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A Comparative Study of Esketamine-Propofol and Sufentanil-Propofol for Analgesia and Sedation During Breast Minimally Invasive Rotary Resection with Local Anesthesia: A Randomized Double-Blind Clinical Trial

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Purpose: Minimally invasive rotary resection (MIRR) is crucial for diagnosing and treating breast tumors, but the optimal intravenous anesthesia regimen is unclear. Esketamine, an NMDA receptor antagonist with anesthetic, analgesic, and sympathomimetic properties, may provide an ideal adjunct to propofol sedation. This study aims to compare the safety and efficacy of esketamine versus sufentanil as adjuncts to propofol for analgesia and sedation during breast MIRR.

Patients and Methods: A total of 90 patients undergoing elective breast MIRR were randomly assigned to receive either sufentanil-propofol or esketamine-propofol for analgesia and sedation. The primary outcome was the occurrence of hypoxia (SpO_2 < 92% for >10s or exhibiting a persistent downward trajectory). Other outcomes included incidence of subclinical respiratory depression (92% ≤ SpO_2 < 95% for >10s), number of airway interventions, awakening time, satisfaction scores, postoperative exhaust time, hemodynamic parameters, and side events.

Results: Finally, 41 patients were assigned to the sufentanil group and 40 to the esketamine group. The occurrence of hypoxia was significantly lower in the esketamine group (17.5%) than in the sufentanil group (39%) (P = 0.032). Subclinical respiratory depression occurred in 32.5% of the esketamine group and 56.1% of the sufentanil group (P = 0.033). The sufentanil group required more airway interventions than the esketamine group (P = 0.032), and patients in the sufentanil group experiencing hypoxia received more mask-assisted ventilation (P = 0.029). Hemodynamic stability was better in the esketamine group. No significant differences were observed in awakening time, satisfaction score, postoperative exhaust time, or side events between groups.

Conclusion: Esketamine-propofol anesthesia significantly reduces the risk of hypoxia (SpO_2 < 92%) compared to sufentanil-propofol, while maintaining similar awakening time, satisfaction, postoperative exhaust time, and side events. Its hemodynamic advantages make it valuable for clinical use, especially in procedures requiring respiratory and hemodynamic stability.

Keywords: esketamine, hypoxia, respiratory depression, minimally invasive rotary resection, breast tumor

Introduction

Minimally invasive rotary mastectomy (MIRR) is an ultrasound-guided technique that uses negative pressure suction to remove breast masses. Compared to open surgery, MIRR offers faster, safer, and less invasive treatment with fewer complications and higher patient satisfaction. It has become the preferred method for diagnosing early breast lesions and

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excising benign tumors.[1] Traditional local anesthesia, is essential for MIRR's advancement; however, it is often associated with issues such as inadequate dosage, drug accumulation, and tissue swelling, leading to inadequate anesthesia and increased patients' discomfort experience and procedure difficulty.[2] In contrast, combining analgesia and sedation with local anesthesia provides a simple, cost-effective, and safe approach to pain relief, ensuring a more comfortable experience and meeting surgical needs effectively during minimally invasive procedures.[3,4]

No single intravenous anesthetic currently provides both sufficient analgesia and sedation with minimal side effects. Therefore, anesthesiologists often combine two or more anesthetics for optimal anesthesia.[5] Propofol is widely used for safe and controlled sedation.[6] However, due to its lack of analgesic properties, it is frequently combined with opioids like sufentanil during minimally invasive procedures to achieve the desired anesthetic effect.[7,8] Nevertheless, researches indicate that both propofol and opioids carry a risk of respiratory depression, which is exacerbated in combination.[9,10] Thus, optimizing anesthetic regimens for breast MIRR by adjusting anesthetic combinations is necessary.

Esketamine, the S-enantiomer of ketamine, offers simultaneously sedative and analgesic effects.[11] Previous studies indicated that low-dose esketamine reduced propofol requirements during endoscopic surgery without increasing side events and affecting patients' and endoscopists' satisfaction.[12] Additionally, esketamine's sympathomimetic property can counteract propofol-induced cardiorespiratory inhibition,[13] making it a potential alternative to opioids as an adjunct to propofol sedation. To achieve widespread acceptance, the anesthetic efficacy and safety of the esketamine-propofol combination must be validated across various procedures.

On this account, we conducted a randomized controlled trial to compare the efficacy and safety of esketamine versus sufentanil combined with propofol for analgesia and sedation in patients undergoing breast MIRR.

