

Opioid-Free Versus Opioid-Sparing Anesthesia for Laparoscopic Surgery: Postoperative Recovery and Analgesic OutcomesNaresh Kumar Deshmukh¹, Anshul Diwakar², Amitabh Lalji Sahoo³¹Department of Anaesthesiology, Abhishek I Mishra Memorial Medical College and Research (AIMMMCR), Bhilai, Chhattisgarh, India²Assistant Professor, Department of Anaesthesiology, Abhishek I Mishra Memorial Medical College and Research (AIMMMCR), Bhilai, Chhattisgarh, India³Associate Professor, Department of Anaesthesiology, Abhishek I Mishra Memorial Medical College and Research (AIMMMCR), Bhilai, Chhattisgarh, India

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Conflict of interest: Nil

Abstract**Background:** Opioid-related adverse effects may delay postoperative recovery following laparoscopic surgery. Multimodal opioid-free anesthesia has emerged as an alternative to opioid-sparing approaches, but its relative effects on postoperative recovery and analgesia remain an area of clinical interest.**Objective:** To compare postoperative recovery and analgesic outcomes between opioid-free and opioid-sparing anesthesia in patients undergoing elective laparoscopic surgery.**Materials and Methods:** This prospective randomized comparative study included 100 adult patients undergoing elective laparoscopic surgery under general anesthesia. Patients were randomly allocated to an opioid-free anesthesia group (OFA, n=50) or an opioid-sparing anesthesia group (OSA, n=50). The primary outcome was quality of recovery assessed using the QoR-15 score at 24 hours. Secondary outcomes included postoperative Numeric Rating Scale (NRS) pain scores, time to first rescue analgesia, 24-hour rescue opioid consumption, PACU stay, ambulation, oral intake, postoperative nausea and vomiting, and adverse events.**Results:** Baseline characteristics were comparable between groups. NRS pain scores were significantly lower in the OFA group at 1, 2, and 6 hours ($p < 0.05$), while scores at 12 and 24 hours were comparable. Time to first rescue analgesia was significantly longer with OFA (6.8 ± 2.5 vs 4.9 ± 2.1 hours; $p < 0.001$), and 24-hour rescue opioid consumption was lower (3.2 ± 4.1 vs 6.5 ± 5.3 mg morphine equivalents; $p = 0.001$). The 24-hour QoR-15 score was significantly higher with OFA (128.6 ± 10.8 vs 121.9 ± 12.4 ; $p = 0.005$). OFA was also associated with shorter PACU stay, earlier ambulation and oral intake, and a lower incidence of postoperative nausea (12.0% vs 30.0%; $p = 0.027$). No significant intergroup differences were observed for major hemodynamic or respiratory adverse events.**Conclusion:** Opioid-free anesthesia was associated with improved early postoperative analgesia, reduced rescue opioid consumption, better quality of recovery, and fewer opioid-related adverse effects compared with opioid-sparing anesthesia. Multimodal OFA may therefore be a useful component of enhanced recovery pathways for appropriately selected patients undergoing laparoscopic surgery.**Keywords:** Opioid-free anesthesia; opioid-sparing anesthesia; laparoscopic surgery; multimodal analgesia; postoperative pain; QoR-15; postoperative recovery; opioid consumption.This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.**Introduction**

Laparoscopic surgery has become an integral part of contemporary surgical practice because of reduced tissue trauma, shorter hospitalization, and faster postoperative recovery. Despite its minimally invasive nature, postoperative pain, nausea, vomiting, and opioid-related adverse effects may delay recovery. Consequently, perioperative strategies aimed at reducing opioid exposure while maintaining effective analgesia have gained increasing attention. [1] Opioid-free anesthesia

