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ORIGINAL RESEARCH

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Effects of inhalation anesthesia combined with intravenous anesthesia on anesthetic efficacy and adverse reactions in female patients with breast cancer: a retrospective study

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Abstract

Background: This study aims to investigate the effects of inhalation anesthesia combined with intravenous anesthesia on anesthesia efficacy and adverse reactions in female breast cancer patients. **Methods**: A retrospective analysis was conducted using clinical data from 78 female breast cancer patients admitted to our hospital between January 2022 and December 2023. Based on the recorded anesthesia methods, the patients were categorized into two groups: the control group (n = 39; received inhalation anesthesia) and the observation group (n = 39; underwent inhalation anesthesia combined with intravenous anesthesia), and their anesthesia effectiveness (mean arterial pressure (MAP), heart rate, arterial oxygen partial pressure (PaO_2), eye opening time, orientation recovery time and extubation time), postoperative pain scores (Visual Analog Scale (VAS) scores), postoperative inflammatory markers (C-Reactive Protein (CRP), Interleukin-6 (IL-6), Tumor Necrosis Factor Alpha (TNF-α), norepinephrine (NE), cortisol and epinephrine (E) and the incidence of adverse reactions, were compared. **Results**: At T1, T2, and T3, they had significantly lower MAP and heart rate and higher Partial Pressure of Oxygen (PaO_2) than the control group ($p < 0.05$). Recovery times, including eye opening, orientation recovery and extubation times, were significantly shorter in the observation group ($p < 0.05$). VAS scores at 5, 45 and 90 minutes post-anesthesia were significantly lower in the observation group than the control group ($p < 0.05$). 24 hours post-surgery, the levels of inflammatory markers (CRP, IL-6, TNF-α, NE, cortisol, E) were significantly reduced ($p < 0.05$), and the incidence of adverse reactions was significantly lower in the observation group ($p < 0.05$). **Conclusions**: The combination of inhalation and intravenous composite anesthesia in breast cancer resection surgery was associated with superior anesthesia outcomes, including reduced postoperative pain and inflammation and a lower incidence of adverse reactions, thereby holding promise for clinical application and warrants further investigation.

Keywords

Breast cancer; Inhalation anesthesia; Inhalation anesthesia combined with intravenous anesthesia; Radical mastectomy

1. Introduction

Breast cancer is among the most prevalent malignancies, representing a significant global health burden for women [1]. According to the latest global cancer statistics published by the International Agency for Research on Cancer (IARC) in 2018, breast cancer remains the most common malignant tumor in females, accounting for 24.2% of all female cancer cases [2]. Radical mastectomy is the primary treatment for breast cancer; however, this procedure often results in postoperative pain and stress reactions, and these responses are influenced by factors such as emotional tension, surgical trauma and intraoperative changes in blood volume [3].

The choice of anesthetic agents during surgery significantly affects circulatory system compliance, hemodynamic stability and stress response and therefore, efficient anesthesia techniques are essential for optimizing surgical outcomes, minimizing stress responses and maintaining stable hemodynamics. The commonly used methods in clinical practice include inhalation anesthesia and the combination of inhalation and intravenous anesthesia [4]. General anesthesia often involves the use of agents such as remifentanil and propofol, which are characterized by their rapid onset and effective analgesic properties. However, these agents are frequently associated

with adverse effects, including postoperative agitation [5]. The combination of inhalation anesthesia with intravenous compound anesthesia provides distinct advantages, including precise control over anesthetic depth and a smoother recovery process [6]. Thus, this approach has gained widespread acceptance and is increasingly utilized in clinical practice.

Although traditional inhalation anesthesia offers some effectiveness, there is growing interest in intravenous composite anesthesia due to its potential to enhance anesthesia outcomes and reduce adverse reactions. This study investigates the effects of combining inhalation anesthesia with intravenous composite anesthesia on anesthesia outcomes and adverse reactions in female breast cancer patients to address a significant gap in existing literatures. While numerous studies have evaluated various anesthesia methods, few have systematically compared approaches specifically targeting breast cancer patients, with most focusing on single techniques and providing limited insight into combined approaches. To address this limitation, we retrospectively analyzed the data of 78 female breast cancer patients to obtain a comprehensive assessment of the benefits of combining inhalation anesthesia with intravenous composite anesthesia. Unlike previous studies that predominantly examined adverse reactions linked to individual anesthesia methods, our present research evaluates the overall impact of different anesthesia combinations and offers critical insights into their safety and effectiveness while guiding clinical decision-making. Through comparisons between control and observation groups in terms of postoperative recovery, pain management and the incidence of adverse reactions, the findings provide valuable evidence to inform clinical practice. Given the increasing incidence of breast cancer, optimizing anesthesia protocols to improve patient quality of life and ensure surgical safety remains a pressing clinical challenge. By evaluating the combination of inhalation anesthesia and intravenous composite anesthesia, this study seeks to provide insights into personalized anesthesia strategies for breast cancer patients and a potential foundation for future clinical applications.

This study addresses a significant need to optimize anesthesia strategies for female breast cancer patients undergoing surgical treatment. Breast cancer remains one of the most prevalent malignancies in women, and anesthesia choice directly affects postoperative recovery, complication rates and quality of life. This study compares the strengths and limitations of inhalation and intravenous anesthesia by evaluating inhalation alone versus a combined approach to identify insights into enhancing recovery and reducing complications. To achieve this, key inflammatory markers, including C-reactive protein (CRP), interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), were analyzed to assess postoperative inflammation triggered by anesthesia and surgery. By determining whether the combined method offers better control of inflammation and improves recovery, the study provides insights that can refine anesthesia management and enhance patient care.

Inflammatory biomarkers, including CRP, IL-6 and TNF-α, are important markers for assessing postoperative inflammatory responses, which can be triggered by both anesthesia and surgery [7]. These biomarkers serve as indicators for determining inflammation severity and are instrumental in evaluating recovery outcomes [8]. By analyzing the impact of different anesthesia methods on these biomarkers, this study aims to determine whether the combination of inhalation and intravenous anesthesia more effectively controls postoperative inflammation, thereby promoting improved recovery. The findings are expected to provide clinicians with valuable insights for optimizing anesthesia protocols, reducing postoperative complications, and enhancing patient quality of life. Overall, this study is methodologically innovative and highly relevant to clinical practice, providing insights into optimizing anesthesia management for female breast cancer patients through robust theoretical and data support for clinical anesthesia strategies. The results may not only advance the understanding of effective anesthesia practices but also inform future research on improving postoperative recovery and outcomes for breast cancer patients.