Material and Methods

Ethics and Trial Registration

The study was conducted at the People's Hospital of Ningxia Hui autonomous region, a tertiary hospital in Yinchuan, China, from February 2024 to June 2024. The study was approved by the ethics committee of the People's Hospital of Ningxia Hui Autonomous Region (2023-NZR-136) and registered in the Chinese Clinical Trial Registry (ChiCTR 2400080406). The clinical trial complies with the Declaration of Helsinki. Prior to participation, written informed consents were obtained from each patient. The protocol strictly adhered to applicable CONSORT (Consolidated Standards of Reporting Trials), as illustrated in Figure 1, providing a detailed overview of the trial procedures. No modifications were made to critical methodologies after the commencement of the trial.

Inclusion and Exclusion Criteria

Patients aged 18–65 years, with American Society of Anesthesiologists physical status (ASA PS) I–II, a body mass index (BMI) of 18–30 kg/m², scheduled for elective breast MIRR surgery under analgesia and sedation, were enrolled. Exclusion criteria included hearing dysfunction, psychiatric or neurological diseases, hypertension (>140/90 mmHg upon admission to the operating room), basic SpO_2<92%, hyperthyroidism, pregnancy, sleep apnea hypopnea syndrome, liver or kidney dysfunction, drug or alcohol abuse history, and allergies or contraindications to study anesthetics. Patients requiring tracheal intubation or experiencing drug allergies during operation were excluded from the final analysis.

Randomization and Blinding

The block randomization allocation scheme, completed by an independent researcher via www.randomizer.org, was sealed in sequentially numbered opaque envelopes. Participants were randomly assigned in a 1:1 ratio to receive either the sufentanil-propofol (sufentanil group) or the esketamine-propofol (esketamine group) combination. Group assignments were blinded to participants, surgeons, and the researcher collecting and analyzing data. Only the anesthesiologists and nurse assistants, who were not involved in assessment or follow-up, were unblinded.

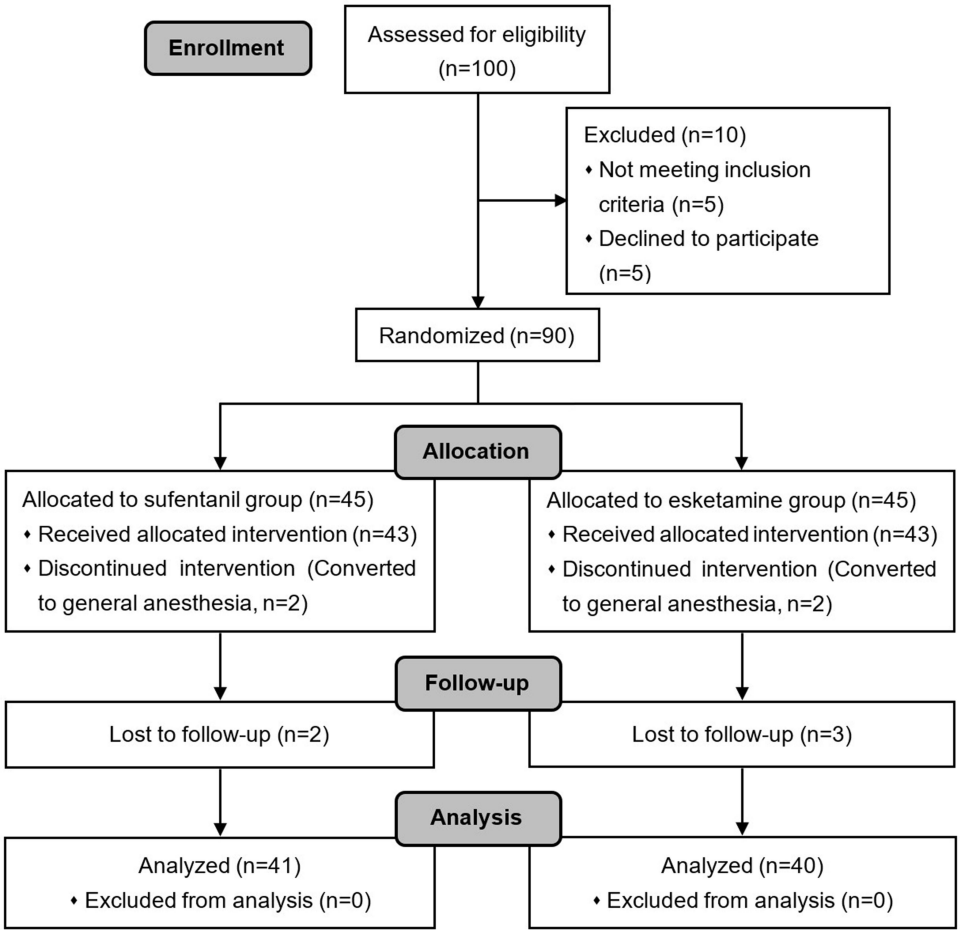

Figure 1 Study protocol flowchart.

