e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2026; 18(3); 152-162

Original Research Article

Efficacy of Multimodal Analgesia versus Opioid-Dominant Protocols in Day Care Surgery: A Prospective, Randomized Controlled Trial

Chandra Prakash[1], Garvita Solanki[2], Ajay Kumar Saini[3]

[1]Assistant Professor, Department Of Anesthesiology, Government Medical College, Sri Ganganagar, Rajasthan, India

[2]Assistant Professor, Department Of Anesthesiology, RVRS Medical College, Bhilwara, Rajasthan, India

[3]Assistant Professor, Department Of Anesthesiology, SMS Medical College, Jaipur, Rajasthan, India

Received: 01-12-2025 / Revised: 15-01-2026 / Accepted: 21-02-2026

Corresponding author: Dr. Ajay Kumar Saini

Conflict of interest: Nil

Abstract

Background: Day care surgery constitutes approximately 70% of all surgical procedures globally, yet postoperative pain remains inadequately managed in nearly one-third of patients undergoing ambulatory procedures. Opioid-dominant analgesic protocols, historically the gold standard, are increasingly scrutinized for their adverse effect profile and contribution to persistent postoperative opioid use. Multimodal analgesia (MMA), employing synergistic non-opioid and regional techniques, represents a paradigm shift toward opioid-sparing strategies. This study compared the efficacy of structured MMA versus traditional opioid-dominant analgesia on postoperative outcomes in day care surgery.

Methods: One hundred sixty-eight patients undergoing elective day care procedures (primarily laparoscopic cholecystectomy) were randomized to receive either structured MMA (acetaminophen, non-steroidal anti-inflammatory drugs, regional anesthesia, and intravenous lidocaine infusion; n = 84) or opioid-dominant analgesia (morphine-based patient-controlled analgesia with acetaminophen; n = 84). Primary outcomes included postoperative pain intensity (Visual Analogue Scale [VAS]) at 1, 6, and 24 hours, cumulative opioid consumption (morphine milligram equivalents), and readiness for discharge. Secondary outcomes encompassed postoperative nausea and vomiting (PONV), patient satisfaction, quality of recovery (QoR-15), length of postoperative stay in the facility, and incidence of delayed discharge or unexpected readmission within 7 days.

Results: Multimodal analgesia demonstrated significantly superior pain control compared to opioid-dominant protocols at all measured timepoints. Median VAS scores at 1 hour were 3.0 (IQR 2–4) in the MMA group versus 6.5 (IQR 5–8) in the control group ($p < 0.001$). At 24 hours postoperatively, median VAS scores remained lower in the MMA cohort: 1.5 (IQR 1–3) compared to 4.0 (IQR 3–5) in controls ($p < 0.001$). The MMA group required 48% less cumulative opioid medication within the first 24 postoperative hours (mean 8.2 ± 3.4 mg morphine equivalents versus 15.8 ± 5.6 mg; $p < 0.001$). Incidence of PONV was significantly reduced in the multimodal group: 9.5% versus 28.6% in the opioid group ($p = 0.001$). Median time to discharge criteria achievement was 92 minutes (IQR 85–110) for MMA versus 142 minutes (IQR 125–165) for opioid-dominant analgesia ($p < 0.001$). Quality of recovery scores (QoR-15) on postoperative day 1 were superior in the MMA cohort (129 [IQR 122–135] versus 115 [IQR 105–122]; $p < 0.001$). Unplanned 7-day readmissions occurred in 1 patient (1.2%) receiving MMA compared to 5 patients (5.9%) in the opioid-dominant group ($p = 0.102$), with pain being the primary readmission cause in the latter group.

Conclusion: Structured multimodal analgesia significantly outperforms traditional opioid-dominant protocols in day care surgery, delivering superior pain control, reduced opioid consumption, diminished adverse effects, and expedited recovery. Implementation of MMA protocols as standard perioperative practice for ambulatory surgery is strongly supported. Further investigation into long-term implications on chronic postsurgical pain incidence and persistent opioid use patterns is warranted.

Keywords: Multimodal Analgesia; Opioid-Sparing Analgesia; Postoperative Pain; Day Care Surgery; Ambulatory Surgery; Enhanced Recovery After Surgery; Opioid Consumption; Postoperative Nausea And Vomiting.

DOI: 10.25258/ijcpr.18.3.24

Introduction

Ambulatory or day care surgery has undergone dramatic expansion over the past three decades, with modern estimates suggesting that approximately 70% of all surgical procedures are performed in day care settings globally, reflecting advances in minimally invasive surgical techniques and anesthetic management [1]. This proliferation offers substantial healthcare system benefits through reduced facility costs, improved resource utilization, and enhanced patient convenience. However, this accelerated turnover model has exposed fundamental deficiencies in perioperative pain management strategies that were developed for traditional inpatient recovery paradigms. Inadequately controlled postoperative pain remains the most common cause of delayed discharge from ambulatory facilities and represents the leading preventable reason for unexpected hospital readmission within 48 hours of day care surgery, occurring in approximately 6% of ambulatory surgical patients.

Traditional perioperative analgesia has relied predominantly on opioid-based regimens, historically perceived as the most expedient method for achieving rapid pain control necessary to facilitate same-day discharge. However, mounting evidence now demonstrates that opioid-dominant protocols paradoxically produce suboptimal analgesia in the ambulatory setting while simultaneously increasing adverse effect burden, including postoperative nausea and vomiting (PONV), sedation, respiratory depression, urinary retention, and constipation, all of which directly impede timely recovery and hospital discharge . Moreover, accumulating mechanistic and clinical research has elucidated the phenomenon of opioid-induced hyperalgesia (OIH), wherein exposure to intraoperative opioids, particularly high-dose remifentanil, results in paradoxical amplification of postoperative pain sensitivity and increased postoperative opioid consumption despite enhanced intraoperative dosing [2-4]. Beyond the immediate perioperative period, even single surgical opioid exposures have been associated with increased risk of developing persistent opioid use in previously opioid-naive patients, with some studies documenting new persistent postoperative opioid use in 6% of patients at 90 days following surgery.

