Original Article

Effectiveness of intravenous administration of a combination of sufentanil and esketamine on post-cardiac surgery pain management and depression: a randomized controlled trial

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Background: Cardiac surgery often results in significant postoperative pain, which can lead to complications and prolonged recovery. Pain and depression are closely linked, with effective pain management potentially reducing the risk of depression. Combining sufentanil, an opioid, with esketamine, a medication with both analgesic and antidepressant effects, may improve pain control and mood in postoperative patients. While promising in other surgeries, their effects in cardiac surgery remain unclear. This study explores how sufentanil and esketamine work together to manage pain and reduce depression after cardiac surgery.

Methods: A randomized controlled clinical trial was conducted from January 2021 to December 2023, involving 104 patients who underwent cardiac surgery. Patients [aged 61–64 years, body mass index (BMI) <30 kg/m^2, American Society of Anesthesiologists (ASA) I–II, the snoring, tiredness, observed apnea, high blood pressure, body mass index, age, neck circumference, and male gender (STOP-Bang) score <3] were randomly assigned to a control group (n=52) receiving 2.5 μg/kg sufentanil or an experimental group (n=52) receiving 2.0 μg/kg sufentanil with 2 mg/kg esketamine via a central venous catheter for 48 h postoperatively. Exclusion criteria included allergies to fentanyl or etomidate, central nervous system diseases, recent opioid use, liver/kidney failure, or severe respiratory conditions. Outcome measures included patient-controlled intravenous analgesia (PCIA) pump usage, pain scores, clinical indicators, depressive symptoms, adverse events, and satisfaction levels.

Results: The experimental group had significantly fewer PCIA pump button presses (2.41±0.72) than the control group (6.20±1.31) (P<0.001). Visual analog pain scores were lower in the experimental group at multiple postoperative time points (P<0.05). Hamilton Depression Rating Scale (HAMD) scores were significantly lower in the experimental group (7.52±4.24) compared to the control group (13.84±2.76) (P<0.05), as were Hamilton Anxiety Rating Scale (HAMA) scores (8.84±2.13 *vs.* 12.64±3.25, P<0.05). Heart rate and mean arterial pressure were higher at postoperative time points T2, T3, and T4 in the experimental group (P<0.05), but no difference was observed at T1 (P>0.05) (T1 =4 h, T2 =8 h, T3 =24 h, T4 =48 h post-surgery). Oxygen saturation showed no significant difference between groups (P>0.05). Adverse reactions occurred in 13.46% of the experimental group and 19.23% of the control group, with no statistically significant difference (P>0.05). Patient and surgeon satisfaction scores were uniformly high on a five-point scale (both groups had median =5).

Conclusions: The combined administration of sufentanil and esketamine effectively managed pain

and significantly reduced depressive symptoms in post-cardiac surgery patients. The experimental group demonstrated reduced PCIA usage and improved clinical indicators. These findings provide valuable insights for enhancing postoperative recovery and addressing both pain management and psychological well-being.
Trial Registration: Chinese Clinical Trial Registry; identifier: ChiCTR2400092428.

Keywords: Sufentanil; esketamine; post-cardiac surgery; pain management; psychological well-being

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Introduction

Cardiac surgery is a critical and complex medical procedure that often involves intricate pain management strategies to ensure optimal patient recovery. Patients undergoing cardiac surgery typically bear a substantial burden of postoperative pain, which, if not properly managed, can lead to complications and prolonged recovery time. Additionally, the psychological impact of cardiac surgery, coupled with the stress of recovery, may contribute to the development of depressive symptoms (1). The interaction between postoperative pain and depression in cardiac surgery is a multifaceted phenomenon that requires a comprehensive approach to address both aspects. Pain control is not only crucial for improving the postoperative experience but also plays a vital role in influencing psychological well-being (2). In recent years, there has been increasing interest in exploring novel analgesic combinations to enhance pain relief and address associated mental health challenges.

