, Cochrane reviews, large meta-analyses, multicenter randomized controlled trials, and the most recent high-quality studies; this hierarchy also guided the interpretation of conflicting findings. The synthesis was conducted using a thematic rather than chronological approach, with evidence organized into five domains: definitions and perioperative philosophy, mechanisms and pharmacology, protocol architecture, patient-centered outcomes, and safety, limitations, and implementation. This structure reflects the multifaceted nature of opioid-free anesthesia (OFA) and opioid-sparing anesthesia (OSA) as composite perioperative strategies, whose effects depend on the specific pharmacologic substitutions employed, the integration of regional anesthesia techniques, approaches to rescue analgesia, and the selection of clinically relevant outcomes.

3. Results

The available evidence does not support a simplistic conclusion that opioid-free anesthesia (OFA) is universally superior to opioid-based anesthesia (OBA). A major 2023 meta-analysis including 38 randomized trials found no clinically relevant difference in postoperative pain scores or postoperative opioid consumption between OFA and OBA. The pooled mean difference in pain was approximately 0.39 points, and the pooled difference in opioid use was approximately 4.02 morphine milligram equivalents (MME), both of which were interpreted as clinically trivial. Nevertheless, the same analysis reported a reduction in postoperative nausea and vomiting (PONV) with OFA, counterbalanced by a higher incidence of bradycardia. Importantly, data on chronic postsurgical pain were almost absent, limiting any claim that OFA improves long-term pain outcomes (Feenstra et al., 2023).

This cautious interpretation is consistent with more recent evidence. A 2025 network meta-analysis concluded that currently studied OFA regimens do not reliably improve pain during the first 24 postoperative hours compared with OBA. The authors also emphasized substantial heterogeneity between protocols and a moderate-to-high risk of bias across many trials (Tripodi et al., 2025). Similarly, a 2025 meta-analysis focused

on recovery quality suggested possible improvements in selected early recovery domains, particularly physical comfort and pain, but did not demonstrate a robust and universally clinically important improvement in global recovery metrics (Liu et al., 2025).

Therefore, the most defensible interpretation is that OFA should not be viewed as a universal replacement for opioid-containing anesthesia. Rather, it should be understood as one possible strategy within a broader opioid-sparing framework, with potential value in carefully selected patients and surgical contexts (Feenstra et al., 2023; Tripodi et al., 2025). In contrast, opioid-sparing anesthesia (OSA) is supported by a stronger conceptual and clinical rationale because it aims to reduce unnecessary opioid exposure without requiring complete opioid elimination (Feenstra et al., 2023).

3.1 Pharmacological Components of Opioid-Free and Opioid-Sparing Anesthesia

3.1.1. Ketamine

Ketamine is one of the best-studied non-opioid adjuncts in perioperative analgesia (Brinck et al., 2018; Schwenk et al., 2018). Its principal analgesic rationale is antagonism of N-methyl-D-aspartate (NMDA) receptors, which are involved in central sensitization, opioid tolerance, and hyperalgesia. For this reason, ketamine is best conceptualized as an anti-hyperalgesic adjunct rather than as a complete replacement for opioids (Schwenk et al., 2018).

The 2018 Cochrane review concluded that perioperative intravenous ketamine probably reduces postoperative analgesic consumption and pain intensity, with additional reductions in nausea and vomiting (Brinck et al., 2018). The 2018 ASRA/AAPM/ASA consensus guideline supports subanesthetic bolus dosing up to 0.35 mg/kg and infusions up to 1 mg/kg/h for acute pain settings, especially when moderate-to-severe postoperative pain is expected or when opioid tolerance is present (Schwenk et al., 2018).

Long-term benefit is less certain. A 2024 systematic review found low-certainty evidence that perioperative ketamine does not clearly reduce chronic postsurgical pain overall, although a possible signal for reducing chronic neuropathic pain at three months remains unresolved (Abouarab et al., 2024). Clinically, ketamine may be most useful in high-pain surgery, opioid-tolerant patients, and settings where hyperalgesia is a major concern, while caution is needed in patients at risk of severe psychotomimetic reactions or uncontrolled cardiovascular disease (Schwenk et al., 2018).

