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CLINICAL TRIAL REPORT

Intraoperative Non-Opiate Anesthesia for Patients Undergoing Arthroscopic Temporomandibular Joint Surgery: A Randomized Controlled Trial

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Background: Pain intensity after temporomandibular joint (TMJ) surgery is often underestimated, and inadequate pain control may relate to poor recovery quality, increased opioid consumption, and longer hospital stay. This trial aims to evaluate whether non-opiate anesthesia provides a promising option of pain management for patients undergoing TMJ surgery.

Methods: Sixty patients receiving TMJ surgery were randomly assigned to either the control group or the non-opiate group. Non-opiate anesthesia used lidocaine, dexmedetomidine, and ketamine infusion therapy for pain management. The primary outcome was the highest documented pain score while in the post-anesthesia care unit (PACU). Secondary outcomes included perioperative opioid consumption, utilization, dosage, and timing of rescue analgesia in the PACU, incidence of postoperative nausea and vomiting in the PACU and at home, pain satisfaction levels, occurrence of opioid-related adverse effects, duration of PACU and hospital stays, and total consumption of oxycodone-acetaminophen tablets at 24 and 48 hours post-surgery.

Results: Patients were predominantly female (88.3%) and had a median age of 37.5 [IQR 26.0, 52.5] years. There were no significant differences observed in the highest documented pain scores (mean difference [MD] −0.36 points, 95% CI: −1.84, 1.12, p = 0.63), postoperative oxycodone-acetaminophen consumption (MD 6.68 mg, 95% CI: −2.48, 15.84, p = 0.15), pain satisfaction (odds ratio [OR] 0.81, 95% CI: 0.23, 2.81, p = 0.74), time to PACU discharge (hazard ratio [HR] 1.24, 95% CI: 0.67, 2.30, p = 0.49) or time to hospital discharge (HR 1.48, 95% CI: 0.80, 2.75, p = 0.21) between the two groups. Similarly, no significant difference was observed in time to rescue analgesia, calculated in minutes from the end of surgery (HR 1.69, 95% CI: 0.79, 3.61, p = 0.18).

Conclusion: Non-opiate anesthesia for pain management shows a similar postoperative analgesia effect, compared to opioid-based anesthesia, in patients undergoing arthroscopic TMJ surgery.

Keywords: non-opiate, anesthesia, temporomandibular joint disorders, temporomandibular joint, surgery

Introduction

Temporomandibular joint disorders (TMD) affect patients in various ways, ranging from headaches to temporomandibular joint (TMJ) misalignment and dysfunction.[1] The goal of TMD management is to alleviate pain, regain function of the joint, and improve quality of life for patients.[2] Treatment typically begins with a conservative but multimodal approach. Surgical intervention is indicated for refractory functional limitations where six months of nonsurgical management have not proven effective, or for significant structural or intraarticular disorders.[2–4] Modalities such as TMJ arthroscopy have proven to be an effective minimally invasive approach to manage TMDs in patients.[4]

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Pain, often underestimated and poorly controlled, is an unavoidable consequence of oral and maxillofacial (OMF) surgery.[5] Treatments for pain are administered through a multimodal approach, though opioid therapy is the primary means. Effective pain control is important because inadequate pain management is associated with poor recovery, increased opioid requirement and hospital stay.[6] Achieving adequate pain control is key for a well-rounded intraoperative anesthetic plan, but determination of the specific approach can be challenging. It is known that opioid therapy can result in undesirable side effects such as respiratory depression, postoperative nausea and vomiting, pruritus, and prolongation of postoperative ileus.[7] In addition, published papers have indicated that young adults are three times more likely to become long term users of opioids, and are about 30% more likely to misuse or abuse therapy in future.[8,9] Therefore, an alternative non-opiate approach to pain management may be a safer option for patients undergoing OMF surgery.

Alternative therapeutic approaches to pain during OMF surgery have not been fully investigated. To our knowledge, while some data indicate that non-opiate anesthesia and opioids may exert similar effect, there are few studies comparing their use in patients undergoing OMF surgery, suggesting that there is a lack of reported studies implementing non-opiate strategies for postoperative OMF pain management; specifically investigating the use of lidocaine, dexmedetomidine, and ketamine. While subanesthetic infusions of these non-opiate drugs supplemented with other intravenous agents and inhaled anesthetics have been used in other surgeries; this has not been previously reported for TMJ surgery. A Cochrane review reveals that lidocaine, when compared to a placebo, positively impacts pain scores and other secondary outcomes in patients undergoing elective or urgent surgery under general anesthesia.[10] Other reviews have reported similar outcomes with use of dexmedetomidine and ketamine as adjuncts for pain control in non-cardiac elective surgery.[11,12]

Given the paucity of data on this question, we conducted a randomized control trial investigating the efficacy and outcomes of non-opiate anesthesia using lidocaine, dexmedetomidine, and ketamine infusions for pain management in patients undergoing OMF surgery. Moreover, dexmedetomidine, ketamine and lidocaine exert strong analgesic effects during the intraoperative and postoperative periods, and do not induce respiratory depression or opioid-related post-operative complications. We hypothesized that by using a non-opiate anesthetic technique, we could reduce postoperative pain scores with fewer side effects than opioids, reduce the time until patients meet discharge criteria from the post-anesthesia care unit (PACU), and reduce postoperative opioid consumption while in the PACU and within the subsequent 48 hours of PACU discharge.

