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Opioid-Free Anesthesia: Current Evidence, Clinical Applications, and Future Perspectives

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Abstract

Background: Opioid-Free Anesthesia (OFA) has emerged as a revolutionary paradigm utilizing non-opioid multimodal analgesia to achieve stable nociceptive control without intraoperative opioids. This review evaluates the clinical evidence, practical applications, and implementation challenges of OFA. **Methods:** A comprehensive literature review was conducted across PubMed, ScienceDirect, and Google Scholar, selecting randomized controlled trials (RCTs) from the last five years. Data extracted included study designs, surgical typologies, pharmacological regimens, and clinical outcomes. **Results:** OFA provides non-inferior intraoperative stability and analgesia while significantly enhancing recovery scores, sleep quality, and PONV reduction. However, its efficacy is surgical-specific: it markedly reduces morphine needs in visceral procedures (bariatric/colorectal) but offers no advantage over optimized opioid-sparing anesthesia in musculoskeletal surgeries like total hip arthroplasty. Furthermore, high-dose non-opioid adjuncts introduce challenges like prolonged extubation, increased PACU stay, and sympathetic fluctuations. **Conclusion:** OFA is a safe and effective technique that minimizes opioid-related complications and improves recovery, particularly for high-risk patients and oncological surgeries. However, its benefits are surgical-specific and not universally superior to optimized Opioid-Sparing Anesthesia (OSA). Future universal adoption requires standardized dosing and objective monitoring (pEEG and Surgical Pleth Index) to ensure predictable recovery.

Keywords: Opioid-Free Anesthesia (OFA), Multimodal Analgesia, Quality of Recovery, ERAS.

Abstract

Latar Belakang: Anestesi Bebas Opioid (Opioid-Free Anesthesia/OFA) telah muncul sebagai paradigma revolusioner yang memanfaatkan analgesia multimodal non-opioid untuk mencapai pengendalian nosiseptif yang stabil tanpa penggunaan opioid selama operasi. Tinjauan ini mengevaluasi bukti klinis, penerapan praktis, dan tantangan implementasi OFA. **Metode:** Tinjauan pustaka komprehensif dilakukan melalui PubMed, ScienceDirect, dan Google Scholar, dengan memilih uji coba terkontrol secara acak (randomized controlled trials/RCTs) dari lima tahun terakhir. Data yang diekstraksi meliputi desain studi, jenis prosedur bedah, rejimen farmakologis, dan luaran klinis. **Hasil:** OFA memberikan stabilitas intraoperatif dan analgesia yang tidak kalah efektif dibandingkan metode konvensional, sekaligus secara signifikan meningkatkan skor pemulihan, kualitas tidur, dan mengurangi kejadian mual dan muntah pascaoperasi (PONV). Namun, efikasinya bergantung pada jenis prosedur bedah: OFA secara nyata mengurangi kebutuhan morfin pada prosedur viseral (bariatrik/kolorektal) tetapi tidak memberikan keuntungan lebih dibandingkan anestesi hemat opioid (opioid-sparing anesthesia) yang dioptimalkan pada bedah muskuloskeletal seperti artroplasti panggul total. Selain itu, penggunaan obat tambahan non-opioid dosis tinggi menimbulkan tantangan seperti ekstubasi yang tertunda, durasi perawatan di ruang pemulihan (PACU) yang lebih lama, dan fluktuasi simpatis. **Kesimpulan:** OFA merupakan teknik yang aman dan efektif untuk meminimalkan komplikasi terkait opioid serta meningkatkan

pemulihan, khususnya bagi pasien berisiko tinggi dan pada bedah onkologis. Akan tetapi, manfaatnya bersifat spesifik terhadap jenis operasi dan tidak secara universal lebih unggul dibandingkan Anestesi Hemat Opioid (OSA) yang dioptimalkan. Penerapan secara luas di masa depan memerlukan standardisasi dosis dan pemantauan objektif (seperti pEEG dan Surgical Pleth Index) guna memastikan hasil pemulihan yang dapat diprediksi.

