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# Opioid-sparing versus opioid-free anesthesia following cancer surgery : Effect on pain severity and patient-reported outcomes

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Systematic Review

## ABSTRACT

Opioid use in anesthesia during cancer surgery causes concerns about adverse effects, including postoperative nausea, vomiting, respiratory depression, and potential impacts regarding cancer recurrence. In response, opioid-sparing and opioid-free anesthesia procedures have emerged as promising strategies to reduce opioid consumption while maintaining effective pain management. This study aimed to analyze the outcome of opioid-sparing anesthesia compared to opioid-free anesthesia on pain severity and patient-reported outcomes following cancer surgery. Randomized controlled trials and observational research that met predefined inclusion criteria were systematically selected, with data extracted and analyzed. The analysis revealed that both opioid-sparing and opioid-free anesthesia techniques reduced postoperative pain severity significantly in comparison to traditional opioid-based anesthesia. Additionally, patients who received opioid-free anesthesia reported better overall outcomes, including reduced nausea, faster recovery times, and improved satisfaction scores. Although pain control differences between opioid-sparing and opioid-free anesthesia techniques were statistically insignificant, both techniques showed substantial as safer, effective alternatives in perioperative cancer care, supporting their broader adoption in clinical practice.

## INTRODUCTION

Historically, opioids have been a cornerstone of anesthesiology. In France, opioid prescriptions surged by 104% from 2004 to 2017, with 1.1% of the population receiving strong opioids in 2017. Overconsumption of opioids was accompanied by a 98% rise in overdose incidents during the same period.[1] Postoperatively, approximately 50% of patients are given prescriptions for strong opioids, and over 3% continue using them three months later.[2] Several unfavorable effects related to opioid use, namely depression of the respiratory system, sedation, chest stiffness, cough depression, bronchoconstriction, and postoperative nausea and vomiting (PONV), affect 25% and 52% of patients, respectively.[3,4] The opioid death rate among cancer patients rose from 0.52 to 0.66 per 100,000. In contrast, the general population's rate increased from 5.33 to 8.97 per 100,000.[5] Furthermore, opioids can lead to hyperalgesia, tolerance, and dependence, complicating pain control and increasing the risk of unfavorable effects.

New anesthetic approaches aim to reduce opioid use through alternative strategies.[5,6] opioid-free anesthesia (OFA) and opioid-reduced anesthesia (ORA) are two such methods. OFA

employs a multimodal analgesia approach, using a combination of regional anesthesia, NMDAR antagonists, anti-inflammatory drugs, and α-2 agonists to minimize opioid use. This approach targets multiple mechanisms of nociception, the sensory process of pain. Despite its potential, OFA remains debated, with mixed findings in recent meta-analyses. Some studies report improved postoperative outcomes and reduced PONV with OFA, while others find no significant differences in analgesia or opioid consumption. ORA, on the other hand, seeks to reduce rather than eliminate opioid use during surgery.[7,8] The findings of this review have the potential to make a significant contribution to healthcare practices in Indonesia, particularly in the management of postoperative pain in cancer patients. Amid limited access to medical opioids and the risk of misuse, approaches such as OFA and ORA may serve as strategic solutions to enhance the safety and effectiveness of anesthesia.

This systematic review evaluates the impacts of opioid-sparing and opioid-free anesthesia regarding pain severity and patient-reported results after cancer surgeries. The focus will be on comparing opioid requirements during and after surgery, pain scores, and side effects related to opioids between traditional opioid-based anesthesia and OFA/ORA protocols.

## METHODS

This systematic review protocol has been registered in the PROSPERO database (registration number: **1059041**)

### Inclusion and Exclusion

For this review, the inclusion criteria were (1) studies involving patients undergoing cancer surgery, (2) comparative studies of opioid-sparing anesthesia (OSA) versus opioid-free anesthesia (OFA), (3) inclusion of randomized controlled trials (RCTs) and observational studies, and (4) availability of full-text versions. Reviewers independently evaluated papers, and data extraction was conducted using a standardized form. Key information extracted included study authorship, publication year, research method, number of samples, and details on anesthesia protocols and outcomes.

