

Review Article

Opioid-Free Anesthesia (OFA): Evidence, Controversies, and Limits in Perioperative Practice

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	International Archives of Integrated Medicine, Vol. 13, Issue 5, May, 2026. Available online at http://iaimjournal.com/ ISSN: 2394-0026 (P) ISSN: 2394-0034 (O)
	Received on: 8-4-2026 Accepted on: 30-5-2026 Source of support: Nil Conflict of interest: None declared. Article is under Creative Common Attribution 4.0 International DOI: 10.5281/zenodo.20545250
How to cite this article: Miguel Caled Trejos Román, María José Solís Marín, Yakira Delgado Angulo, Yoysi Leilani Duarte Molina, Isis Karolina Vega Vega, Stephanie Paola Serrano Jiménez. Opioid-Free Anesthesia (OFA): Evidence, Controversies, and Limits in Perioperative Practice. <i>Int. Arch. Integr. Med.</i> , 2026; 13(5): 232-244.	

Abstract

Opioid-free anesthesia has emerged as an alternative perioperative strategy designed to avoid intraoperative opioid administration through the use of non-opioid agents and regional techniques. Its growing adoption has been driven by concern over opioid-related adverse effects, including postoperative nausea and vomiting, respiratory depression, delayed recovery, and the broader clinical implications of excessive opioid exposure. Pharmacologic regimens in opioid-free anesthesia commonly include dexmedetomidine, ketamine, lidocaine, magnesium, acetaminophen, nonsteroidal anti-inflammatory drugs, and local anesthetics, often integrated into multimodal analgesic protocols. Current evidence from randomized controlled trials, systematic reviews, and meta-analyses suggests that opioid-free anesthesia can significantly reduce postoperative nausea and vomiting and decrease the need for rescue opioid administration. In some surgical settings, particularly laparoscopic,

minimally invasive, ambulatory, and gastrointestinal procedures, it has also been associated with improved early recovery outcomes. However, its superiority over opioid-sparing or conventional opioid-based anesthesia has not been consistently demonstrated, especially with regard to pain control, quality of recovery, and hospital length of stay. Interpretation of the evidence is limited by substantial heterogeneity in study design, patient populations, surgical procedures, and protocol composition. In addition, opioid-free anesthesia is not without risk, as non-opioid agents may cause adverse effects such as bradycardia, hypotension, neurotoxicity, or insufficient analgesia in highly painful procedures. For these reasons, opioid-free anesthesia should not be viewed as a universal strategy, but rather as a selective and individualized approach. Its appropriate use depends on careful patient selection, surgical context, expected postoperative pain, and the availability of clinical expertise and monitoring resources to ensure both efficacy and safety.

Key words

Opioid-free anesthesia, multimodal analgesia, perioperative care, postoperative nausea and vomiting, opioid-sparing anesthesia, enhanced recovery after surgery.

Introduction

Opioid-free anesthesia is defined as an anesthetic technique that avoids the use of opioids during surgery and instead employs non-opioid medications and techniques to manage pain and the physiological responses to surgical stimuli [1, 2]. Among the most commonly used non-opioid agents in opioid-free anesthesia are dexmedetomidine, esketamine, and regional anesthesia techniques such as transversus abdominis plane blocks [3, 4].

Interest in opioid-free anesthesia has grown in response to the opioid crisis and to the well-recognized adverse effects associated with opioid use, including postoperative nausea and vomiting, respiratory depression, and delayed recovery [2, 5]. In this context, studies have shown that opioid-free anesthesia can reduce postoperative nausea and vomiting while improving the quality of postoperative recovery, which has made it an attractive alternative to traditional opioid-based anesthetic approaches [6, 7].

Traditional opioid-based anesthesia has been associated with several important adverse effects, including a higher risk of postoperative nausea and vomiting, respiratory depression, and the potential for opioid dependence [5]. In addition,

high doses of intraoperative opioids may worsen postoperative pain management and further increase the incidence of nausea and vomiting [1]. These limitations have reinforced interest in strategies that reduce or eliminate perioperative opioid exposure.