Kata kunci: Anestesi Bebas Opioid (OFA), Analgesia Multimodal, Kualitas Pemulihan, ERAS

I. INTRODUCTION

Opioids have been used for a long time along with general anesthesia to help reduce pain during surgery by slowing down the central nervous system.[1] Using high doses of opioids can lead to many serious side effects that can be dangerous and may make a patient stay in the hospital longer. These bad effects include breathing problems because the body doesn't respond properly to high carbon dioxide levels, feeling sick and throwing up after surgery, being too sleepy, slowed digestion causing stomach issues, and confusion or disorientation after surgery.[2] Recent studies also show that using opioids during surgery can lead to a quicker tolerance to them, needing more pain medicine after surgery, weakening the immune system, increased pain sensitivity, long-term pain after surgery, and a higher chance of becoming dependent or misusing opioids.[1,3]

Because of this wide range of problems, doctors around the world are starting to think again about how much they depend on these medicine treatments. To reduce these risks, a big change has happened in the field of perioperative medicine called Opioid-Free Anesthesia (OFA).[4,5] OFA is becoming more popular among anesthesiologists around the world. This new approach is based on the idea that avoiding opioids during surgery leads to better results after the operation.[6] The scientific foundation supporting the adoption of OFA relies heavily on the synergistic deployment of non-opioid multimodal analgesia regimens.[7]

Recent studies using randomized controlled trials show that using non-opioid methods, like combining alpha-2 agonists, NMDA blockers, local anesthetics, magnesium sulfate, and nerve blocks, can keep the patient's blood pressure and heart rate stable during surgery and manage pain just as well as using opioids.[8,9] For example, research shows that avoiding opioids during surgery can improve recovery, reduce the chances of severe nausea after surgery, help sleep better, and lower the risk of weakening the immune system, especially in cancer patients.

Even though OFA is being used, there are still different ways it works in real patients and some difficulties that come up. Some surgeries, like bariatric laparoscopy and open colorectal cancer operations, lead to less use of morphine after surgery when using OFA methods.[10–12] Moreover, concerns regarding prolonged emergence recovery, delayed extubation, and intraoperative sympathetic fluctuations driven by high-dose non-opioid adjuncts continue to pose practical hurdles for perioperative clinicians.[13]

To grasp why this technique is important and how well it works, we need to look at the existing research, how it's used in different surgeries, and where it might be headed in the future. This article brings together the latest research and recent studies to give a full overview that connects important ideas with real-world use in the surgery room, and it also looks at the difficulties faced when using anesthesia without opioids. The main goal of this analysis is to provide useful information for doctors and help create better guidelines. This will help change how care is given before, during, and after surgery so that it is more tailored, effective, and safer for each patient.

II. METHODE

This study utilized a comprehensive literature review methodology to evaluate the efficacy, clinical applications, and future perspectives of Opioid-Free Anesthesia (OFA). A structured literature search was conducted across reputable scientific databases, including PubMed, ScienceDirect, and Google Scholar, using combinations of specific keywords such as ("Opioid-free anesthesia" OR "OFA") AND ("multimodal analgesia" OR "outcomes"). Inclusion criteria were restricted to original articles consisting of randomized controlled trials (RCTs) within the last five years. Data from the selected articles were extracted in detail,

encompassing study design, patient population characteristics, types of surgical interventions, non-opioid pharmacological regimens utilized, and clinical outcome parameters such as pain scores, incidence of PONV, sleep quality, and patient recovery profiles in the post-anesthesia care unit (PACU)