3.1.2. Lidocaine

Intravenous lidocaine occupies a more ambiguous position in OFA and OSA protocols (Weibel et al., 2018). Its proposed effects include sodium-channel blockade, anti-inflammatory activity, attenuation of central sensitization, and improvement in postoperative gastrointestinal recovery. Nevertheless, its clinical value appears distinctly procedure-specific rather than universal (Chen et al., 2022; Weibel et al., 2018).

The 2018 Cochrane review concluded that uncertainty remained regarding the magnitude and consistency of benefit across adult surgical populations (Weibel et al., 2018). Later meta-analytic work suggested improvements in pain and selected recovery parameters in some procedures, particularly abdominal surgery, where earlier return of bowel function may be clinically relevant (Cooke et al., 2019). However, this should not be extrapolated automatically to all surgical fields (Weibel et al., 2018).

Safety is central to lidocaine use. A 2021 international consensus statement recommended that, if intravenous lidocaine is used, the initial dose should not exceed 1.5 mg/kg calculated using ideal body weight, and excessive or prolonged dosing should be avoided. The potential benefit must therefore be balanced against systemic toxicity risk, particularly when other local anesthetic techniques are used simultaneously (Foo et al., 2021).

3.1.3. Dexmedetomidine

Dexmedetomidine is arguably the most influential non-opioid anesthetic adjunct in the OFA literature (Yu et al., 2023). By acting at alpha-2 adrenergic receptors, it provides sedation, sympatholysis, and opioid-sparing effects with comparatively little direct respiratory depression (Weerink et al., 2017). Typical intraoperative regimens in recent studies include a bolus of 0.5-1 microgram/kg followed by infusions of approximately 0.2-0.7 microgram/kg/h (Sun et al., 2026).

Meta-analytic evidence indicates that dexmedetomidine can reduce postoperative opioid use and lower pain scores. More recent analyses suggest an approximately 30% reduction in 24-hour postoperative opioid requirement in mixed adult surgical populations. These findings make dexmedetomidine clinically attractive, particularly in patients in whom opioid-induced respiratory depression or PONV is a concern (Sun et al., 2026; Weerink et al., 2017).

However, its adverse-effect profile is clinically important. Older and newer evidence consistently associates dexmedetomidine with bradycardia and, in some contexts, hypotension. These effects are particularly relevant when loading doses are aggressive, when baseline vagal tone is high, or when the patient is elderly, hypovolemic, or hemodynamically fragile (Sun et al., 2026; Weerink et al., 2017). Thus, dexmedetomidine is best used as a titrated adjunct rather than as a default foundation for all OFA protocols (Sun et al., 2026).

3.1.4 Gabapentinoids

Gabapentinoids provide the clearest example of an intervention whose theoretical appeal exceeded its contemporary evidence. Their perioperative use was originally justified by modulation of calcium-channel-mediated neuronal excitability and the possibility of reducing central sensitization. However, more recent high-quality evidence has substantially weakened support for routine use (Park et al., 2022; Verret et al., 2020).

The meta-analysis by Verret and colleagues found no clinically significant analgesic benefit for routine perioperative gabapentin or pregabalin use, despite modest statistical effects in selected endpoints. Any reduction in PONV was offset by increased dizziness and visual disturbance, and no meaningful benefit was demonstrated for pain at 72 hours or for prevention of chronic postsurgical pain (Verret et al., 2020).

Safety concerns intensified after a large 2022 cohort study in older adults, in which perioperative gabapentin use was associated with increased delirium, new antipsychotic use, and pneumonia (Park et al., 2022). Consequently, gabapentinoids should not be used as routine default components of adult multimodal analgesia, particularly in older, frail, cognitively vulnerable, or renally impaired patients (Park et al., 2022; Verret et al., 2020).