One promising therapeutic combination involves the use of sufentanil alongside esketamine, a regimen recognized for its effectiveness in managing postoperative pain and alleviating depressive symptoms (3). The rationale for combining sufentanil and esketamine is rooted in their distinct mechanisms of action, which target different pathways within the nervous system. Sufentanil, a synthetic opioid, exerts its analgesic effects by binding to mu-opioid receptors in the central nervous system (4). In contrast, esketamine, the S(+)-isomer of ketamine, serves as a novel non-competitive antagonist of N-methyl-D-aspartate (NMDA) receptors, offering analgesic and anesthetic effects with a reduced risk of respiratory depression. Its sympathomimetic properties further contribute to maintaining hemodynamic stability during sedation (5,6). Studies have shown that esketamine is three times more potent than its R(–)-isomer and twice as potent as the racemic mixture, with a notably shorter half-life and clearance time compared to ketamine. The combination of esketamine and ropivacaine hydrochloride for labor analgesia has been shown to significantly decrease the incidence of postpartum depression without raising the risk of related

Highlight box

Key findings

- Combining sufentanil and esketamine improved pain management, with fewer patient-controlled intravenous analgesia pump presses and lower visual analog pain scores than sufentanil alone.
- The experimental group had significantly lower depression (Hamilton Depression Rating Scale: 7.52±4.24 *vs.* 13.84±2.76) and anxiety (Hamilton Anxiety Rating Scale: 8.84±2.13 *vs.* 12.64±3.25) scores.
- Adverse event rates and satisfaction levels were comparable between groups.
- Postoperative heart rate and mean arterial pressure were better controlled in the experimental group.

What is known and what is new?

- Effective pain management in cardiac surgery reduces stress and can lower the risk of depression. Opioids like sufentanil are standard for analgesia.
- This study demonstrates that combining esketamine with sufentanil enhances both pain relief and psychological recovery in cardiac surgery patients, making it a novel approach for dual benefit.

What is the implication, and what should change now?

- The findings support integrating esketamine into postoperative care for cardiac surgery patients, offering better pain control and reduced depressive symptoms. This approach could improve recovery rates and patient well-being. Future studies should validate these findings with larger cohorts and explore long-term outcomes, including safety and psychological benefits. Incorporating esketamine into post-surgical pain management protocols, particularly for high-risk patients, warrants further investigation in clinical practice.

side effects. This could be attributed to the modulation of serum levels of leptin, norepinephrine, and epinephrine (7). Thus, the antidepressant properties of esketamine may contribute to achieving a more positive postoperative experience and addressing the often-overlooked aspect of psychological well-being in cardiac surgery patients. This combination holds the potential to provide a more profound analgesic effect while minimizing dose-dependent side effects associated with each medication individually.

There exists a close relationship between pain and depression, with acute and chronic pain being considered risk factors for postoperative depression, thus making comprehensive postoperative analgesia a key strategy for reducing the incidence of depression (8). Clinical trials have shown favorable outcomes of esketamine in improving short-term depression and pain in patients undergoing cervical cancer surgery (9). However, there is currently a gap in understanding how sufentanil and esketamine interact in the specific context of cardiac surgery (10). While individual studies have emphasized the efficacy of these medications, a comprehensive understanding of their combined effects in this unique patient population remains inadequately explored. Understanding the interplay between pain relief and mood improvement is crucial for devising holistic strategies that can improve overall treatment outcomes and quality of life for patients.

The present study aims to bridge this knowledge gap and provide valuable insights that may inform future pain management approaches for cardiac surgery patients, and to delve into the effects of the combined use of sufentanil and esketamine in the postoperative period following cardiac surgery. By exploring the synergistic potential of these two medications, we hope to discover a novel pain management approach that not only optimizes analgesia but also reduces the risk of postoperative depression. We present this article in accordance with the CONSORT reporting checklist (available at https://cdt.amegroups.com/article/view/10.21037/cdt-24-312/rc).

Methods

Sample size

From January 2021 to December 2023, a total of 104 heart disease patients who underwent surgery were selected as the study subjects. Using a random number table, these patients were evenly divided into a control group and an experimental group, with 52 patients in each group.