### Search Strategy and Information Sources

Following the Preferred Reporting Items for systematic reviews and meta-analysis (PRISMA) guidelines, the authors systematically searched English-language studies published between 2014 and 2024 across several databases: PubMed, ScienceDirect, Sage Database, and Cochrane. Relevant articles were identified using the keywords ("analgesics opioid"[Pharmacological Action] OR "analgesics, opioid"[MeSH Terms] OR ("analgesics"[All Fields] AND "opioid"[All Fields]) OR "opioid analgesics"[All Fields] OR "opioid"[All Fields] OR "opioids"[All Fields] OR "opioid s"[All Fields]) AND "free"[All Fields] AND ("anaesthesia"[All Fields] OR "anesthesia"[MeSH Terms] OR "anesthesia"[All Fields] OR "anaesthesias"[All Fields] OR "anesthesias"[All Fields]) AND ("cancer s"[All Fields] OR "cancerated"[All Fields] OR "canceration"[All Fields] OR "cancerization"[All Fields] OR "cancerized"[All Fields] OR "cancerous"[All Fields] OR "neoplasms"[MeSH Terms] OR "neoplasms"[All Fields] OR "cancer"[All Fields] OR "cancers"[All Fields]) AND ("surgery"[MeSH Subheading] OR "surgery"[All Fields] OR "surgical procedures, operative"[MeSH Terms] OR ("surgical"[All Fields] AND "procedures"[All Fields] AND "operative"[All Fields]) OR "operative surgical procedures"[All Fields] OR "general surgery"[MeSH Terms] OR ("general"[All Fields] AND "surgery"[All Fields]) OR "general surgery"[All Fields] OR "surgery s"[All Fields] OR "surgerys"[All Fields] OR "surgeries"[All Fields])) AND (y_10[Filter]) AND Additionally, we reviewed reference lists of key papers to identify further relevant studies manually.

### Description of Studies Based on Criteria

A total of 1530 entries were found during the identification phase by searching databases. 1230 records were left for screening after 300 duplicates were eliminated. A total of 330 full-text articles were assesed for their eligibility after 900 records were excluded during the screening

phase due to title and abstract screening. 275 of these papers were disqualified for a variety of reasons, including failure to meet inclusion requirements, insufficient data, or results that were not pertinent. Ultimately, the systematic review contained 55 studies. This graphic clearly illustrates the exacting procedure of screening and selecting research to ensure that only those that fulfill specific criteria are incorporated into the final analysis.

**Quality Assessment and Risk of Bias Assessment**

The authors applied the risk of bias in non-randomized studies of exposure (ROBINS-E) to assess potential bias in observational studies. Figure 2 provides a visual representation of the results. Any disagreements were settled by consensus. Based on an evaluation of the thirteen examined studies, the majority show a minimal risk of bias in terms of blinding of outcome assessment and random sequence generation.