2. Materials and methods

2.1 Patient and general information

Sample Size Calculation and Grouping Method: the sample size was calculated using the following formula:

$n = \pi_t \times (1 - \pi_t) \times \pi_c \times (1 - \pi_c)/[(\pi_t - \pi_c - \Delta)] \times (\mu_{\alpha/2} + \mu_\beta)^2$.

Explanation of Parameters and Their Sources:

π_t and π_c (Event Occurrence Rate): π_t: the expected event occurrence rate in the observation group (inhalational anesthesia combined with intravenous anesthesia), representing outcomes such as adverse reactions or effective treatment rates. π_c: the expected event occurrence rate in the control group (pure inhalational anesthesia).

Source: these values were derived from previous literature, clinical data or preliminary experimental results, with relevant studies consulted to ensure reasonable estimates.

Δ (Delta, Minimum Acceptable Difference): represents the smallest clinically significant difference in event rates between the observation and control groups, reflecting the desired effect size.

Source: this value is determined by the researcher based on clinical significance and relevant literature, typically set according to clinical practice and the needs of patients to establish a reasonable minimum difference.

$\mu_{\alpha/2}$ and μ_β (Z-values): $\mu_{\alpha/2}$: the Z-value associated with the significance level (α), typically 1.96 for a two-tailed test at $\alpha = 0.05$. μ_β: The Z-value related to statistical power ($1 - \beta$), typically 0.84 when $\beta = 0.2$ (representing 80% power).

Source: these values are based on standard statistical principles, where the choices of α and β reflect the researcher's tolerance for Type I (false positive) and Type II (false negative) errors.

To enhance the credibility of the study, the following additional steps were performed:

Literature Support: relevant references were used to justify the selected event occurrence rates and effect sizes.

Preliminary Data: a small-scale pretrial was conducted, where possible, to validate the parameters chosen and confirm their applicability.

Sensitivity Analysis: sensitivity analyses were performed to

evaluate the impact of varying parameter choices on sample size calculations, ensuring the robustness and reliability of the results.

This retrospective cohort study evaluated fixed variables as the primary efficacy outcomes. A superiority design with a 1:1 ratio was adopted, using parameters set at $\alpha = 0.025$ (one-sided), $\beta = 0.20$ (one-sided) and $\Delta = 5\%$. Based on these settings, the required sample size for each group was calculated to be 33 patients. To account for a 20% dropout rate, 39 patients were included in each group, resulting in a total of 78 patients. The study ultimately included 39 patients in the observation group and 39 patients in the control group, with participants assigned to their respective groups based on recorded treatment methods.

Clinical data from 78 female breast cancer patients treated between January 2022 and December 2023 were retrospectively reviewed and the patients were grouped according to the treatment methods documented in their medical records, with 39 patients in the observation group and 39 in the control group.

Inclusion Criteria: (1) Female patients meeting the diagnostic and treatment standards for breast cancer as outlined in the 2022 National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines for Breast Cancer [9], with diagnosis confirmed by imaging and pathological examinations. (2) Underwent either a nipple-sparing mastectomy (NSM) or radical mastectomy. (3) Presented with a single tumor focus. (4) No evidence of distant metastasis or invasion. (5) Scheduled for elective unilateral radical mastectomy for breast cancer. (6) Demonstrated normal results in preoperative laboratory tests for cardiac, pulmonary, liver, kidney, and coagulation functions, meeting the following criteria: Forced vital capacity (FVC): 4.0–5.0 L; Forced expiratory volume in 1 second (FEV1): 3.5–4.5 L; FEV1/FVC ratio: $>$70%; Hemoglobin: $>$12 g/dL; Creatinine clearance: $>$60 mL/min; Serum creatinine: 0.6–1.2 mg/dL; Blood urea nitrogen (BUN): 7–20 mg/dL; Platelet count: 150,000–400,000/μL; D-dimer: $<$0.5 mg/L. (7) Complete medical records were available for review.

Exclusion criteria: (1) Patients with severe cardiac, liver, or renal dysfunction; (2) had received preoperative chemoradiotherapy or immunotherapy; (3) with severe immune dysfunction; (4) those allergic to anesthesia-related drugs or with contraindications to anesthesia; (5) had a history of mental illness or drug addiction.

2.2 Interventions

As this is a retrospective study, the intervention methods were retrieved from the patients' existing case records. All patients from both groups underwent radical mastectomy. Preoperatively, the clinical staging of the axilla and the results of axillary lymph node fine needle aspiration (FNA) biopsy were evaluated to guide management. For patients with positive FNA biopsy results, axillary lymph node dissection was performed. In cases without axillary lymph node enlargement and with negative FNA results, a sentinel lymph node biopsy was conducted. If the sentinel lymph node biopsy was positive, axillary lymph node dissection was subsequently performed.

All surgeries were conducted under general anesthesia by the same surgical team. Patients in both groups underwent traditional radical mastectomy procedures. For those with tumors not involving the pectoralis major or minor muscles, a modified radical mastectomy (MRM) was performed, which involved the removal of most breast skin, the nipple-areola complex, the entire breast tissue, and axillary lymph nodes (if sentinel nodes were positive), while preserving the pectoralis major and minor muscles. For patients with tumors involving the pectoralis muscles, a radical mastectomy (RM) was performed, which included resection of the pectoralis muscles in addition to the MRM.

Breast reconstruction surgery was performed based on patient preference and clinical condition, either immediately (Stage I) or as a delayed procedure (Stage II). Postoperatively, all patients received adjuvant chemotherapy, radiotherapy, endocrine therapy and targeted therapy in accordance with NCCN guidelines. The specific regimens and timing of these adjuvant treatments were tailored to each patient's clinical condition and pathological findings. Any other comorbidities were managed with appropriate medications as required.

2.2.1 Preoperative patient assessment

The preoperative assessment comprised a thorough review of the patient's medical history, a detailed physical examination, and essential preoperative tests such as electrocardiograms and imaging studies to assess overall health status and anesthetic risk. Informed consent was obtained after providing the patient with comprehensive information about the anesthesia process, potential risks and expected outcomes.

2.2.2 Pre-anesthesia preparation

Intravenous Access: a suitable vein was selected on the patient's arm or forearm, and an 18–20 G intravenous catheter was inserted to establish intravenous access. Monitoring Equipment: basic monitoring devices, including an electrocardiogram, blood pressure cuff and pulse oximeter (SpO_2), were installed to continuously monitor the patient's vital signs.