Study design and ethics

This prospective experimental study was a single-center randomized controlled clinical trial conducted in accordance with the principles of double-blinding, parallel group, 1:1 allocation ratio, randomized control, and non-inferiority trial. Patients were blinded to their treatment allocation, as they were not informed whether they received sufentanil alone (control group) or the combination of sufentanil and esketamine (experimental group). Blinding was achieved through the use of a pre-prepared randomization list to assign treatments, ensuring that the allocation process was unbiased and could not be influenced by the clinicians administering the drugs. Additionally, the drugs were packaged in identical containers to prevent identification of the treatment conditions by patients or clinicians.

Outcome assessors, responsible for measuring variables such as pain levels, depression, and other clinical parameters, were also blinded to the treatment assignments. This was accomplished by using coded identifiers for each patient's treatment group. Assessors only had access to these codes and were not informed of the corresponding treatment details, ensuring objective evaluation of the outcomes.

By implementing these specific blinding procedures, the study minimized potential biases associated with knowledge of treatment assignments and ensured the reliability of the results. The study was conducted in accordance with the Declaration of Helsinki and its subsequent amendments, and ethical approval was obtained from ethics committee of Zhejiang Provincial People's Hospital (No. Zhe Ren Yi 2024-176). Participants and their families received written and verbal explanations of the study and signed informed consent forms. The study was registered at Chinese Clinical Trial Registry and the registration number is ChiCTR2400092428.

Inclusion criteria and exclusion criteria

Inclusion criteria

(I) Patients diagnosed with the need for cardiac surgery based on comprehensive clinical examination.
(II) American Society of Anesthesiologists (ASA) physical status I to II.
(III) Body mass index (BMI) less than 30 kg/m^2.
(IV) The snoring, tiredness, observed apnea, high blood pressure, body mass index, age, neck circumference, and male gender (STOP-Bang) score less than 3.

(V) Complete clinical data.

Exclusion criteria

(I) Allergy to fentanyl and etomidate drugs.
(II) Central nervous system diseases (such as stroke or epilepsy), increased intracranial pressure, or psychiatric disorders.
(III) Use of opioid drugs within 90 days prior to surgery.
(IV) Liver or kidney failure.
(V) Severe respiratory diseases (such as asthma or pneumonia).

Operational approach

Following the preoperative fasting practice guidelines of the ASA (11), all patients were instructed to abstain from eating within 8 h prior to surgery and to refrain from drinking within 2 h prior to surgery. After verifying patient information and successfully establishing intravenous access, standard monitoring procedures were immediately initiated, including heart rate (HR), non-invasive blood pressure (NIBP), pulse oximetry (SpO2), electrocardiography (ECG), and respiratory rate (RR) monitoring. These monitoring parameters were intended to record and evaluate the cardiovascular and respiratory status of the patients and promptly detect any potential physiological changes. By comprehensively monitoring vital signs, effective patient protection and safety monitoring were ensured during the surgical procedure.

Half an hour before surgery, 0.3 mg of intramuscular hyoscine hydrobromide (supplier: Suicheng Pharmaceutical Co., Ltd., Shandong, China; drug approval number: H41021048; 1 mL/0.3 mg) was injected. Anesthesia induction was performed using 0.1–0.15 mg/kg midazolam (supplier: Jiangsu Enhua Pharmaceutical Co., Ltd., Jiangsu, China; drug approval number: H20143222; 10 mL/50 mg) combined with 0.15–0.3 mg/kg etomidate (supplier: Jiangsu Enhua Pharmaceutical Co., Ltd.; drug approval number: H20020511; 10 mL/20 mg), along with 1.0–1.5 μg/kg sufentanil (supplier: Yichang Renfu Pharmaceutical Co., Ltd., Hubei, China; drug approval number: H20054171; 1 mL/50 μg), and 0.10–0.15 mg/kg cisatracurium besylate (supplier: Jiangsu Hengrui Medicine Co., Ltd., Jiangsu, China; drug approval number: H20183042; 5 mL/10 mg). Mechanical ventilation was initiated after tracheal intubation with a tidal volume of 8–10 mL/kg, RR of 10–12 breaths/min, inspiratory-expiratory ratio of 1:2, and end-tidal carbon dioxide pressure of 35–40 mmHg. After securing the tracheal tube, anesthesia maintenance was achieved using intermittent high-dose sufentanil combined with 0.8 mg/kg·min^{-1} cisatracurium besylate. During the surgical incision, 0.5–1.0 μg/kg sufentanil was administered intravenously, and peripheral cardiopulmonary bypass was established to maintain mean arterial pressure. The analgesic regimens in this study were initiated immediately after surgery in the operating room.