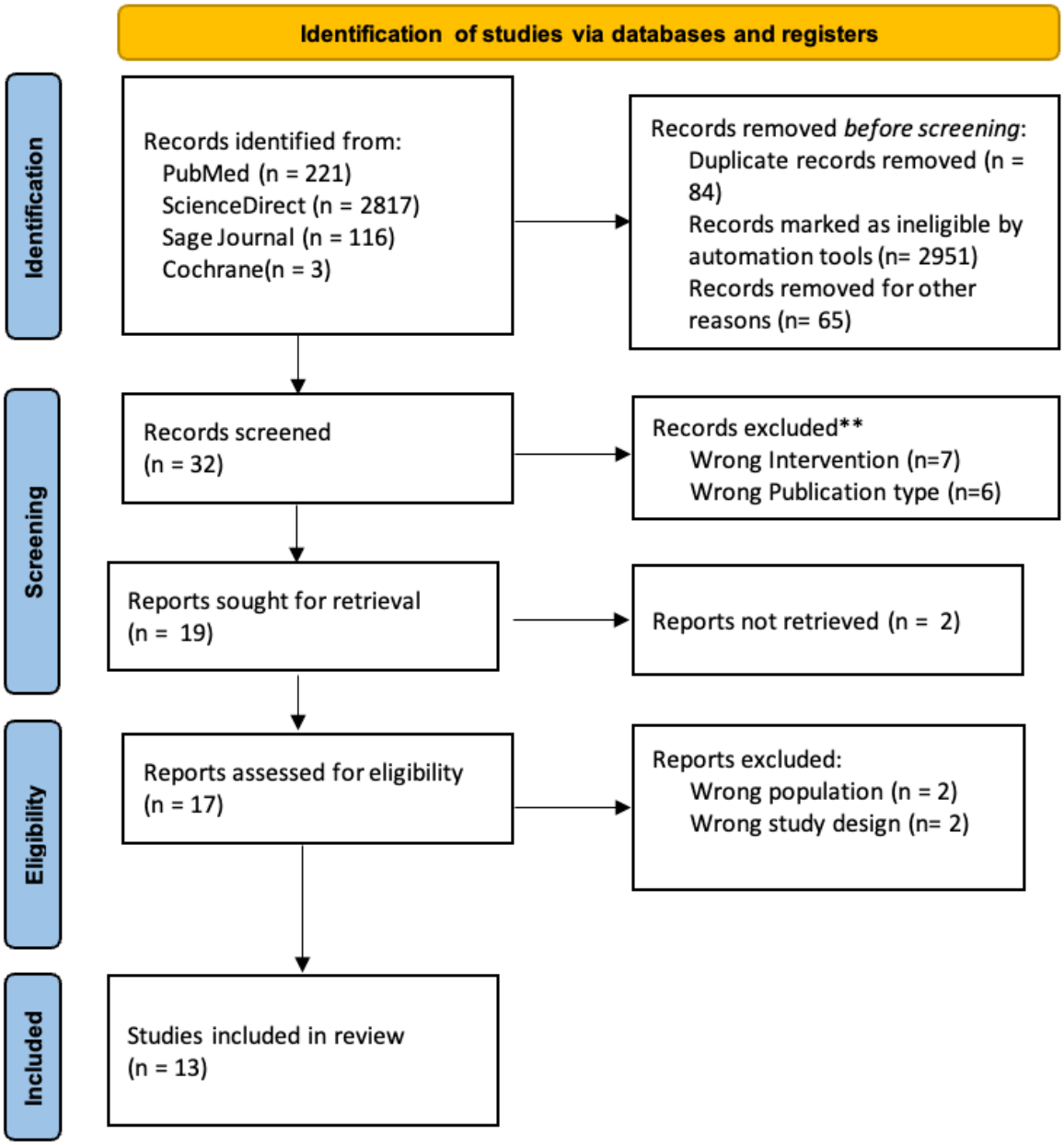


Figure 1. Flowchart of the study

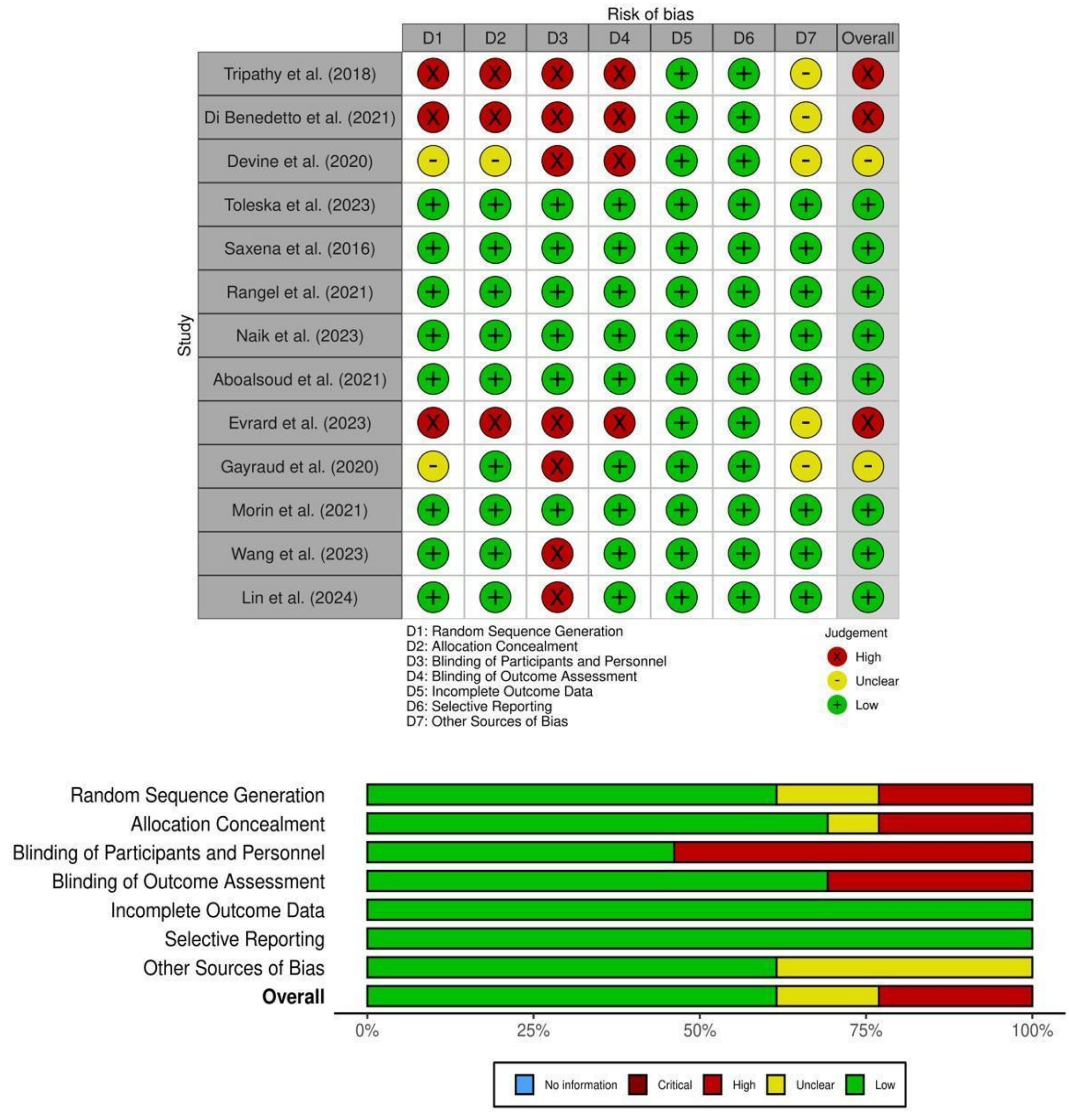


Figure 2. Risk of bias assessment

## RESULTS

### Study Characteristics

The studies explored various aspects of opioid-free and opioid-sparing anesthesia across a variety of surgical procedures and settings. Thirteen studies were included in this systematic review. The Various aspects of opioid-free and opioid-sparing anesthesia across different surgical procedures are listed in (Table 1).

In India, Tripathy et al. conducted an observational study analyzing participants who received opioid-free compared to opioid-based anesthesia in breast malignancy surgeries. They found that opioid-free anesthesia reduced recovery time, less nausea, decreased analgesic requirements, and improved overall patient satisfaction.[11] Similarly, Di-Benedetto et al. performed a cross-sectional study on quadrantectomy patients. Previous study observed the effect of opioid-free anesthesia in the reduction of pain severity, nausea, and vomiting after surgeries.[12]

Table 1. Various aspects of opioid-free and opioid-sparing anesthesia across different surgical procedures

| No. | Author | Study (Year) | Country | Study design | Sample | Post Surgery Anesthesia | Description |
|---|---|---|---|---|---|---|---|
| 1. | Tripathy et al.[11] | 2018 | India | Observational study | 24 patients | Opioid free vs Opioid anesthesia | Opioid-free anesthesia resulted in less recovery time, nausea, and analgesic use. Better overall satisfaction. |
| 2. | Di Benedetto et al.[12] | 2020 | India | Cross-sectional Study | 89 patients | Opioid free vs Opioid anesthesia | Opioid-free group experienced lower pain scores and nausea/vomiting, with similar patient satisfaction. |
