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Opioid-Free Anesthesia in Adult Surgery: A Narrative Review of Current Evidence and Clinical Implications

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ABSTRACT

Opioid-free anesthesia (OFA) is a type of general anesthesia that avoids using opioid medications during surgery. Instead, it relies on a combination of non-opioid drugs like dexmedetomidine, ketamine, intravenous lidocaine, clonidine, and regional anesthesia techniques. The main aim of OFA is to lower the risk of opioid-related side effects, such as postoperative nausea and vomiting (PONV), breathing problems, constipation, drowsiness, and opioid-induced hyperalgesia. *Aim:* This narrative review presents a summary of what is known regarding the use of OFA in adult patients. *Methods:* The authors carried out a literature search using PubMed, the Cochrane Library, Scopus, and Google Scholar. They analyzed the studies that were published between 2020 and 2026. Randomized controlled trials, systematic reviews, and meta-analyses that assessed the efficacy and safety of opioid-free anesthesia were included. *Results:* Evidence indicates that opioid-free anesthesia significantly reduces postoperative nausea and vomiting and may improve postoperative quality of recovery in surgical populations. However, no consistent superiority has been demonstrated regarding postoperative pain intensity or postoperative opioid consumption compared with opioid-sparing or conventional opioid-based anesthesia. OFA protocols based on $\alpha 2$ -agonists may increase the risk of bradycardia and prolonged recovery time. *Conclusion:* Its clearest benefit appears to be in patients in whom opioid-related adverse effects, especially postoperative nausea and vomiting, are a particular concern. At present, the evidence is insufficient to justify replacing opioid-sparing anesthesia with OFA as a routine strategy. In practice, the decision to avoid intraoperative opioids should therefore depend on the individual patient, the type of surgery, and the expected benefits and risks of the drugs included in the anesthetic protocol.

Keywords: opioid-free anesthesia, opioid-sparing anesthesia, multimodal anesthesia, perioperative care

1. INTRODUCTION

Surgical procedures are performed using a variety of techniques, including open, laparoscopic, and minimally invasive approaches. Regardless of the surgical method, effective perioperative pain management remains one of the fundamental components of modern anesthetic practice (Blum et al., 2024; Shanthanna and Joshi, 2024).

Opioids have for a long time been seen as the main component of pain relief during surgery since they have strong pain-killing properties, work synergistically with anesthetic agents, and can reduce the body's physiological stress response to surgery. Their action is achieved via opioid receptors which are found in both the central and peripheral nervous systems and they are still commonly used in general anaesthesia. On the other hand, the administration of opioids is also linked to a variety of adverse effects, such as respiratory depression, postoperative nausea and vomiting (PONV), constipation, urinary retention, pruritus, bradycardia, prolonged sedation, and a delayed postoperative recovery (Blum et al., 2024; Shanthanna and Joshi, 2024).

Because of growing awareness of the adverse effects associated with opioids and concerns about the global opioid crisis, there has been increasing interest in anesthetic methods which either reduce or get rid of the use of opioids during surgery. On the other hand, progress in multimodal analgesia and the fact that effective non-opioid pain relief drugs are now available have allowed for the creation of alternative strategies for pain management during the perioperative period (Blum et al., 2024; Tripodi et al., 2025).

In the OFA approach opioids are not used during general anaesthesia and analgesia is achieved by combining a number of different methods. There is no one standard OFA protocol since the drugs employed differ from one protocol to another and can include dexmedetomidine, ketamine, lidocaine, clonidine or magnesium sulphate. Regional anaesthesia may also be incorporated as part of the technique (Blum et al., 2024; Tripodi et al., 2025). The aim is to ensure sufficient analgesia while, as much as possible, avoiding the adverse effects linked with exposure to opioids during the perioperative period (Blum et al., 2024; Shanthanna and Joshi, 2024).

The clinical results reported with OFA have not been uniform. Several studies have found less postoperative nausea and vomiting, particularly after thoracic and bariatric procedures (Feng et al., 2024; Bao et al., 2024; Ao et al., 2025). Findings for postoperative opioid requirements are less consistent, however. On the basis of currently available evidence, OFA cannot therefore be considered consistently superior to opioid-sparing or conventional opioid-based anesthesia (Feenstra et al., 2023; Chassery et al., 2024; Tripodi et al., 2025).