3.1.5 NSAIDs and Acetaminophen

Non-steroidal anti-inflammatory drugs (NSAIDs) and acetaminophen are not usually presented as “headline” OFA agents, but they remain foundational components of most OSA pathways. Their value lies in reliable opioid-sparing effects, broad availability, and compatibility with enhanced recovery protocols when contraindications are absent (El-Boghdadly et al., 2024). Cochrane evidence supports preventive NSAID use for reducing postoperative pain and morphine consumption (Doleman et al., 2021). More recent reviews suggest that short-term perioperative NSAID use may be safer than some historical concerns implied, although risk remains procedure- and patient-specific (Halvey et al., 2023). Contemporary perioperative guidance continues to recommend multimodal foundational analgesia with paracetamol and NSAIDs when clinically appropriate (El-Boghdadly et al., 2024).

The major limitation is not lack of efficacy but patient selection. NSAIDs require caution or avoidance in renal impairment, high gastrointestinal bleeding risk, severe cardiovascular disease, selected anastomotic-risk procedures, and bone-fusion contexts (Halvey et al., 2023). Non-steroidal anti-inflammatory drugs (NSAIDs) and acetaminophen are not usually presented as “headline” OFA agents, but they remain foundational components of most OSA pathways (El-Boghdadly et al., 2024). Their value lies in reliable opioid-sparing effects, broad availability, and compatibility with enhanced recovery protocols when contraindications are absent (El-Boghdadly et al., 2024; McDaid et al., 2010).

Cochrane evidence supports preventive NSAID use for reducing postoperative pain and morphine consumption (Doleman et al., 2021). More recent reviews suggest that short-term perioperative NSAID use may be safer than some historical concerns implied, although risk remains procedure- and patient-specific (Halvey et al., 2023; Joshi et al., 2025). Contemporary perioperative guidance continues to recommend multimodal foundational analgesia with paracetamol and NSAIDs when clinically appropriate (El-Boghdadly et al., 2024).

The major limitation is not lack of efficacy but patient selection (Halvey et al., 2023). NSAIDs require caution or avoidance in renal impairment, high gastrointestinal bleeding risk, severe cardiovascular disease, selected anastomotic-risk procedures, and bone-fusion contexts. Acetaminophen is generally safer but must be dosed appropriately in patients with hepatic impairment or low body weight (El-Boghdadly et al., 2024; Halvey et al., 2023).

3.2. Regional Anesthesia as the Structural Core of Opioid-Sparing Care

Regional anesthesia represents one of the most clinically robust components of opioid-sparing perioperative care. Its value does not result from ideological opioid avoidance, but from direct interruption of nociceptive transmission from the operative field (Chitnis et al., 2020). By reducing afferent input at the level of peripheral nerves, plexuses, fascial planes, or the neuraxis, regional techniques can decrease intraoperative and postoperative systemic analgesic requirements, improve dynamic pain control, and facilitate recovery-oriented outcomes such as coughing, deep breathing, mobilization, and participation in early rehabilitation (Cheung et al., 2022; Chitnis et al., 2020).

The main regional techniques used in opioid-sparing pathways include neuraxial anesthesia and analgesia, peripheral nerve blocks, fascial plane blocks, wound infiltration, and continuous catheter-based local anesthetic techniques (Chitnis et al., 2020). Neuraxial approaches, particularly epidural analgesia, have historically played a major role in thoracic, abdominal, vascular, and major orthopedic surgery (Viderman et al., 2022). Peripheral nerve blocks are especially relevant in limb surgery, including shoulder, upper-limb, knee, hip, foot, and ankle procedures (Kamel et al., 2022). Fascial plane blocks, such as transversus abdominis plane block, erector spinae plane block, quadratus lumborum block, rectus sheath block, and pectoral nerve blocks, have expanded the applicability of regional analgesia in abdominal, thoracic, breast, and minimally invasive surgery (Hamilton et al., 2022; Viderman et al., 2022). Although these techniques differ in anatomical precision and analgesic density, their common goal is to reduce reliance on systemic opioids while preserving analgesic quality (Chitnis et al., 2020; Kamel et al., 2022).