| 3. | Devineet et al.[13] | 2020 | Australia | Retrospective, propensity-matched, case-control study. | 83 patients | Opioid free vs control (standard technique) | Opioid-free group had less pain at 1 hour post-surgery; pain scores and morphine use were similar at 24 hours. |
| 4. | Toleska et al.[14] | 2019 | Israel | Prospective and randomized clinical | 27 patients | Opioid based vs Opioid Sparing vs Opioid Free Anesthesia | Opioid-free anesthesia resulted in lower pain scores and no nausea/vomiting, with reduced need for additional analgesics. |
| 5. | Saxena, et al.[15] | 2016 | Belgium | A prospective, randomized, controlled trial | 66 patients | Opioid free vs control | Opioid-free group had better quality of recovery scores and used less piritramide. |
| 6. | Rangel et al.[16] | 2021 | Brazil | A randomized prospective clinical trial | 146 patients | opioid-free anesthesia vs opioid-based anesthesia groups. | Biochemical recurrence rates were similar; other factors influenced recurrence more than anesthesia type. |
| 7. | Naik et al.[17] | 2023 | India | Randomized control trial | 130 patients | Opioid-Based vs Opioid-Free Anesthesia | Opioid-free anesthesia reduced nausea/vomiting and maintained stable hemodynamics. |
| 8. | Rana et al.[18] | 2021 | Egypt | Randomized control trial | 40 patients | Opioid free versus opioid based anesthesia | Opioid-free group had lower pain scores, less nausea/vomiting, and higher patient satisfaction. |
| 9. | Evrardet al.[19] | 2023 | France | A retrospective study | 172 patients | Opioid Reduced vs control | Opioid-reduced anesthesia used less morphine, had fewer complications, but more bradycardia and hypoxemia. |
| 10. | Guillaume et al.[20] | 2020 | France | Retrospective study with propensity-adjusted analysis. | 175 patients | Opioid sparing | Opioid-sparing anesthesia reduced opioid use, pain scores, and incidence of nausea/vomiting. |