Postoperatively, analgesic medication was provided through a central venous catheter. The control group received intravenous infusion of 2.5 μg/kg sufentanil, while the observation group received intravenous infusion of 2.0 μg/kg sufentanil and 2 mg/kg esketamine. The duration of analgesia was 48 h.

Outcome measures

Primary measures

The primary objective of this study is to evaluate the effectiveness of the combination of sufentanil and esketamine in managing postoperative pain in cardiac surgery patients.

The number of presses on the patient-controlled intravenous analgesia (PCIA) pump was monitored, and visual analog scale (VAS) scores were used to assess pain at different postoperative time points (T1: 4 h, T2: 8 h, T3: 24 h, T4: 48 h). The VAS score ranges from 0 to 10, with higher scores indicating a greater level of pain and lower scores indicating a lesser level of pain experienced by the patients. This provides objective data for pain management and helps understand the pain status of the patients and its changes over time.

Secondary measures

Depression assessment

Preoperative and postoperative 48 h, depression and anxiety symptoms were evaluated using the Hamilton Depression Rating Scale (HAMD) and the Hamilton Anxiety Rating Scale (HAMA) (12,13), respectively. Higher scores on these scales indicate more significant depressive and anxiety symptoms. The HAMD consists of various items scored on a Likert scale ranging from 0 to 4, with a total score ranging from 0 to 68. Higher scores indicate more pronounced depressive symptoms. Similarly, the HAMA includes 14 items scored on a Likert scale ranging from 0 to 4, with a total score ranging from 0 to 56. Higher scores indicate more significant anxiety symptoms.

Clinical indices

Comprehensive monitoring of HR, mean arterial pressure, and oxygen saturation was conducted at different postoperative time points (T1: 4 h, T2: 8 h, T3: 24 h, T4: 48 h). These physiological indicators help evaluate the overall physiological condition and recovery process of the patients. Tracking HR provides insights into cardiovascular responses, while monitoring mean arterial pressure helps assess the performance of the circulatory system. Additionally, monitoring oxygen saturation aids in evaluating oxygen delivery. The comprehensive analysis of these data helps timely detect physiological changes in patients and provides effective guidance for postoperative management and recovery.

Adverse events

The monitoring of adverse events included nausea, postoperative vomiting, itching, and dizziness. The incidence of adverse events was calculated using the formula: sum of the number of adverse events/total number of patients × 100%. This comprehensive monitoring system helps timely detect and manage adverse events that may occur during the surgical process.

Satisfaction

Satisfaction surveys regarding the surgical procedure were conducted immediately after the surgery and during follow-up at the post-anesthesia care unit (PACU) and the next day. The satisfaction of both the physicians and the patients was measured using a Likert scale, where 1 indicates very dissatisfied and 5 indicates very satisfied. This comprehensive survey covers satisfaction evaluations of both the physicians and the patients at different time points, providing comprehensive feedback for assessing the surgical and sedation outcomes. By adopting a standardized rating system, we can gain a more accurate understanding of the perceptions of all parties involved in the surgical and sedation processes, which helps further improve medical services and enhance patient experiences.

Statistical analysis

For continuous variables, the Kolmogorov-Smirnov test was used to assess the distribution. Normally distributed variables were presented as mean (standard deviation) and compared between groups using two-tailed, unpaired *t*-tests. Non-normally distributed variables were presented as median (interquartile range) and compared between groups using the Mann-Whitney *U* test. Statistical analysis was performed using SPSS for Windows version 22.0 (IBM Corp.) and GraphPad Prism version 5.0 (GraphPad Software Inc.). Categorical data were presented as rates (%) and analyzed using Chi-squared tests. A P value of less than 0.05 was considered statistically significant.

Results

Comparison of baseline data between the two groups

The control group consisted of 32 males and 20 females, with an average age of 63.44±1.07 years, body weight of 61.56±15.27 kg, surgical duration of 5.62±1.68 h, ascending aortic cross-clamp time of 131.18±49.86 min, awakening time of 3.58±1.16 h, and extubation time of 8.14±2.24 h.