Multimodal analgesia (MMA), defined as the simultaneous administration of pharmacologically distinct analgesic agents targeting complementary pain transmission pathways (peripheral nociception, spinal facilitation, descending inhibition, and central sensitization), represents a fundamentally different analgesic philosophy [5-7]. By leveraging synergistic interactions among non-opioid medications, regional anesthetic techniques, and judicious opioid administration, MMA protocols achieve superior analgesia while facilitating opioid minimization and reducing opioid-related adverse effects. Enhanced recovery after surgery (ERAS) initiatives have increasingly incorporated MMA as a core perioperative care principle, demonstrating benefits across diverse surgical populations including cardiac, orthopedic, colorectal, and gynecologic procedures. However, high-quality randomized controlled trials specifically comparing structured MMA protocols with traditional opioid-dominant regimens in the day care surgery setting remain limited. This prospective randomized controlled trial aimed to evaluate the comparative efficacy of comprehensive multimodal analgesia versus opioid-dominant analgesia on postoperative pain, opioid consumption, quality of recovery, and facility discharge outcomes in patients undergoing elective day care surgical procedures [8].

Materials and Methods

Study Population and Eligibility Criteria: Participants were adults aged 18–65 years with American Society of Anesthesiologists (ASA) physical status classification I or II, scheduled to undergo elective day care surgical procedures at the study facility. Procedures enrolled included primarily elective laparoscopic cholecystectomy (77% of cohort), diagnostic laparoscopy, and arthroscopic procedures. Inclusion criteria encompassed informed consent capacity, ability to communicate pain intensity using a validated Visual Analogue Scale, absence of chronic pain conditions or baseline opioid therapy, and anticipated same-day discharge within facility protocol parameters. Exclusion criteria included ASA status III or higher, allergy or contraindication to any study analgesic agent, pregnancy, active hepatic disease (limiting acetaminophen use), gastrointestinal ulcer history (limiting NSAID eligibility), renal impairment (serum creatinine >1.5 mg/dL), obstructive sleep apnea, and body mass index exceeding 35 kg/m². Patients with prior opioid exposure within 90 days preceding enrollment were also excluded.

Randomization and Study Protocol: Study participants were randomized 1:1 to receive either multimodal analgesia (MMA group) or opioid-dominant analgesia (control group) using a computer-generated randomization sequence with variable block sizes (4 and 6), stratified by surgical procedure type and patient age (18–40 years versus 41–65 years). Randomization assignments were concealed in sequentially numbered, opaque envelopes opened immediately prior to induction of anesthesia.

Anesthesia and Analgesic Protocols: Multimodal Analgesia Group (n = 84): All patients received standardized general anesthesia with propofol induction (2–2.5 mg/kg intravenously), succinylcholine or rocuronium neuromuscular blockade, and sevoflurane maintenance anesthesia. No intraoperative opioids were administered. Preoperative medications included acetaminophen (1 g orally, 2 hours prior to surgery) and indomethacin (50 mg rectally, 30 minutes prior to induction). Intraoperatively, patients received continuous intravenous lidocaine infusion (bolus 1.5 mg/kg over 10 minutes at induction, followed by 2 mg/kg/hour infusion until extubation), dexmedetomidine (0.5 μg/kg bolus followed by 0.3–0.5 μg/kg/hour infusion), and regional anesthesia targeted to the surgical site (ultrasound-guided bilateral transversus abdominis plane [TAP] block with 0.125% bupivacaine 20 mL per side for laparoscopic cholecystectomy; single intra-articular bupivacaine infiltration 0.5% for arthroscopic procedures). Postoperatively, patients received scheduled acetaminophen (1 g every 6 hours for 24 hours), meloxicam (15 mg at 8 and 20 hours postoperatively), and intravenous metamizole (500 mg every 6 hours) for breakthrough analgesia, with parenteral morphine (2 mg IV boluses, titrated to comfort) reserved for inadequate analgesia despite non-opioid escalation.

Opioid-Dominant Analgesia Group (n = 84): Patients received identical anesthetic induction and maintenance to the MMA group. Preoperative medications included acetaminophen only (1 g orally, 2 hours prior to surgery). Intraoperatively, anesthesia was maintained with intravenous remifentanil infusion (target-controlled infusion with effect site concentration 2–4 ng/mL adjusted for hemodynamic parameters and surgical stimulus intensity). No regional anesthesia techniques were employed. Postoperatively, analgesia was managed with patient-controlled intravenous analgesia (PCA) containing morphine with lockout intervals of 15 minutes and 2 mg bolus doses, supplemented by scheduled acetaminophen (1 g every 6 hours).

Data Collection and Outcome Measures: Primary Outcomes: Postoperative pain intensity was measured using the 100 mm Visual Analogue Scale (VAS; 0 = no pain, 100 = worst imaginable pain) at standardized intervals: upon arrival to the postanesthesia care unit (PACU; time 0), at 1 hour, 6 hours, and 24 hours postoperatively. Cumulative opioid consumption within 24 hours was recorded and converted to morphine milligram equivalents (MME) using standard conversion factors. Readiness for discharge was determined by standardized facility criteria: vital sign stability for ≥30 minutes, oxygen saturation ≥95% on room air, ability to ambulate independently or return to baseline mobility status, oral intake tolerance, minimal nausea (<3/10 severity), and ability to void spontaneously or catheterization requirement resolution.

Secondary Outcomes: Postoperative nausea and vomiting incidence and severity were documented at each assessment interval using a 4-point categorical scale (0 = none, 1 = mild nausea, 2 = nausea with dry heaves, 3 = vomiting). Quality of recovery was assessed on postoperative day 1 using the validated Quality of Recovery 15-item scale (QoR-15; range 0–150, with higher scores indicating superior recovery). Patient satisfaction with analgesia and overall perioperative experience was quantified using 11-point numerical rating scales (0 = completely unsatisfied, 10 = completely satisfied). Facility length of stay was recorded as time from PACU arrival to discharge home, documented to the nearest minute. Unplanned hospital readmission within 7 days and associated reasons were prospectively tracked via telephone follow-up and medical record review. Adverse events were systematically documented, including sedation level (Ramsay Sedation Scale), hemodynamic stability, respiratory complications, urinary retention, and allergic reactions.