| No. | Author | Study (Year) | Country | Study design | Sample | Post Surgery Anesthesia | Description |
|---|---|---|---|---|---|---|---|
| 11. | Morin et al.[21] | 2021 | US | Prospective cohort | 1153 patients | Opioid sparing anesthesia vs control | Opioid-sparing group had lower pain scores and opioid use, with fewer severe pain episodes. |
| 12. | Wang et al.[22] | 2023 | China | An open-label, randomized, controlled, non-inferiority trial | 106 patients | opioid-free postoperative pain management strategy versus a conventional opioid-based | Both groups had similar pain control; opioid-free group had lower nausea/vomiting rates. |
| 13. | Lin et al.[23] | 2024 | China | An open-label, randomized, controlled, non-inferiority trial. | 96 patients | opioid-free postoperative pain management strategy versus a conventional opioid-based | No significant difference in pain levels; opioid-free group had quicker recovery and less nausea/vomiting. |

Across various regions, studies have compared opioid-free anesthesia (OFA) with opioid-based or opioid-sparing techniques, offering valuable insights into its postoperative outcomes. In Australia, Devine et al. conducted a case-control study on lung cancer resections and reported that OFA provided comparable pain control at 24 hours but significantly reduced pain severity one hour after surgery, with similar morphine usage between groups. [13] In Israel, Toleska et al. found that OFA in colorectal malignancy surgery resulted in the lowest pain scores, absence of nausea/vomiting, and reduced need for rescue analgesics compared to opioid-based and opioid-sparing methods.[14] In Belgium, a randomized controlled trial demonstrated that OFA improved postoperative recovery quality and reduced piritramide consumption. [15]

In Brazil, a study assessing recurrence in prostate cancer after OFA found no significant difference compared to opioid-based anesthesia, suggesting that other clinical factors may play a more dominant role in recurrence. [16] Similarly, in India, Naik et al. evaluated breast cancer surgeries and found that OFA resulted in fewer episodes of postoperative nausea and vomiting, with more stable hemodynamic parameters. [17] In Egypt, Aboalsoud et al. conducted a randomized controlled trial in breast cancer patients and showed that OFA led to significantly lower pain severity, fewer nausea/vomiting events, and greater patient satisfaction. [18]

In France, two retrospective studies further support the use of reduced-opioid approaches. Evrard et al. observed lower morphine usage in opioid-reduced anesthesia during head and neck oncological surgery, albeit with increased rates of bradycardia and hypoxemia. [19] Gaylot et al. reported decreased opioid consumption, pain intensity, and postoperative nausea/vomiting in opioid-sparing anesthesia cases. [20] In the United States, Morin et al. found that OFA during tumor resections was associated with lower pain scores, decreased opioid consumption, and reduced incidence of severe postoperative pain. [21] Lastly, in China, Wang et al. showed in a randomized study that OFA provided comparable pain control but reduced nausea/vomiting in major hepatectomy[22], while Lin et al. found similar pain scores but faster recovery and less nausea/vomiting in patients undergoing laparoscopic radical gastrectomy. [23]

Those studies highlight the possible advantages of both opioid-free and opioid-assisted anesthesia methods, including reduced postoperative pain, lower rates of nausea/vomiting, and greater patient satisfaction. However, the specific benefits may differ depending on the type of surgery and anesthesia used.