(OFA) avoids intraoperative opioids and relies on multimodal combinations of agents such as dexmedetomidine, ketamine, lidocaine, non-steroidal anti-inflammatory drugs, paracetamol, and regional analgesic techniques. Recent randomized studies have demonstrated that OFA can provide satisfactory postoperative recovery and analgesia in patients undergoing laparoscopic procedures. [2,3] Integration of OFA with enhanced recovery protocols may further improve postoperative

quality of recovery by reducing opioid-related adverse effects and facilitating early mobilization. [4] However, complete opioid avoidance may not always provide clinically important advantages over carefully designed opioid-sparing anesthesia (OSA), particularly in patients with relatively low postoperative pain requirements. [5] Studies involving laparoscopic bariatric surgery have similarly shown that opioid-free multimodal approaches may reduce perioperative opioid exposure while maintaining acceptable analgesia. [6]

More recent evidence comparing opioid-free and opioid-sparing techniques in laparoscopic surgery suggests potential differences in postoperative pain, rescue analgesic requirements, nausea and vomiting, and early recovery. [7] However, the relative clinical benefits of these strategies remain incompletely established. Therefore, the present study was undertaken to compare opioid-free versus opioid-sparing anesthesia for laparoscopic surgery, with particular emphasis on postoperative recovery and analgesic outcomes.

Materials and Methods

Study Design and Setting: The present study was designed as a prospective, randomized, comparative study conducted in the Department of Anaesthesiology of a tertiary care teaching hospital. Adult patients scheduled for elective laparoscopic surgery under general anesthesia were screened for eligibility and enrolled after obtaining written informed consent.

Sample Size: The sample size was calculated for comparison of a continuous postoperative recovery outcome between two independent groups. Assuming a two-sided significance level of 5%, statistical power of 80%, expected standard deviation of approximately 15 points, and a clinically relevant intergroup difference of approximately 9 points, the sample size was calculated using:

$$[n = \frac{2(Z_{\alpha/2} + Z_{\beta})^2 \sigma^2}{d^2}]$$

The minimum requirement was approximately 44 patients in each group. After allowing for approximately 10–12% attrition or incomplete observations, 100 patients were included, with 50 patients in each group.

Inclusion Criteria: Patients aged 18–65 years, belonging to American Society of Anesthesiologists (ASA) physical status I or II, and scheduled for elective laparoscopic surgery under general anesthesia were included.

Exclusion Criteria: Patients with known allergy or contraindication to any study medication, chronic opioid use, chronic pain requiring regular

analgesics, significant hepatic or renal dysfunction, uncontrolled cardiovascular disease, pregnancy, psychiatric or neurological disorders interfering with assessment, conversion to open surgery, or refusal to participate were excluded.

Randomization and Group Allocation: The enrolled patients were randomly allocated using a computer-generated randomization sequence into two equal groups:

Group OFA (n=50): Patients received an opioid-free multimodal anesthesia regimen, without administration of intraoperative opioids.

Group OSA (n=50): Patients received opioid-sparing anesthesia, consisting of multimodal non-opioid analgesia supplemented with a limited dose of an opioid when clinically indicated.

Allocation was concealed using sequentially numbered, opaque, sealed envelopes opened immediately before induction of anesthesia.

Anesthetic Technique: Standard monitoring comprising electrocardiography, non-invasive blood pressure, pulse oximetry, capnography, and temperature monitoring was applied. Intravenous access was established, and baseline hemodynamic parameters were recorded.

In Group OFA, anesthesia was provided using a multimodal opioid-free technique incorporating intravenous agents such as dexmedetomidine, ketamine, paracetamol and/or lidocaine, according to the predefined institutional protocol. No intraoperative opioid was administered.

In Group OSA, patients received standard general anesthesia with multimodal non-opioid analgesics along with a reduced intraoperative opioid dose, such as fentanyl, according to body weight and clinical requirements. General anesthesia was induced with propofol, and neuromuscular blockade was achieved with an appropriate non-depolarizing muscle relaxant. Endotracheal intubation was performed, and anesthesia was maintained using an inhalational anesthetic or intravenous anesthetic technique with an oxygen-air mixture. Ventilation was adjusted to maintain normocapnia. At completion of surgery, neuromuscular blockade was reversed and patients were extubated after fulfilling standard extubation criteria.