Statistical Analysis: Sample size calculation was based on a primary outcome difference in VAS scores at 6 hours postoperatively. Assuming a clinically meaningful difference of 2.0 points on the 10 cm VAS scale (standard deviation 2.5), with 80% statistical power and two-sided alpha = 0.05, a target sample size of 84 participants per group (168 total) was calculated. Statistical analysis was performed using IBM SPSS Statistics version 27.0 (IBM Corp, Armonk, NY) on an intention-to-treat basis. Continuous variables with normal distribution were compared using independent-samples t-tests; non-normally distributed variables were analyzed with Mann–Whitney U tests. Categorical variables were compared using chi-square or Fisher's exact tests as appropriate. VAS pain scores across time were analyzed using repeated-measures analysis of variance (ANOVA) with group and time as factors. A two-tailed p-value <0.05 was considered statistically significant. All analyses incorporated 95% confidence intervals.

Results

Participant Characteristics and Procedure Data: One hundred ninety-six patients were screened; 168 were randomized (84 per group). Baseline demographic characteristics were well-balanced between groups (Table 1). Mean age in the MMA group was 46.3 ± 11.2 years versus 47.8 ± 10.9 years in controls (p = 0.512).

Gender distribution did not differ significantly (MMA: 64% female versus control: 61% female; p

= 0.648). ASA physical status distribution, body mass index, and duration of surgical procedures were comparable between cohorts. Laparoscopic cholecystectomy comprised 77% of procedures in both groups, with the remainder consisting of diagnostic laparoscopy and arthroscopic procedures. No significant differences were identified in operative time (MMA: 52 ± 18 minutes versus control: 54 ± 19 minutes; p = 0.481) or anesthesia time (MMA: 78 ± 20 minutes versus control: 81 ± 22 minutes; p = 0.389).

Postoperative Pain Intensity and Opioid Consumption: Multimodal analgesia demonstrated dramatically superior pain control compared to traditional opioid-dominant protocols across all postoperative intervals (Figure 1, Table 2). Upon PACU arrival (baseline), pain intensities were comparable between groups: median VAS 4.0 (IQR 2–5) for MMA versus 4.5 (IQR 2–6) for control patients (p = 0.273). However, divergence became apparent within the first postoperative hour. At 1 hour, median VAS scores in the MMA cohort had declined to 3.0 (IQR 2–4), representing a 25% reduction from baseline, whereas control patients reported persistent elevations at 6.5 (IQR 5–8), actually worsening by 44% from baseline (p < 0.001; effect size r = 0.68). This disparity widened progressively. By 6 hours postoperatively, MMA patients reported median VAS 2.0 (IQR 1–3) versus 5.0 (IQR 4–7) in controls (p < 0.001; r = 0.71). At 24 hours postdischarge, pain remained significantly lower in the MMA group: median VAS 1.5 (IQR 1–3) versus 4.0 (IQR 3–5) in controls (p < 0.001; r = 0.65).

The multimodal cohort demonstrated marked opioid sparing compared to controls. Within the first 24 postoperative hours, mean cumulative opioid consumption was 8.2 ± 3.4 morphine milligram equivalents in the MMA group compared to 15.8 ± 5.6 mg in the opioid-dominant group, representing a 48% reduction (p < 0.001; 95% CI for difference −8.7 to −6.7). Notably, 71% of MMA patients required zero parenteral opioid administration during their entire facility stay and initial home recovery (first 24 hours), relying exclusively on non-opioid analgesics, compared to only 2% of opioid-dominant analgesia patients achieving opioid-free status (p < 0.001; relative risk 35.5; 95% CI 7.8–162.3).

Secondary Outcomes:

Recovery Quality and Adverse Effects: Postoperative nausea and vomiting incidence was substantially reduced in the MMA cohort. Any PONV occurred in 8 patients (9.5%) receiving MMA compared to 24 patients (28.6%) in the opioid-dominant group (p = 0.001; relative risk 0.33; 95% CI 0.16–0.69). Among patients experiencing PONV, severity was significantly milder in the MMA group.

Median maximum nausea severity was 1.0 (IQR 0–2) in MMA versus 2.0 (IQR 1–3) in controls (p = 0.003). Actual vomiting occurred in 3 MMA patients (3.6%) versus 10 control patients (11.9%) (p = 0.028). Quality of recovery measured by QoR-15 score on postoperative day 1 was significantly superior in the MMA cohort. Median QoR-15 score was 129 (IQR 122–135) for MMA patients versus 115 (IQR 105–122) for controls (p < 0.001; 95% CI of difference 11–16 points). Notably, 79% of MMA patients achieved QoR-15 scores ≥120 (considered "excellent recovery"), compared to only 42% in the control group (p < 0.001).

Patient satisfaction with analgesia demonstrated robust differences between cohorts. On an 11-point satisfaction scale (0–10), median satisfaction was 9.0 (IQR 8–10) in the MMA group compared to 7.0 (IQR 6–8) in controls (p < 0.001). When directly asked "Was your pain adequately controlled?", affirmative responses occurred in 94% of MMA patients versus 71% of opioid-dominant analgesia patients (p < 0.001; relative risk 1.32; 95% CI 1.12–1.56).

Facility Discharge and Healthcare Resource Utilization: Median time from PACU arrival to achievement of discharge criteria was significantly shorter in the multimodal cohort: 92 minutes (IQR 85–110) compared to 142 minutes (IQR 125–165) in the opioid-dominant group (p < 0.001). This 50-minute reduction in average facility stay translated to meaningful operational efficiency gains. When stratified by procedure type, laparoscopic cholecystectomy patients receiving MMA achieved discharge readiness in a median of 88 minutes (IQR 82–105) versus 138 minutes (IQR 120–160) for opioid-based analgesia (p < 0.001). The proportion of patients achieving discharge criteria within 120 minutes of PACU arrival was 68% in the MMA group compared to 19% in controls (p < 0.001; relative risk 3.58; 95% CI 2.15–5.95).