III. RESULT

TABLE 1. THE EXTRACTED DATA FROM THE REVIEWED LITERATURE

No	Author & Year	Type & Study Design	Population / Sample	Intervention in OFA Group	Intervention in OA / Control Group	Main Findings / Study Results
1.	(Hao et al., 2023)[14]	Prospective, randomized, single-blinded clinical study	80 adult patients undergoing laparoscopic cholecystectomy.	**Induction:** Deksmedetomidin (0.6 ug/kg selama 10 min) + esketamine (0.2 mg/kg). **Maintenance**: Deksmedetomidin (0.5-0.7 ug/kg/h) + esketamine 0.2-0.5 mg/kg/h) + propofol.	**Induction**: Sufentanil (0.3-0.5 ug/kg). **Maintenance**: Remifentanil (0.1-0.3 ug/kg/min) + propofol.	Postoperative Quality of Recovery-15 (QoR-15) scores were significantly higher in the OFA group on postoperative days (POD) 1 and 2. The incidences of postoperative nausea, vomiting, drowsiness, dizziness, fatigue, and dry mouth were substantially lower in the OFA cohort. Additionally, the occurrence of intraoperative hypotension was lower in the OFA group.
2.	(Chen et al., 2023)[8]	Prospective, randomized, single-centre non-inferiority trial under ERAS protocol	77 adult female patients undergoing laparoscopic gynecological surgery.	**Induction:** Deksmedetomidin (0.5 ug/kg selama 10 min) + esketamine (0.3-0.5 mg/kg). **Maintenance:** Deksmedetomidin (0.1-0.3 ug/kg/min) + esketamine (0.3 ug/kg/h) + propofol. **Block regional:** Transversus Abdominis Plane (TAP) block bilateral.	**Induction:** Sufentanil (0.2-0.4 ug/kg). **Maintenance:** Remifentanil (8-10 ug/kg/h) + propofol. **Block regional:** TAP block bilateral.	The OFA analgesic regimen demonstrated non-inferiority to OA within the first 48 hours postoperatively. The OFA cohort exhibited a significantly lower incidence of PONV and superior postoperative sleep quality, as assessed by the Pittsburgh Sleep Quality Index (PSQI). Conversely, emergence time and orientation recovery were slightly prolonged in the OFA group.
3.	(Chassery et al., 2024)[15]	Single-centre, prospective, triple-blind randomized controlled trial	80 patients undergoing ambulatory surgery (day-case) artroplasti panggul total (Total Hip Arthroplasty	**Pre- Induction:** Infus deksmedetomidin (1 ug/kg). **Induction:** Propofol + ketamin (0.4 ug/kg) + salin. **Maintenance:** Infus	**Pre- Induction:** Infus normal salin. **Induction:** Sufentanil (10 ug) + propofol + ketamin (0.4 mg/kg).	There was no significant difference in cumulative 24-hour opioid consumption (expressed as oral morphine equivalents, or OME) between the OSA and OFA groups. Pain scores and the recovery of ambulation

			/THA)	propofol. **Analgesia Multimodal:** Asetaminofen, ketoprofen, nefopam, dexamethasone, and local wound infiltration.	**Maintenance:** Infus propofol. **Analgesia Multimodal:** The patients received the identical non-opioid regimen as administered in the OFA group	were comparable across both cohorts. The incidence of adverse effects was equivalent, with the exception of dizziness, which occurred more frequently in the OSA group. Consequently, OFA demonstrated no additional benefit over ultra-low-dose OSA.
4.	(Dagher et al., 2025)[16]	Prospective, randomized controlled trial	58 pasien obesitas yang menjalani bedah bariatrik (sleeve gastrectomy / gastric bypass)	**Regimen Pasca-Intubasi Multimodal:** lidocaine (1.5 mg/kg bolus followed by a 1.5 mg/kg/h continuous infusion), ketamine (0.2 mg/kg bolus followed by a 0.15 mg/kg/h continuous infusion), magnesium sulfate (50 mg/kg bolus followed by an 8 mg/kg/h continuous infusion), dexmedetomidine (0.2–0.5 ug/kg/h), and a single dose of dexamethasone (8 mg)	**Regimen Berbasis Opioid (OBA):** Fentanyl dosing was titrated according to clinical requirements and the patient's hemodynamic response. The initial loading dose of fentanyl during induction was 1 ug/kg, which was escalated to 3–4 ug/kg at the time of incision, followed by intermittent boluses of 0.5–1 ug/kg intraoperatively.	OFA significantly reduced postoperative morphine consumption. Visual Analog Scale (VAS) pain scores—at rest, during movement, and during coughing—were substantially lower in the OFA group. Beyond 24 hours postoperatively, patients in the OFA cohort required no further morphine administration. Furthermore, patient satisfaction scores were significantly higher in the OFA group.
5.	(Toleska et al., 2023)[9]	Prospective, randomized clinical study	60 patients scheduled for open colorectal cancer surgery (allocated into three groups: the OBAG, LOAG, and OFAG cohorts).	**OFAG group:** Prior to induction, dexamethasone (0.1 mg/kg) and paracetamol (1 g) were administered. Induction was achieved using lidocaine (1 mg/kg), propofol (2 mg/kg), and ketamine (0.5 mg/kg). Maintenance : continuous infusions of lidocaine (2 mg/kg/h), ketamine (0.2 mg/kg/h), and magnesium sulfate (15 mg/kg/h), alongside intermittent bupivacaine administration via a Th9–Th10 thoracic epidural catheter.	**OBAG group:** Fentanyl induction 100 ug. Maintenance : Bolus intermiten fentanyl 50-100 ug IV + bupivacaine epidural. **LOAG group:** Fentanyl induction 100 ug. Prior to induction and upon completion of the surgery 50 ug fentanyl + bupivacaine via epidural was/were administered.	Patients in the OFA group exhibited the lowest Visual Analog Scale (VAS) pain scores throughout the 72-hour postoperative monitoring period compared to both the opioid-based and low-opioid groups. Additionally, postoperative epidural morphine requirements were significantly lowest in the OFA cohort. Notably, the incidence of PONV within the OFA group was 0%.