**Outcomes of Opioid-Free and Opioid-Sparing Post-Surgery Anesthesia**

Tripathy et al. conducted an observational study in India comparing OFA with opioid-based anaesthesia (OBA) in 24 radical mastectomies with axillary dissection. The study concluded that opioid-free anesthesia was effective, significantly shortened recovery room time, reduced postoperative nausea, decreased analgesic use, and improved the score of the visual analog scale (VAS) compared to opioid-based anesthesia. Surgeons and patients reported high satisfaction and good quality of life on the seventh postoperative day.[11] Di-Benedetto et al. performed a retrospective analysis of 89 patients who underwent quadrantectomy and compared patients who obtained OFA evaluated accesed between those given opioid-inclusive anesthesia (OIA). Results showed that postoperative pain scores at various time points in OFA group were lower, and the need for additional analgesics was reduced. The PONV was also lower in the OFA group, while patient satisfaction remained similar in both groups.[12]

A study conducted by Devine et al. in Australia involving 83 patients undergoing lung cancer resection in both the OFA and standard anesthesia (STD) groups reported that the difference in pain severity at 0 or 24 hours after the surgical procedure was not significant. However, the OFA group reported significantly lower pain levels one hour after surgery. Although mean patient-controlled analgesia morphine consumption and recovery time were comparable in both groups, the OFA group spent less time in the hospital.[13]

Toleska et al. report on a randomized clinical study in Israel comparing OBA, low-opioid anesthesia (LOA), and OFA in 60 patients undergoing colorectal tumor surgery. The OFA group showed significantly lower VAS at 2, 12, 24, and 48 hours postoperatively compared with the OBA and LOA groups. Furthermore, the OFA group experienced a decreased incidence of PONV and

less reliance on additional analgesics.[14]

Saxena et al. carried out an RCT study in Belgium in 66 patients to analyze opioid-free anesthesia versus opioid-based anesthesia. The OFA Group shown a doubtful clinical significance of this difference, but in comparison to the OBA group, the postoperative recovery rating 40 (Qor-40) was higher. The OFA Group has little use of piritramide after surgery, indicating a decrease in opioid consumption.[15]

Rangel et al. conducted a prospective randomized clinical study in 146 subjects undergoing prostate cancer surgery in Brazil, analyzing non-opioid anesthesia versus opioid-based anesthesia. No significant differences were found in biochemical recurrence-free survival accross different categories. There was a correlation between obesity, high risk of dummy colon, laparoscopic surgery, stage 3 tumor pathology, and positive surgical margins with shorter biochemical recurrence-free survival, whereas the choice of anesthesia had no impact on these outcomes.[16]

Naik et al. in a randomized controlled study in India, included 130 patients in breast malignancy surgical procedure, opioid-free anesthesia was superior in minimizing side effects, namely postoperative nausea, vomiting, stabilizing bleeding, compared to opioid-based anesthesia.[17]

Aboalsud et al. noted that in a randomized controlled trial in Egypt of 40 patients in unilateral radical mastectomy, the OFA group had significantly diminished pain severity at rest and on mobilization, lower nausea and vomiting after surgery, and higher patient satisfaction scores relative to the opioid-based anesthesia group. Furthermore, the OFA group showed a reduced incidence of neuropathic pain and significant changes in inflammatory markers.[18]

Ebrard et al. compared opioid-reduced anesthesia with standard anesthesia in a retrospective study conducted in France in 172 patients undergoing major head and neck tumor surgery and found that opioid-reduced anesthesia consumed less morphine at the end of the surgical operation. However, a study observed no differences in the postoperative pain management and also pain scores between the two categories, although this group had a higher incidence of bradycardia and hypoxemia.[19]

Gayraud et al on a retrospective study in France to analyze the impact of a single preoperative paravertebral block on opioid use and postoperative pain in radical mastectomy with immediate reconstruction. Their results have shown that the use of the paravertebral block reduced the administration of opioids during the operation, reduced the severity of pain, and reduced the occurrence of nausea and vomiting after surgery.[20]

Morin et al. compared participants who were given an opioid-sparing multimodality analgesia protocol with those who did not in a United States prospective cohort study of 1,153 tumor resection patients. The study found that the opioid-sparing protocol significantly reduced mean pain scores and decreased the occurrence of severe pain. Participants in the previous study with the opioid-free group were also given reduced doses of opioid medications after discharge.[21]

A previous study conducted a randomized controlled non-inferiority trial to compare opioid-free pain management for postoperative recovery with a conventional opioid-based approach following major hepatectomy in China. There were no significant differences in the need for additional analgesics or in pain scores among groups. However, the opioid-free group experienced a decrease rate of nausea and vomiting after surgery, as well as fewer serious complications.[22]

Lin et al. on a randomized controlled trial in China that was compared opioid-free postoperative pain control with conventional opioid-based treatment after laparoscopic radical gastrectomy. Although the difference in pain scores was not significant, groups that did not include opioids experienced faster recovery time, such as previous defecation, post -operative nausea and vomiting.[23]