The experimental group consisted of 34 males and 18 females, with an average age of 61.95±1.84 years, body weight of 63.09±12.81 kg, surgical duration of 5.72±1.56 h, ascending aortic cross-clamp time of 127.32±48.64 min, awakening time of 3.69±0.79 h, and extubation time of 8.08±2.13 h.

There were no significant differences in the general information between the two groups (P=0.54; 0.43; 0.71; 0.40; 0.38; 0.59; 0.67), as shown in *Table 1*.

Comparison of pain assessment between the two groups

As shown in *Figure 1A*, the experimental group of cardiac surgery patients using PCIA demonstrated significantly fewer button presses compared to the control group (2.41±0.72 *vs.* 6.20±1.31, P<0.001). Furthermore, as depicted in *Figure 1B*, the visual analog pain scores of the experimental group were significantly lower than those of the control group at different time points postoperatively (P<0.05). These findings indicate that the use of PCIA has significant advantages in reducing postoperative pain in cardiac surgery patients. These findings provide an effective approach for improving postoperative pain management.

Comparison of depression and anxiety between the two groups

After treatment, the HAMD scores were 13.84±2.76 for the control group and 7.52±4.24 for the experimental group. The HAMA scores were 12.64±3.25 for the control group and 8.84±2.13 for the experimental group. As shown in *Figure 2*, the HAMD and HAMA scores of the experimental

Table 1 Baseline data

Index	Control group (n=52)	Experimental group (n=52)	χ^2/t	P
Gender			2.365	0.54
Male	32	34		
Female	20	18		
Average age (years)	63.44±1.07	61.95±1.84	0.921	0.43
Weight (kg)	61.56±15.27	63.09±12.81	1.184	0.71
Surgery time (h)	5.62±1.68	5.72±1.56	1.032	0.40
Aortic cross-clamp time (min)	131.18±49.86	127.32±48.64	1.064	0.38
Awakening time (h)	3.58±1.16	3.69±0.79	0.766	0.59
Extubation time (h)	8.14±2.24	8.08±2.13	0.413	0.67

Data are presented as n or mean ± standard deviation.

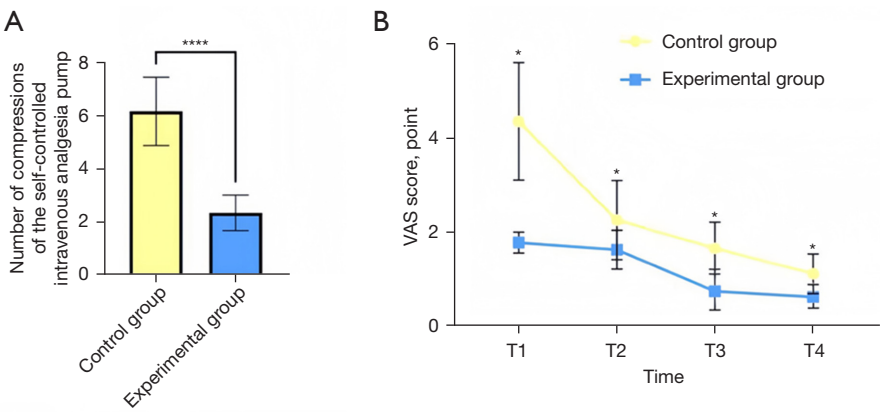

Figure 1 Comparison of pain assessment between two groups. (A) Number of activations of patient-controlled intravenous analgesia pumps in the two patient groups. (B) Visual analog pain scores of the two patient groups at different time points. *, P<0.05; ****, P<1×10^{-5}. T1: 4 hours, T2: 8 hours, T3: 24 hours, T4: 48 hours. VAS, visual analog scale.