Methods

Study Design and Participants

This study was approved by the Mass General Brigham Institutional Review Board (IRB Protocol Number 2020P003873), and written informed consent was obtained from all subjects. The name of the approved IRB for this study was "The effect of opioid-free anesthesia in TMJ surgery: a prospective study". The trial was registered prior to patient enrollment at clinicaltrials.gov (Identifier: NCT04724759, Principal Investigator: Dr. Jingping Wang), and conducted in accordance with the Declaration of Helsinki. The date of our clinical trial's prospective registration was 2021–01-26, and the date of first patient enrollment was 2021–06-18.

This study enrolled eligible patients undergoing TMJ surgery at Massachusetts General Hospital. Specific inclusion criteria were detailed below: (1) Patients aged 18 to 75 (inclusive); (2) Scheduled for TMJ surgery (including both unilateral and bilateral procedures); (3) Planned arthroscopic surgical procedure; (4) Preoperative plan to discharge the same day. Specific exclusion criteria were as follows: (1) Inability to provide written informed consent; (2) Pregnant patients; (3) Open TMJ surgeries; (4) Planned overnight admission; (5) Mental status disorder or patient who are unable to communicate.

Randomization and Masking

Patients who consented to participate were randomized to one of two groups in a 1:1 fashion using permuted block randomization. The randomization schema was developed by a statistician and displayed in the Research Electronic Data Capture (REDCap) randomization module. This study involves two distinctly different medication administration strategies in the operating room, thus, it was not possible to blind the treating anesthesiologist. Patients and outcome-

assessors remained blinded to randomization groups to obtain unbiased assessments of pain and anesthesia outcomes postoperatively.

Drug Administration

Prior to surgery patients were randomized to one of two groups: Group 1, receiving non-opiate anesthesia, and Group 2, receiving opioid-based anesthesia. All other anesthetic care was standardized according to current institutional standards of care. All patients were given oral acetaminophen (950 mg) before entering the operating room unless contraindicated. General anesthesia was administered to all patients, involving proper oxygenation, propofol (2–2.5 mg•kg−1), succinylcholine (1 mg•kg−1), and intravenous lidocaine (1–1.5 mg•kg−1 bolus) for induction before nasal intubation.

In this study, patients were randomized into two groups: the non-opiate anesthesia group and the control group (opioid-based anesthesia). In the non-opiate group, lidocaine (1–1.5 mg•kg−1 bolus), ketamine (5 mcg•kg−1•min−1), and dexmedetomidine (0.5–1.0 μg•kg−1•hr−1) were continuously infused from induction until approximately one hour before the anticipated end of surgery. In the control group, standard opioid-based anesthesia was used, which included fentanyl (1 mcg•kg−1) during induction and redosed every 45 minutes until the end of surgery, supplemented as necessary. No opioids were used intraoperatively in the non-opiate group. Anesthesia maintenance for both groups was achieved with sevoflurane (0.7–1.3 MAC). Importantly, no opioids were used intraoperatively in the non-opiate group.

Both groups received routine perioperative care according to the standard clinical practice for TMJ surgery at our institution. All TMJ arthroscopic surgeries were performed by a single surgeon. At the end of TMJ arthroscopy, patients in both groups received an intra-articular administration of approximately 2–3 mL of a multi-modal solution containing ropivacaine, epinephrine, clonidine, and ketorolac.

Multimodal anti-emetics, including dexamethasone (12 mg IV), ondansetron (2–4 mg IV), and haloperidol (1 mg IV), were administered before emergence in accordance with the standard of care unless contraindicated.

Rescue analgesia was administered when patients exhibited signs of inadequate pain control. Specifically, it was provided if patients displayed hemodynamic changes indicative of pain (eg, an increase in heart rate or blood pressure exceeding 20% of baseline values), or if the patients themselves expressed that they could not tolerate their current level of pain and requested additional analgesia in the PACU. The goal was to ensure effective pain management in response to these clinical signs and patient-reported discomfort. The rescue analgesics given to patients during the PACU period for pain included oral and intravenous hydromorphone, intravenous fentanyl, and oxycodone. The doses of these medications were titrated based on the patient's pain level and clinical response. For example, intravenous fentanyl and hydromorphone were administered in small, incremental doses to manage pain while avoiding excessive sedation. The primary routes of administration for rescue analgesia were oral for oxycodone and intravenous (IV) for hydromorphone and fentanyl. All doses of opioid medications were converted to oral milligram morphine equivalents (MME) for analysis.