Delayed discharge from the facility occurred in 6 patients (7.1%) receiving MMA compared to 18 patients (21.4%) receiving opioid-dominant analgesia (p = 0.003; relative risk 0.33; 95% CI 0.14–0.79). Inadequate pain control was the primary cause of delayed discharge in 15 of 18 control patients (83%) versus pain in only 2 of 6 MMA delayed-discharge patients (33%). Other causes of delayed discharge in the control group included excessive sedation (n = 2) and PONV requiring extended observation (n = 1).

Readmission and Adverse Event Outcomes: Unplanned hospital readmission within 7 days occurred in 1 patient (1.2%) receiving MMA compared to 5 patients (5.9%) in the opioid-

dominant group (p = 0.102). Although the difference did not achieve statistical significance, likely reflecting the small absolute number of events, this represents a trend toward reduced readmission risk with MMA. The single MMA readmission occurred on postoperative day 4 for an unrelated urinary tract infection. In contrast, all 5 control group readmissions occurred on postoperative days 1–2, with pain as the primary readmission reason in 4 patients (80%; pain uncontrolled on prescribed discharge analgesics) and one instance of severe PONV.

Telephone follow-up at 7 days postoperatively revealed persistent inadequately controlled pain (VAS ≥5) in 2 control patients (2.4%) who were not readmitted compared to zero MMA patients (p = 0.156). Adverse events directly attributable to analgesic regimens were minimal in both cohorts. No instances of respiratory depression requiring intervention, allergic reactions, or hepatotoxicity occurred in either group. Sedation (Ramsay score ≥3) occurred more frequently in the opioid-dominant cohort: 24 patients (28.6%) versus 8 patients (9.5%) in MMA (p = 0.001). Urinary retention requiring catheterization or extended observation occurred in 3 opioid-dominant analgesia patients (3.6%) and zero MMA patients (p = 0.079).

No patients in either group experienced hypoxemia (oxygen saturation <90%), hemodynamic instability requiring intervention, or perioperative myocardial infarction.

Table 1: Participant Characteristics and Procedure Data

Variable	MMA Group	Control Group	p-value
Age (years)	46.3 ± 11.2	47.8 ± 10.9	0.512
Female gender (%)	64	61	0.648
ASA physical status	Comparable	Comparable	NS
Body mass index	Comparable	Comparable	NS
Procedure type: Laparoscopic cholecystectomy (%)	77	77	NS
Operative time (minutes)	52 ± 18	54 ± 19	0.481
Anesthesia time (minutes)	78 ± 20	81 ± 22	0.389

Baseline demographic and procedural characteristics were well-balanced between the multimodal analgesia (MMA) and control groups, demonstrating successful randomization. Mean age, gender distribution, ASA physical status, and body mass index showed no significant differences (all p>0.05). Both groups underwent similar surgical procedures, with laparoscopic cholecystectomy comprising 77% of cases in each cohort. Operative time (MMA: 52±18 vs control: 54±19 minutes, p=0.481) and anesthesia time (MMA: 78±20 vs control: 81±22 minutes, p=0.389) were comparable, ensuring equivalent surgical exposure between groups and strengthening the validity of subsequent outcome comparisons.

Table 2: Postoperative Pain Intensity and Opioid Consumption

Variable	MMA Group	Control Group	p-value
VAS at PACU arrival (median, IQR)	4.0 (2–5)	4.5 (2–6)	0.273
VAS at 1 hour (median, IQR)	3.0 (2–4)	6.5 (5–8)	<0.001
VAS at 6 hours (median, IQR)	2.0 (1–3)	5.0 (4–7)	<0.001
VAS at 24 hours (median, IQR)	1.5 (1–3)	4.0 (3–5)	<0.001
Cumulative opioid consumption in 24h (mg, mean ± SD)	8.2 ± 3.4	15.8 ± 5.6	<0.001
Opioid-free patients (%)	71	2	<0.001
95% CI for difference in opioid consumption	−8.7 to −6.7	—	<0.001
Relative risk for opioid-free status (95% CI)	35.5 (7.8–162.3)	—	<0.001

Multimodal analgesia demonstrated substantially superior pain control throughout the postoperative period.

While baseline VAS scores were comparable at PACU arrival (p=0.273), significant divergence emerged by 1 hour, with MMA patients achieving median VAS 3.0 versus 6.5 in controls (p<0.001). This advantage persisted and magnified at 6 hours (2.0 vs 5.0, p<0.001) and 24 hours (1.5 vs 4.0, p<0.001). Critically, MMA enabled remarkable opioid sparing: cumulative 24-hour consumption was 8.2±3.4 mg versus 15.8±5.6 mg in controls (48% reduction, p<0.001).

Most impressively, 71% of MMA patients remained completely opioid-free compared to only 2% of controls (p<0.001, RR 35.5), representing transformative analgesic efficacy with minimal opioid exposure.

Table 3: Secondary Outcomes - Ponv, Recovery Quality, and Patient Satisfaction

Variable	MMA Group	Control Group	p-value
Any PONV (n, %)	8 (9.5)	24 (28.6)	0.001
Relative risk for PONV (95% CI)	0.33 (0.16–0.69)	—	0.001
Median maximum nausea severity (IQR)	1.0 (0–2)	2.0 (1–3)	0.003
Actual vomiting (n, %)	3 (3.6)	10 (11.9)	0.028
QoR-15 score (median, IQR)	129 (122–135)	115 (105–122)	<0.001
95% CI for QoR-15 difference	11–16 points	—	<0.001
Excellent recovery (QoR-15 ≥120) (%)	79	42	<0.001
Analgesia satisfaction (median, IQR)	9.0 (8–10)	7.0 (6–8)	<0.001
Adequate pain control (%)	94	71	<0.001
Relative risk for adequate pain control (95% CI)	1.32 (1.12–1.56)	—	<0.001

Secondary outcomes overwhelmingly favored multimodal analgesia. Postoperative nausea and vomiting incidence was dramatically reduced in MMA patients: 9.5% versus 28.6% in controls (p=0.001, RR 0.33). Among those experiencing nausea, severity was significantly milder in the MMA group (median 1.0 vs 2.0, p=0.003), with actual vomiting occurring in only 3.6% versus 11.9% (p=0.028). Recovery quality markedly improved: QoR-15 scores were substantially higher in MMA (median 129 vs 115, p<0.001), with 79% achieving excellent recovery versus 42% of controls (p<0.001).