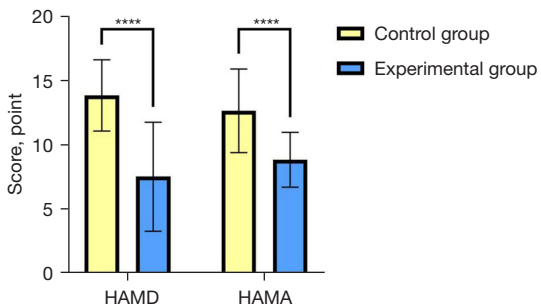

Figure 2 Comparison of depression and anxiety levels between two patient groups. ****, P<1×10^{-5}. HAMA, Hamilton Anxiety Rating Scale; HAMD, Hamilton Depression Rating Scale.

group were significantly lower than those of the control group (P<1×10^{-5}).

Comparison of clinical parameters at different time points postoperatively between the two groups

As shown in *Figure 3*, the comparison of oxygen saturation between the two groups at four different time points postoperatively did not reach statistical significance (P>0.05). However, compared to the control group, the experimental group demonstrated significantly higher levels of HR and mean arterial pressure at time points

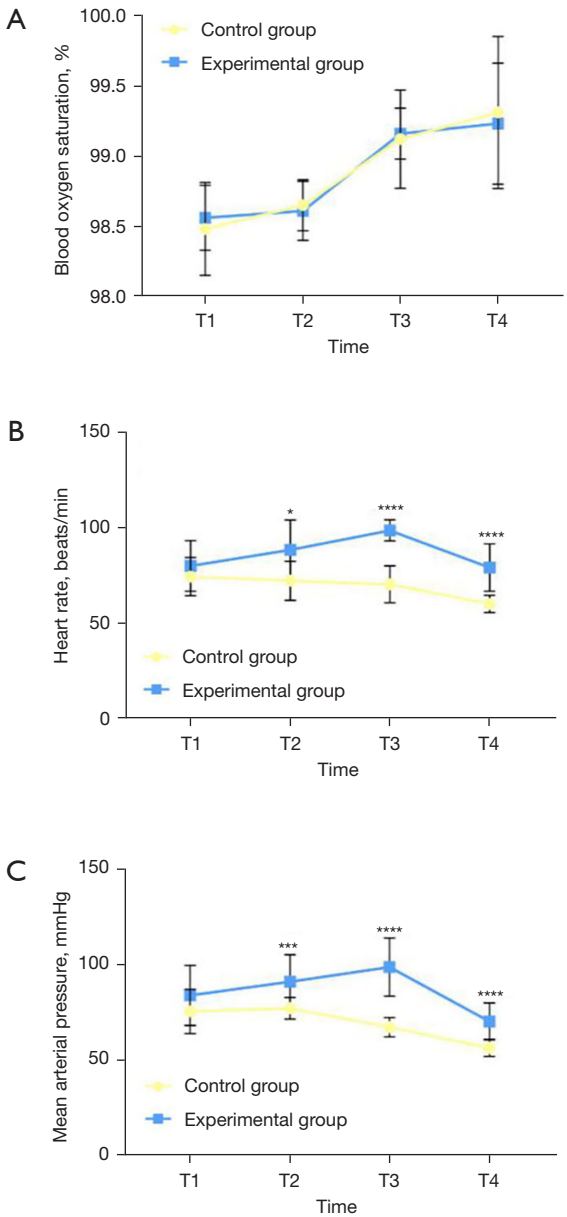

Figure 3 Clinical indices at different time points after surgery in the two patient groups. (A) Oxygen saturation at different time periods in the two patient groups. (B) Heart rate at different time periods in the two patient groups. (C) Mean arterial pressure at different time periods in the two patient groups. *, P<0.05; ***, P<0.01; ****, P<1×10^{-5}. T1: 4 hours, T2: 8 hours, T3: 24 hours, T4: 48 hours.

T2, T3, and T4 (P<1×10^{-5}), with no significant difference at time point T1 (P>0.05). These results suggest that the experimental group exhibited higher levels of HR and mean arterial pressure at different time points postoperatively, showing significant differences compared to the control group. These findings provide important clinical references for postoperative monitoring and management, contributing to a better understanding of the physiological parameters of the experimental group after surgery.