Patients had a preoperative plan to be discharged on the same day with the following standardized discharge medications for TMJ arthroscopic surgery (unless contraindicated). This included oxycodone-acetaminophen (5/325 mg, orally every six hours as needed for pain; dispensed: 20 tablets), meloxicam (7.5 mg orally once daily; dispensed: 60 tablets), and a muscle relaxant (5 mg orally every bedtime; dispensed: 60 tablets).

Study Procedures

Following intraoperative drug administration, patients were followed by blinded personnel until discharge from the PACU to assess study endpoints while in the hospital. Clinically documented PACU pain scores were abstracted from the medical record based on nursing documentation. Medication administration, particularly with respect to postoperative opioids, and anesthesia-related complication (postoperative nausea, vomiting, etc.) were also recorded.

At the time of discharge from the PACU, members of the study team asked each patient to complete a brief survey on their satisfaction with pain management. At the time of hospital discharge, patients were provided with medication and symptom diaries. These were used to record pain medication administration post-hospital discharge during the first 48 hours after surgery, and any pain or postoperative complications they might have experienced at home. Patients were contacted by the study team after postoperative day two to collect the information from these diaries. Patients were asked

to mail or Email a copy of the completed diaries to the study team. If these could not be returned, a complete record was obtained verbally during the phone call. At this point, the participation of subjects was considered complete.

Withdrawal or Early Termination of Study Procedures

Regardless of the randomization group patients were assigned to, the attending anesthesiologist had the discretion to treat any pain or discomfort, as needed clinically, as deemed appropriate. If subjects required additional pain medication dosing to achieve comfort, it was provided to ensure adequate analgesia for both of groups. We attempted to minimize crossover from the non-opiate group by standardizing the anesthetic regimen, as outlined above in the Drug Administration Section, while providing adjuvant non-opioid strategies first in the intraoperative period. If crossover occurred, this did not constitute termination of the study, as patients were analyzed according to the intention-to-treat principle. Participants were encouraged to complete the study, as planned, through postoperative day two. As with any research study, participation was completely voluntary. In the event that a patient requested to be withdrawn, study procedures were concluded. Data collected up until the point of withdrawal was used in the analysis.

Study Endpoints and Outcomes

The primary outcome assessed in this study was the worst recorded PACU pain score. Pain was measured using the eleven point (0 to 10) numeric rating scale. Pain scores were abstracted from nursing documentation in the electronic medical record from the end of surgery through discharge from the PACU. Secondary outcomes assessed included opioid consumption in MME during the first 12, 24, and 48 hours postoperatively, the use, dose, and time to use of rescue analgesia in the PACU (MME), the incidence of postoperative nausea and vomiting in PACU and at home after surgery, pain satisfaction (self-reported at the time of PACU discharge using the Revised American Pain Society Patient Outcome Questionnaire [APS-POQ-R]), the incidence of opioid related adverse effects (ileus, nausea, vomiting, and pruritus), the length of PACU and hospital stay, and the total dose of oxycodone-acetaminophen used at 24 and 48 hours after surgery.

Statistical Analysis

Descriptive statistics are summarized and reported. Categorical variables are reported as frequency counts (percent), and continuous variables are reported as median [quartile 1, quartile 3]. Normality of continuous data was assessed via visual inspection of the data (eg, histogram). Standardized mean differences (SMDs) are reported to understand differences between patients randomized to receive non-opiate anesthesia compared to those randomized to the control group. An SMD > 0.10 was used to suggested imbalance between groups.[13]

In this study, the primary outcome of worst PACU pain score was evaluated, along with secondary outcomes of postoperative oxycodone-acetaminophen use, postoperative opioid use, self-reported patient pain satisfaction, time to rescue analgesia, time to PACU discharge, and time to hospital discharge. All models were adjusted for prognostic covariates including age, sex, history of depression, and preoperative pain score. The primary outcome was evaluated using a generalized linear model with a gaussian distribution and identity link conditional on randomization group assignment and prognostic covariates. For secondary outcomes, the dose of oxycodone-acetaminophen used postoperatively was recorded via self-reported patient medication diaries. Patients recorded the dose taken in milligrams; therefore, postoperative oxycodone-acetaminophen use was evaluated as a continuous outcome, using the same methods as the primary outcome. Postoperative opioid use was analyzed as a binary outcome and was evaluated using a generalized linear model with a logit link, and patient pain satisfaction was analyzed as an ordinal outcome and evaluated using an ordered logistic regression. Time to rescue analgesia, PACU discharge, and hospital discharge were analyzed as time-to-event data using Cox Proportional Hazards models. Results for continuously scaled, binary and ordinal, as well as time-to event outcomes are reported as adjusted mean differences (MD), odds ratios (OR) or hazard ratios (HR), respectively, and their associated 95% confidence intervals (CI). Results of each model were evaluated using two-sided p-values, with less than 0.05 considered statistically significant.