2.2.3 Anesthesia induction

Premedication: premedication, such as atropine or diazepam, was administered when necessary to reduce anxiety and suppress salivation. Intravenous Anesthetics: propofol was administered through the intravenous catheter to achieve rapid anesthesia induction. The dosage was adjusted based on the patient's weight, age and clinical condition. Airway Management: after induction, the patient's airway was evaluated. Depending on the patient's condition, appropriate airway management techniques were employed, including mask ventilation, laryngeal mask airway placement or endotracheal intubation to maintain an open airway.

2.2.4 Anesthesia maintenance

Inhalation Anesthetics: after successful endotracheal intubation, inhalation anesthetic agents were administered via the anesthesia machine, and the concentrations were adjusted to maintain an appropriate depth of anesthesia.

Control Group Anesthesia Protocol: patients in the control group received inhalational anesthesia with isoflurane (Hebei

Jiupai Pharmaceutical Co. Ltd., Shijiazhuang, Hebei, China, National Drug Standard H19980141) at a concentration of 1.5%–3.0%. During the maintenance phase, vecuronium and fentanyl were administered based on the patient's clinical status and surgical requirements to ensure adequate anesthesia depth and effective pain relief.

Observation Group Anesthesia Protocol: in the observation group, an intravenous combined anesthesia regimen was implemented in addition to the control group protocol. Upon entering the operating room, vital signs, including heart rate (HR), blood pressure (BP) and oxygen saturation (SpO_2), were continuously monitored for real-time assessment of the patient's physiological status. During induction, propofol (Fresenius Kabi AB, Uppsala, Sweden, National Drug Standard J20080023) was administered at a dose of 1.5–2.5 mg/kg, adjusted according to the patient's weight, age and overall condition to achieve the desired depth of anesthesia. For analgesia, sufentanil (Yichang Renfu Pharmaceutical Co. Ltd., Yichang, Hubei, China, National Drug Standard H20054172) was administered intravenously at a dose of 0.2–0.5 μg/kg, with adjustments made in response to the patient's pain level and the degree of surgical stimulation. Muscle relaxation was achieved using cisatracurium (Jiangsu Heng Pharmaceutical Co., Ltd., Changzhou, Jiangsu, China, National Drug Standard H20060869) at a dose of 0.2–0.3 mg/kg, tailored to meet the surgical requirements and patient responses.

After intubation, inhalational isoflurane was continued at a concentration of 1.0%–2.0% to maintain effective anesthesia depth while avoiding over-sedation. Additionally, a continuous intravenous infusion of propofol (500 mg) and fentanyl (500 μg) was initiated, and the infusion rates were adjusted according to the patient's vital signs and depth of anesthesia to maintain stable anesthesia throughout the surgery.

Intravenous infusion rates were carefully modified based on the patient's physiological responses, the intensity of surgical stimulation, and the required depth of anesthesia. This individualized and precise management ensured optimal anesthesia control, contributing to enhanced surgical safety and improved patient comfort.

2.2.5 Intraoperative monitoring

During surgery, the anesthesiologist continuously monitored the patient's vital signs and adjusted anesthetic agents as needed to ensure safe and effective anesthesia. The key components of intraoperative monitoring included:

(1) Vital Sign Monitoring: HR: continuously assessed to monitor cardiac function. BP: dynamically measured, including systolic, diastolic and mean arterial pressures (MAP), to ensure hemodynamic stability. SpO_2: blood oxygen levels were continuously measured using a pulse oximeter to confirm adequate oxygenation. Respiratory Rate (RR): monitored to ensure airway patency and effective ventilation.

(2) Anesthesia Depth Monitoring: the depth of anesthesia was assessed using specialized anesthesia monitors or electroencephalogram (EEG) monitoring to prevent complications from over- or under-sedation.

(3) Temperature Monitoring: the patient's body temperature was closely monitored to prevent hypothermia or hyperthermia. Temperature control measures, such as warming blankets or heaters, were used as needed to maintain normothermia.

(4) Medication Monitoring: the administration of anesthetic medications, including intravenous agents (*e.g.*, propofol, alfentanil) and inhalation anesthetics (*e.g.*, isoflurane, sevoflurane), was carefully documented, such as recording dosages, infusion rates and any adjustments made based on patient responses.

(5) Surgical Site Monitoring: the surgical site was continuously observed for bleeding and other potential complications to ensure smooth surgical progression and minimize risks.

2.2.6 Postoperative analgesia

Effective postoperative pain management is essential following breast cancer radical mastectomy. Both groups of patients were typically prescribed analgesic medications, including non-steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen or ketoprofen. For ibuprofen, the standard dosage ranged from 400 mg to 600 mg every 6 to 8 hours, with a maximum daily dose of $\leq$2400 mg, which may occasionally be increased to 3200 mg under physician supervision. For ketoprofen, the usual dosage was 50 mg to 100 mg every 6 to 8 hours, with a maximum daily dose of 300 mg. Dosages were adjusted based on individual factors such as age, weight and renal function. Careful monitoring was performed for patients with gastrointestinal disorders or other conditions that may affect NSAID use. NSAIDs were often combined with other analgesics to enhance pain relief and minimize side effects, as monotherapy may not adequately control postoperative pain.

2.2.7 Postoperative nausea and vomiting (PONV)

To prevent and manage PONV, the following medications were utilized: (1) 5-HT3 Receptor Antagonists: ondansetron was commonly administered at a dosage of 4 mg intravenously immediately after surgery. An additional dose was given preoperatively for PONV prevention, with repeat dosing based on the patient's response. (2) Dopamine Antagonists: droperidol was typically administered at 0.625 mg to 1.25 mg intravenously, with dosage adjustments as needed but not exceeding 2.5 mg. (3) Antihistamines: meclizine, at an adult dosage of 25 mg to 50 mg, was usually administered 1 hour before surgery. While primarily used for motion sickness, its use for PONV required physician guidance.

The treatment was individualized to optimize outcomes, considering variability in patient responses to these medications.

2.2.8 Muscle relaxant reversal agents

During total intravenous anesthesia (TIVA), muscle relaxants were used to facilitate surgery, and reversal agents were often necessary postoperatively to counteract their effects. The most commonly used reversal agents included: (1) Neostigmine: administered at a typical dosage of 0.05 mg/kg, with a maximum dose of 5 mg. This was often combined with atropine or glycopyrrolate to mitigate side effects such as excessive salivation. (2) Sugammadex: used for the rapid reversal of certain muscle relaxants, such as rocuronium. The initial dose typically ranged from 0.6 mg/kg to 1.2 mg/kg and was adjusted based on surgical requirements and patient weight. Higher

doses, such as 1.0 mg/kg, were used for faster induction, while maintenance doses ranged from 0.1 mg/kg to 0.2 mg/kg for continuous administration during prolonged surgeries.