Guidelines and perioperative reviews consistently identify regional anesthesia as a major opioid-sparing strategy, particularly when it is integrated into a broader multimodal analgesic protocol rather than used as an isolated intervention (Cheung et al., 2022; Schwenk & Mariano, 2018). A nerve block may reduce early opioid requirements, but its benefit is maximized when combined with scheduled acetaminophen, NSAIDs or COX-2 inhibitors when not contraindicated, local anesthetic infiltration, antiemetic prophylaxis, early mobilization, and procedure-specific rehabilitation (Cheung et al., 2022; El-Boghdadly et al., 2024).

Therefore, regional anesthesia should be understood as a structural element of enhanced recovery rather than as a stand-alone substitute for all analgesic planning (Cheung et al., 2022; Schwenk & Mariano, 2018).

Evidence supporting regional anesthesia is strongest for reduction of early postoperative opioid consumption and improvement of pain scores in procedure-specific settings (Chitnis et al., 2020; Kamel et al., 2022). In orthopedic surgery, peripheral nerve blocks can substantially reduce early opioid use after shoulder, knee, hip, and limb procedures, although the balance between analgesia and motor impairment must be considered (Kamel et al., 2022; Niyonkuru et al., 2024). For example, femoral nerve block and lumbar plexus techniques may provide strong analgesia after knee or hip surgery, but may also impair quadriceps strength and increase fall risk; this concern has encouraged increasing use of more motor-sparing approaches such as adductor canal block in selected knee procedures (Johnson et al., 2013; Koh et al., 2017). In thoracic and abdominal surgery, epidural analgesia and newer fascial plane blocks can reduce opioid exposure and improve dynamic pain control, although the relative superiority of one technique depends on the operation, local expertise, and institutional protocols (Hamilton et al., 2022; Viderman et al., 2022).

A particularly important argument for regional anesthesia concerns long-term outcomes. A 2024 meta-analysis suggested that perioperative regional anesthesia may reduce persistent opioid use after non-cardiac surgery, with a reported relative risk of 0.48, and may also reduce chronic postsurgical pain up to six months. This finding is highly relevant for opioid stewardship, because the long-term harm associated with perioperative opioids is not limited to immediate adverse effects such as nausea, sedation, or respiratory depression (Hyland et al., 2021; Pepper et al., 2024). Persistent opioid use after surgery may begin with legitimate acute pain treatment and then continue beyond the expected period of tissue healing. By reducing early opioid exposure and improving early pain control, regional anesthesia may help decrease the transition from acute postoperative opioid use to prolonged use in selected patients (Pepper et al., 2024).

However, the available evidence should be interpreted carefully. The effect of regional anesthesia is not uniform across surgical populations. A well-performed block for a procedure with a clearly defined neural target is more likely to reduce opioid consumption than a poorly matched or technically incomplete block. Similarly, the benefit may be greater in surgeries associated with intense early pain, such as major orthopedic, thoracic, breast, and abdominal wall procedures, than in operations where postoperative pain is mild or already well controlled with basic multimodal analgesia (Chitnis et al., 2020; Kamel et al., 2022). In addition, studies differ in block type, local anesthetic dose, use of catheters, background analgesic regimens, rescue opioid

protocols, and outcome definitions. These sources of heterogeneity make it difficult to translate pooled results into a single universal recommendation (Chitnis et al., 2020; Pepper et al., 2024).

The limitations of regional anesthesia must also be acknowledged. Block failure, incomplete dermatomal coverage, rebound pain after single-shot blocks, local anesthetic systemic toxicity, bleeding risk in anticoagulated patients, infection, nerve injury, delayed mobilization due to motor block, and dependence on operator expertise all limit indiscriminate use. In some contexts, regional anesthesia may also increase workflow complexity, require ultrasound equipment and trained staff, and prolong preoperative preparation time. Continuous catheter techniques can extend analgesic benefit but introduce additional issues such as catheter dislodgement, infection surveillance, pump management, and patient education (Chitnis et al., 2020; Jeng et al., 2010).