A power calculation was performed using data from a previous study,[14] in which the worst postoperative pain score in the standard of care group was 6. Assuming increased variability (standard deviation of 2.5) in the standard of care group in the current study and a two-point reduction in the non-opiate group, 1:1 sampling ratio, type I error of 0.05 and power

of 0.80, a total of 26 subjects per group were required. Thus, this study aimed to enroll 30 patients per group. All analyses were conducted using RStudio version 4.2.3.[15]

Results

From June 2021, to April 2023, a total of 130 patients were screened for inclusion, and 60 patients were ultimately enrolled (Figure 1). Descriptive statistics for baseline characteristics are summarized and reported (Table 1). Patient age was well balanced between treatment groups. Females made up 88.3% of the study cohort. Meaningful differences between groups were additionally identified in patient race, presence of preoperative depression, rheumatoid arthritis, and American Society of Anesthesiologists (ASA) physical status score. Preoperative pain scores were not meaningfully different between groups (0.0 [0.0, 4.0] in non-opiate, 1.0 [0.0, 3.5] in control, Table 1).

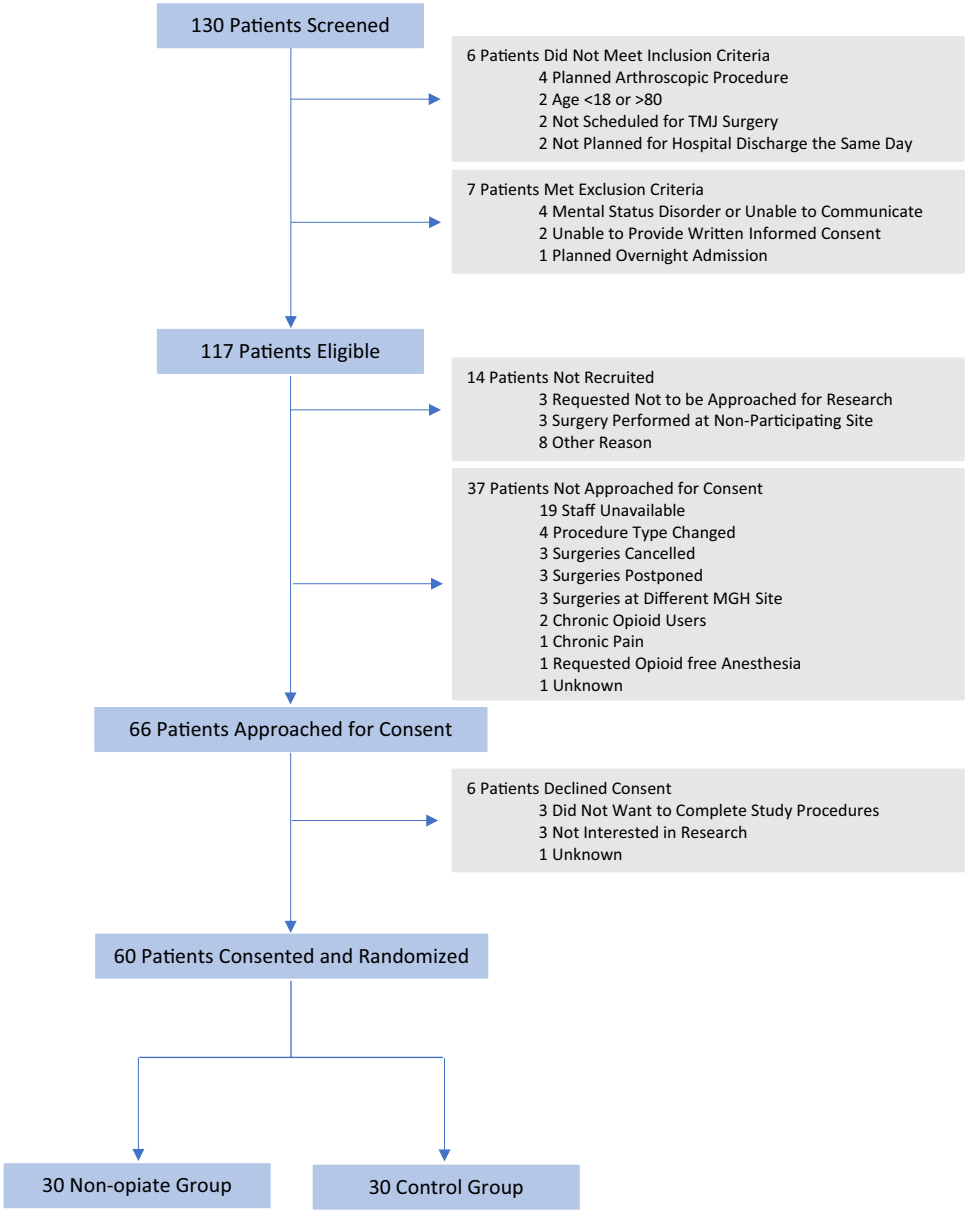

Figure 1 Consort Diagram. Patient flow is outlined at each step. Of the 130 patients screened, 60 were ultimately consented and randomized. There were 30 patients in each treatment group.

Table 1 Baseline Characteristics

	Non-opiate	Control	SMD
	N = 30	N = 30	
Age	38.0 [26.0, 51.8]	36.5 [27.5, 53.3]	0.026
Male Sex	3 (10.0)	4 (13.3)	0.104
Race			0.604
White	23 (76.7)	24 (80.0)	
Black	0 (0.0)	1 (3.3)	
Asian	1 (3.3)	4 (13.3)	
Other	3 (10.0)	0 (0.0)	
Unknown/Unspecified	2 (6.7)	1 (3.3)	
Hispanic	3 (10.0)	0 (0.0)	0.499
Preoperative Pain Score	0.0 [0.0, 4.0]	1.0 [0.0, 3.5]	0.152
Anxiety	16 (53.3)	17 (56.7)	0.067
Depression	17 (56.7)	11 (36.7)	0.409
Previous Anesthesia Complication	3 (10.0)	3 (10.0)	<0.001
Rheumatoid Arthritis	2 (6.7)	0 (0.0)	0.378
Psoriatic Arthritis	0 (0.0)	0 (0.0)	<0.001
Ankylosing Spondylitis	0 (0.0)	1 (3.3)	0.263
Osteoarthritis	3 (10.0)	3 (10.0)	<0.001
ASA			0.479
I	5 (16.7)	11 (36.7)	
II	21 (70.0)	15 (50.0)	
III	4 (13.3)	4 (13.3)	

Note: [a]Data is presented as n (percent) or median [quartile 1, quartile 3] with standard mean differences.