The selection of reversal agents and dosages was individualized, accounting for factors such as the patient's weight, depth of anesthesia, type of surgery and clinical condition. When using neostigmine to reverse muscle relaxants like rocuronium, it was essential to confirm that the patient had regained adequate respiratory function and muscle strength before extubation. Neuromuscular function was closely monitored to ensure patient safety and proper recovery.

2.2.9 Other antidotes

During anesthesia and surgery, antidotes may be required to counteract side effects or overdose reactions from specific drugs. The following antidotes were commonly used:

Opioid Antagonists (Naloxone): Dosage and Administration: naloxone was administered intravenously, intramuscularly, or subcutaneously at an initial dose of 0.4 mg to 2 mg. If no significant response was observed within 2–3 minutes, the dose was repeated every 2–3 minutes, up to a maximum total dose of 10 mg. For sustained effects, naloxone could be continuously infused at a rate of 0.1 mg/h to 0.4 mg/h. Precautions: It was used only in patients who had received opioid medications. Respiratory and consciousness status were closely monitored, as opioid reversal could cause withdrawal symptoms and respiratory distress.

Antidotes: Dopamine Antagonists (Droperidol): Dosage and Administration: droperidol was typically administered intravenously at a dose of 0.625 mg to 1.25 mg, with adjustments made based on clinical needs. The maximum dose was generally $\leq$2.5 mg. Precautions: patients receiving dopamine antagonists were monitored for side effects, including sedation, hypotension and cardiovascular reactions, such as QT interval prolongation.

General Precautions: antidote regimens and dosages were tailored to the patient's condition, type of surgery and anesthesia plan. Careful monitoring and adherence to medical guidelines were essential to ensure safety and effectiveness.

2.2.10 Postoperative monitoring and recovery

(1) Recovery Room Monitoring: (i) Vital Signs: HR, BP, RR and SpO_2 were continuously monitored to assess the patient's recovery status. (ii) Consciousness Status: the patient's level of consciousness and responsiveness were regularly evaluated to ensure normal recovery. (iii) Pain Assessment: postoperative pain was assessed using a standardized pain scale, such as the Visual Analog Scale (VAS), and analgesics were administered as needed based on the patient's reported pain level.

(2) Monitoring for Complications: patients were closely observed for any signs of postoperative complications, including respiratory depression, cardiovascular instability or allergic reactions.

(3) Fluid Balance Monitoring: postoperative fluid intake and output were recorded to maintain fluid balance and prevent dehydration or fluid overload.

(4) Limb Activity Monitoring: postoperative limb mobility was assessed to confirm the return of normal neuromuscular function and to help prevent complications such as deep vein thrombosis (DVT).

(5) Discontinuation of Anesthetic Drugs: the concentration of inhaled anesthetics was gradually reduced as the patient transitioned to full recovery, ensuring a smooth and safe emergence from anesthesia.

(6) Postoperative Care: patients were continuously monitored in the recovery room for any complications related to anesthesia or the surgical procedure. Once fully conscious and stable, they were transferred to the ward for further observation and care.

(7) Discharge Preparation: discharge was assessed based on factors such as independent activity, normal eating and urination functions and stable vital signs.

2.2.11 Monitoring anesthesia depth

The depth of anesthesia can be monitored through various methods to ensure patient safety and effective anesthesia management:

(1) Clinical Assessment: (i) Consciousness Level: the patient's responsiveness to external stimuli and ability to follow commands are evaluated to determine the depth of anesthesia. (ii) Muscle Relaxation: muscle tone and spontaneous breathing are assessed as indicators of muscle relaxation, providing an indirect measure of anesthesia depth.

(2) Physiological Monitoring: (i) HR and BP: Changes in these parameters can reflect anesthesia depth, with increases or decreases often signaling levels that are too shallow or too deep. (ii) RR: Alterations in respiratory patterns or rates, including respiratory depression, help gauge the effects of anesthesia on the respiratory system and indicate depth.

(3) Electroencephalographic (EEG) Monitoring: (i) Bispectral Index (BIS): BIS monitoring interprets EEG signals, with values between 40 and 60 typically indicating an appropriate anesthesia depth. Values outside this range may suggest insufficient or excessive anesthesia. (ii) Entropy Monitoring: similar to BIS, entropy monitoring was conducted to analyze EEG signals to provide a continuous and reliable assessment of anesthesia depth.

(4) Drug Concentration Monitoring: Plasma Drug Concentration: monitoring the plasma levels of intravenous anesthetics, such as propofol, offers direct insight into anesthesia depth and helps guide drug dosing and administration.

(5) Other Physiological Parameters: Oxygenation Status: continuous monitoring of blood SpO_2 and arterial blood gas parameters (Partial Pressure of Oxygen (PaO_2), Partial Pressure of Carbon Dioxide ($PaCO_2$)) helps evaluate respiratory function and indirectly assess anesthesia depth.

2.3 Outcome indicators

The outcome indicators were retrospectively derived from the case records.

2.3.1 Primary outcomes

Vital Signs: vital signs, including HR, MAP, RR, SpO_2 and arterial oxygen partial pressure (PaO_2), were measured at four time points: before anesthesia (T0), during endotracheal intubation (T1), during surgical incision (T2) and at the end of

surgery (T3).

HR: measured using electrodes connected to an electrocardiogram (ECG) monitor, which automatically calculates and displays the HR.

MAP: BP was measured with a mercury or electronic sphygmomanometer. MAP was calculated using the formula: MAP = Diastolic Blood Pressure (DBP) + (SBP − DBP)/3.

RR: Measured using a respiratory monitor. SpO_2: Measured with a pulse oximeter attached to the fingertip, earlobe or toe, using infrared and red light to calculate SpO_2. The results are shown in seconds.

Arterial Oxygen Partial Pressure (PaO_2): (i) Sample Collection: The radial artery was the preferred site for arterial blood sampling, although the femoral or brachial arteries may also be used if necessary. Briefly, the site was disinfected using an antiseptic solution, such as alcohol or iodine, the artery was located through palpation, and a dedicated arterial blood collection needle was used to draw approximately 1–2 mL of blood. To prevent hematoma formation, a firm pressure was applied to the puncture site immediately after collection and maintained for 5–10 minutes. (ii) Sample Analysis: the collected blood sample was placed on ice and promptly transported to the laboratory to minimize metabolic changes. A blood gas analyzer was then used to measure and report PaO_2 levels accurately.