Postoperative Assessment: After surgery, patients were transferred to the post-anesthesia care unit. Postoperative pain was assessed using the Numeric Rating Scale (NRS; 0–10) at predetermined intervals, such as immediately after recovery and at 1, 2, 6, 12, and 24 hours postoperatively. Rescue analgesia was administered according to a predefined NRS threshold. The time to first rescue analgesic request and total rescue analgesic/opioid

consumption during the first 24 hours were recorded.

Postoperative nausea and vomiting (PONV), sedation, dizziness, bradycardia, hypotension, respiratory depression, and other anesthesia-related adverse events were documented.

Quality of postoperative recovery was assessed using a validated recovery instrument such as the Quality of Recovery-15 (QoR-15) score.

Outcome Measures: The primary outcome was postoperative quality of recovery assessed using the QoR-15 score at 24 hours.

Secondary outcomes included postoperative NRS pain scores, time to first rescue analgesia, 24-hour rescue opioid/analgesic consumption, and incidence of PONV, postoperative sedation, hemodynamic adverse events, PACU stay, and other anesthesia-related complications.

Statistical Analysis: Data were entered into Microsoft Excel and analyzed using IBM SPSS

Statistics. Continuous variables were expressed as mean $\pm$ standard deviation or median with interquartile range according to their distribution, whereas categorical variables were presented as frequencies and percentages. Independent-samples t-test or Mann–Whitney U test was used for comparison of continuous variables between groups. Categorical variables were compared using the Chi-square test or Fisher's exact test. Repeated postoperative pain measurements were analyzed using an appropriate repeated-measures model. A p-value <0.05 was considered statistically significant.

Results

A total of 100 patients undergoing elective laparoscopic surgery were included and equally allocated to the opioid-free anesthesia (OFA) group (n=50) and opioid-sparing anesthesia (OSA) group (n=50). All included patients completed the 24-hour postoperative assessment.

Table 1: Baseline demographic and perioperative characteristics

Parameter	OFA group (n=50)	OSA group (n=50)	p-value
Age (years), mean $\pm$ SD	41.8 $\pm$ 10.6	42.5 $\pm$ 11.1	0.748
Male/Female, n	19/31	21/29	0.684
BMI (kg/m ²), mean $\pm$ SD	25.7 $\pm$ 3.4	26.1 $\pm$ 3.6	0.569
ASA I/II, n	29/21	27/23	0.687
Duration of surgery (min), mean $\pm$ SD	82.6 $\pm$ 18.9	80.9 $\pm$ 19.5	0.659
Duration of anesthesia (min), mean $\pm$ SD	101.4 $\pm$ 21.2	99.7 $\pm$ 22.0	0.695

The two groups were comparable with respect to age, sex distribution, BMI, ASA physical status, duration of surgery, and duration of anesthesia (all $p>0.05$), indicating adequate baseline comparability.

Table 2: Postoperative pain scores and rescue analgesic requirements

Outcome	OFA group (n=50)	OSA group (n=50)	p-value
NRS at 1 hour	2.7 $\pm$ 1.0	3.3 $\pm$ 1.1	0.005
NRS at 2 hours	2.5 $\pm$ 0.9	3.0 $\pm$ 1.0	0.010
NRS at 6 hours	2.4 $\pm$ 0.9	2.8 $\pm$ 1.0	0.039
NRS at 12 hours	2.2 $\pm$ 0.8	2.4 $\pm$ 0.9	0.242
NRS at 24 hours	1.8 $\pm$ 0.7	2.0 $\pm$ 0.8	0.186
Time to first rescue analgesia (hours)	6.8 $\pm$ 2.5	4.9 $\pm$ 2.1	<0.001
Patients requiring rescue opioid, n (%)	14 (28.0)	26 (52.0)	0.014
24-hour rescue opioid consumption (morphine equivalents, mg)	3.2 $\pm$ 4.1	6.5 $\pm$ 5.3	0.001

Postoperative pain scores were significantly lower in the OFA group during the early postoperative period at 1, 2, and 6 hours. By 12 and 24 hours, the difference between groups was no longer statistically significant. The OFA group also demonstrated a significantly longer time to first rescue analgesia and lower 24-hour rescue opioid consumption.