Study Interventions

No premedication was given. The operating room was kept warm to prevent shivering. Peripheral venous access was obtained in a large forearm vein for fluid and drug administration. Lactated Ringer's solution was infused at 10 mL/kg/h for pre-hydration. Routine monitoring included mean arterial pressure (MAP), pulse oximetry saturation (SpO_2), heart rate (HR), and respiratory rate (RR). Oxygen was continuously supplied via nasal catheter at 6L/min. Patients were positioned flat, head tilted 30°–45°to one side, without a pillow.

The study drugs were prepared by an assistant as follows: esketamine (one ampoule containing 50mg in a concentration of 25mg/mL, Jiangsu Hengrui Pharmaceutical Co., Ltd.) was diluted with saline to 20 mL, yielding a concentration of 2.5mg/mL, and sufentanil (one ampoule containing 50μg in a concentration of 50μg/mL, Yichang Renfu Pharmaceutical Co., Ltd) was similarly diluted to 20 mL, yielding a concentration of 2.5μg/mL. After disinfecting the surgical site, patients in the sufentanil group received 0.1μg/kg of sufentanil intravenously, while those in the esketamine group received 0.25mg/kg of esketamine. Subsequently, each patient received 1mg/kg of propofol (AstraZeneca Corporation, London, England) intravenously over 10–20 seconds. The modified Observer's Assessment of Alertness/Sedation (MOAA/S) score was used to assess sedation level.[12]

During surgery, the target MOAA/S score for sedation was 1, with the patient responding only after a painful trapezius squeeze. If the MOAA/S score > 1 one minute after propofol administration, an additional 0.1 mg/kg dose was given as needed. The incision block with a combination of 10 mL of 0.375% ropivacaine and 1% lidocaine was performed by the physician before the procedure. All patients received continuous propofol infusion at 4–12 mg/kg/h during procedure. If intraoperative body movement (eg, spontaneous limb movements, pain reflexes, muscle rigidity, or

agitation) occurred or the MOAA/S score > 1, 0.5mg/kg of propofol was administered first, followed by 0.05mg/kg esketamine (in the esketamine group) or 0.05μg/kg sufentanil (in the sufentanil group). Maximum doses were 0.5 mg/kg for esketamine and 0.3 μg/kg for sufentanil. Propofol infusion was stopped at the end of procedure and 2mg of tropisetron (Hangzhou Minsheng Pharmaceutical Co., Ltd.) was administered intravenously to all patients.

Subclinical respiratory depression is defined as SpO_2 between 92% and 95% for more than 10 seconds. Hypoxia is defined as SpO_2 below 92% for more than 10 seconds or showing a continuous decline. Patients will sequentially receive interventions such as head position adjustment, jaw-lifting or mask-assisted ventilation. If the prior intervention does not improve hypoxia within 10 seconds (SpO_2 remains below 90% or continues to decrease), the next intervention will be applied.

Hypotension is defined as MAP below 65mmHg or a 30% decrease from baseline, treated with 5–10 mg of intravenous ephedrine. Hypertension is defined as a 30% increase from baseline, treated with 10 mg of intravenous urapidil. For HR < 50 beats per minute, 0.25–0.5mg of atropine is administered intravenously. All drug dosages are recorded.

All procedures were conducted by an experienced breast surgeon, while the same anesthesiologist carried out anesthesia. Data collection and recording were performed by another trained physician.