Anesthetic effect: this was determined based on the maintenance time of anesthesia, time to eye opening, time to directional force recovery and extubation time.

Adverse Reactions: these were recorded and included postoperative nausea and vomiting (PONV), bradycardia, respiratory depression and restlessness.

2.3.2 Secondary outcomes

VAS Scores: pain intensity was assessed using the VAS [10] during anesthesia at specific time points, and the scale ranged from 0 to 10, with higher scores indicating more severe pain.

Inflammatory Markers: peripheral venous blood samples (5 mL) were collected before anesthesia and at the end of surgery. Briefly, the samples were separated via centrifugation for 10 minutes at 3000 r/min, and the levels of CRP, IL-6 and TNF-α were measured using enzyme-linked immunosorbent assay (ELISA).

Stress Response Indicators: peripheral venous blood samples (5 mL) were similarly collected and centrifuged before anesthesia and at the end of surgery. Cortisol (Cor), norepinephrine (NE) and epinephrine (E) levels were measured using ELISA.

2.4 Statistical analysis

Data analysis was conducted using SPSS 21.0 (IBM, Armonk, NY, USA) and GraphPad Prism 8.0.2 software (GraphPad Software Inc., San Diego, CA, USA). Continuous variables with a normal distribution are presented as mean ± standard deviation (SD), and comparisons between groups were conducted using an independent sample *t*-test. For intra-group comparisons, a paired sample *t*-test was applied. For data with a skewed distribution or unequal variances, the Mann-Whitney U test was used, and results are reported as median (M) and interquartile range (P25, P75). Categorical variables are expressed as frequencies and percentages (%). Group comparisons for categorical data were performed using the chi-square test or Fisher's exact test, depending on the expected frequencies within the contingency table. $p < 0.05$ was considered statistically significant for all analyses.

3. Results

3.1 General information

The general characteristics of the control and observation groups are presented in Table 1.

3.2 Vital sign indicators

The comparison of vital sign indicators between the two groups is shown in Table 2. No significant differences were observed in vital signs during the T0 period ($p > 0.05$). However, at T1, T2 and T3, the observation group exhibited significantly lower MAP and HR, as well as significantly higher PaO_2 compared to the control group ($p < 0.05$, Fig. 1).

3.3 Anesthetic effects

The eye opening time, directional force recovery time and extubation time in observation group were statistically shorter

TABLE 1. General characteristics of the control and observation groups.

Variables	Control group	Observation group	χ^2/t	p
Age (yr)	45.35 ± 5.67	46.60 ± 4.85	1.051	0.296
Complication				
Hypertension	10 (25.64)	8 (20.51)	0.289	0.591
Diabetes	5 (12.82)	7 (17.95)	0.394	0.530
Cardiovascular disease	8 (20.51)	6 (15.38)	0.348	0.555
ASA classification				
ASA level I	16 (41.03)	14 (35.90)	0.217	0.642
ASA level II	23 (58.97)	25 (64.10)		
BMI (kg/m^2)	23.50 ± 0.57	23.35 ± 0.36	1.393	0.168

ASA: American Society of Anesthesiologists; BMI: Body mass index.

TABLE 2. Comparison of vital signs indicators between the control and observation groups ($\bar{x} \pm s$).

Variables	Groups	n	T0	T1	T2	T3
MAP (mmHg)						
	Control group	39	82.77 ± 5.60	91.69 ± 6.43	92.15 ± 8.24	93.59 ± 5.08
	Observation group	39	81.72 ± 7.89	79.33 ± 7.04	78.82 ± 8.26	81.41 ± 8.98
	t		0.679	8.092	7.138	7.370
	p		0.499	<0.001	<0.001	<0.001
Heart rate (beats/min)						
	Control group	39	72.72 ± 2.81	75.64 ± 3.10	76.08 ± 3.49	72.54 ± 4.91
	Observation group	39	71.64 ± 2.93	63.38 ± 2.10	65.97 ± 2.16	67.38 ± 2.54
	t		1.656	20.453	15.376	5.823
	p		0.102	<0.001	<0.001	<0.001
SpO_2 (%)						
	Control group	39	96.28 ± 1.02	95.82 ± 0.85	97.44 ± 0.75	96.74 ± 1.21
	Observation group	39	96.54 ± 1.12	96.10 ± 0.75	97.13 ± 0.83	96.41 ± 1.23
	t		1.055	1.546	1.711	1.208
	p		0.295	0.126	0.091	0.231

MAP: mean arterial pressure; SpO_2: blood pressure cuff and pulse oximeter; T0: before anesthesia; T1: during endotracheal intubation; T2: during surgical incision; T3: at the end of surgery.