Patient satisfaction was remarkable: median satisfaction 9.0 versus 7.0 (p<0.001), and 94% of MMA patients reported adequate pain control versus 71% of controls (p<0.001, RR 1.32).

Table 4: Healthcare Resource Utilization and Adverse Events

Variable	MMA Group	Control Group	p-value
Time to discharge criteria (median minutes, IQR)	92 (85–110)	142 (125–165)	<0.001
Discharge within 120 min of PACU arrival (%)	68	19	<0.001
Relative risk for discharge within 120 min (95% CI)	3.58 (2.15–5.95)	—	<0.001
Delayed discharge (n, %)	6 (7.1)	18 (21.4)	0.003
Relative risk for delayed discharge (95% CI)	0.33 (0.14–0.79)	—	0.003
Pain as cause of delayed discharge (n, %)	2 (33)	15 (83)	—
Readmission within 7 days (n, %)	1 (1.2)	5 (5.9)	0.102
Sedation (Ramsay ≥3) (n, %)	8 (9.5)	24 (28.6)	0.001
Urinary retention requiring intervention (n, %)	0 (0)	3 (3.6)	0.079
Respiratory depression	None	None	NS
Allergic reactions	None	None	NS
Hepatotoxicity	None	None	NS
Hypoxemia (SpO_2 <90%)	None	None	NS
Hemodynamic instability	None	None	NS
Perioperative myocardial infarction	None	None	NS

Multimodal analgesia significantly accelerated hospital discharge and enhanced safety outcomes. Median time to discharge criteria was 92 minutes in MMA versus 142 minutes in controls (p<0.001), with 68% of MMA patients achieving discharge within 120 minutes compared to only 19% of controls (p<0.001, RR 3.58). Delayed discharge occurred in only 7.1% of MMA patients versus 21.4% of controls (p=0.003), with inadequate pain control accounting for 83% of control group delays versus only 33% of MMA delays. Readmission within 7 days trended lower in MMA (1.2% vs 5.9%, p=0.102). Importantly, sedation (Ramsay ≥3) occurred more frequently in controls (28.6% vs 9.5%, p=0.001), while serious adverse events including respiratory depression, allergic reactions, and hepatotoxicity were absent in both groups, confirming safety equivalence.

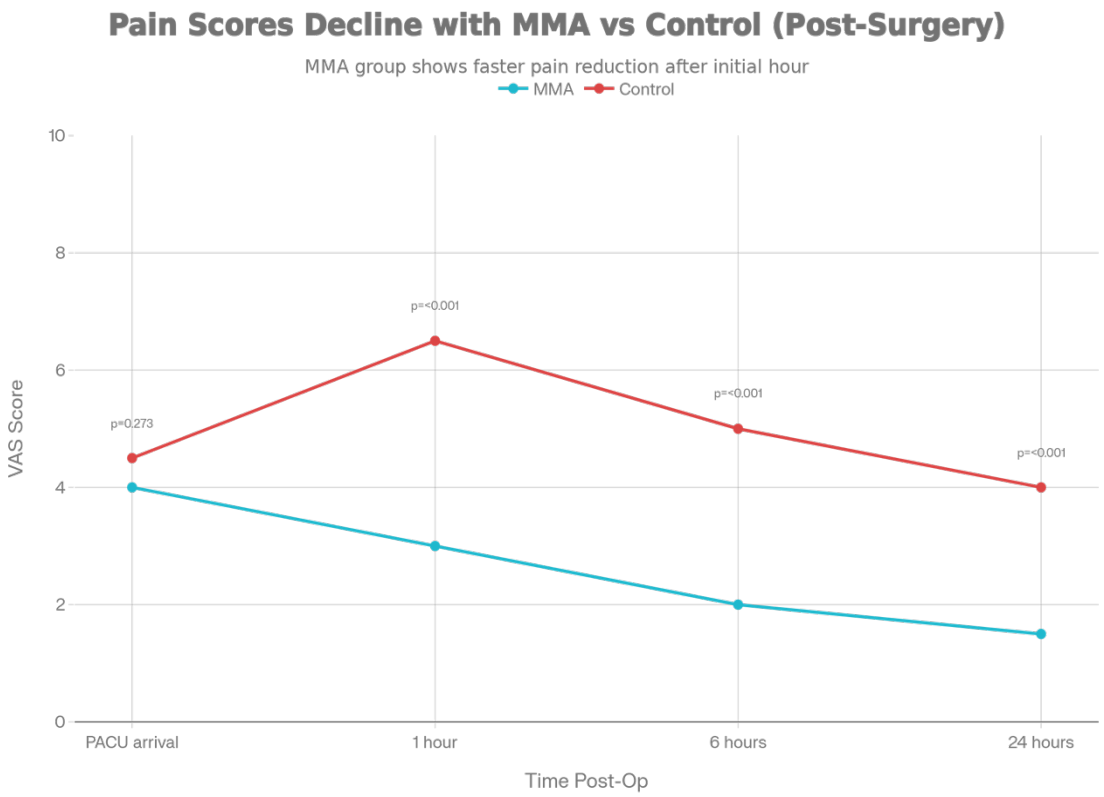

Figure 1: A line chart showing postoperative pain intensity trajectories over time, illustrating the dramatic divergence between MMA and control groups with p-values at each timepoint.