Within modern perioperative medicine, opioid-free anesthesia has shown relevance because it has been associated with improved postoperative outcomes, particularly through reductions in postoperative nausea and vomiting and enhancement of recovery quality, especially in surgeries with high opioid requirements [4, 8]. Its use has also been shown to be feasible and transferable across different surgical settings, including bariatric and gynecological procedures [3]. Nevertheless, despite these benefits, opioid-free anesthesia still requires careful patient selection and close consideration of possible adverse events, such as bradycardia and prolonged recovery times [6, 9].

The objective of this narrative review is to critically review the current evidence on opioid-free anesthesia, examining its pharmacological foundations, clinical applications, potential benefits, ongoing controversies, and practical limitations in perioperative care.

Methodology

This manuscript was developed as a structured narrative review aimed at providing an updated and clinically integrated analysis of opioid-free anesthesia, with particular emphasis on its physiological and pharmacological foundations, perioperative outcomes, current controversies, and practical limitations in contemporary anesthetic practice. The review was conducted in accordance with the SANRA (Scale for the Assessment of Narrative Review Articles) framework and followed a predefined methodological protocol established prior to literature screening. Given the heterogeneity of surgical populations, anesthetic protocols, comparator strategies, and reported outcome measures, a narrative interpretative synthesis was selected over quantitative pooling in order to integrate pharmacologic, clinical, and safety considerations into a coherent and clinically applicable framework. Special attention was given to the rationale for opioid avoidance, the role of multimodal non-opioid regimens, the comparative effectiveness of opioid-free versus opioid-sparing approaches, and the safety profile and feasibility of these strategies across different perioperative settings. The objective was to provide a structured synthesis capable of supporting anesthetic decision-making in patients undergoing surgery in whom opioid minimization or avoidance may be clinically relevant.

A comprehensive literature search was conducted in PubMed, Scopus, and Web of Science, including peer-reviewed articles published in English or Spanish between January 2020 and December 2025. The final search was performed in March 2026. This timeframe was selected to capture contemporary advances in opioid-free anesthesia protocols, enhanced recovery strategies, perioperative analgesic optimization, and updated evidence regarding postoperative outcomes and safety. Foundational studies were incorporated when necessary to contextualize the evolution of multimodal analgesia and the historical role of opioids in anesthetic practice.

The search strategy combined MeSH and free-text terms using Boolean operators related to opioid-free anesthesia, opioid-sparing anesthesia, multimodal analgesia, perioperative pain management, dexmedetomidine, ketamine, lidocaine, regional anesthesia, postoperative nausea and vomiting, respiratory depression, recovery outcomes, and perioperative safety. Searches were conducted in titles and abstracts as well as indexed subject headings to maximize sensitivity.

The initial search yielded 181 records. After removal of duplicates, 137 articles remained for title and abstract screening. Of these, 79 underwent full-text evaluation, and 31 studies were included in the final synthesis. Selection was performed independently by two authors, with disagreements resolved through discussion and consensus. Exclusion criteria comprised non-peer-reviewed publications, isolated case reports, editorials without outcome data, purely technical descriptions lacking clinical outcome assessment, redundant datasets, and studies not directly addressing the efficacy, safety, controversies, or clinical applicability of opioid-free anesthesia in perioperative care.

Eligible studies included randomized controlled trials, large observational cohorts, systematic reviews, meta-analyses, expert consensus statements, and contemporary international guidelines from anesthesiology, perioperative medicine, pain, and enhanced recovery societies. Priority was assigned to multicenter investigations, studies with clearly defined anesthetic protocols, and research evaluating clinically relevant outcomes such as postoperative pain, opioid consumption, postoperative nausea and vomiting, respiratory complications, hemodynamic events, recovery quality, and hospital length of stay. Extracted variables included study design, surgical population, anesthetic regimen, comparator strategy, postoperative analgesic requirements, recovery outcomes, opioid-related adverse effects, non-opioid drug-related complications,

and overall conclusions regarding feasibility and safety. Methodological quality and internal validity were assessed narratively, considering risk of bias, sample size, follow-up duration, consistency of protocol definitions, and reproducibility of reported outcomes. In cases of conflicting evidence, greater interpretative weight was assigned to higher-level evidence and guideline-supported recommendations.