There was no significant difference observed in the worst documented PACU pain score in the control group compared to the non-opiate group (MD −0.36 points, 95% CI: −1.84, 1.12, p = 0.63). The median opioid use while in the PACU was the same in both groups (median 5.0 [IQR 0.0, 25.0] MME), and there was no significant difference in whether patients used opioids postoperatively in the control group compared to the non-opiate group (OR 0.72, 95% CI: 0.18, 2.66, p = 0.62) (Table 2, 3). There were higher frequencies of all opioid-related adverse effects (nausea, vomiting, pruritus, and ileus) documented in the 48 hours after discharge from the PACU by patients in the control group compared to the non-opiate group (Table 2). No significant differences were observed in postoperative oxycodone-acetaminophen consumption, or pain satisfaction in the control group compared to the non-opiate group (MD 6.68 mg, 95% CI: −2.48, 15.84, p = 0.15; OR 0.81, 95% CI: 0.23, 2.81, p = 0.74), respectively (Table 3). For time to event outcomes, there were no significant differences in time to PACU or hospital discharge (HR 1.24, 95% CI: 0.67, 2.30, p = 0.49; Hospital HR 1.48, 95% CI: 0.80, 2.75, p = 0.21), respectively. Similarly, there was no significant difference in time to rescue analgesia in the control group compared to the non-opiate group (HR 1.69, 95% CI: 0.79, 3.61, p = 0.18; Table 3). Patients in the control group did have a lower median time to rescue compared to the non-opiate group (Figure 2; Table 2).

Discussion

The comparison of opioid and non-opioid anesthesia in our study revealed important insights into their efficacy in managing postoperative pain. While our findings suggest no statistical difference between the two regimens in the context of low-intensity pain, as indicated by the highest mean pain score of 4.9, it is essential to interpret these results with caution. The observed pain levels may have been influenced by various factors, including the administration of local anesthetic agents such as ropivacaine, clonidine, and ketorolac, which may have mitigated postoperative discomfort. Therefore, while our study provides valuable information on the comparative effectiveness of opioid and non-opioid anesthesia, further research is warranted to validate these findings across a broader spectrum of pain intensities and surgical procedures.