From a clinical perspective, the strongest conclusion is that regional anesthesia is not simply an optional addition to opioid-sparing care, but one of its most evidence-consistent foundations (Cheung et al., 2022; Chitnis et al., 2020). It should be prioritized when the surgical procedure has a clear regional target, when dynamic pain control is important, when opioid-related adverse effects would be particularly harmful, or when the patient has risk factors for persistent opioid use. Regional anesthesia is especially valuable in patients at increased risk of opioid-induced respiratory depression, postoperative nausea and vomiting, ileus, delirium, or prolonged hospitalization. Nevertheless, its use should remain individualized and procedure-specific, with attention to contraindications, expected duration of pain, motor effects, anticoagulation status, and local expertise (Cheung et al., 2022; Chitnis et al., 2020; Pepper et al., 2024).

4. Discussion

The central interpretive conclusion of this review is that opioid-sparing anesthesia, rather than universal opioid-free anesthesia, currently represents the more evidence-based direction of modern perioperative care (Feenstra et al., 2023; Tripodi et al., 2025). Contemporary perioperative practice has clearly moved away from opioid-heavy monotherapy toward multimodal, recovery-oriented analgesia; however, the available evidence does not support the routine elimination of all intraoperative opioids as a universally superior strategy (Chou et al., 2016; Feenstra et al., 2023; Hyland et al., 2021). Major society guidelines and consensus statements increasingly emphasize multimodal analgesia, regional anesthesia, procedure-specific pain management, functional recovery, prevention of opioid-related adverse effects, and responsible discharge prescribing (Chitnis et al., 2020; El-Boghdadly et al., 2024; Gan et al., 2020). This framework is fully compatible with selective and individualized opioid use. Therefore, the current paradigm should not be interpreted as a shift from opioids to complete opioid avoidance, but rather as a transition from opioid-dominant analgesia to mechanism-based, opioid-minimizing perioperative care (Chou et al., 2016; Feenstra et al., 2023; Ghai et al., 2022).

Ketamine may reduce central sensitization and opioid-induced hyperalgesia through N-methyl-D-aspartate receptor antagonism (Schwenk et al., 2018). Dexmedetomidine provides sympatholysis, sedation, and opioid-sparing effects through α_2 -adrenergic mechanisms (Weerink et al., 2017). Intravenous lidocaine may attenuate inflammatory responses and central sensitization in selected surgical populations (Cooke et al., 2019; Weibel et al., 2018). Propofol-based total intravenous anesthesia reduces exposure to volatile anesthetics and is associated with a lower risk of postoperative nausea and vomiting (Yang et al., 2020). Regional anesthesia directly blocks afferent nociceptive transmission from the surgical site, while acetaminophen and NSAIDs provide reproducible opioid-sparing effects in many perioperative pathways (Chitnis et al., 2020; Doleman et al., 2021; El-Boghdadly et al., 2024). When these interventions are combined within an opioid-free protocol, the entire package may outperform opioid-inclusive comparators, particularly if the control group relies heavily on opioids or lacks robust multimodal analgesia. However, when the comparator arm already includes optimized opioid-sparing care, the incremental clinical benefit of eliminating the final intraoperative dose of fentanyl or remifentanyl appears substantially smaller (Feenstra et al., 2023; Tripodi et al., 2025).