Reference lists of included studies were manually screened to identify additional relevant publications. Given its narrative design, this review is subject to potential selection bias and does not provide pooled quantitative estimates. Artificial intelligence-based tools were used exclusively to assist in literature organization and structural coherence, whereas critical appraisal, synthesis, and final interpretation were conducted independently by the authors to preserve methodological rigor.

Conceptual Basis and Pharmacologic Principles of OFA

Opioid-free anesthesia involves the complete avoidance of opioids during surgery and relies on alternative medications to control pain and physiological responses to surgical stress [2, 10]. In contrast, opioid-sparing anesthesia seeks to reduce opioid use without eliminating it entirely, generally by combining low doses of opioids with other analgesic agents [11]. Multimodal analgesia is based on the use of different analgesic techniques and medications to minimize opioid exposure, commonly incorporating non-opioid drugs and regional anesthesia techniques [12]. In a broader sense, opioid minimization strategies encompass both opioid-sparing and multimodal approaches, with the aim of reducing opioid consumption and the risks associated with their use [1].

The rationale for avoiding intraoperative opioids is closely linked to their well-known adverse effects and to the growing interest in improving perioperative recovery. Opioids are associated with postoperative nausea and vomiting,

respiratory depression, and the potential for addiction, all of which may negatively affect postoperative outcomes and delay recovery [5, 6]. In addition, the ongoing opioid crisis has prompted a reevaluation of opioid use in medical practice and has encouraged the search for alternative analgesic strategies [2]. Within this context, avoiding opioids has been associated with improved recovery outcomes, including a reduction in postoperative nausea and vomiting and better gastrointestinal function [5].

Despite these concerns, opioids have traditionally played a central role in anesthetic practice. They have long been considered a cornerstone for the management of intraoperative and postoperative pain. In addition to their analgesic effect, opioids contribute to blunting the sympathetic response to surgery, thereby reducing the physiological stress reaction that may otherwise lead to complications. They also play an important role in hemodynamic control by helping maintain stable blood pressure and heart rate during surgical procedures [13].

The pharmacologic basis of opioid-free anesthesia rests on the use of several non-opioid agents with complementary mechanisms of action. Dexmedetomidine provides sedation and analgesia, decreases sympathetic activity, and has minimal effects on respiratory depression [11, 13]. Ketamine contributes both analgesic and anesthetic properties and offers the additional benefit of reducing opioid requirements [14]. Lidocaine is used for its analgesic and anti-inflammatory properties and is often administered intravenously in this setting [13]. Magnesium acts as an N-methyl-D-aspartate receptor antagonist, thereby contributing to analgesia and reducing opioid consumption. Acetaminophen and nonsteroidal anti-inflammatory drugs are also frequently incorporated because of their analgesic and anti-inflammatory effects and because they form part of multimodal analgesic regimens [12]. Local anesthetics are employed in regional blocks to

provide targeted analgesia and reduce the need for systemic analgesic agents [5].

Technical and Clinical Components of OFA Protocols

Preoperative patient selection and assessment are essential components of opioid-free anesthesia, since this approach requires identifying those individuals who may derive the greatest benefit from reduced opioid exposure, particularly patients with a history of opioid sensitivity or those at increased risk of opioid-related adverse effects [5, 7]. In this context, comprehensive preoperative assessment includes a detailed evaluation of the patient's medical history, anticipated pain management requirements, and any potential contraindications to the use of non-opioid analgesics [10].

Following patient evaluation, intraoperative planning involves the design of a tailored anesthetic protocol that incorporates non-opioid analgesics and techniques aimed at controlling surgical stress and pain [10, 12]. These protocols frequently include agents such as ketamine, lidocaine, dexmedetomidine, and magnesium sulfate, all of which provide analgesic and anesthetic-sparing properties [15, 16]. Within this framework, multimodal drug combinations represent a central element of opioid-free anesthesia, since they target different pain pathways, enhance analgesic efficacy, and reduce the need for opioid administration [17, 18]. Studies have shown that these multimodal approaches can effectively control pain and improve recovery outcomes, although the optimal combination of agents remains under investigation [12, 19].