The fact that the various studies differ raises a number of issues regarding the clinical application of OFA which remain unanswered. Specifically, it is not yet clear which patients are most likely to gain from avoiding opioids during anaesthesia and whether or not this benefit varies depending on the type of surgical procedure. In order to answer these questions it will be necessary to conduct studies that use more comparable OFA protocols and that define their clinical outcomes clearly (Tripodi et al., 2025; Feenstra et al., 2023; Shanthanna and Joshi, 2024).

The aim of this narrative review was to summarize the current evidence regarding the use of opioid-free anesthesia in adult surgical patients, with particular emphasis on:

1. the parts of opioid-free anesthesia protocols;
2. a comparison of the effectiveness and safety of OFA with those of opioid-sparing and opioid-based anesthesia;
3. the possible clinical benefits, limitations, and areas for future research regarding the use of OFA in adult surgery.

2. REVIEW METHODS

The purpose of this review is to summarize the current evidence on opioid-free anesthesia (OFA) in adult surgical patients. A literature search was carried out using PubMed, the Cochrane Library, Scopus, and Google Scholar, and only studies published in English or Polish from January 2020 to May 2026 were included. The search strategy used combinations of these keywords: "opioid-free anesthesia," "opioid-sparing anesthesia," "multimodal analgesia," "dexmedetomidine," "ketamine," "lidocaine infusion," "adult surgical patients," "postoperative pain," and "postoperative nausea and vomiting (PONV)." We used the Boolean operators AND and OR as needed.

The only publications that were considered were randomized controlled trials, systematic reviews, and meta-analyses relating to OFA in adult surgical patients. We have only included full-text, peer-reviewed articles which reported on the efficacy or safety of this method. Studies in children and experimental animal studies were left out of the review. We also omitted case reports, conference abstracts, editorials, and letters. Articles without a direct clinical focus on OFA in adult surgery were not included in the final selection.

The selected studies were analyzed with particular attention to postoperative pain intensity, postoperative opioid consumption, postoperative nausea and vomiting, quality of recovery, perioperative safety, hemodynamic complications, and recovery time. Due to the heterogeneity of the included studies in terms of surgical procedures, anesthetic protocols, and reported outcomes, the findings were synthesized narratively. The literature search and study selection process is presented in Figure 1.