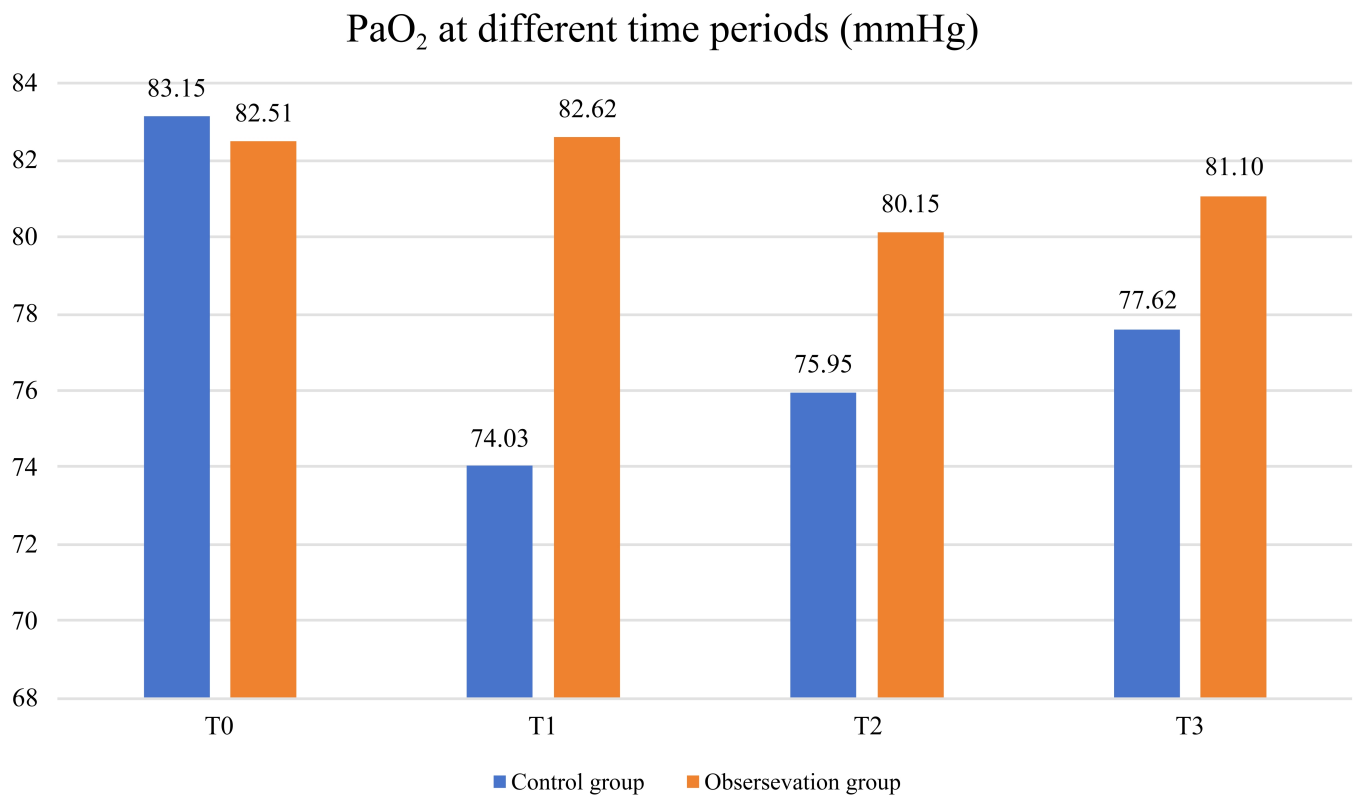

FIGURE 1. Comparison of PaO_2 between the two groups. PaO_2: arterial oxygen partial pressure; T0: before anesthesia; T1: during endotracheal intubation; T2: during surgical incision; T3: at the end of surgery.

than control group ($p < 0.05$), and there was no significant difference in the duration of anesthesia maintenance between the two groups (Table 3, $p > 0.05$).

3.4 Adverse reactions

The incidence of adverse reactions in the observation group was significantly lower (Table 4, $p < 0.05$).

3.5 VAS scores

At 5 minutes, 45 minutes and 90 minutes post-anesthesia, the VAS scores of the observation group were significantly lower than those of the control group (Fig. 2, $p < 0.05$).

3.6 Inflammation level

The levels of CRP, IL-6 and TNF-α in the observation group were significantly lower than the control group 24 hours after operation (Table 5, $p < 0.05$).

3.7 Stress response indicators

The levels of NE, Cor and E in the observation group were significantly lower than the control group 24 hours after operation (Table 6, $p < 0.05$).

4. Discussion

Radical mastectomy is a common surgical approach for the treatment of breast cancer [11]. However, the physical trauma associated with tissue manipulation during the procedure often induces stress and inflammatory responses, which can complicate surgery and increase patient discomfort. As such, selecting an appropriate anesthesia technique is essential to ensuring surgical success while minimizing patient pain and distress.

Inhalation anesthesia combined with intravenous anesthesia offers several advantages over single-agent anesthesia. Among the agents used, sufentanil is a potent analgesic that contributes to maintaining hemodynamic stability, while propofol is an intravenous anesthetic with rapid onset and minimal side effects, making it an ideal choice for general anesthesia. Propofol acts quickly and has a short duration of effect, functioning by binding to specific β-subunits of the γ-aminobutyric acid (GABA) receptor, which enhances inward chloride currents, inhibiting central nervous system activity to produce sedative and hypnotic effects [12, 13]. The drug is metabolized primarily by the liver, contributing to its favorable safety profile, and is widely used for both induction and maintenance of general anesthesia [14]. Sufentanil, a potent μ-opioid receptor agonist, inhibits adenylate cyclase and downstream protein kinase A activity through cascade reactions, leading to ion channel closure. This mechanism effectively blocks pain signal transmission and reduces pain perception. Although sufentanil's analgesic duration is relatively short, its rapid clearance from the bloodstream minimizes the risk of prolonged adverse effects [15]. Combining inhalation and intravenous anesthesia mitigates the cardiovascular impact associated with inhalation anesthesia alone, allowing for quicker postoperative recovery. This combined approach compensates for the limitations of single-agent anesthesia by optimizing the depth of anesthesia while minimizing respiratory and circulatory side effects. Despite their benefits, both propofol and sufentanil exhibit inhibitory effects on respiratory and circulatory functions, potentially reducing blood SpO_2 and affecting physiological stability [16].

In this study, the observation group, which received a combination of inhalation anesthesia and intravenous anesthesia, exhibited more stable vital signs compared to the control group, and this may be attributed to the precise control of anesthesia depth achieved through the use of intravenous agents such as propofol and fentanyl. The reduced reliance on inhalation anesthetics minimized their adverse effects on the respiratory and cardiovascular systems, contributing to better physiological stability throughout the procedure. Additionally, the combined anesthesia approach acted on the

TABLE 3. Comparison of anesthetic effect between two groups ($\bar{x} \pm s$, min).

Variables	Control group (n = 39)	Observation group (n = 39)	t	p
Maintenance time of anesthesia	171.51 ± 35.17	164.38 ± 35.20	0.895	0.374
Eye opening time	7.26 ± 1.31	5.82 ± 0.91	5.607	<0.001
Directional force recovery time	18.95 ± 3.55	14.03 ± 3.15	6.474	<0.001
Extubation time	12.64 ± 1.65	9.59 ± 1.50	8.558	<0.001

TABLE 4. Comparison of adverse reactions (n (%)).

Variables	n	Postoperative nausea and vomiting	Bradycardia	Respiratory depression	Restlessness	Total
Control group	39	3 (7.69)	2 (5.13)	5 (12.82)	4 (10.26)	14 (35.90)
Observation group	39	1 (2.56)	0	1 (2.56)	1 (2.56)	3 (7.69)
χ^2		Fisher	Fisher	Fisher	Fisher	9.101
p		0.615	0.494	0.200	0.358	0.003