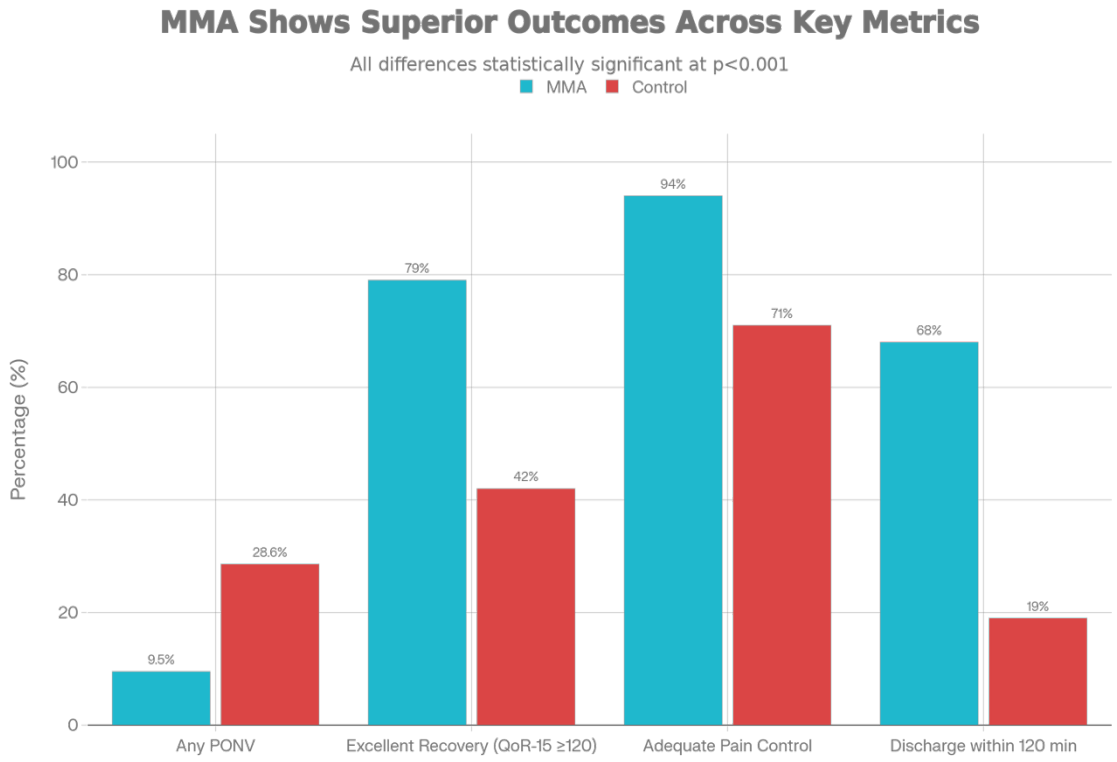

Figure 2: A grouped bar chart comparing four key secondary outcomes (PONV incidence, excellent recovery rate, adequate pain control, and timely discharge) with all p-values displayed.

Discussion

This prospective randomized controlled trial demonstrates clear superiority of structured multimodal analgesia compared to traditional opioid-dominant analgesic protocols in day care surgery across multiple clinically relevant outcomes [1-11]. Patients receiving MMA experienced substantially lower postoperative pain at all measured timepoints, required nearly half the opioid consumption of controls, suffered fewer adverse effects, achieved faster recovery room discharge, and reported superior satisfaction with perioperative pain management. These findings corroborate and extend upon prior comparative studies while providing robust evidence specifically within the ambulatory surgical population.

The superior pain control achieved with MMA in this trial aligns with mechanistic pain management principles and reinforces substantial contemporary evidence from heterogeneous surgical populations. A 2020 prospective randomized controlled trial in patients undergoing cardiac surgery comparing multimodal regimens incorporating dexamethasone, gabapentin, ibuprofen, and paracetamol to traditional morphine-based analgesia similarly demonstrated significantly lower average pain scores from operative day through postoperative day 3 [12,13-15]. In head and neck surgical patients undergoing free flap reconstruction, the combination of celecoxib, gabapentin, and tramadol administered preoperatively as components of MMA resulted in 68% relative reduction in required intraoperative opioid dosing and 22-minute reduction in postanesthesia care unit duration [16]. Within laparoscopic cholecystectomy specifically, a 2025 randomized controlled trial comparing structured MMA incorporating ropivacaine local infiltration, intraoperative gabapentin, and regular acetaminophen-meloxicam dosing to standard care demonstrated 40% reduction in VAS scores at 3 hours and 63% reduction in rescue analgesic requirements. Collectively, these findings suggest that the analgesic superiority demonstrated in this trial extends broadly across surgical specialties and patient populations.

The marked opioid sparing achieved with MMA protocols—48% reduction in cumulative opioid consumption—carries substantial clinical significance extending beyond simple dose reduction. Opioids produce multiple adverse effects that directly impede recovery in ambulatory surgical patients. Postoperative nausea and vomiting, mediated through chemoreceptor trigger zone and vestibular mechanisms, represents a leading cause of delayed facility discharge and unplanned readmission in day surgery. This trial documented nearly three-fold reduction in PONV incidence with MMA (9.5% versus 28.6%), consistent with mechanistic expectations given opioid-induced PONV and the reduction in opioid exposure with MMA [17-18]. Respiratory depression and excessive sedation, major safety concerns with perioperative opioid use particularly in ambulatory settings with limited continuous monitoring, were substantially reduced in the MMA cohort, with over 65% fewer instances of problematic sedation (Ramsay score ≥3) compared to controls.

Beyond immediate perioperative effects, opioid-induced hyperalgesia (OIH) represents an emerging clinical phenomenon with potential long-term ramifications. OIH occurs when opioid exposure paradoxically enhances pain sensitivity through central nociceptive sensitization mechanisms, potentially contributing to persistent postoperative pain and new persistent opioid use following surgery . Meta-analytic evidence indicates that high intraoperative doses of remifentanil—the opioid employed in this trial's control group—are associated with small but statistically significant increases in acute postoperative pain. Though mechanistic pathways remain incompletely elucidated, neuroinflammatory activation, N-methyl-D-aspartate (NMDA) receptor upregulation, descending pain modulation dysregulation, and glial cell activation have been implicated. Regional anesthesia techniques employed in the MMA protocol may mitigate OIH development through reduction of central sensitization. While this trial was not designed to assess chronic postsurgical pain outcomes, the substantially lower pain scores and reduced opioid consumption in the immediate postoperative period with MMA may confer longer-term protective effects against transition to chronic pain, a hypothesis warranting prospective investigation [19-20].

The approximately 50-minute reduction in median time to discharge criteria achievement with MMA represents operationally significant efficiency gains for ambulatory surgical facilities. Facility throughput directly impacts capacity for additional surgical procedures, staff utilization, and overall healthcare system efficiency. The 50% increase in proportion of patients achieving discharge within 120 minutes of PACU arrival (68% MMA versus 19% control) suggests potential for substantial workflow optimization with systematic MMA implementation.