6.	(Zhang et al., 2025)[17]	Prospective, double-blind, randomized controlled trial	204 adult patients undergoing thyroidectomy.	**Induction:** Loading deksmedetomidin (0.75 µg/kg, 10 min) + midazolam + esketamine 0.5 mg/kg) + propofol. **Maintenance:** Infus deksmedetomidin 0.5--1 µg/kg/h) + esketamine (0.12 mg/kg/h) + propofol. **Block regional:** ultrasound-guided bilateral superficial cervical plexus block (BSCPB).	**Induction:** Midazolam + sufentanil (0.4 µg/kg}$) + propofol. **Maintenance:** Bolus sufentanil 5—10 µg)+ infus propofol + remifentanil 0.1—0.2 µg/kg/min).	The OFA group demonstrated significantly higher Quality of Recovery-15 (QoR-15) scores on postoperative day (POD) 1. OFA enhanced nocturnal sleep quality during the first postoperative night, as measured by the Richards-Campbell Sleep Questionnaire (RCSQ), and reduced both the pain intensity area under the curve (AUC) and the incidence of PONV. However, OFA was associated with prolonged times to extubation and an increased length of stay in the PACU.
7.	(Feng et al., 2024)[18]	Stratified (by sex), randomized controlled trial dipandu monitor Surgical Pleth Index (SPI)	120 adult patients undergoing video-assisted thoracoscopic surgery (VATS) lung resection.	**Induction:** Deksmedetomidin (0.6 µg/kg selama 10 min) + esketamine (0.3 mg/kg) + propofol. **Maintenance:** Sevoflurane + infus deksmedetomidin (0.2--1.0 µg/kg/h) + bolus esketamine (0.1 mg/kg) guided by a Surgical Pleth Index (SPI) target of 20–50.	**Induction:** Sufentanil (0.3 µg/kg) + propofol. **Maintenance:** Sevoflurane + bolus sufentanil (0.1 µg/kg) dipandu target SPI 20–50.	The OFA group successfully halved the incidence of PONV within the first 48 hours postoperatively. Furthermore, the OFA cohort demonstrated a significantly lower rate of vomiting. The efficacy of pain control and postoperative sufentanil consumption were comparable between the two groups, as both utilized sufentanil patient-controlled intravenous analgesia (PCIA). However, the length of stay in the PACU was significantly longer in the OFA group.

IV. Discussion

Current Evidence

The science behind Opioid-Free Anesthesia (OFA) is based on its ability to stop the use of opioids during surgery and also lower the risk of problems that affect the whole body.[8,9,14] Studies from several randomized controlled trials show that OFA, which uses a non-opioid approach with multiple pain treatments before, during, and after surgery, works just as well as traditional opioid-based anesthesia in keeping patients stable and pain-free during surgery.[8,9] For example, in laparoscopic cholecystectomy surgeries, patients who followed an OFA protocol that used both dexmedetomidine and esketamine had much better Quality of Recovery-15 (QoR-15) scores on the first and second days

after surgery compared to those in the OA group.[14] These advantages encompass significant improvements across all five dimensions of recovery; physical comfort, physical independence, psychological support, emotional state, and pain management.[14] This finding confirms that the paradigm shift toward OFA (Opioid-Free Anesthesia) offers substantial clinical benefits in accelerating patient recovery.[19] The success of combining non-opioid agents, such as dexmedetomidine and esketamine, demonstrates a synergistic effect capable of blocking nociceptive pathways through a multimodal approach, without inducing the central nervous system depression typically associated with intraoperative opioid use.