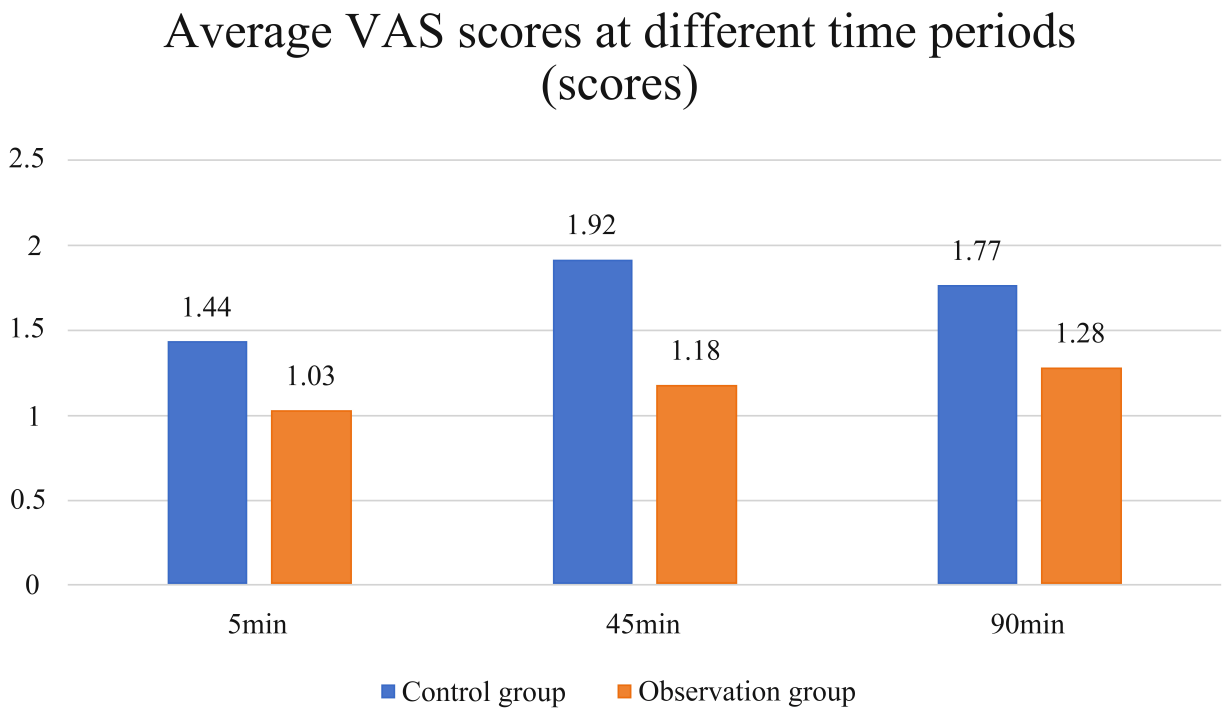

FIGURE 2. Comparison of VAS scores between the two groups. VAS: Visual Analog Scale.

TABLE 5. Comparison of inflammation levels between the control and observation groups ($\bar{x} \pm s$).

Variables	Time	Control group (n = 39)	Observation group (n = 39)	*t*	*p*
CRP (mg/mL)					
	Before anesthesia	19.22 ± 3.56	20.17 ± 3.79	1.136	0.260
	24 h after operation	46.60 ± 4.64	37.26 ± 4.95	8.591	<0.001
IL-6 (pg/mL)					
	Before anesthesia	34.79 ± 6.48	35.10 ± 6.04	0.217	0.829
	24 h after operation	75.50 ± 9.34	59.22 ± 9.15	7.775	<0.001
TNF-α (mg/mL)					
	Before anesthesia	46.84 ± 6.20	47.09 ± 6.92	0.170	0.866
	24 h after operation	77.44 ± 7.45	62.58 ± 7.32	8.885	<0.001

CRP: C-reactive protein; IL-6: interleukin-6; TNF-α: tumor necrosis factor-alpha.

TABLE 6. Comparison of stress response indicators between the control and observation groups ($\bar{x} \pm s$).

Variables	Time	Control group (n = 39)	Observation group (n = 39)	*t*	*p*
NE (ng/mL)					
	Before anesthesia	193.97 ± 26.46	204.63 ± 35.22	1.512	0.135
	24 h after operation	293.10 ± 43.21	264.49 ± 38.19	3.098	0.003
Cor (ng/mL)					
	Before anesthesia	208.36 ± 32.34	203.22 ± 38.17	0.642	0.523
	24 h after operation	280.37 ± 44.73	247.55 ± 41.42	3.361	0.001
E (ng/mL)					
	Before anesthesia	117.03 ± 37.28	123.01 ± 37.96	0.701	0.485
	24 h after operation	211.58 ± 50.57	161.19 ± 40.72	4.847	<0.001

NE: norepinephrine; Cor: Cortisol; E: epinephrine.

central nervous system through complementary mechanisms, enhancing the safety and efficacy of anesthesia. This approach also increased the patients' resistance to external stimuli during surgery, further ensuring procedural success and patient comfort [17].

The observation group demonstrated significantly shorter eye-opening times, orientation recovery times, and extubation times compared to the control group, which can be attributed to several factors. First, the use of intravenous combined anesthesia facilitates faster recovery due to the short half-life of agents such as propofol, allowing for quicker wakefulness and minimizing postoperative drowsiness and confusion [18]. Second, the shorter orientation recovery time observed in the observation group may be linked to the optimized selection and precise dosage of anesthetic drugs. Intravenous anesthetics are rapidly metabolized following surgery, thereby reducing the likelihood of postoperative cognitive dysfunction. The combination of anesthetic techniques in the observation group may also have contributed to smoother airway management, which facilitated faster recovery of respiratory function after intubation. Furthermore, intravenous combined anesthesia promotes earlier recovery of spontaneous breathing, reduces extubation complications, and significantly shortens the extubation time. These benefits highlight the advantages of this multimodal approach in achieving more efficient postoperative recovery. Taken together, inhalation anesthesia combined with intravenous anesthesia was found to be more effective than inhalation anesthesia alone in maintaining hemodynamic stability and achieving a greater depth of anesthesia, ensuring complete muscle relaxation, providing a clearer surgical field and reducing the risk of damage to surrounding organs, as well as promoting better postoperative recovery without adversely affecting liver or kidney function.

Additionally, at 5, 45 and 90 minutes post-anesthesia, the VAS scores of the observation group were significantly lower than those of the control group, indicating that the combination of inhalation and intravenous anesthesia significantly improves postoperative pain management. This improvement can be attributed to several underlying factors. For instance, the lower VAS scores in the observation group reflect the enhanced analgesic effect provided by combined anesthesia. Intravenous anesthetics, such as fentanyl and other opioids, offer potent pain relief, effectively reducing postoperative discomfort. The synergistic action of these agents enhances pain control compared to inhalation of anesthesia alone. The mechanism behind this improved analgesia lies in the ability of intravenous combined anesthesia to target multiple pain pathways simultaneously. This synergistic effect leads to more effective alleviation of early postoperative pain, ensuring greater patient comfort during the recovery period. The findings further demonstrate that the anesthesia process in the observation group had significant advantages in maintaining stable vital signs, promoting rapid recovery and providing superior pain relief. The multiple mechanisms and flexibility of this combined anesthesia strategy make it an optimal choice for radical mastectomy in breast cancer patients, and by addressing both intraoperative and postoperative needs, this approach enhances the surgical experience and supports improved recovery outcomes.