Outcomes

The primary outcome was the occurrence of hypoxia. Other outcomes included the incidence of subclinical respiratory depression, the number of body movements, the number of each airway intervention, the duration of anesthesia and procedure, and the awakening time (defined as the time between cessation of propofol pumping and MOAA/S of 4). Furthermore, we also recorded anesthetic dosages, as well as the amount and average size of breast nodules. MAP and HR were recorded at multiple time points: resting for 5 minutes after the patient enters the operating room serves as the baseline value (T_0), 1 min after propofol administration (T_1), and 1 min (T_2), 3 min (T_3) after skin incision, and at the end of the procedure (T_4). Post-procedure, the surgeon assessed procedure difficulty using a three-point scoring system (easy = 1, moderate = 2, complex = 3). Surgeon's and patients' satisfaction with anesthesia were evaluated using a five-point Likert scale (very dissatisfied = 1 to highly satisfied = 5).[12] The Modified Aldrete score[14] was employed to assess postoperative recovery at various intervals: upon admission to the PACU (T_a), and at 15 (T_b), 30 (T_c), 45 (T_d), and 60 (T_e) min thereafter. We also documented the highest Numerical rating scale (NRS) score in the PACU and time to first postoperative exhaust. Finally, perioperative side reactions, including nausea or vomiting, injection pain, hypotension, hypertension, bradycardia, dizziness, and delirium were noted.

Sample Size

The sample size was calculated using PASS 15 software, with hypoxia incidence as the primary evaluation index. Pilot results showed a hypoxia rate of 45% in the sufentanil group, and we estimated a reduction of 15% in the esketamine group. Assuming a = 0.05 and 1-β = 0.8, the sample size of each group was determined to be 36 using the sample size calculation formula for effectiveness test. Considering the 20% shedding rate, 90 patients were planned for enrollment, 45 in each group.

Statistical Analysis

SPSS ver. 23.0 for Windows (SPSS Inc., IL, USA) was used for statistical analysis. Measurement data were detected for normal distribution using the Shapiro–Wilk test. For normally distributed data, variables were analyzed by two independent-sample *t*-test between groups and repeated measures ANOVA within groups, and Bonferroni method was used for pairwise comparisons of post hoc tests. If a significant difference in MAP or HR between groups was observed at a given time point, the variables at that time point were included as a covariate, and group differences at the subsequent time point were analyzed using ANCOVA, and data are expressed as the Mean ± SD. Non-normally distributed data were compared using the Mann–Whitney *U*-test between groups and the Friedman test within groups. For post hoc tests following the Friedman test, the Wilcoxon signed-rank test was used with a Bonferroni correction to adjust the significance level, and data are expressed as the Median (IQR). Categorical data were analyzed using a chi-square (χ^2) test or Fisher's exact test, and data were expressed as n (%). Missing data were tested to determine if they were missing at random; if not, the last observation carried forward method was used. Additionally, to precisely analyze

the differences in HR and MAP between the two groups at each time point, as well as the changes within each group over different time points, we further employed a mixed-effects model. This model incorporated treatment intervention and time points as fixed effects while also considering the interaction between intervention and time. A P value of < 0.05 was considered statistically significant.

Results

Patient Inclusion and Exclusion

The CONSORT flow diagram is shown in Figure 1. From February 2024 to July 2024, 100 patients were assessed for eligibility. Five patients did not meet the inclusion criteria, and five declined participation, leaving 90 patients randomly assigned to either sufentanil or esketamine in combination with propofol. Two patients in each group converted to general anesthesia due to changes in the procedure, while two in the sufentanil group and three in the esketamine group were lost to follow-up. Ultimately, 41 patients in the sufentanil group and 40 in the esketamine group were included in the final statistical analysis.

Patient Characteristics and Baseline Values

The patients' demographic characteristics and baseline values are shown in Table 1. SpO_2 was higher in the sufentanil group compared to the esketamine group [98.0(97.0, 100.0) vs 97.5(96.0, 99.0), P = 0.044], but this difference is clinically insignificant. Although the proportion of patients with motion sickness was higher in the sufentanil group, there were no significant differences between the two groups (sufentanil vs esketamine, 24.4% vs 15.0%; P = 0.289).

The Procedure and Related Outcomes

In the sufentanil group, more bilateral minimally invasive resections were performed compared to the esketamine group (61% vs 37.5%, P = 0.035), leading to longer procedure [22 (14, 30) vs 14 (10.3, 25.5), P = 0.015] and anesthesia [27