Table 2 Outcome Measures

	Non-opiate N = 30	Control N = 30
Worst Documented PACU Pain Score	4.9 (2.4)	4.4 (2.8)
Patients with Postoperative Opioid Use[b]	21 (70.0)	20 (66.7)
Postoperative Opioid Use in Hospital *(MME)*	5.0 [0.0, 10.0]	5.0 [0.0, 10.0]
Postoperative Oxycodone-Acetaminophen Use at Home[c] *(mg)*	0.0 [0.0, 25.0]	5.0 [0.0, 25.0]
Opioid Related Adverse Effects in Hospital	0 (0.0)	0 (0.0)
Opioid Related Adverse Effects at Home		
Nausea	5 (16.7)	9 (30.0)
Vomiting	0 (0.0)	1 (3.3)
Pruritus	2 (6.7)	3 (10.0)
Ileus	2 (6.7)	5 (16.7)
Patient Pain Satisfaction		
0	1 (3.3)	0 (0.0)
1	1 (3.3)	0 (0.0)
2	0 (0.0)	0 (0.0)
3	0 (0.0)	1 (3.3)
4	0 (0.0)	0 (0.0)
5	1 (3.3)	1 (3.3)
6	0 (0.0)	0 (0.0)
7	0 (0.0)	1 (3.3)
8	5 (16.7)	6 (20.0)
9	2 (6.7)	2 (6.7)
10	18 (60.0)	14 (46.7)
No Survey	2 (6.7)	5 (16.7)
Procedure Length *(minutes)*	109.5 [80.0, 137.3]	109.5 [86.3, 129.0]
Time to Rescue Analgesia *(minutes)*[d]	90.0 [65.3, 100.3]	62.0 [44.5, 82.3]
Time to PACU Discharge *(minutes)*[e]	227.0 [192.5, 268.0]	206.0 [176.3, 244.8]
Time to Hospital Discharge *(hours)*[f]	4.1 [3.4, 4.8]	3.8 [3.0, 4.3]

Notes: [a]Data is presented as mean (standard deviation), median [quartile 1, quartile 3], or n (percent). [b]Postoperative opioid use refers to opioids that were administered while patients were in the PACU. Due to the brief length of stay in the hospital, no opioids were administered to patients other than while in the PACU. [c]Postoperative oxycodone-acetaminophen use is specified separately as it was self-administered, post-discharge, and recorded in patient medication diaries. [d]Time to Rescue Analgesia was measured from the end of surgery to the time of rescue medication. [e]Time to PACU Discharge was measured from the end of surgery to the time of PACU discharge. [f]Time to Hospital Discharge was measured from the end of surgery to the time of hospital discharge.
Abbreviations: MME, Milligram Morphine Equivalents; PACU, Post-anesthesia Care Unit.

Table 3 Results

	N	Estimate[a]	95% CI	p
Continuous Outcomes		*Mean Difference*		
Worst PACU Pain Score *(primary outcome)*	50	−0.36	−1.84, 1.12	0.63
Postoperative Oxycodone-Acetaminophen Use *(mg)*	50	6.68	−2.48, 15.84	0.15
Binary & Ordinal Outcomes		*Odds Ratio*		
Postoperative Opioid Use[b]	50	0.72	0.18, 2.66	0.62
Patient Pain Satisfaction	43	0.81	0.23, 2.81	0.74
Time to Event Outcomes		*Hazard Ratio*		
Time to Rescue Analgesia[c]	50	1.69	0.79, 3.61	0.18
Time to PACU Discharge[d]	50	1.24	0.67, 2.30	0.49
Time to Hospital Discharge[e]	50	1.48	0.80, 2.75	0.21

Notes: [a]Model estimates are control group compared to non-opiate group, all models are adjusted for prognostic covariates age, sex, preoperative pain score, and depression. [b]Postoperative opioid use was assessed as a binary outcome, whether or not patients used opioids while in the PACU. [c]Time to Rescue Analgesia was measured from the end of surgery to the time of rescue medication. [d]Time to PACU Discharge was measured from the end of surgery to the time of PACU discharge. [e]Time to Hospital Discharge was measured from the end of surgery to the time of hospital discharge.
Abbreviation: PACU, Post-anesthesia Care Unit.