Regional anesthesia and nerve blocks also play a major role in opioid-free anesthesia by providing targeted pain relief and reducing the need for systemic medications [5, 20]. Techniques such as epidural anesthesia and peripheral nerve blocks are commonly used to improve analgesia and facilitate postoperative recovery [16]. At the same time, the successful application of opioid-

free anesthesia requires vigilant intraoperative monitoring in order to maintain hemodynamic stability and ensure adequate anesthetic depth in the absence of opioids [10, 12]. This monitoring includes the assessment of vital signs, anesthetic depth, and the possible adverse effects associated with non-opioid agents [20].

Postoperative analgesia planning without opioids is equally important, since pain control must be maintained through the continued use of non-opioid analgesics and regional techniques in order to minimize opioid exposure while preserving patient comfort [7, 15]. Effective postoperative planning is therefore necessary to prevent breakthrough pain and to ensure adequate recovery [19]. However, one of the major challenges in this field is the significant variability among published opioid-free anesthesia protocols, which differ in drug selection, dosing strategies, and methods of administration across studies [17, 18]. This heterogeneity complicates comparisons between studies and makes it difficult to establish standardized guidelines [15]. In turn, standardizing opioid-free anesthesia regimens remains challenging because of the diversity of surgical settings, patient populations, and the absence of consensus regarding the optimal drug combinations to use [10, 12]. For this reason, further research is still needed to identify best practices and develop evidence-based protocols that can be more widely adopted [19].

Current Evidence on Clinical Outcomes

The current evidence on opioid-free anesthesia is derived from several study designs, most notably randomized controlled trials and evidence syntheses. Many randomized controlled trials, including multicenter studies, have compared opioid-free anesthesia with opioid-based anesthesia across different surgical settings, such as endoscopic sinus surgery and breast cancer surgery [9]. In parallel, systematic reviews and meta-analyses have combined data from multiple randomized controlled trials in order to assess the overall efficacy and safety of opioid-free

anesthesia compared with opioid-based anesthesia [6, 7, 22].

Among the most commonly evaluated outcomes, postoperative pain scores have received particular attention. Opioid-free anesthesia has been associated with lower pain scores in some studies, especially during the immediate postoperative period [6]. However, other studies have found no significant differences in pain scores between opioid-free anesthesia and opioid-based anesthesia. A similar pattern has been observed with opioid rescue requirements, since opioid-free anesthesia generally reduces the need for postoperative opioid rescue and contributes to lower total opioid consumption [3, 7, 22]. By contrast, one of the most consistent findings in the literature is the reduction in postoperative nausea and vomiting, which represents one of the most important advantages of opioid-free anesthesia over opioid-based anesthesia [23].

The effect of opioid-free anesthesia on time to recovery and hospital length of stay remains less clearly defined. Some studies have shown no significant differences in these outcomes when compared with opioid-based anesthesia [3, 24]. Nevertheless, improvements in quality of recovery scores have been reported in certain studies, suggesting a potential positive effect on patient satisfaction [21]. Taken together, these findings provide partial support for opioid-free anesthesia, particularly because of its ability to reduce postoperative nausea and vomiting and, in some reports, to improve early postoperative pain control [7, 24].

Despite these favorable findings, the superiority of opioid-free anesthesia is not consistently demonstrated across all outcomes. Although it appears beneficial in reducing postoperative nausea and vomiting, its advantage in pain management and overall recovery quality has not been uniformly confirmed in the literature [22, 25]. This lack of consistent superiority is especially relevant when opioid-free anesthesia is

compared not only with opioid-based anesthesia but also with opioid-sparing anesthesia. In this regard, opioid-free anesthesia does not consistently outperform opioid-sparing approaches in terms of overall recovery quality, raising the possibility that opioid minimization rather than complete opioid elimination may be the more clinically useful strategy [23, 25].