Table 1 Baseline Patient Characteristics

Variable	Sufentanil group (n=41)	Esketamine group (n=40)	$t/\chi^2/Z$	P value
Age, Mean ± SD	39.9±11.4	38.9±10.7	0.399	0.691
Weight, kg, Median (IQR)	60.0(52.8, 65.0)	60.0(52.0, 67.88)	−1.249	0.212
Height, cm, Mean ± SD	161.5±4.3	162.5±5.5	−0.927	0.357
BMI, kg/m^2, Mean ± SD	22.6±3.0	23.1±3.5	−0.904	0.369
ASA Physical Status Classification	17(41.5)	10(25.0)	2.470	0.116
I, n (%)	24(58.5)	30(75.0)		
II, n (%)				
Mallampati score	28(68.3)	20(50.0)	2.806	0.094
I, n (%)				
II, n (%)	13(31.7)	20(50.0)		
Heart rate, Mean ± SD	76.2±9.2	75.9±8.5	0.162	0.872
MAP, Mean ± SD	91.3±10.3	94.6±8.9	−1.531	0.130
SpO_2, Median (IQR)*	98.0(97.0, 100.0)	97.5(96.0, 99.0)	−2.017	0.044
Smoking history, n (%)	0(0)	0(0)	–	1.000-
Alcohol intake, n (%)	0(0)	0(0)	-	1.000
Motion sickness, n (%)	10(24.4)	6(15.0)	1.126	0.289
Degree of education, n (%)	2(4.8)	3(7.5)	1.184	0.780
Without education, n (%)	5(12.2)	5(12.5)		
Elementary school, n (%)	12(29.3)	8(20)		
Secondary school, n (%)	22(53.7)	24(60)		
University school, n (%)				

Notes: BMI: Body Mass Index, SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure, ASA: American Society of Anesthesiologists, IQR: Interquartile Range, SD: Standard Deviation. *$P<0.05$ between groups.

Table 2 Perioperative Outcomes

Variable	Sufentanil group (n=41)	Esketamine group (n=40)	t/χ^2/Z	P value
Type of procedure, n (%) *	16(39.0)	25(62.5)	4.464	0.035
Unilateral minimally invasive resection	25(61.0)	15(37.5)		
Bilateral minimally invasive resection				
The amount of breast nodules, Median (IQR)	3(2, 4)	2(1, 3)	−1.362	0.173
The average size of breast nodules, cm, Median (IQR)	1.0(0.9, 1.4)	1(1.0, 1.8)	−1.796	0.072
Difficulty level of procedure 1/2/3, (n)	20/20/1	19/20/1	0.274	1.000
Procedure duration, min, Median (IQR)*	22 (14, 30)	14(10.3, 25.5)	−2.430	0.015
Anesthesia duration, min, Median (IQR)*	27(18, 38.5)	22(13, 30)	−2.156	0.031
Awakening time, min, Median (IQR)	5(4, 7)	5(3.3, 7)	−0.590	0.555
The induction dosage of Propofol (MOAA/S=1), mg, Median (IQR)	60(53.5, 65.0)	61(52.5, 69.5)	−0.691	0.489
The maintain dosage of Propofol, mg, Median (IQR)	170 (116, 205)	183 (92.5, 297.5)	–0.874	0.382
Infusion volume, mL, Median (IQR)	500(500, 600)	500(400, 600)	−0.693	0.489
Highest NRS score in PACU, Median (IQR)	0(0, 1)	0(0, 2)	−0.760	0.447
Surgeon satisfaction, Median (IQR)	5(5, 5)	5(4, 5)	−1.514	0.130
Patient satisfaction, Median (IQR)	5(5, 5)	5(5, 5)	−1.932	0.053
The time to first postoperative exhaust, min, Mean ± SD	443.8±197.3	419.9±201.1	0.460	0.647

Notes: NRS: Numerical rating scale, IQR: Interquartile Range, SD: Standard Deviation. *P<0.05 between groups.

(18, 38.5) vs 22 (13, 30), P = 0.031] durations (Table 2). However, the amount, average size of breast nodules, and procedure difficulty level were evenly distributed between groups, resulting in similar maintenance dosages of propofol. Surgeon's and patients' satisfaction, as well as the highest NRS score in the PACU, showed no significant difference between groups (all P > 0.05). The time to first postoperative exhaust was also similar: 443.8 ± 197.3 min in the sufentanil group and 419.9 ± 201.1 min in the esketamine group (P = 0.647).