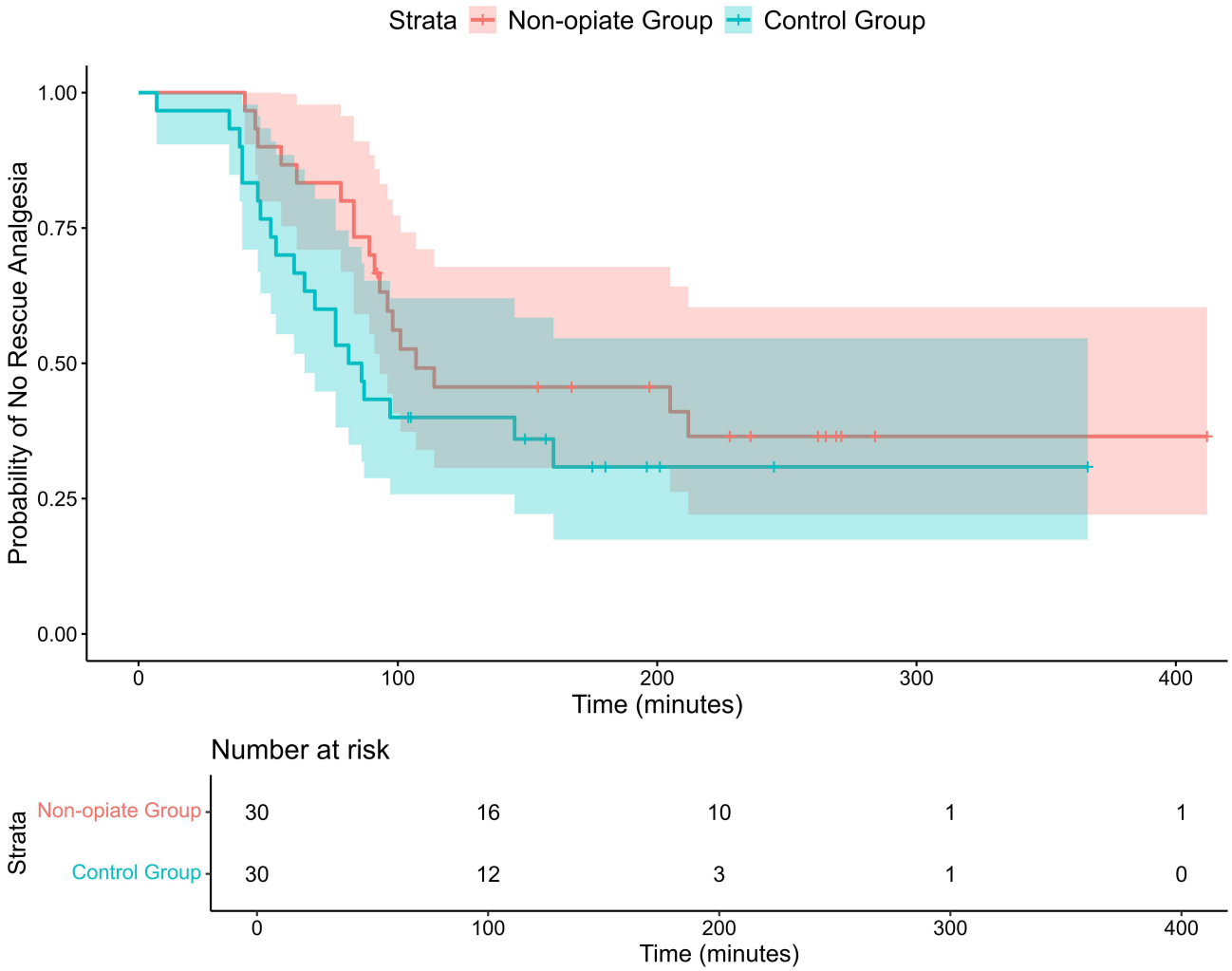

Figure 2 Time to Rescue Analgesia in the PACU. The unadjusted model for time to rescue analgesia in the PACU is reported, stratified by treatment group. Patients in the control group are reported in blue and patients in the non-opiate group are reported in red.

Our study results suggest that opioid therapy for TMJ surgery is not statistically different compared to a non-opiate approach. Given these findings, it could be speculated that either approach would be sufficient to provide analgesia for patients undergoing TMJ surgery. These results are clinically relevant because opioid therapy does not come without risks, and some patient populations may benefit by avoiding opioid therapy altogether. A similar non-opiate anesthesia protocol using lidocaine, dexmedetomidine and ketamine was performed by Mulier, and has been reported to improve postoperative recovery and opioid-related complications, especially in obese and maternal patients.[16,17] Based on our study results that there is no significant difference, a non-opiate therapy could be considered for obese patients with risk factors such as obesity and diabetes. Providers with high risk patients can tailor an anesthetic plan specific to their patients' needs and determine whether they would benefit from a non-opiate therapy, reassured that adequate analgesia can be provided regardless of the approach.