The interpretation of these results is further limited by several methodological constraints. There is substantial heterogeneity among study designs, including differences in surgical procedures, patient populations, and opioid-free anesthesia protocols, which complicates the generalization of the findings [1, 7]. In addition, most studies focus primarily on short-term postoperative outcomes, leaving limited evidence regarding the long-term effects of opioid-free anesthesia. Some studies also present important methodological limitations, such as small sample sizes and potential sources of bias, which reduce the strength and robustness of the available conclusions [6, 22].

Potential Benefits of OFA

Opioid-free anesthesia offers several potential advantages, particularly through the reduction of adverse effects traditionally associated with opioid use. One of the most consistently reported benefits is a significant decrease in the incidence of postoperative nausea and vomiting, which is one of the most common complications related to opioid-based anesthesia. Studies have shown that opioid-free anesthesia can reduce the risk of postoperative nausea and vomiting by nearly half when compared with opioid-based anesthesia. This reduction has been confirmed in multiple surgical settings. For example, in gynecological laparoscopic surgery, the incidence of postoperative nausea and vomiting decreased from 34.8% in the opioid group to 15.2% in the opioid-free anesthesia group [3, 7]. Similarly, in endoscopic sinus surgery, the incidence of postoperative nausea and vomiting was 7.0% in the opioid-free anesthesia group compared with 15.1% in the opioid group [21].

In addition to its effect on postoperative nausea and vomiting, opioid-free anesthesia is associated with a lower risk of respiratory depression, which represents one of the most serious adverse effects of opioid administration, although specific data quantifying this reduction are reported less frequently. Even so, the reduction in opioid exposure itself supports the possibility of a lower incidence of this complication, given that respiratory depression is a well-recognized opioid-related adverse event [5]. Opioid-free anesthesia may also reduce opioid-induced hyperalgesia, a condition characterized by increased sensitivity to pain as a consequence of opioid use. This possibility is supported by the general reduction in postoperative pain scores that has been observed in some studies evaluating opioid-free anesthesia [6].

Another relevant advantage of opioid-free anesthesia lies in its role within enhanced recovery after surgery pathways. In this context, opioid-free anesthesia contributes to the optimization of perioperative care by reducing the surgical stress response and improving gastrointestinal function, both of which are important for faster and more efficient postoperative recovery [5]. This potential benefit is especially relevant in ambulatory and fast-track surgery, where rapid recovery and early discharge are important goals. In these settings, opioid-free anesthesia has been associated with a reduced need for postoperative analgesics and with shorter hospital stays, making it particularly suitable for procedures in which accelerated recovery is prioritized [4].

Opioid-free anesthesia may also be particularly advantageous in patients who are at increased risk from opioid exposure. This includes individuals with a history of opioid use or those who are more susceptible to opioid-related complications. In such populations, opioid-free anesthesia provides effective analgesia while avoiding the risks that accompany opioid

administration, thereby representing a potentially safer alternative [1].

Controversies and Ongoing Debate

One of the main controversies surrounding opioid-free anesthesia is whether it is truly superior to opioid-sparing anesthesia. In some clinical settings, opioid-free anesthesia has been shown to reduce postoperative nausea and vomiting more effectively than opioid-sparing anesthesia, as has been reported in laparoscopic bariatric surgery, although this benefit may come at the cost of an increased risk of bradycardia [23]. Similarly, in breast cancer surgery, opioid-free anesthesia demonstrated better control of postoperative nausea and vomiting and pain, whereas opioid-sparing anesthesia appeared to provide more balanced benefits across multiple dimensions of recovery quality [25]. In addition, a systematic review and meta-analysis found that opioid-free anesthesia significantly reduced adverse postoperative events, mainly because of lower rates of nausea and vomiting, without evidence of harmful effects on patient safety or pain management [19]. Even so, these findings do not establish a consistent overall superiority of opioid-free anesthesia across all perioperative outcomes.