Incidence of Hypoxia and Need for Airway Intervention

Table 3 lists the primary and secondary outcomes. Hypoxia occurred in 7 patients (17.5%) in the esketamine group and 16 patients (39%) in the sufentanil group (P = 0.032). The sufentanil group also had a higher incidence of subclinical respiratory suppression (56.1% vs 32.5%, P = 0.033) and more frequent need for airway intervention due to hypoxia (P =

Table 3 Primary and Secondary Outcomes

Variable	Sufentanil group (n=41)	Esketamine group (n=40)	χ^2	P value
Primary outcome				
Hypoxia, n (%)*	16(39)	7(17.5)	4.614	0.032
Secondary outcomes	23(56.1)	13(32.5)	4.566	0.033
Subclinical respiratory suppression, n (%)*	16(39)	7(17.5)	4.614	0.032
Need for airway intervention, n (%)*	3(7.3)	3(7.5)	0.001	0.975
Methods of airway intervention, n (%)	12(29.3)	6(15)	2.385	0.123
Adjust head position	12(29.3)	4(10)	4.742	0.029
Jaw-lift				
Mask-assisted ventilation*				
Body movement, n (%)	15(36.6)	16(40)	0.100	0.752

Notes: *P<0.05 between groups.

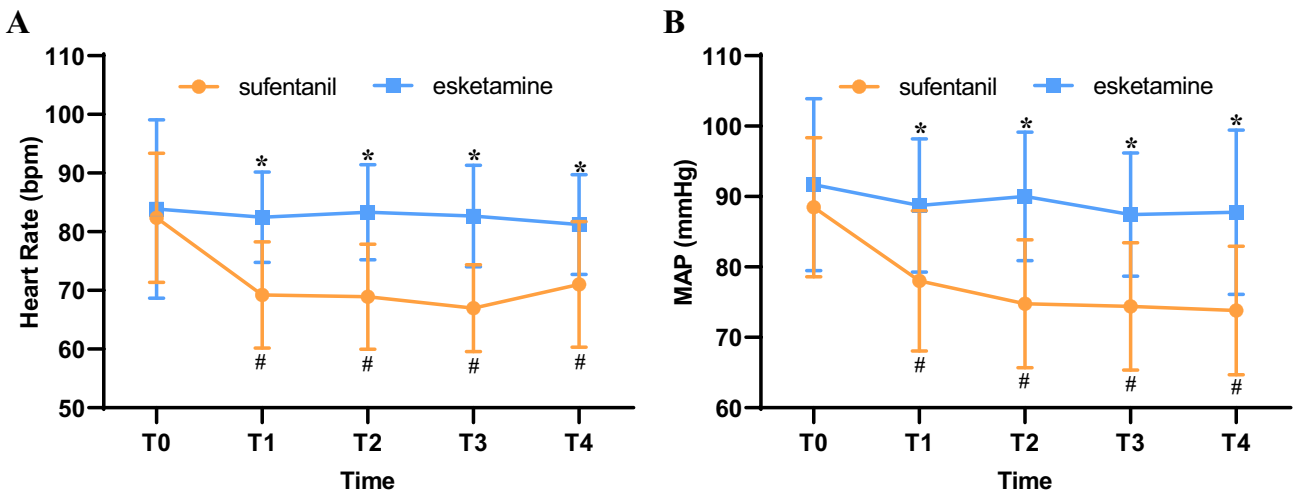

Figure 2 Changes in vital signs against elapsed anesthesia time. HR: heart rate **(A)**, bpm: beat per minute, MAP: mean arterial pressure **(B)**. T_0, the baseline; T_1, 1 min after administration of propofol; T_2, 1 min after skin incision; T_3, 3 min after skin incision; T_4, the end of the procedure. (*P< 0.05 between groups; #P< 0.05 compared with T_0 within group).

0.032). More patients required mask-assisted ventilation in the sufentanil group compared to the esketamine group (29.3% vs 10%, P = 0.029).

Hemodynamic Results

Figure 2 shows the changes in vital signs during analgesia and sedation. There was no significant difference in MAP and HR between groups at T_0 (P > 0.05). HR and MAP were significantly lower in the sufentanil group compared to the esketamine group at T_1, T_2, T_3, and T_4 (all P < 0.05). While the esketamine group showed no significant changes in MAP and HR at these time points compared to baseline, the sufentanil group exhibited a marked decrease (all P < 0.05). Additionally, the linear mixed-effects model also revealed that groups, time points, and the interaction between groups and time points had a significant impact on HR and MAP (Tables S1 and S2, all P < 0.05).