Previous studies have demonstrated that dexmedetomidine, ketamine and lidocaine have significant analgesic effects during the intraoperative and postoperative periods without respiratory depression or opioid-related postoperative complications. Intraoperative pain usually comes from the stimulation of the surgical operation while postoperative pain is principally attributed to inflammatory pain, neuropathic pain, or hyperalgesia.[18] Intravenous lidocaine produces prolonged analgesic effects through anti-inflammatory effects and inhibiting neuropathic pain.[19,20] The anti-inflammatory effects of lidocaine are in connection with interactions with polymorphonuclear cells and the inhibition of G protein-coupled receptors.[21,22] Also, lidocaine can inhibit spontaneous impulse generation from injured peripheral nerves and

dorsal root ganglions proximal to the injured fibers and suppress polysynaptic reflexes in the spinal dorsal horn.[23] Dexmedetomidine is a highly selective α2 adrenergic agonist and exhibits analgesic effects through peripheral and central pathways.[24] In the central nervous system, dexmedetomidine can activate α2 adrenoceptors in the spinal level in neurons of the dorsal horn and in the locus coeruleus at a supraspinal level.[25] The peripheral analgesic effects may attribute to relief of surgical stress responses and anti-inflammatory shift in immunological responses. However, the anti-inflammatory effects of dexmedetomidine are not entirely clear.[26,27] Ketamine is an analgesic and acts as a noncompetitive antagonist to NMDA receptor in the central nervous system, particularly in the prefrontal cortex and hippocampus.[28,29] Ketamine also can produce antagonistic effects on other receptors relating to pain regulation including nicotinic and muscarinic cholinergic receptors and sodium and potassium channels.[30,31] Though ketamine has been proven to alleviate opioid tolerance and hyperalgesia in preclinical studies, the clinical effects are limited in perioperative opioid dosage and analgesia.[32,33] Thus, non-opiate pain control in our study is a multimodal analgesic approach to pain management and achieved similar analgesic effects when compared with the opioid-based anesthetic regimen.

The potential for synergistic effects among ketamine, dexmedetomidine, and lidocaine is indeed significant and merits further exploration. While individual studies may offer insights into the effects of each agent, understanding their combined impact in clinical practice remains an area of ongoing interest. The unique pharmacological properties of each drug suggest the possibility of synergism, particularly in modulating pain perception, sedation, and hemodynamic stability.

Despite promising points, non-opiate anesthesia may be associated with potential complications that were not explicitly observed or evaluated in this study. Firstly, ketamine, as a dissociative anesthetic, may induce hallucinations, delirium, and vivid dreams, especially at higher doses. Secondly, dexmedetomidine, as a selective α2-adrenergic agonist, may lead to bradycardia and hypotension, particularly during anesthesia induction and maintenance. Additionally, as a local anesthetic, lidocaine could result in systemic toxicity if administered in excessive doses or inadvertently injected into a blood vessel, manifesting as central nervous system excitation followed by depression, cardiovascular collapse, and seizures. In future research, sufficient attention to the aforementioned side effects should be considered and formally measured.

Potential limitations in our study include the short duration of arthroscopic TMJ surgery and the low dosage of intraoperative opioid consumption. In the context of this study, the effects of opioids may be too small to result in a detectable difference between groups. Additionally, our study did not distinguish between unilateral and bilateral surgical patients. The assessment of a larger study population is needed to draw more definitive conclusions. It is also pertinent to acknowledge the limitations of the demographic composition of our study population. Our subjects were predominantly Caucasian females, which aligns with the demographic profile of patients commonly affected by this condition; however, this lack of diversity in race and gender representation raises questions about the generalizability of our results. Future studies should aim to recruit a more diverse sample to ensure that the findings can be extrapolated to a wider range of patient demographics. In addition, the effect of non-opiate anesthesia on postoperative pain may not appear significant because the drugs were stopped 1 hour before surgery ends. Therefore, it is probably suitable for a short duration procedure. In our study of patients undergoing arthroscopic TMJ surgery, non-opiate anesthesia resulted in postoperative analgesic effects that were not statistically different when compared to the standard opioid-based regimen. Future research is needed with a larger, more diverse patient population to draw any strong conclusions regarding which method may be optimal for pain management.

Conclusion

Non-opiate anesthetic techniques offer a viable alternative for achieving comparable analgesic effects to opioid medications in patients undergoing arthroscopic TMJ surgery. This presents a novel option for surgical patients who either cannot use opioids or prefer to avoid them. Contrary to our initial expectations, we found that a combination of lidocaine, dexmedetomidine, and ketamine infusion therapy for pain management in these patients resulted in postoperative analgesia that was not significantly different than that provided by opioids. Our study also sets the stage for broader application of non-opiate general anesthetic techniques across various surgical procedures.

Data Sharing Statement

The data generated during the current study are available from the corresponding author (Jingping Wang) upon reasonable request. The study protocol, statistical analysis plan, and clinical study report will also be available.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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