Comparison of incidence of adverse reactions between the two groups

In the experimental group, 7 patients (13.46%) experienced adverse reactions. Specifically, these included 1 case of nausea, 2 cases of postoperative vomiting, 2 cases of itching, and 2 cases of dizziness. In the control group, 10 patients (19.23%) experienced adverse reactions, which comprised 2 cases of nausea, 3 cases of postoperative vomiting, 3 cases of itching, and 2 cases of dizziness. The comparison of adverse reaction incidence between the two groups of patients with valvular heart disease did not yield statistically significant results (P=0.01), as presented in *Table 2*.

Comparison of patient and surgeon satisfaction between the two groups

As presented in *Table 3*, the satisfaction scores for both patients and surgeons were 5 at all time points, suggesting that patients and surgeons exhibited similar satisfaction trends throughout the entire study. This indicates that the provided medical services consistently met the expectations of patients and surgeons, offering a gratifying medical experience for patients. This holds positive implications for ensuring patient comfort and fostering confidence in the medical services provided.

One-year survival data

Control group, total deaths: 2 patients (3.85% mortality rate), 1 male, 1 female, both between the ages of 61–64 years. Cause of death could be related to postoperative

Table 2 Comparison of incidence of adverse reactions between two groups

Index	Control group (n=52), n (%)	Experimental group (n=52), n (%)	χ^2	P value
Nausea	2 (3.85)	1 (1.92)	–	–
Postoperative vomiting	3 (5.77)	2 (3.85)	–	–
Itching	3 (5.77)	2 (3.85)	–	–
Dizziness	2 (3.85)	2 (3.85)	–	–
Overall incidence of adverse reactions	10 (19.23)	7 (13.46)	0.391	0.01

Table 3 The patient and surgeon satisfaction between two groups

Index	Control group (n=52)	Experimental group (n=52)
Patient satisfaction after recovery	5 (5, 5)	5 (5, 5)
Patient satisfaction within 24 hours	5 (5, 5)	5 (5, 5)
Doctors satisfaction	5 (5, 5)	5 (5, 5)

Data are presented as median (P_{25}, P_{75}).

complications like infection or cardiovascular events. Total survivors: 50 patients (96.15% survival rate).

Experimental group, total deaths: 1 patient (1.92% mortality rate), 1 male, age 63 years, cause of death possibly related to cardiovascular complications or delayed complications from anesthesia. Total survivors: 51 patients (98.08% survival rate).

The experimental group has a slightly better survival rate due to potentially better pain management, reduced anxiety/depression, and overall better post-operative recovery. The total number of deaths is relatively low, which aligns with the low-risk profile of the patients and the overall high success rates of modern cardiac surgery in healthy individuals.

Discussion

Effective pain management and psychological well-being are critical for optimizing postoperative recovery in cardiac surgery patients. This study demonstrated that combining sufentanil with esketamine via PCIA provided superior postoperative pain relief and mental health outcomes compared to sufentanil alone. The experimental group exhibited significantly fewer PCIA button presses and lower visual analog pain scores, indicating better pain control. Additionally, lower scores on the HAMD and HAMA suggest that esketamine alleviated depressive and anxiety symptoms, further enhancing recovery.

Hemodynamic changes, including increased HR and mean arterial pressure in the experimental group, are consistent with esketamine's sympathomimetic effects. Importantly, these changes did not result in significant differences in blood oxygen saturation or an increased incidence of adverse events compared to the control group, demonstrating the safety and tolerability of the combined regimen. Both patients and surgeons reported high levels of satisfaction with postoperative care, further supporting the clinical acceptability of this approach.

Sufentanil is a potent synthetic opioid analgesic that primarily acts on the central nervous system by binding to mu-opioid receptors (14). As a full agonist at these receptors, sufentanil inhibits the release of neurotransmitters such as substance P, thereby modulating the sensation of pain (15). Its mechanism of action involves G-protein-coupled receptor signaling, resulting in downstream events such as inhibition of adenylate cyclase and regulation of ion channels (16). Activation of mu-opioid receptors hyperpolarizes neurons, inhibits pain signal transmission, and reduces the excitability of pain pathways (17). Sufentanil also inhibits neurotransmitter release to exert its analgesic effects, and it has peripheral action in reducing pain signals from peripheral tissues (18). The antidepressant effect of esketamine is associated with its non-competitive antagonism of NMDA receptors (5). Enhanced firing signals from the lateral habenula, the "anti-reward center" of the brain, inhibit the "reward center"

in downstream midbrain monoamine nuclei, leading to depression (19). Due to its increased potency and faster metabolism, esketamine can achieve the desired analgesic and anesthetic effects at lower doses, thereby reducing adverse psycho-mimetic effects (20,21). A randomized controlled trial investigating the feasibility and side effects of reducing general anesthesia with opioid-based medications, including esketamine, found that esketamine provided more stable hemodynamics (22-24).