Incidence of Side Events

Nausea or vomiting occurred in three patients in both the sufentanil group (7.3%) and the esketamine group (7.5%) (P = 1.000) (Table 4). Furthermore, 39% of patients receiving sufentanil and 20% receiving esketamine experienced propofol injection pain, with no significant difference (P = 0.061). One patient in the sufentanil group developed hypotension, and four patients in the esketamine group experienced dizziness. No patients in either group developed delirium.

Table 4 Side Reactions

Variable	Sufentanil Group (n=41)	Esketamine Group (n=40)	χ^2	P value
Nausea or vomiting, n (%)	3(7.3)	3(7.5)	0.000	1.000
Injection pain, n (%)	16(39)	8(20)	3.515	0.061
Hypotension, n (%)	1(2.4)	0(0)	–	1.000
Hypertension, n (%)	0(0)	0(0)	–	1.000
Bradycardia, n (%)	1(2.4)	0(0)	–	1.000
Dizziness, n (%)	0(0)	4(10)	2.446	0.118
Delirium, n (%)	0(0)	0(0)	–	1.000

Discussion

This randomized clinical trial evaluated the efficacy and safety of esketamine-based anesthesia in breast MIRR procedures, revealing fewer hypoxia cases with esketamine compared to sufentanil when combined with propofol. As previous studies had not assessed esketamine's effects on MIRR, our findings first suggest that esketamine combined with propofol may provide a more effective and safer anesthesia option for this procedure.

While general anesthesia provides sufficient analgesic effects, combining sedation and analgesia with local anesthesia has become the preferred approach for minimally invasive surgeries due to its simplicity, cost-effectiveness, safety, and fewer side effects associated with general anesthesia.[15] To ensure adequate analgesia and due to drug administration habits, sufentanil has become our center's most commonly used intravenous analgesic for breast MIRR. Its dosage ranges from high (8–50 μg/kg), medium (2–8 μg/kg), to low (0.1–2 μg/kg). To minimize respiratory depression, low-dose regimens are typically used for anesthesia induction and outpatient minimally invasive procedures.[8] In this study, the sufentanil group had a 39% incidence of hypoxia, significantly higher than the esketamine group. This finding suggests that esketamine may enhance respiratory function in patients undergoing breast MIRR. A potential mechanism underlying this effect could be attributed to the sympathomimetic properties of esketamine, which may help maintain spontaneous breathing and airway reflexes, thereby stabilizing respiratory function. Additionally, esketamine can enhance CO_2 chemosensitivity during hypoventilation, thus ameliorating respiratory depression.[16] Notably, the hypoxia incidence was higher than previously reported,[10,17] likely due to our stricter criterion of $SpO_2 < 92\%$ for more than 10 seconds[18,19] compared to $SpO_2 < 90\%$ used in earlier studies.[10] In clinical practice, patients with hypoxia often experience a rapid and sustained drop in oxygen saturation, thus making the <92% threshold safer for management. Additionally, the use of nasal cannula oxygen delivery may have also contributed to this higher incidence.

Ketamine is known as the only clinical anesthetic providing both analgesic and sedative effects. However, its use is associated with higher rates of postoperative side reactions, such as headache, dissociation, dizziness, prolonged recovery, and lower satisfaction degree.[20,21] Esketamine, a higher-affinity non-competitive NMDA receptor antagonist, offers approximately twice the anesthetic potency of racemic ketamine with fewer psychiatric side effects. It also results in lower incidences of nausea, and vomiting, and faster recovery, making it preferable for clinical use.[11,13] Studies have demonstrated esketamine's effective analgesia in opioid-free anesthesia.[22,23] In breast cancer procedures, combining it with pregabalin reduced opioid consumption and chronic pain,[24] which might contribute to the prevention of central sensitization.[25] In our study, there were no significant differences in patients' and surgeon's satisfaction, as well as the highest NRS score in PACU between groups, indicating esketamine's excellent analgesic effect in breast MIRR surgery.

Subanesthetic doses of ketamine (<1mg/kg) refer to doses below the clinical anesthetic threshold, providing significant analgesic and anti-hyperalgesic effects without dissociative anesthesia. However, no standardized subanesthetic dosage for esketamine exists. Chen et al found that esketamine exposure was an independent risk factor for emergence delirium (ED) in preschool children, recommending a dose of ≤0.3 mg/kg during anesthesia induction to minimize ED.[26] In obese patients undergoing painless gastroscopy, 0.25 mg/kg of esketamine combined with propofol enhanced safety and reduced the incidence of side events.[10] Additionally, the dosage of 0.25mg/kg esketamine, but not below 0.2mg/kg, provided hemodynamic stabilization benefits.[17,27] Furthermore, considering esketamine's potency relative to ketamine and its dose-dependent psychiatric effects, we selected 0.25 mg/kg as the subanesthetic dose for our research.[28]