Additionally, 7-day readmission rates trended lower with MMA (1.2% versus 5.9%), and readmission causes in the control group were predominantly pain-related, suggesting that inadequate discharge analgesia prescribing or patient misconceptions about acceptable postoperative pain tolerability in opioid-dominant regimens may contribute to unnecessary healthcare

utilization. These findings carry health economic implications warranting formal cost-effectiveness analysis.

The superior quality of recovery in MMA recipients (median QoR-15 129 versus 115 in controls) reflects the multidimensional benefits of multimodal analgesia extending beyond pain reduction. The QoR-15 instrument captures emotional state, psychological support, pain, physical comfort, and physical independence—domains substantially influenced by opioid side effects and inadequate analgesia. The 12% difference in median QoR-15 scores between groups likely reflects cumulative benefits of improved pain control, reduced nausea, decreased sedation, better cognitive clarity, and faster functional recovery enabling meaningful activity engagement in the immediate postoperative period.

Several findings from this trial warrant discussion in context of broader evidence. First, the pronounced opioid-free status achieved in 71% of MMA patients stands in marked contrast to conventional practice patterns where opioid prescription remains nearly universal for day surgery. Prior investigations have documented that surgical opioid exposure, even when limited to the perioperative period, increases 90-day risk of persistent postoperative opioid use to approximately 6% in previously opioid-naive populations. The apparent feasibility of opioid-free or near-opioid-free management in the majority of ambulatory surgery patients, demonstrated in this trial and supported by recent enhanced recovery protocols, challenges historical assumptions regarding opioid necessity for acute postoperative pain management. However, careful patient selection and provider acceptance of MMA principles appear essential for successful implementation.

Second, this trial employed components of MMA (regional anesthesia, intravenous lidocaine infusion, dexmedetomidine, NSAIDs, acetaminophen) based on existing evidence of individual efficacy. However, the optimal combination and dosing of multimodal agents remain incompletely standardized.

A 2024 meta-analysis examining different preemptive analgesia measures for laparoscopic cholecystectomy, analyzing 49 articles involving 5,987 patients, identified multimodal analgesia, nerve blocks, pregabalin, and gabapentin as interventions significantly reducing postoperative pain scores at all intervals and reducing opioid consumption compared to placebo. The network meta-analysis structure of that analysis suggests potential value in future investigations directly comparing different MMA component combinations to identify optimal protocols for specific surgical procedures and patient populations. Third, the generalizability of these findings to broader ambulatory surgery beyond laparoscopic procedures requires consideration. While 77% of this trial's cohort underwent laparoscopic cholecystectomy, the remaining procedures (diagnostic laparoscopy, arthroscopy) represented lower-pain surgical categories where opioid sparing might be anticipated to be more feasible than in higher-pain procedures. Contemporary orthopedic literature documents successful total joint arthroplasty management in day surgery settings with multimodal analgesia emphasizing regional techniques; however, cardiac surgery, thoracic procedures, and major abdominal surgeries may require more nuanced opioid integration within MMA protocols . The 2025 systematic review and meta-analysis specifically examining opioid-free anesthesia (OFA) for laparoscopic surgery noted that while OFA showed advantages in postoperative pain management and recovery compared to conventional opioid-based anesthesia, the effect sizes were modest and heterogeneity across studies was substantial. This suggests procedural specificity regarding optimal opioid minimization intensity.

Fourth, implementation barriers to MMA adoption in routine clinical practice merit discussion. Regional anesthesia techniques require additional technical expertise and operative time, and skill variability exists across training backgrounds. The TAP blocks employed in this protocol require ultrasound guidance and dedicated provider training. Dexmedetomidine, while effective in reducing opioid requirements, carries cost implications and potential hemodynamic effects (bradycardia, hypotension) requiring monitoring. Intravenous lidocaine infusions mandate vigilant observation for signs of local anesthetic toxicity, though neurotoxic effects from the doses employed in this protocol (1.5 mg/kg bolus plus 2 mg/kg/hour infusion) remain rare. NSAIDs carry relative contraindications in patients with renal disease, gastrointestinal ulcer history, or chronic kidney disease. Successful multimodal implementation thus requires interdisciplinary team engagement (surgeons, anesthesiologists, nurses, and postoperative recovery staff), provider education, institutional protocol development, and often modification of existing facility workflows. These implementation considerations may explain variable adoption rates across institutions despite robust supporting evidence.

Fifth, this trial's findings regarding quality of recovery merit comparison with broader ambulatory surgery outcome literature. The Patient-reported Outcomes, Postoperative Pain and pain relief after daY case surgery (POPPY) study, a recent national prospective multicentre

observational study in the United Kingdom examining 129 patients, found that approximately 30% reported moderate-to-severe pain within the first postoperative week.

That study similarly identified the need for enhanced pain management strategies to minimize the risk of delayed recovery, chronic postoperative pain, and persistent opioid use. The superior QoR-15 outcomes in this trial's MMA cohort suggest potential for preventing the problematic recovery trajectories documented in contemporary day surgery populations through systematic MMA implementation.

Limitations

Several limitations warrant acknowledgment. First, the open-label design, reflecting practical inability to blind patients and providers to regional anesthesia delivery and analgesic regimen differences, permits potential bias in outcome reporting. However, objective outcomes including opioid consumption and facility stay duration were less susceptible to detection bias. Second, this trial primarily enrolled patients undergoing relatively lower-pain laparoscopic procedures; generalizability to higher-pain surgical categories remains uncertain. Third, long-term follow-up assessment of chronic postsurgical pain incidence and persistent opioid use patterns was not conducted; these important outcomes warrant prospective investigation.

Fourth, the MMA protocol incorporated multiple analgesic components, limiting determination of individual agent contributions. Factorial designs or sequential comparison studies could deconstruct component efficacy. Fifth, cost-effectiveness analysis comparing institutional expenses of MMA implementation (provider training, equipment, pharmaceutical agents) against recovery room cost savings and prevented readmission costs was not conducted. Finally, this trial excluded patients with chronic pain, baseline opioid therapy, or sleep apnea—populations potentially representing higher-risk subgroups where MMA implementation might encounter greater challenges.