The stress response triggered by surgical manipulation during radical mastectomy exacerbates tissue injury by activating the sympathetic-adrenal system, leading to the release of substances such as adrenaline, Cor and NE [19]. This increased stress response further exacerbates the inflammatory response, increasing the release of inflammatory mediators (*i.e.*, CRP, IL-6 and TNF-α) [20]. In the observation group, inflammatory factors (CRP, IL-6, TNF-α) and stress indexes (NE, Cor, E) were significantly elevated 24 hours after surgery. However, these markers were markedly lower compared to the control group, suggesting that the combination of inhalation and intravenous anesthesia effectively attenuates the inflammatory and stress responses. This mitigation likely contributes to improved patient outcomes by reducing the extent of postoperative physiological stress and inflammation. In terms of safety, the combined approach of inhalation and intravenous anesthesia did not lead to an increased incidence of adverse reactions such as agitation, respiratory depression, bradycardia or reflux, indicating that the technique is relatively safe for clinical application. Furthermore, this combination strategy significantly alleviates postoperative pain and reduces the total anesthetic drug dosage required. Therefore, it decreases the incidence of postoperative complications such as nausea and vomiting, thereby positively influencing the overall recovery process.

In the study of anesthetic effects in female breast cancer patients, the implementation of safety measures was essential for reducing complications during the anesthesia process and ensuring patient safety. Comprehensive preoperative evaluations were conducted for all patients, including a detailed medical history review, physical examinations and laboratory tests such as blood work and liver and kidney function tests. These evaluations helped identify potential anesthesia risks, and patients were classified according to the American Society of Anesthesiologists (ASA) classification to assess risk levels and develop appropriate anesthesia plans. Individualized anesthesia plans were created based on the specific condition of each patient, the characteristics of the tumor and any comorbidities. Suitable anesthetic agents and methods, such as a combination of inhalation and intravenous anesthesia, were selected to meet the patient's needs. During surgery, anesthesia doses and methods were adjusted in real-time based on continuous monitoring of key parameters, including HR, BP and SpO_2. Intraoperative monitoring played a central role in maintaining patient safety. Continuous tracking of vital signs, such as electrocardiography, pulse oximetry, and non-invasive BP, allowed for the early detection of any abnormalities. Anesthesia depth was monitored using the BIS to avoid the risks associated with both excessive and insufficient anesthesia. Airway management strategies were carefully planned based on a preoperative airway assessment. Necessary equipment, including tools for intubation, masks and ventilators, was prepared to address any potential emergencies. Postoperative care involves continuous monitoring in the recovery room to evaluate vital signs, consciousness recovery and pain levels, ensuring a smooth and safe recovery process. Pain management was tailored to patients' needs using VAS scores to alleviate discomfort and minimize stress responses. To address potential complications, a rapid response mechanism

was established to manage anesthetic-related issues such as allergic reactions, respiratory suppression, and cardiovascular instability. Postoperative follow-ups were also conducted to document and address any adverse reactions in a timely manner. Training and teamwork were integral to the success of these measures. The anesthesia team underwent regular training to ensure proficiency in the latest techniques, equipment, and emergency protocols. Collaboration among anesthesiologists, surgeons, nurses and other healthcare professionals fostered effective communication, further enhancing patient safety. The implementation of these comprehensive safety measures effectively reduced anesthesia risks and improved the safety and comfort of female breast cancer patients during surgery, which not only enhanced anesthetic outcomes but also facilitated smoother postoperative recovery, highlighting the importance of a systematic and multidisciplinary approach to anesthetic management.

This study has several limitations. First, the sample size was relatively small, and the collection of baseline disease characteristics and other general data was limited, which together with the single-center design might have reduced the generalizability of the findings to broader populations. Second, as a retrospective study, patient allocation was based on previously recorded treatment plans rather than randomized assignment, potentially introducing certain levels of biases. Third, the study did not explore factors influencing patient recurrence rates, leaving a gap in understanding the potential impact of different anesthesia methods on recurrence. Lastly, the analysis of risk factors associated with postoperative complications was not comprehensive, limiting insights that could improve surgical and clinical management strategies. Future research could address these limitations by including larger sample sizes, incorporating diverse patient demographics, and adopting multicenter designs to improve the applicability of findings. Additionally, further investigation into postoperative complications and factors affecting recurrence rates is needed to provide a more accurate and comprehensive understanding of the impact of anesthesia methods on long-term patient outcomes.

5. Conclusions

In conclusion, this study demonstrates that the combination of inhalation anesthesia and intravenous anesthesia offers significant advantages over inhalation anesthesia alone for female breast cancer patients in several key areas. First, the depth of anesthesia was more stable during surgery, with better-maintained intraoperative hemodynamic indicators, reducing the risks associated with fluctuations in anesthesia depth. Second, postoperative pain scores were significantly lower in the combined anesthesia group, reflecting superior analgesic effects and a reduced need for postoperative pain medications. Third, inflammatory markers were notably decreased following combined anesthesia, suggesting that this method positively impacts postoperative recovery, potentially leading to shorter hospital stays and faster rehabilitation. Finally, the incidence of adverse reactions was significantly lower in the combined anesthesia group, underscoring the safety benefits of this approach and enhancing the overall anesthetic experience for patients.

Based on these findings, inhalation anesthesia combined with intravenous anesthesia is recommended as the preferred method for breast cancer surgery. This approach not only improves anesthetic outcomes and alleviates postoperative pain and inflammation but also enhances the overall recovery experience for patients, and its implementation in clinical practice could be encouraged to optimize anesthesia management and improve surgical outcomes for breast cancer patients.

AVAILABILITY OF DATA AND MATERIALS

The authors declare that all data supporting the findings of this study are available within the paper and any raw data can be obtained from the corresponding author upon request.

AUTHOR CONTRIBUTIONS

EJ, RM—designed the study and carried them out, prepared the manuscript for publication and reviewed the draft of the manuscript. EJ, RM, JW—supervised the data collection, analyzed the data, interpreted the data. All authors have read and approved the manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethical approval was obtained from the Ethics Committee of The First People's Hospital of Aksu (Approval no. 2023-32). Written informed consent was obtained from a legally authorized representatives for anonymized patient information to be published in this article.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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