Accordingly, the main clinical question is not whether opioids should be categorically avoided, but whether their use can be reduced without compromising analgesic quality, recovery, or patient safety (Feenstra et al., 2023; Ghai et al., 2022). The strongest rationale for opioid-sparing strategies relates to reduction of opioid-associated adverse effects, including postoperative nausea and vomiting, sedation, ileus, pruritus, urinary retention, respiratory depression, and delayed mobilization (Gan et al., 2020; Hyland et al., 2021). In this context, opioid reduction may contribute to enhanced recovery goals such as earlier oral intake, improved respiratory mechanics, more effective coughing, earlier ambulation, and discharge readiness (Cheung et al.,

2022; Hyland et al., 2021). Nevertheless, complete opioid avoidance should not become a goal in itself if it leads to inadequate analgesia, excessive reliance on sedating adjuncts, hemodynamic instability, or delayed recovery (Feenstra et al., 2023; Tripodi et al., 2025). A clinically rational approach should prioritize patient-centered outcomes rather than the formal label of “opioid-free” anesthesia (Chou et al., 2016; Ghai et al., 2022).

The interpretation of the literature is complicated by several methodological limitations. Definitions of opioid-free and opioid-sparing anesthesia vary considerably between studies, and there is no universally accepted threshold that distinguishes one approach from the other (Feenstra et al., 2023; Tripodi et al., 2025). Some studies define opioid-free anesthesia as complete avoidance of intraoperative opioids but allow postoperative rescue opioids, whereas others assess the total perioperative opioid burden. Rescue opioid protocols are also inconsistent, which makes comparison of postoperative opioid consumption difficult (Feenstra et al., 2023). Moreover, many trials compare complex anesthetic packages rather than isolated interventions. As a result, it is often unclear whether observed benefits are caused by opioid avoidance itself, regional anesthesia, dexmedetomidine, ketamine, propofol-based maintenance, antiemetic optimization, or differences in postoperative care pathways (Feenstra et al., 2023; Liu et al., 2025; Tripodi et al., 2025).

Heterogeneity is another major limitation. The included studies differ in surgical population, baseline pain burden, anesthetic technique, type and dose of non-opioid adjuncts, use of regional anesthesia, antiemetic prophylaxis, postoperative analgesic protocols, and outcome definitions (Feenstra et al., 2023; Tripodi et al., 2025). Many positive randomized trials are single-center and procedure-specific, while meta-analyses often pool pharmacologically heterogeneous opioid-free regimens across different types of surgery. This creates a paradox in the evidence base: individual trials may suggest benefit in selected clinical contexts, while pooled analyses may show little or no clinically meaningful advantage because the interventions and populations are too diverse (Feenstra et al., 2023; Liu et al., 2025; Tripodi et al., 2025). Therefore, broad conclusions about the superiority or inferiority of opioid-free anesthesia should be made cautiously (Feenstra et al., 2023; Tripodi et al., 2025).

Another important weakness is the dominance of short-term outcomes. Many studies focus on pain scores in the post-anesthesia care unit, 24-hour opioid consumption, early postoperative nausea and vomiting, or immediate recovery scores (Feenstra et al., 2023; Liu et al., 2025). Although these outcomes are relevant, they do not fully capture the aims of modern perioperative medicine. More clinically meaningful endpoints include functional recovery, quality of sleep, mobilization, respiratory events detected with adequate monitoring, return of bowel function, discharge readiness, unplanned admission after ambulatory surgery, persistent opioid use, chronic postsurgical pain, delirium in vulnerable patients, and patient-reported recovery (Cheung et al., 2022; Hyland et al., 2021). These longer-term and function-based outcomes remain underreported in the opioid-free anesthesia literature (Feenstra et al., 2023; Tripodi et al., 2025).

For current clinical practice, several pragmatic conclusions can be drawn. The foundational implication is that baseline multimodal analgesia should be considered routine unless contraindicated (Chou et al., 2016; El-Boghdady et al., 2024). Scheduled acetaminophen, NSAIDs or COX-2 inhibitors, and procedure-appropriate regional anesthesia should generally be implemented before considering stricter opioid-free protocols (Chitnis et al., 2020; Doleman et al., 2021; El-Boghdady et al., 2024). These interventions have a stronger and more consistent evidence base than many newer or more “fashionable” non-opioid adjuvants (Cheung et al., 2022; Verret et al., 2020).