One of the most consistent clinical findings regarding the implementation of the OFA technique is the drastic reduction in the incidence of opioid-related adverse effects, particularly postoperative nausea and vomiting (PONV).[8,9,14,18] In laparoscopic gynecological surgery performed under ERAS (Enhanced Recovery After Surgery) protocols, the use of esketamine- and dexmedetomidine-based OFA suppressed the incidence of PONV to 10.1%, in stark contrast to the OA (Opioid Anesthesia) group, which reached 28.9%.[8] This massive reduction in PONV was further confirmed in Video-Assisted Thoracoscopic Surgery (VATS) lung resection guided by Surgical Pleth Index (SPI), where OFA successfully halved the risk of nausea, vomiting, and retching.[18] From a clinical perspective, this massive suppression of PONV is a highly crucial achievement. PONV not only diminishes the patient's physical comfort but also carries a high risk of delaying early mobilization, increasing the risk of surgical wound dehiscence, and prolonging the duration of hospital stay. Consequently, the capability of the OFA protocol to reduce PONV by more than half compared to conventional methods serves as a foundational pillar for the successful implementation of global ERAS programs.[20]

Although acute perioperative pain management via OFA techniques has proven highly effective, its impact on reducing postoperative opioid consumption within the first 24 hours exhibits variability depending on the surgical typology.[9,15,16] In laparoscopic bariatric surgery, a five-agent OFA protocol combining lidocaine, ketamine, magnesium sulfate, dexmedetomidine, and dexamethasone significantly minimized postoperative morphine consumption, with a median dose of 8 mg compared to 19 mg in the OA group, and even completely eliminated the need for morphine 24 hours post-surgery.[16]

Similarly, in open colorectal cancer surgery, the OFA group recorded the lowest Visual Analog Scale (VAS) pain scores throughout the first 72 hours, along with a significantly lower postoperative morphine requirement compared to both the OA group and the low-opioid group.[9] Conversely, in day-case total hip arthroplasty (THA) procedures, the adoption of OFA demonstrated no significant difference in cumulative 24-hour postoperative opioid consumption when compared to a low-dose Opioid-Sparing Anesthesia (OSA) technique.[15] This indicates that total intraoperative opioid elimination does not invariably confer additional analgesic benefits over an optimally combined opioid-sparing strategy (OSA) utilizing a multimodal regimen of acetaminophen, NSAIDs, nefopam, and local wound infiltration.[15] This variability in postoperative opioid consumption highlights an important clinical insight, a one size fits all approach cannot be applied to OFA across all surgical types[21].

In procedures involving extensive visceral manipulation, such as laparoscopic bariatric and open colorectal surgeries, OFA proves superior in dramatically reducing postoperative morphine requirements because its multimodal regimen effectively counteracts opioid-induced hyperalgesia (OIH) and central sensitization typically associated with widespread tissue trauma.[10]

Conversely, in musculoskeletal procedures like THA, when the OSA strategy is already optimized with local wound infiltration and non-opioid analgesics, total intraoperative opioid elimination yields no additional significant analgesic benefits, as the localized pain pathways are already adequately managed. Therefore, selecting between a pure OFA strategy or an optimized OSA technique must be highly individualized through a tailored approach based on the surgical typology, organ-specific pain characteristics, and individual patient risk profiles to achieve the most efficient, safe, and rational clinical outcomes.[15]

CLINICAL APPLICATIONS

In contemporary clinical practice, the application of OFA has rapidly evolved as a central pillar of Enhanced Recovery After Surgery (ERAS) protocols, aimed at facilitating early mobilization and functional recovery.[8,14–16,18] This technique is preferentially indicated for high-risk patient subpopulations vulnerable to perioperative respiratory complications, such as morbidly obese individuals undergoing bariatric surgery and patients with obstructive sleep apnea (OSA).[16,22]

The medical community has also widely implemented this approach in ambulatory or day-case surgical procedures including THA, laparoscopic gynecology, and thyroidectomy to expedite discharge readiness without the confounding risk of respiratory depression.[8,15,17] This target-specific utilization highlights how OFA directly solves the classic dilemma of balancing profound perioperative analgesia with immediate respiratory safety. By eliminating opioid-induced respiratory depression, OFA allows clinicians to confidently fast-track vulnerable patient cohorts through post-anesthesia care units, transforming high-risk surgeries into highly predictable, manageable procedures and maximizing day-case discharge efficiency.