Table 3: Postoperative recovery outcomes

Recovery parameter	OFA group (n=50)	OSA group (n=50)	p-value
QoR-15 score at 24 hours	128.6 $\pm$ 10.8	121.9 $\pm$ 12.4	0.005
Time to eye opening (min)	7.8 $\pm$ 2.6	8.5 $\pm$ 2.9	0.126
Time to extubation (min)	10.3 $\pm$ 3.1	11.1 $\pm$ 3.4	0.222
PACU stay (min)	52.4 $\pm$ 13.7	61.8 $\pm$ 16.2	0.002
Time to first ambulation (hours)	7.1 $\pm$ 2.0	8.3 $\pm$ 2.4	0.008
Time to oral intake (hours)	5.4 $\pm$ 1.7	6.2 $\pm$ 2.0	0.034

The mean QoR-15 score at 24 hours was significantly higher in the OFA group (128.6 ± 10.8) than in the OSA group (121.9 ± 12.4 ; $p=0.005$), suggesting better overall postoperative recovery. PACU stay, time to ambulation, and time to oral intake were also significantly shorter in the OFA group. No significant differences were observed in time to eye opening or extubation.

Table 4: Postoperative adverse events

Adverse event	OFA group (n=50), n (%)	OSA group (n=50), n (%)	p-value
Postoperative nausea	6 (12.0)	15 (30.0)	0.027
Vomiting	3 (6.0)	9 (18.0)	0.065
Rescue antiemetic required	5 (10.0)	13 (26.0)	0.037
Sedation	5 (10.0)	9 (18.0)	0.249
Dizziness	4 (8.0)	7 (14.0)	0.338
Bradycardia	6 (12.0)	2 (4.0)	0.140
Hypotension	7 (14.0)	4 (8.0)	0.338
Respiratory depression	0 (0)	2 (4.0)	0.495

Postoperative nausea occurred significantly less frequently with OFA (12.0%) than with OSA (30.0%; $p=0.027$). Similarly, fewer patients in the OFA group required rescue antiemetic therapy. Bradycardia and hypotension were numerically more frequent in the OFA group, although these differences were not statistically significant. No respiratory depression occurred in the OFA group.

Discussion

The present study compared opioid-free anesthesia (OFA) with opioid-sparing anesthesia (OSA) in 100 patients undergoing elective laparoscopic surgery. The principal findings demonstrated that OFA was associated with lower early postoperative pain scores, reduced rescue opioid requirements, prolonged time to first rescue analgesia, improved QoR-15 scores, shorter PACU stay, and a lower incidence of postoperative nausea. These findings suggest that complete intraoperative opioid avoidance within a multimodal regimen may provide clinically meaningful benefits during early postoperative recovery.

The favorable analgesic outcomes observed with OFA are supported by Cheng et al., who, in a systematic review and meta-analysis of laparoscopic surgery, reported that multimodal opioid-free anesthesia could reduce postoperative pain and opioid requirements while improving selected recovery outcomes. [8]

Similarly, da Silveira et al., in a systematic review and meta-analysis of minimally invasive abdominal surgery, demonstrated that opioid-free techniques reduced postoperative opioid consumption and some opioid-related adverse effects, although the magnitude of benefit varied according to the anesthetic regimen and surgical procedure. [9] In the present study, NRS pain scores were significantly lower with OFA at 1, 2, and 6 hours, whereas differences at 12 and 24 hours were not significant. This predominantly early benefit is consistent with the meta-analysis by Gao et al., which demonstrated favorable postoperative

analgesic effects of opioid-free general anesthesia in laparoscopic procedures. [10] The diminishing difference over time may reflect the relatively short duration of action of several components of multimodal OFA and the subsequent use of postoperative rescue analgesics in both groups.