Another clinically relevant implication is that opioid-free anesthesia appears most defensible in selected scenarios, particularly in patients at high risk of postoperative nausea and vomiting, patients with opioid intolerance, patients in whom opioid-related respiratory depression is a major concern, and procedures where regional anesthesia and multimodal pathways are well established (Chitnis et al., 2020; Feenstra et al., 2023; Ghai et al., 2022). Potentially suitable contexts include selected laparoscopic, thoracic, bariatric, breast, and ambulatory procedures, although the choice should remain procedure- and patient-specific (Kamel et al., 2022; Tripodi et al., 2025; Viderman et al., 2022).

The safety profile of non-opioid adjuncts also requires careful consideration. Dexmedetomidine may reduce opioid requirements and improve selected recovery outcomes, but it is consistently associated with bradycardia and may cause hypotension, particularly in patients with conduction abnormalities, baseline bradycardia, hypovolemia, or limited cardiovascular reserve (Sun et al., 2026; Weerink et al., 2017). Ketamine may be useful in opioid-tolerant patients or in procedures associated with severe postoperative pain, but psychotomimetic effects and patient selection require attention (Brinck et al., 2018; Schwenk et al., 2018). Intravenous lidocaine may be valuable in selected abdominal surgery, but dosing must remain within safety limits because of the risk of systemic toxicity (Foo et al., 2021; Weibel et al., 2018). Gabapentinoids represent

a particularly important cautionary example: although theoretically attractive, contemporary evidence does not support their routine perioperative use, especially in older adults, frail patients, patients at risk of delirium, and those with renal impairment (Park et al., 2022; Verret et al., 2020).

Finally, rescue opioids should remain available as part of a patient-centered analgesic strategy. Poorly controlled acute pain may impair breathing, coughing, mobilization, sleep, and rehabilitation, and may contribute to central sensitization (Chou et al., 2016; Hyland et al., 2021). A rational opioid-sparing strategy should therefore reduce unnecessary opioid exposure while preserving opioids as rescue therapy when non-opioid measures are insufficient (Ghai et al., 2022; Hyland et al., 2021). In this sense, selective opioid use is not a failure of multimodal analgesia, but an appropriate component of individualized perioperative care (Chou et al., 2016; Feenstra et al., 2023).

Overall, the most defensible interpretation of the current evidence is that opioid-free anesthesia may be useful in selected clinical contexts, but opioid-sparing anesthesia provides a broader and more clinically balanced framework (Feenstra et al., 2023; Tripodi et al., 2025). Modern perioperative care should aim to minimize avoidable opioid exposure, prevent opioid-related adverse effects, and support functional recovery, while maintaining adequate analgesia and individualized rescue options (Cheung et al., 2022; Gan et al., 2020; Hyland et al., 2021). The future of perioperative analgesia is therefore unlikely to be defined by the complete abandonment of opioids, but by their more selective, rational, and patient-centered use within high-quality multimodal care (Chou et al., 2016; Ghai et al., 2022; Hyland et al., 2021).

5. Conclusions

Modern perioperative anesthesia is moving decisively toward opioid stewardship, multimodal analgesia, and individualized recovery-centered care. That transition is strongly evidence-based. What remains unproven is the claim that strict OFA should routinely replace all opioid-inclusive anesthesia in adult elective non-cardiac surgery. Current data show that OFA can reduce PONV and may improve selected recovery domains in some procedures, but average benefits for postoperative pain and 24-hour opioid use are small or clinically trivial, while safety risks such as dexmedetomidine-related bradycardia remain real. The most defensible contemporary position is therefore neither “opioids for everyone” nor “opioids never,” but rather patient-specific OSA built on regional anesthesia, foundational non-opioid analgesics, careful TIVA where appropriate, selective use of ketamine or lidocaine, and restrained, rescue-oriented opioid prescribing when needed.

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