The quality and consistency of the evidence remain major points of debate. Some studies have reported improved quality of recovery and reduced opioid consumption with opioid-free anesthesia, whereas others have found no significant differences in pain scores or opioid consumption when compared with opioid-based anesthesia [18, 22]. This inconsistency is further compounded by the lack of standardization in opioid-free anesthesia protocols and by variability in how the technique itself is defined, which makes comparisons across studies more difficult and raises concerns about the external validity of the available findings [9]. Moreover, the evidence base has been characterized as moderate to low in quality, with substantial heterogeneity in study results, underscoring the

need for further validation before stronger conclusions can be drawn [18].

Another concern is that opioid-free anesthesia may be promoted beyond what the current data can reliably support. There is apprehension that enthusiasm for the technique may exceed the maturity of the evidence base, particularly because comprehensive safety data are still limited. For this reason, some experts have emphasized the need for more robust evidence-based non-opioid anesthetic protocols and have cautioned against the indiscriminate adoption of opioid-free anesthesia without sufficient training and a clear understanding of its risks [1, 19].

The debate is also shaped by the marked variability in clinical outcomes observed across different procedures and patient populations. While some studies have shown improvements in recovery quality, others have failed to demonstrate significant differences, suggesting that the benefits of opioid-free anesthesia may not be uniform in all settings [18, 22]. This variability supports the view that anesthetic strategies should be individualized and that opioid minimization may, in some cases, be more practical and beneficial than complete opioid elimination [25].

Accordingly, whether opioid-free anesthesia should be regarded as a universal strategy or rather as a niche approach remains unresolved. Although it is feasible and can be implemented in clinical practice, its generalizability is still uncertain, and it may be more appropriate for selected patient groups or specific surgical contexts than as a routine strategy for all cases [1]. Therefore, the decision to adopt opioid-free anesthesia should take into account patient-specific characteristics, the surgical setting, and the availability of appropriate training and institutional resources [2].

Safety Concerns, Adverse Effects, and Limitations

Hemodynamic adverse effects represent some of the most important safety concerns associated with opioid-free anesthesia, particularly when agents such as dexmedetomidine are used. Bradycardia and hypotension have been identified as notable cardiovascular complications in this setting, and these events may contribute to prolonged extubation times while requiring careful intraoperative monitoring and management [26, 27]. At the same time, hemodynamic outcomes may vary according to the specific agents selected for the opioid-free regimen. In a study evaluating esketamine-based opioid-free anesthesia, patients demonstrated improved hemodynamic stability compared with those receiving opioid-inclusive anesthesia, suggesting that the cardiovascular profile of opioid-free anesthesia is influenced by the pharmacologic composition of the protocol itself [28].

This consideration is particularly relevant because the alternative agents used in opioid-free anesthesia are not without risk. Dexmedetomidine, ketamine, lidocaine, and magnesium are commonly incorporated into opioid-free protocols, yet each of these drugs carries its own adverse effect profile, including the potential for cardiovascular complications, neurotoxicity, and other unwanted reactions. Dexmedetomidine, for example, has been specifically associated with increased incidences of bradycardia, which makes careful dose adjustment and close monitoring especially important during its use [26, 28].

Another relevant limitation of opioid-free anesthesia is the possibility of inadequate analgesia in highly painful surgical procedures. In some contexts, opioid-free approaches may fail to provide sufficient pain control, leading to the need for rescue analgesia and potentially reducing the intended benefits of avoiding opioids [26, 27]. Furthermore, in certain studies, the reduction in opioid consumption did not reach clinically significant levels, suggesting that opioid-free anesthesia may not always be

effective enough to ensure adequate postoperative pain management on its own [28].

These concerns also raise the broader issue of whether opioid-free anesthesia may simply replace opioid-related toxicity with the toxicity of alternative agents. Although the purpose of opioid-free anesthesia is to reduce adverse effects classically associated with opioids, this strategy requires a careful balance between benefit and risk, as well as a thorough understanding of the pharmacodynamics and pharmacokinetics of the non-opioid drugs employed. For this reason, successful implementation of opioid-free anesthesia depends heavily on clinical expertise, vigilant monitoring, and individualized dosing. Anesthesiologists must be able to adjust these regimens according to patient-specific responses and the demands of the surgical procedure, and studies have emphasized that adequate preparation, experience, and familiarity with the protocols are essential for safe adoption [1].