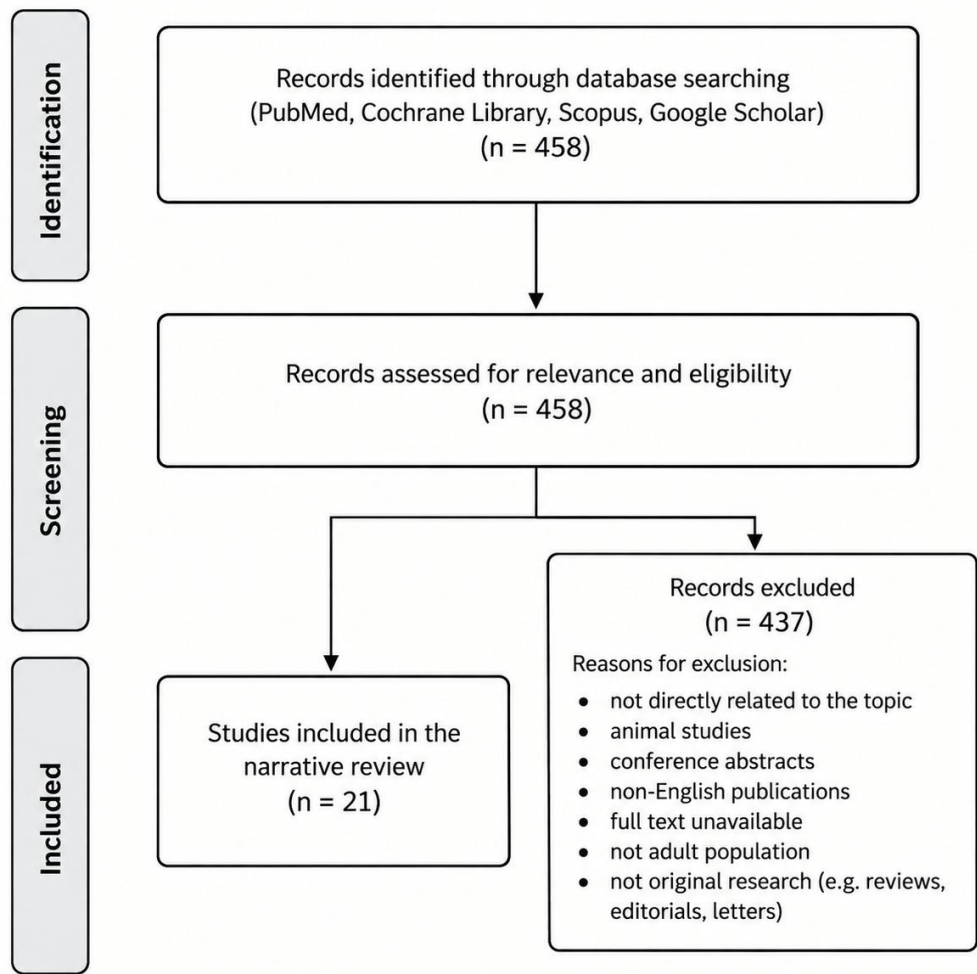


Figure 1. Flow diagram of the literature search and study selection process.

3. RESULTS AND DISCUSSION

Postoperative pain (NRS/VAS) and opioid consumption after surgery

Two scales are commonly used to assess postoperative pain: the Numerical Rating Scale (NRS) and the Visual Analogue Scale (VAS). The NRS is an 11-point scale on which patients rate pain intensity from 0 to 10, where 0 indicates no pain and 10 indicates the worst possible pain. It is commonly used in adults and older children, and pain may be assessed both at rest and during movement. The VAS involves the use of a line that is 10 centimeters in length on which the patient indicates the point that most accurately reflects the intensity of their pain, the scale extending from 0 (meaning no pain) to 10 (representing the worst possible pain).

According to the available evidence, OFA does not reliably lead to a reduction in postoperative pain or in opioid use when compared with opioid-based or opioid-sparing anesthesia. In the case of ambulatory total hip arthroplasty, OFA did not result in a lower 24-hour oral morphine equivalent consumption and pain scores were similar to those seen with opioid-sparing anesthesia (Chassery et al., 2024). With regard to bariatric surgery, the evidence also indicates that OFA and opioid-sparing methods may help reduce PONV, although the differences in pain and opioid consumption remain inconsistent (Ao et al., 2025).

Overall, the available evidence does not demonstrate a consistent advantage of OFA in terms of postoperative pain or oral morphine equivalent (OME) consumption, although exceptions have been reported.

PONV (postoperative nausea and vomiting)

Postoperative nausea and vomiting (PONV) remain frequent problems after general anesthesia and can interfere with early recovery. In more severe cases, persistent symptoms may contribute to dehydration, delayed discharge, or aspiration. Avoiding opioids during anesthesia has therefore been investigated as one way of reducing PONV.

Two randomized trials in the field of thoracic surgery found that opioid-free anesthesia was associated with a lower incidence of postoperative nausea and vomiting (PONV). The study by Feng et al., (2024), which involved patients having a thoracoscopic lung resection, showed that the rate of PONV was lower in the group given opioid-free anesthesia. Similarly, Bao et al., (2024), who looked at patients following video-assisted thoracoscopic surgery, also observed a reduction in the number of PONV episodes when opioid-free anesthesia was used. Importantly, however, this decrease was not linked to a clinically significant worsening of postoperative pain relief. Thus, the results of these trials indicate that opioid-free anesthesia has an antiemetic effect in thoracic surgery, but the findings cannot be simply applied to other types of operations or to other opioid-free anesthesia protocols.

Safety and adverse effects (hemodynamics, bradycardia, hypotension)

Even though OFA has some advantages, the adverse effects will vary according to the drugs used in the multimodal regimen. Pooled analyses in the case of dexmedetomidine-based OFA are especially linked to a higher risk of bradycardia (Yu et al., 2023; Feenstra et al., 2023). The effect on recovery can also depend on the particular OFA protocol; in the trial involving thoracoscopic lung resection, OFA was linked to a longer stay in the PACU (Feng et al., 2024). Some OFA regimens may result in adverse hemodynamic effects such as bradycardia and hypotension, and these effects should be understood in light of the specific drugs and doses employed rather than simply because opioids have been avoided (Yu et al., 2023; Feenstra et al., 2023).

OFA may reduce exposure to opioid-related adverse effects, including respiratory depression and constipation. Nevertheless, the technique is not free of risk, and adverse effects associated with individual non-opioid agents must also be considered.