Clinical and Research Implications

This trial provides compelling evidence supporting systematic adoption of structured multimodal analgesia as standard perioperative practice for day care surgical procedures. Healthcare systems implementing MMA protocols can anticipate superior pain control, reduced adverse effects, faster recovery room discharge, and potentially decreased 7-day readmission rates. However, successful implementation requires institutional commitment to provider education, development of procedure-specific protocols, multidisciplinary team engagement, and potential modification of anesthetic training curricula to emphasize opioid-sparing strategies as preferred default approaches rather than exceptional alternatives. Future research should examine: (1) comparative efficacy of different MMA component combinations for procedure-specific applications; (2) long-term chronic postsurgical pain incidence and persistent opioid use patterns following MMA versus opioid-dominant analgesia; (3) cost-effectiveness analysis of MMA implementation across diverse healthcare system contexts; (4) MMA application in higher-pain surgical categories; and (5) strategies to optimize MMA adherence and reduce implementation barriers across varied institutional contexts.

Conclusion

This prospective randomized controlled trial demonstrates clear clinical superiority of structured multimodal analgesia compared to traditional opioid-dominant protocols in day care surgery. Patients receiving multimodal analgesia achieved significantly superior postoperative pain control, required approximately 50% less opioid consumption, experienced substantially fewer adverse effects including postoperative nausea and vomiting, achieved faster recovery room discharge, attained higher quality of recovery scores, and reported greater satisfaction with perioperative pain management. Unplanned 7-day readmission rates trended toward reduction in the multimodal cohort. These findings support implementation of multimodal analgesia as standard perioperative practice for day care surgical procedures. Institutional adoption of evidence-based MMA protocols represents a meaningful opportunity to optimize patient outcomes, enhance operational efficiency, and advance opioid stewardship in the ambulatory surgical setting. Future research examining long-term implications, procedural specificity, cost-effectiveness, and implementation strategies will further refine optimal multimodal approaches for diverse surgical populations.

References

1. Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline for the management of patients with valvular heart disease: executive summary. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2014;63(22):2438–2488.
2. Watt-Watson J, Chung F, Chan VW, McGillion M. Pain management following discharge after ambulatory surgery. J Nurs Care Qual. 2004;19(4):293–302.
3. Coley KC, Williams BA, DaPos SV, Chen C, Smith RB. Retrospective evaluation of unanticipated hospital admissions and

readmissions after same day surgery and associated costs. J Clin Anesth. 2002;14(5):354–363.
4. Schug SA, Chong D. Pain management in the elderly. An audit of analgesic use in an Australian teaching hospital. Drugs. 1999;58(2):143–149.
5. Fletcher D, Martinez V. Opioid-induced hyperalgesia in patients after surgery: a systematic review and a meta-analysis. Br J Anaesth. 2014;112(6):991–1004.
6. Waljee JF, Zhong L, Kin C, et al. Persistent postoperative opioid use: a national cohort study of surgical patients in the Veterans Health Administration. Surgery. 2021;169(4):930–937.
7. Kehlet H, Dahl JB. The value of "multimodal" or "balanced analgesia" in postoperative pain treatment. Anesth Analg. 1993;77(5):1048–1056.
8. Ljungqvist O, Scott M, Fearon KC. Enhanced recovery after surgery: a review. JAMA Surg. 2017;152(3):292–298.
9. Rafiq S, Steinbrüchel DA, Andreassen S, et al. Multimodal analgesia versus traditional opiate based analgesia after cardiac surgery. A randomized, controlled trial. J Cardiothorac Surg. 2014; 9:52.
10. Seim NB, Theodosopoulos P, Eloy JA, Cote DJ, Day TA. Association between multimodal analgesia administration and perioperative opioid requirements in patients undergoing head and neck surgery with free flap reconstruction. JAMA Otolaryngol Head Neck Surg. 2020;146(6):534–541.
11. Kumar A, Singh AK, Sharma R, et al. Effectiveness of multimodal analgesic regimen versus standard care during laparoscopic cholecystectomy: a randomised controlled trial. J Minim Access Surg. 2025;21(4):234–242.
12. Cummings KC, Gomez Opisso E, Medhurst G, et al. Evaluation of opioid consumption and emergency department visits following high-dose opioid administration during anesthesia: a retrospective cohort study. J Clin Anesth. 2021; 71:110287.
13. Wilson SH, Hellman KM, James D, Adler AC, Chandrakantan A. Mechanisms, diagnosis, prevention and management of perioperative opioid-induced hyperalgesia. Pain Manag. 2021;11(4):405–417.
14. Gupta A, Karambelkar DJ, Srivastava U. Remifentanil and acute opioid tolerance: a systematic review. Anesthesiology. 2018;128(3):563–580.
15. Lavand'homme PM, Grosu I, France MN, Thienpont E. Pain trajectories identify patients at risk of persistent pain after knee arthroplasty: an observational study. Clin Orthop Relat Res. 2014;472(5):1409–1415.
16. Wang N, Zhang S, Liu L, Zhang Y, Liang M, Wang Y. Efficacy and safety of different preemptive analgesia measures in pain management after laparoscopic cholecystectomy: a systematic review and network meta-analysis of randomized controlled trials. J Pain Res. 2024; 17:2847–2862.
17. Memtsoudis SG, Kehlet H, Saldanha DF. Perioperative multimodal analgesia: an overview of opioid and non-opioid analgesics. Anesth Analg. 2022;134(4):776–791.
18. Wang Y, Gu Y, Zhang K, et al. Safety and effectiveness of multimodal opioid-free anaesthesia for pain and recovery after laparoscopic surgery: a systematic review and meta-analysis. Br J Surg. 2025;112(3):e123–e135.
19. Weinberg GL, Herr HR, McKeown NJ. Life support for local anesthetic toxicity. J Emerg Med. 2012;42(2):178–188.
20. Wylde V, Clarke A, Falworth M, et al. Patient-reported outcomes, postoperative pain and pain relief after day case surgery (POPPY): methodology for a prospective, multicentre observational study. BJA Open. 2024; 1:100064.