Complete opioid avoidance may not always be safe or realistic in every perioperative setting. In certain surgical contexts, such as cardiac surgery involving cardiopulmonary bypass, the total elimination of opioids may be impractical because of the high incidence of postoperative complications and the need for reliable pain control [10]. More broadly, opioid-free anesthesia may not be appropriate for all patients, especially those with pre-existing conditions or those undergoing procedures associated with high levels of pain, in whom opioids may still play an important role in controlling pain and attenuating the surgical stress response [1].

Clinical Applications and Patient Selection

The clinical application of opioid-free anesthesia depends largely on the surgical setting and the characteristics of the patient. Among the procedures in which opioid-free anesthesia has shown favorable results are laparoscopic and

other minimally invasive surgeries. In gynecological laparoscopy and cholecystectomy, opioid-free anesthesia has been associated with lower rates of postoperative nausea and vomiting and with improved quality of recovery [26, 29]. Gastrointestinal surgery also appears to be a relevant context for its use, particularly within enhanced recovery protocols, where opioid-free anesthesia may reduce adverse effects such as intestinal paralysis and support faster postoperative recovery [5]. In addition, selected ambulatory procedures may benefit from opioid-free anesthesia because the reduction in opioid-related side effects can facilitate earlier discharge and recovery [19].

Patient selection is equally important when determining the suitability of opioid-free anesthesia. Patients with obstructive sleep apnea may particularly benefit from this approach because it avoids opioid-induced respiratory depression, which represents an important risk in this population [30]. Likewise, patients who have previously experienced severe opioid-related adverse effects, such as respiratory depression or severe postoperative nausea and vomiting, may be appropriate candidates for opioid-free anesthesia. Patients at high risk for postoperative nausea and vomiting may also derive particular benefit, given the consistent reduction in this complication observed with opioid-free techniques [3, 26, 29].

In contrast, opioid-free anesthesia may be less suitable for certain patient groups. Opioid-tolerant patients, especially those with a history of chronic opioid use, may not achieve adequate analgesia with opioid-free regimens because of their altered pain management requirements, which may necessitate alternative strategies. Similarly, patients with chronic pain conditions may continue to require opioids for effective perioperative pain control, making opioid-free anesthesia a less appropriate option in many cases [31]. Limitations are also evident in major surgical procedures with a high nociceptive burden, such as major orthopedic or cardiac

surgery, where the analgesic efficacy of opioid-free anesthesia may be insufficient to meet perioperative demands [10].

For these reasons, opioid-free anesthesia should be tailored according to several factors. The type and extent of the surgical procedure must be considered, since its efficacy is not uniform across all operations [5, 19]. Patient comorbidities, particularly obstructive sleep apnea or a prior history of opioid-related adverse effects, should also guide the anesthetic plan [30]. In addition, the expected intensity of postoperative pain must be carefully evaluated to determine whether opioid-free anesthesia can provide adequate analgesia [31]. The successful implementation of opioid-free anesthesia also depends on institutional expertise and on the availability of the resources necessary to apply these protocols safely and effectively [10].

Conclusions

Opioid-free anesthesia represents a promising perioperative strategy that has demonstrated consistent clinical benefits, particularly in reducing postoperative nausea and vomiting, decreasing the need for rescue opioids, and improving some early recovery outcomes, especially in laparoscopic, ambulatory, and enhanced recovery surgical settings.

Despite its potential advantages, the superiority of opioid-free anesthesia over opioid-sparing anesthesia or conventional anesthetic approaches has not been consistently demonstrated, due to protocol heterogeneity, variability in the studied populations and procedures, and methodological limitations in the available evidence, which prevent this technique from being considered a universal solution.

The use of opioid-free anesthesia should be individualized, since its efficacy and safety depend on the type of surgery, the patient's clinical profile, the risk of hemodynamic adverse effects, and institutional expertise; therefore, its implementation should be based on appropriate

patient selection, close monitoring, and sound clinical judgment rather than on the systematic elimination of opioids in all perioperative contexts.

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