The linear mixed-effects model showed a significant difference in the trend of HR and MAP changes over time between the two groups. Specifically, patients experienced varying increases in MAP and HR after administrating esketamine, though these remained within 20% of baseline and returned to baseline within one minute after propofol administration. In contrast, MAP and HR began to drop significantly in the sufentanil group with one minute after propofol administration. Nonetheless, only one patient in the sufentanil group developed hypotension and bradycardia, likely due to the participants were young women, who generally exhibited good resistance to cardiovascular depressant effects of propofol and sufentanil.[29]

Opioids can inhibit perioperative bowel function recovery in a dose-dependent manner, with severe cases potentially leading to postoperative obstruction.[30] Previous research showed that opioid-free anesthesia with

esketamine shortens the time to first flatus in patients undergoing laparoscopic cholecystectomy, suggesting esketamine may aid in promoting gastrointestinal function recovery.[23] However, in our study, there was no significant difference in the time to first postoperative exhaust between groups. Esketamine also did not reduce the incidence of postoperative nausea or vomiting compared to the sufentanil group, aligning with Lin et al's findings.[31] Variations in surgery type, medication doses, and sample size indicators likely explain these inconsistencies.

The avoidance of esketamine is often due to its potential for psychotomimetic side effects, such as visual impairment, headache, and hallucinations (misinterpretations of real external sensory experiences). However, in our study, apart from four patients who experienced postoperative dizziness that improved significantly after 2–3 hours of bed rest, no other psychotomimetic reactions were observed in the esketamine group. We attribute this to two relevant factors: first, the esketamine dose used in the current study was appropriate, avoiding severe side effects.[26] Second, esketamine's psychotomimetic side effects are primarily linked to c-fos expression in the posterior cingulate cortex, which propofol can inhibit.[12]

Previous studies suggested that esketamine anesthesia could prolong postoperative recovery time.[32] However, in obese patients undergoing painless gastroscopy, combining esketamine with propofol significantly shortened awakening time compared to propofol alone.[10] Another study showed no effect of esketamine on recovery time,[17] which is consistent with our findings, as both groups showed a similar awakening time of about 5 minutes. Variations in surgical type, drug dosage, and patient populations may explain these discrepancies. Additionally, modified Aldrete and Ramsay scores assess postoperative recovery and sedation levels at 0, 15, 30, 45, and 60 minutes after entering PACU. No differences were observed at any time point between the groups, and all patients demonstrated improved postoperative recovery and sedation state.

Finally, an important consideration is the equi-analgesic effects of esketamine and sufentanil, which differ significantly in their analgesic mechanisms and actions. Consequently, determining equi-analgesic doses for these two drugs, as is typically done with opioids, is challenging due to limited data. Therefore, standard practice doses of esketamine and sufentanil combined with propofol were used to achieve a target MOAA/S score of 1 during the procedure. Including a propofol-only group would be interesting, however, the pain associated with the MIRR procedure makes it unethical to withhold analgesia entirely.

Our study has several limitations. First, being a single-center trial, its validity may be limited, necessitating further multi-institutional prospective studies. Second, the relatively small sample size may not capture rare drug-related complications. Third, since most patients undergoing MIRR procedure at our center had no comorbidities, caution is needed when generalizing the results to high-risk patients. Lastly, the study only evaluated a subanesthetic dose of esketamine, which, while effective, may not fully represent the optimal dosage.

Conclusion

In conclusion, esketamine-propofol anesthesia significantly reduces the incidence of hypoxia (SpO_2 < 92%) without affecting awakening time, surgeon's and patients' satisfaction, postoperative exhaust time, or side events compared to sufentanil-propofol in elective breast MIRR procedure. Additionally, the esketamine-propofol group experienced hemodynamic advantages, making it a promising option for further clinical use.

Data Sharing Statement

The data collected during the study are available from the corresponding author (Qingshan Ye) upon request. The authors intend to share individual deidentified participant data that underline the results reported in this article only. Data are available indefinitely on the Clinical Trial Management Public Platform (http://www.medresman.org.cn.), a website recommended in the Chinese Clinical Trial Registry from 3 months following article publication.

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Disclosure

The authors report no conflicts of interest in this work.

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