Wake-up time, PACU, and hospitalization

The recovery that follows OFA is not simply due to avoiding opioids but is instead affected by the specific mixture of drugs used; OFA protocols vary a great deal and may involve lidocaine, dexmedetomidine, clonidine, ketamine or esketamine, magnesium, as well as regional analgesic methods (Blum et al., 2024). The doses and combinations of these drugs also differ from one patient and one procedure to another. It cannot be assumed that the recovery time will be shorter if the opioids are left out; some of the drugs used in OFA have sedative or other pharmacological effects which may delay emergence from anesthesia or prolong the early postoperative recovery (Shanthanna and Joshi, 2024).

The randomized trial carried out by Hao et al., (2023) showed that the patients in the opioid-free anesthesia (OFA) group had a better postoperative quality of recovery. Yet, there were no significant differences between the groups in terms of their length of stay in the post-anesthesia care unit (PACU) or their extubation time. A further randomized study noted that the time until the first passage of flatus was shorter in the OFA group. On the other hand, in patients who had high pain sensitivity, acute postoperative pain was more common in the OFA group than in either the opioid-sparing or the opioid-based groups (Wang et al., 2025b).

Analyses by surgical field

In surgery involving thoracoscopy, the use of OFA can lessen the occurrence of nausea and vomiting after the operation, and the results regarding postoperative pain were the same for OFA and opioid-based anesthesia in the randomized trial carried out by Feng et al. (2024). In patients who have undergone bariatric surgery, various studies have generally found a lower incidence of postoperative nausea and vomiting (PONV) when using an opioid-free analgesic (OFA) regimen, although the level of postoperative pain has been found to be similar to that seen with opioid-based or opioid-sparing methods (Dagher et al., 2025; Almeida et al., 2026). The hemodynamic results are less clear-cut: a meta-analysis of laparoscopic procedures failed to identify a consistent difference in the occurrence of bradycardia or hypotension, indicating that these effects may depend on the specific drugs and doses contained in each patient's individual OFA protocol (Cheng et al., 2025).

In the case of ambulatory total hip arthroplasty, OFA did not offer any advantage in terms of postoperative pain relief when compared with opioid-sparing anesthesia (Chassery et al., 2024). Again, for patients at a low risk of experiencing acute postoperative pain who underwent laparoscopic surgery, OFA was no less effective with regard to acute pain but it neither improved postoperative recovery nor had any effect on PONV (Mogianos et al., 2026). In the SOFA trial involving major elective surgery, OFA led to a

statistically significant improvement in QoR-15, even though the difference over 24 hours did not amount to a clinically important extent (Léger et al., 2024).

Thyroidectomy — Compared with opioid-based anesthesia, OFA has been associated with better quality of recovery and a lower incidence of PONV.

Gynecological surgery - A systematic review and meta-analysis found that OFA significantly reduced postoperative nausea and vomiting and antiemetic use after gynecological surgery, while postoperative pain scores and analgesic use were not significantly different (Zhang et al., 2024).

Quality of recovery (QoR: QoR-15/QoR-40)

QoR (Quality of Recovery) is a validated patient-reported outcome measure which is used for the assessment of multidimensional recovery following surgery and anaesthesia, and the QoR-15 is a more concise validated version of the instrument (Morales-Ariza et al., 2023). Opioid-free anaesthesia might lead to a better early quality of recovery after surgery, but there is still a great deal of variability between the different protocols and surgical patient groups (Tripodi et al., 2025).

A randomized controlled trial carried out in the setting of thyroid surgery found that the QoR-15 score on the first day after surgery was 9.4 points higher in cases where OFA was used; the patients also suffered less nausea and vomiting and enjoyed better sleep quality (Zhang et al., 2025). Moreover, other randomized and pooled data indicate a possible benefit in terms of early recovery, although the effects on emergence and recovery time differ from study to study (Xiong et al., 2025; Wang et al., 2025a). The main findings regarding the efficacy, safety, and postoperative outcomes of opioid-free anesthesia are summarized in Table 1.

Table 1. Summary of the main findings regarding opioid-free anesthesia in adult surgery.