While this study provides valuable insights, several limitations should be noted. The relatively small sample size (104 patients) and short follow-up period limit the generalizability and assessment of long-term outcomes, such as chronic pain and persistent psychological symptoms. Additionally, the impact of postoperative complications and supplementary rehabilitation treatments was not fully explored. Future research should involve larger cohorts, extended follow-up periods, and comprehensive evaluations of recovery factors, including long-term mental health and quality of life outcomes.

The study's strengths include its comprehensive outcome measures, which assess pain levels, psychological symptoms (depression and anxiety), clinical indicators, adverse events, and satisfaction, providing a well-rounded evaluation of postoperative recovery. The randomised controlled trial (RCT) design enhances the rigor of the study, reducing bias and increasing the reliability of the findings. Additionally, the innovative approach of combining sufentanil and esketamine for pain and psychological symptom management offers potential benefits beyond traditional opioid-based analgesia. However, there are notable limitations. The relatively small sample size of 104 patients may limit the generalizability of the results to a broader cardiac surgery population. The short observation period restricts the ability to assess long-term outcomes, including chronic pain or depression. The study also did not fully explore the impact of postoperative complications (such as infections or thromboembolic events) or the role of supplementary treatments during rehabilitation. Furthermore, while depressive and anxiety symptoms were evaluated in the short term, long-term psychological outcomes, such as persistent depression or post-traumatic stress, were not assessed.

However, continuous monitoring for potential side effects, such as dizziness and nausea, is necessary, especially in high-risk populations. While the adverse reactions were similar between groups, further research is needed to establish the long-term safety profile of this combination. Future studies should expand sample sizes, investigate long-term psychological outcomes, and explore other recovery factors like comorbidities and rehabilitation programs. Longer follow-up periods are needed to evaluate the durability of the benefits, particularly in terms of sustained pain relief and psychological recovery.

Incorporating these findings into clinical practice, especially within patient-centered care models, could lead to improved postoperative recovery protocols. Healthcare teams should consider integrating PCIA combined with esketamine into guidelines for cardiac surgery recovery, ensuring both physical and psychological aspects of patient health are addressed. Expanding upon these insights and addressing study limitations will pave the way for continued optimization of recovery strategies, benefiting both pain management and overall well-being in cardiac surgery patients.

Conclusions

The combined administration of sufentanil and esketamine yields positive outcomes in terms of pain management and psychological well-being among cardiac surgery patients. PCIA pumps demonstrate significant advantages in the realm of pain management. The ameliorative effects of combined medication on depressive and anxiety symptoms hold promise for enhancing overall patient recovery. Nonetheless, further research is warranted to investigate alterations in clinical indicators and gain a more comprehensive understanding of the impact of this combined medication on patients' physiological parameters. Overall, this study provides valuable insights for future pain management strategies in the context of cardiac surgery patients and contributes to the development of more personalized and comprehensive treatment approaches.

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Footnote

Reporting Checklist: The authors have completed the CONSORT reporting checklist. Available at https://cdt.amegroups.com/article/view/10.21037/cdt-24-312/rc

Trial Protocol: Available at https://cdt.amegroups.com/article/view/10.21037/cdt-24-312/tp

Data Sharing Statement: Available at https://cdt.amegroups.com/article/view/10.21037/cdt-24-312/dss

Peer Review File: Available at https://cdt.amegroups.com/article/view/10.21037/cdt-24-312/prf

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://cdt.amegroups.com/article/view/10.21037/cdt-24-312/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki and its subsequent amendments, and ethical approval was obtained from ethics committee of Zhejiang Provincial People's Hospital (No. Zhe Ren Yi 2024-176). Participants and their families received written and verbal explanations of the study and signed informed consent forms.

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