## DISCUSSION

The Efficacy OFA versus OBA has been investigated in several studies, reflecting a growing interest in minimizing opioid consumption due to their associated side effects. Each study

contributes to understanding the efficacy and safety of opioid-free techniques in various surgical contexts. An observational study comparing opioid-free and opioid-anesthesia for modified radical mastectomy was carried out in India by Tripathy et al. According to their findings, anesthesia without opioids decreased postoperative nausea, reduced the need for analgesics, and increased patient satisfaction.[11] This aligns with the study by Naik et al, which supports opioid-free anesthesia's effectiveness in reducing postoperative nausea and vomiting while maintaining stable hemodynamics. Both studies emphasize improved recovery metrics and patient satisfaction with opioid-free approaches in breast malignancy surgical procedure.[17]

Devine et al. and Wang et al. explored opioid-free anesthesia in different contexts. Devine's case-control study revealed that opioid-free techniques did not show significant differences in pain scores compared to standard techniques, although opioid-free groups reported lower pain scores at specific intervals.[13] Similarly to Wang's study on major hepatectomy found similar postoperative pain management efficacy between opioid-free and conventional methods, with opioid-free strategies leading to fewer complications such as nausea and vomiting. These studies underscore the promising advantages of opioid-free anesthesia in lowering certain side effects while maintaining similar pain control.[22]

Toleska et al. and Lin et al. provided insights into opioid-sparing and opioid-free approaches for colorectal and gastrectomy surgeries, respectively.[14,23] Toleska's randomized clinical trial highlighted that opioid-free anesthesia resulted in lower VAS (visual analog scale) scores for pain compared to opioid-based and low-opioid strategies. Similarly, Lin's study found opioid-free postoperative pain management to be non-inferior to conventional methods yet superior in terms of faster recovery and reduced nausea. These results suggest that opioid-free techniques may offer both analgesic efficacy and improved recovery profiles.[14]

Two previous studies investigated the broader implications of opioid-free anesthesia. Rangel's study biochemical recurrence rates were comparable between groups for prostate cancer patients between opioid-free and opioid-based groups, indicating that the choice of anesthesia might not influence cancer recurrence.[16] On the other hand, Aboalsoud's research on breast cancer surgery found opioid-free anesthesia associated with decreased pain scores, reduced incidence of neuropathic pain, and improved immune response markers. These findings suggest potential benefits of opioid-free anesthesia beyond pain management.[18]

When comparing opioid-reduced anesthesia to control groups in major cervicofacial surgery, Evrart et al. saw lower opioid use and fewer postoperative problems.[19] Guillaume et al. explored paravertebral blocks, highlighting their role in reducing opioid use and postoperative pain.[20] Similarly, Morin et al. reported superior pain control with opioid-sparing multimodal analgesia in lumpectomy patients, supporting the practice of various opioid-sparing techniques to improve pain control.[21] These studies collectively suggest that opioid-free and opioid-sparing anesthetic strategies can be efficient in managing postoperative pain, reducing opioid-related side effects, and improving patient outcomes across various types of surgeries. The opioid method is expected to improve patient recovery and satisfaction, but opioid and standard approaches need to adapt to individual patients and surgical contexts.

By 2030, low- and middle-income countries (LMICs) are projected to face 24.1 million new cancer cases annually, with 70% of global cancer deaths occurring in these regions. This highlights the urgent need to strengthen cancer care and broader noncommunicable disease (NCD) management as part of global health strategies. Achieving Sustainable Development Goal (SDG) 3.4—which targets a one-third reduction in premature mortality from NCDs by 2030—is increasingly uncertain, particularly in LMICs where health systems remain under-resourced and fragmented. [24,25] While prevention is essential, it is insufficient on its own. According to WHO's Best Buys for NCDs, effective reduction also requires accessible treatment and well-integrated care systems. Many LMICs still lack the infrastructure, trained personnel, and service delivery models needed for optimal cancer care. Strengthening these systems through cost-effective interventions across the care continuum not only improves cancer outcomes but also reinforces health system resilience. Ultimately, a healthy population is both a prerequisite for and a product of sustainable development. [24,25]

The case reports and findings presented in this review have important implications for achieving the Sustainable Development Goals (SDGs) in Indonesia, particularly SDG 3.4, which aims to reduce premature mortality from non-communicable diseases (NCDs), including cancer, by one-third through prevention, health promotion, and improved healthcare services. The OFA and ORA approaches have the potential to improve the quality of postoperative pain management in cancer patients more safely and effectively, especially amid limited healthcare resources and the risk of opioid misuse in Indonesia. [26]

Adopting evidence-based and cost-effective anesthetic strategies, Indonesia can strengthen its national health system in the context of cancer surgery services—which remains a significant challenge in regional hospitals and oncology centers. This aligns with the country's health system transformation policies, which emphasize quality, accessibility, and sustainability in healthcare services.