Outcome	Main findings
Postoperative pain	OFA does not consistently reduce postoperative pain compared with opioid-sparing or opioid-based anesthesia. Similar pain scores have been reported in several studies.
Postoperative opioid consumption	Avoiding intraoperative opioids does not consistently reduce postoperative opioid requirements.
Postoperative nausea and vomiting (PONV)	A reduction in PONV is one of the most consistently reported benefits of OFA, although the effect varies between surgical populations and OFA protocols.
Quality of recovery (QoR)	OFA may improve early postoperative quality of recovery in selected surgical populations, although the magnitude of benefit varies between studies.
Recovery time and PACU stay	OFA does not consistently shorten recovery time. Some protocols have been associated with prolonged PACU stay or delayed postoperative recovery.
Hemodynamic safety	Safety depends on the drugs included in the OFA protocol. Dexmedetomidine-based regimens may increase the risk of bradycardia, while findings regarding hypotension are inconsistent.
Overall clinical role	OFA may be useful in selected patients, particularly when avoiding opioid-related adverse effects is important, but current evidence does not support its routine replacement of opioid-sparing anesthesia.

Key findings from the review of scientific studies

The studies that have been reviewed indicate that undergoing anesthesia without opioids is a promising method of achieving general anesthesia; this approach is especially advantageous for reducing postoperative nausea and vomiting (PONV) and may also lead to better early quality of recovery (QoR) (Feenstra et al., 2023; Wang et al., 2025a; Zhang et al., 2024). These results are in agreement with recent meta-analyses which have found an antiemetic effect of OFA and possible advantages regarding patient-reported postoperative recovery (Feenstra et al., 2023; Wang et al., 2025a). At the same time, though, no definite benefit of opioid-free anesthesia has been shown with respect to the intensity of postoperative pain or opioid use during the postoperative period. This indicates that removing opioids from anesthesia doesn't always result in lower analgesic demands after surgery (Feenstra et al., 2023; Tripodi et al., 2025).

Differences in results between scientific studies

When analyzing these results, one has to take into account the considerable variety of protocols used in OFA. The scientific papers examined employed different drug regimens, usually involving different doses, rates, and times of administration. Such variations could have a substantial effect on the results of the studies and make it hard to assign any effects on PONV or QoR to the avoidance of opioids rather than to the particular drug combinations and doses (Blum et al., 2024; Tripodi et al., 2025). In addition, the review includes studies from several surgical fields, including gynecological, bariatric, thoracic, orthopedic, and thyroid surgery. Each of these procedures differs in terms of the incidence of postoperative pain, vomiting, and nausea, as well as the quality of recovery, making it difficult to draw a clear conclusion (Cheng et al., 2025; Tripodi et al., 2025).

The extent of the beneficial effect also seems to depend on the group undergoing surgery; in some gynaecological studies there have been more noticeable reductions in nausea and vomiting than in the orthopaedic groups (Chassery et al., 2024; Zhang et al., 2024).

Mechanisms of benefits in analgesia without the use of opioid drugs

The reduction in postoperative nausea and vomiting may be explained by several mechanisms:

- a full stopping of the use of opioid drugs; for opioids act on receptors found in the vomiting centre.
- the analgesic effects of lidocaine and ketamine without respiratory depression
- the sedative and sympatholytic effects of dexmedetomidine—it stabilizes the stress response

The higher quality of recovery noted in certain studies is most likely due to a number of factors; it might be that less exposure to opioids helps because it leads to fewer opioid-related adverse effects, and also that the various elements of the OFA protocol may affect the body's stress response during and after surgery and improve patients' postoperative comfort. Nevertheless, these effects depend on the specific protocol and therefore cannot be considered as features that are common to all OFA techniques (Blum et al., 2024; Tripodi et al., 2025; Wang et al., 2025a).

No clear advantage of OFA in pain control

The control of pain is still one of the less consistently reported results in studies involving opioid-free anesthesia. In a number of trials, patients who were managed with OFA had pain scores similar to those seen after either opioid-sparing or opioid-based anesthesia (Chassery et al., 2024; Mogianos et al., 2026; Xiong et al., 2025). This is also shown by their postoperative need for analgesics, since avoiding the use of opioids during anesthesia did not reliably stop the need for rescue opioid medication afterward (Ao et al., 2025; Chassery et al., 2024; Feenstra et al., 2023).

A possible reason for the analgesic effect of OFA is that it relies greatly on the drugs contained in the protocol and on the surgical procedure itself. Although non-opioid drugs can help to provide analgesia during and after surgery, their effect might be inadequate if the postoperative pain is more severe. Moreover, the level of postoperative pain is affected by the degree of tissue damage, the individual's sensitivity to pain, and the analgesic treatment given after surgery. Since the patients in the various study groups generally receive similar postoperative regimens, such as paracetamol and NSAIDs, it may be hard to identify differences that are due only to the intraoperative anesthetic technique (Shanthanna and Joshi, 2024; Tripodi et al., 2025).