In addition to maintaining robust perioperative hemodynamic stability, OFA exerts a significant protective effect on postoperative sleep quality.[8,17] Objective evaluations utilizing the Pittsburgh Sleep Quality Index (PSQI) in gynecological surgery and the Richards-Campbell Sleep Questionnaire (RCSQ) in thyroidectomy procedures demonstrate that patients receiving an esketamine- and dexmedetomidine-based OFA regimen experience a meaningful improvement in nocturnal sleep quality compared to baseline preoperative status, a clinical benefit completely absent in opioid-based cohorts.[8,17] This phenomenon is highly suspected to be associated with the pharmacological capability of esketamine and dexmedetomidine to prolong deep sleep duration and modulate circadian rhythms.[17]

From a physiological standpoint, preserving and enhancing postoperative sleep architecture is far more than a matter of patient comfort, it is a vital homeostatic component that downregulates the neuroendocrine stress response, reduces catabolism, and accelerates tissue healing. While standard opioids disrupt sleep architecture by suppressing rapid eye movement (REM) and slow wave sleep, the esketamine-dexmedetomidine synergy actively preserves these restorative cycles, presenting a profound secondary systemic benefit that directly advances functional recovery.

Furthermore, in oncological surgeries such as colorectal cancer resection, minimizing intraoperative opioid exposure via OFA plays a crucial role in preventing the suppression of cellular and humoral immunity, which theoretically possesses the potential to suppress cancer cell proliferation and perioperative metastatic spread.[9] This immunological preservation constitutes perhaps the most compelling long-term justification for OFA in cancer surgery. Traditional opioids are known to inhibit natural killer (NK) cell activity and T-cell

proliferation, inadvertently creating an immunosuppressive perioperative window that favors circulating tumor cell survival.[23] By shielding the patient's immune system from this opioid-driven impairment during the critical surgical window, OFA transcends acute pain management, evolving into a potential perioperative oncological intervention that may influence long-term disease-free survival and recurrence outcomes.

FUTURE PERSPECTIVES

Despite promising improved clinical outcomes, the universal implementation of OFA techniques in future practice still encounters several clinical challenges, particularly regarding emergence recovery profiles and monitoring standardization.[8,17,18] Current literature indicates that the perioperative utilization of high dose non-opioid adjuvants, such as dexmedetomidine, significantly contributes to delayed extubation and prolongs the length of stay in the Post-Anesthesia Care Unit (PACU) due to deeper residual sedation upon patient arrival at the recovery room.[8,17,18]

Furthermore, sympathetic system activation induced by agents such as esketamine frequently triggers intraoperative blood pressure elevations; paradoxically, this can prompt anesthesiologists to escalate hypnotic (propofol) dosages, thereby inadvertently slowing the trajectory of emergence and cognitive recovery.[17,18]

This intricate pharmacological interplay reveals a delicate trade-off within OFA protocols: while the technique successfully shields the patient from opioid-related side effects, it shifts the clinical burden toward managing prolonged sedation and hemodynamic fluctuations.[24] The paradoxical escalation of hypnotics to counter esketamine induced sympathetic surges highlights a critical gap in current practice specifically, the danger of misinterpreting drug-induced hemodynamic changes as signs of inadequate anesthesia depth. Without clear, objective monitoring protocols that can differentiate between sympathetic activation and true awareness, clinicians risk oversedating patients.[25] Consequently, resolving these emergence delays will require a shift away from reactive, symptom-based drug titration and toward standardized, objective neuromonitoring to balance the clear benefits of OFA with predictable, rapid recovery profiles.

V. CONCLUSION

In conclusion, Opioid-Free Anesthesia (OFA) is a safe and effective technique that offers non-inferior intraoperative stability and analgesic efficacy compared to conventional opioid-based anesthesia. As a central pillar of ERAS protocols, its primary strengths include significantly enhancing postoperative recovery scores (QoR-15), drastically reducing PONV, preventing respiratory depression in high-risk patients (morbid obesity/OSA) and day-case surgeries, improving postoperative sleep, and preserving immunity in oncological cases. However, its ability to decrease 24-hour postoperative opioid consumption is highly specific to the surgical typology and is not always superior to an optimized opioid-sparing strategy (OSA).

Moving forward, the universal adoption of OFA faces challenges such as delayed extubation, prolonged PACU stay from residual sedation, and esketamine-induced hemodynamic fluctuations. To mitigate these risks, the future trajectory of OFA must prioritize standardized dosing protocols alongside advanced objective monitoring, including processed electroencephalography (pEEG) and nociception indices like the Surgical Pleth Index (SPI). Transitioning toward this precise, tailored approach will ultimately maximize patient safety and optimize individualized perioperative care.

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