The OFA group also had a significantly longer interval before first rescue analgesia and substantially lower 24-hour rescue opioid consumption. Vishnuraj et al. evaluated a combination of ketamine and dexmedetomidine during laparoscopic cholecystectomy and reported that an opioid-free technique provided effective perioperative analgesia and reduced postoperative analgesic requirements. [11] These effects may be attributable to the complementary mechanisms of multimodal agents, including α_2 -adrenergic agonism, NMDA receptor antagonism, and systemic non-opioid analgesia.

Our findings further demonstrated a higher mean QoR-15 score in the OFA group, together with shorter PACU stay and earlier ambulation and oral intake. Coeckelenbergh et al., in a randomized trial involving bariatric surgery, compared opioid-free and opioid-based multimodal strategies and highlighted the potential of opioid-free approaches to limit perioperative opioid exposure while maintaining satisfactory recovery and analgesia. [12] Improved early recovery with OFA may therefore result not only from analgesic efficacy but also from reduced opioid-associated sedation, nausea, and gastrointestinal dysfunction.

Hao et al. reported improved postoperative quality of recovery following an opioid-free anesthetic strategy in patients undergoing laparoscopic cholecystectomy. [13] Their findings support the higher QoR-15 scores observed in our study. Quality-of-recovery instruments provide a broader assessment than pain scores alone because they incorporate physical comfort, emotional status, independence, psychological support, and pain, making them particularly relevant when evaluating enhanced recovery strategies.

An important finding of the present study was the lower incidence of postoperative nausea in the OFA group (12.0% vs 30.0%). The requirement for rescue antiemetic medication was also significantly reduced. Yu et al. demonstrated favorable analgesic and recovery outcomes with opioid-free anesthesia following laparoscopic cholecystectomy, including benefits related to postoperative opioid-associated adverse effects. [14]

Avoidance of intraoperative opioids provides a plausible explanation for the reduced nausea observed in the present study, particularly because laparoscopic procedures themselves are associated with an appreciable risk of PONV.

Similarly, Chen et al., in a randomized controlled trial of gynecological laparoscopic surgery conducted within an enhanced recovery framework, demonstrated that opioid-free general anesthesia could provide recovery outcomes comparable with conventional opioid-containing anesthesia while reducing opioid exposure.¹⁵ Taken together with our findings, this suggests that OFA can be incorporated successfully into multimodal enhanced-recovery pathways in appropriately selected patients. Although bradycardia and hypotension were numerically more frequent with OFA in the present study, these differences were not statistically significant. This observation remains clinically important because agents frequently used in OFA, particularly dexmedetomidine, can produce dose-dependent bradycardia and hypotension. Consequently, OFA should not simply be interpreted as elimination of opioid-related adverse effects; rather, careful patient selection, appropriate drug dosing, and close hemodynamic monitoring are necessary.

The present study had certain limitations. It was conducted at a single centre with a relatively modest sample size, which may limit generalizability. Different laparoscopic procedures may produce different postoperative pain intensities, and the findings may therefore be influenced by surgical heterogeneity. Furthermore, recovery was assessed primarily during the first 24 postoperative hours, and longer-term outcomes such as persistent postoperative pain, functional recovery, patient satisfaction, and opioid use after discharge were not evaluated. Larger multicentre randomized studies with standardized OFA protocols and longer follow-up are warranted.

Conclusion

Opioid-free anesthesia provided better early postoperative analgesia and recovery than opioid-sparing anesthesia in patients undergoing laparoscopic surgery. It was associated with lower early postoperative pain scores, longer time to first rescue analgesia, reduced 24-hour opioid

consumption, higher QoR-15 scores, shorter PACU stay, earlier ambulation and oral intake, and reduced postoperative nausea and antiemetic requirements.

Although hemodynamic adverse events such as bradycardia and hypotension were numerically more frequent with OFA, no significant difference was observed between groups. Thus, a carefully designed multimodal opioid-free anesthetic technique may represent an effective strategy for enhancing early recovery while minimizing perioperative opioid exposure in appropriately selected patients undergoing laparoscopic surgery.

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