Because of this, it is incorrect to conclude that OFA is ineffective on the basis of similar postoperative pain scores. On the contrary, the findings indicate that removing intraoperative opioids does not necessarily result in better postoperative analgesia or a reduced need for opioids (Feenstra et al., 2023; Tripodi et al., 2025).

Safety of OFA

Safety depends largely on the agents included in the OFA protocol. Dexmedetomidine deserves particular attention because its use has been associated with bradycardia (Feenstra et al., 2023; Yu et al., 2023). Certain drug combinations have also been linked to slower postoperative recovery or a longer stay in the PACU (Feng et al., 2024; Yu et al., 2023). For this reason, OFA does not eliminate the need for close hemodynamic monitoring. The cardiovascular effects of the individual drugs used in the protocol should be considered when planning anesthesia (Cheng et al., 2025; Yu et al., 2023).

The role of OFA vs. OSA

OFA and OSA are not equivalent strategies and it is not necessary in all patients to completely avoid opioids. In the case of OSA, small amounts of opioids are still administered if required, along with non-opioid pain relievers and other multimodal methods. The

approach that is preferred should be based on the anticipated degree of postoperative pain, the patient's susceptibility to adverse effects related to opioids, and the safety of the drugs used in the anesthetic plan (Ao et al., 2025; Chassery et al., 2024; Shanthanna and Joshi, 2024).

Significance of results in clinical practice

From a clinical perspective, OFA may be particularly relevant in the following situations:

- OFA could prove to be of benefit in cases where patients have suffered nausea and vomiting as a result of anesthesia following surgical operations (Feenstra et al., 2023; Feng et al., 2024; Zhang et al., 2024).

Limitations in access to data

This review has several important limitations:

- only a small proportion of studies evaluate the long-term effects of anesthesia without the use of opioids
- there is no uniform definition of OFA
- many of the studies conducted involve a small group of patients, which is a statistical limitation
- it is hard to compare OFA protocols directly because they are so different from each other.

Directions for future research

The available evidence highlights several priorities for future research:

- The impact of OFA on long-term outcomes warrants further investigation.
- Standardization of OFA protocols remains necessary.
- Future research should include larger patient cohorts.
- there is still not enough health economics data to support broader decisions.

OFA is a modern anesthetic approach and the most consistently reported advantages of it are a decrease in PONV and a possible improvement in early postoperative recovery. However, according to the data currently available, it cannot be definitely said that OFA is better than opioid-sparing techniques or conventional anesthesia with regard to pain control or the reduction of postoperative opioids (Feenstra et al., 2023; Tripodi et al., 2025; Wang et al., 2025a).

In numerous instances OFA can be of particular advantage, but its use must be tailored to the individual, properly supervised, and guided by established protocols (Shanthanna and Joshi, 2024; Tripodi et al., 2025).

4. CONCLUSION

Opioid-free anesthesia (OFA) represents a promising alternative to conventional anesthetic techniques based on opioids in certain patients, since it has the potential to reduce the occurrence of postoperative nausea and vomiting; moreover, an ever-growing amount of evidence indicates that OFA may lead to an improved early quality of recovery in particular surgical groups. However, the available data do not clearly demonstrate superiority of OFA in postoperative pain control or in reducing total postoperative opioid consumption.

Opioid-free techniques also require careful use because the non-opioid agents involved may cause adverse effects. Reported adverse effects include bradycardia and, with some regimens, prolonged postoperative recovery; these effects may be associated with agents such as dexmedetomidine. OFA is unlikely to be appropriate for every surgical patient. It may be more useful when avoiding opioid-related complications is an important part of the anesthetic plan, for example in patients with a high risk of PONV, opioid intolerance, or obstructive sleep apnea. The assessment of OFA effectiveness is limited by small study populations, differences among surgical procedures, and substantial heterogeneity in anesthetic protocols. Further research involving larger patient populations and a broader range of surgical procedures is needed to define the role of OFA more clearly. Taken together, the available evidence suggests that OFA has a place in perioperative care, but not as a standard approach for every patient.

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Informed consent

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Conflict of interest

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Data and materials availability

All data associated with this study will be available based on the reasonable request to the corresponding author.

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