Moreover, implementing OFA and ORA techniques may reduce dependence on costly and high-risk opioid medications, supporting national efforts toward pharmaceutical self-reliance and efficiency. The application of these practices in healthcare facilities could lead to fewer postoperative complications, faster patient recovery, and reduced treatment costs, all of which contribute to sustainable development goals in health and community well-being.

The systematic review presents several strengths that support its overall credibility. A key advantage is encompassing a broad variety of study designs and populations, including randomized controlled trials, cohort studies, and observational studies. This variety enhances the applicability of the findings across various surgeries and patient demographics. The comparative evaluation of OFA against OBA in numerous contexts allows for a thorough examination of OFA's effectiveness and safety. Furthermore, the review considers an extensive array of outcomes, namely pain severity, postoperative nausea and vomiting, opioid usage, recovery duration, and patient satisfaction, thus providing a comprehensive understanding of OFA's impact. By including recent studies, the review ensures that its findings are aligned with contemporary practices and advancements in anesthesia techniques, keeping the results relevant.

Nevertheless, there are several limitations to be mindful of. The diversity among the included studies regarding surgical procedures, anesthesia methods, and outcome metrics introduces variability in the results, making it challenging to draw firm conclusions. Some studies may exhibit methodological flaws, such as small sample sizes, retrospective approaches, or inadequate blinding, which could undermine the reliability of the findings. Additionally, discrepancies in how outcomes are reported and measured across studies further complicate the synthesis of results and hinder the possibility of conducting a thorough meta-analysis. Moreover, the review predominantly emphasizes short-term outcomes, such as immediate postoperative pain and recovery, with insufficient data addressing long-term effects and quality of life. There is also the potential for bias, as research with promising results tends to be presented, which could skew the perceived advantages of OFA over OBA.

## CONCLUSION

The findings from this systematic review demonstrate the potential advantages of OFA and OSA over conventional OBA in the perioperative management of cancer surgeries. The OFA and OSA were consistently associated with improved postoperative results, such as lower pain severity, reduced PONV, and better patient satisfaction. Notably, several studies highlighted that OFA led to reduced recovery times, fewer analgesic requirements, and more stable hemodynamics, emphasizing its utility in minimizing opioid-related side effects. Studies on the impact of OFA and OSA on patient-reported outcomes revealed improvements in postoperative quality of recovery and reduced reliance on opioids post-discharge.

## CONFLICT OF INTEREST

There is no conflict of interest in this study.

## REGISTRATION AND PROTOCOL

The protocol for this review has been registered with the PROSPERO database (registration number: 105904) to maintain transparency and avoid duplication of efforts.

## ACKNOWLEDGMENTS

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## DATA AVAILABILITY STATEMENT

The authors kindly note that they did not receive any outside funding, institutional support, or outside help in the development of this work

## SUPPLEMENTARY MATERIAL(S)

No supplementary materials are provided with this article. All relevant content is included within the main text and reference list.

## AUTHOR CONTRIBUTION

All authors are responsible for conceptualization until writing, reviewing, and editing the manuscript.

## DECLARATION OF USING AI

The authors manually evaluated and validated each selection, however Rayyan AI software was used to help with the article selection process in compliance with the PRISMA guidelines. Furthermore, this review article's typographical and grammatical problems were fixed by artificial intelligence techniques before being proofread by a professional. The authors affirm that the study data was neither generated or interpreted by artificial intelligence (AI) and that all intellectual content, interpretation, and findings are wholly original.

## LIST OF ABBREVIATIONS

LOA : Low opioid anesthesia; PONV : Postoperative nausea and vomiting; OBA : Opioid-based anesthesia; OFA : Opioid-Free Anesthesia; OLA : Opioid-inclusive anesthesia; ORA : Opioid-Reduced Anesthesia; OSA : Opioid-sparing anesthesia; PRISMA : Preferred Reporting Items for Systematic Reviews and Meta-Analysis; QoR-40 : Quality of Recovery-40; RCT : Randomized controlled trial; ROBINS- E : Risk of Bias in Non-randomized Studies of Exposure; STD : Standard anesthesia; VAS : Visual analog scale.

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