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Original Article

Impacts of sufentanil/remifentanil plus sevoflurane versus propofol in adults undergoing laparoscopic herniorrhaphy

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Abstract: Objective: To retrospectively explore how sevoflurane + sufentanil/remifentanil versus propofol + sufentanil/remifentanil impacts clinical outcomes in laparoscopic herniorrhaphy-treated adults. Methods: We enrolled 102 adult patients grouped into propofol (n=50) and sevoflurane (n=52) groups. Inter-group comparisons were made regarding operative duration, time to induction, extubation, emergence, and consciousness recovery, agitation incidence, first ambulation time, length of stay, and gastrointestinal recovery. Adverse events, hemodynamic parameters, as well as preoperative and postoperative stress markers, inflammatory cytokines, and pain mediators, were also discussed. Results: The sevoflurane group had statistically shorter times to extubation, consciousness recovery, first ambulation, and gastrointestinal restoration, along with lower agitation and overall adverse event rates. Shorter anesthesia emergence time and more stable hemodynamic parameters were also found in patients receiving sevoflurane compared to the propofol cohort. Better performance in postoperative stress response, inflammatory markers, and pain mediators (except for a milder decrease in β-endorphin [β-EP]) was also determined in sevoflurane-treated patients. No notable intergroup differences were identified in the durations of surgery, induction, and hospitalization. Conclusion: Compared to the propofol combination, the sevoflurane-sufentanil/remifentanil regimen applied to adult laparoscopic hernia repair patients contributed to superior clinical outcomes.

Keywords: Sufentanil, sevoflurane, propofol, remifentanil, laparoscopic herniorrhaphy in adults, anesthesia efficacy

Introduction

Hernias constitute a prevalent global health concern, involving the abnormal protrusion of internal organs or tissues beyond their typical anatomical boundaries. The main categories include inguinal hernia, femoral hernia and abdominal wall hernia [1]. Among them, the clinical incidence of inguinal hernia is the highest, which occurs when the abdominal contents protrude through the weak part of the lower abdominal myofascial structure, affecting people of all ages [2]. The global epidemiological trend from 1990 to 2019 showed that its prevalence increased by 36%, the total cases increased to 32.53 million, and the average survival rate decreased by 31% [3]. The gender difference is obvious, and the lifetime risk of inguinal hernia in men is close to 30%, which is significantly higher than 3% in women [4]. The etiology of adult inguinal hernia is multifactorial, which is affected by environmental, genetic and behavioral factors. Male sex, increasing age, lean body mass, and chronic obstructive pulmonary disease are clinically recognized risk factors [5, 6]. Although laparoscopic hernia repair is the dominant method for adult inguinal hernia surgery, there are still specific anesthesia challenges during the perioperative period. Clinicians must address risks such as respiratory depression or the stress caused by tracheal intubation. Therefore, there is a need to optimize the anesthesia plan to ensure patient safety and improve prognosis [7-9].

Sufentanil has attracted much clinical attention because of its significant analgesic effect as a potent μ-opioid receptor agonist. Its main char-

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acteristics include fast onset, long analgesia time and short anesthesia recovery time. In addition, it is effective in inhibiting the stress response caused by intubation and maintaining hemodynamic balance [10]. However, clinical evidence suggests several risks, including the risk of cough and respiratory depression in postoperative cases [11, 12]. Sevoflurane is widely used in anesthesia, which can sedate patients, relieve pain, and reduce blood pressure, while being anti-inflammatory. Its efficacy in reducing surgical stress, physiological stability and improving postoperative comfort has also been documented [13]. A randomized controlled trial reported that the cough caused by sufentanil was significantly reduced in pediatric patients after pre-administration of sevoflurane, and the hemodynamic stability was not significantly affected [14]. According to the data, the combination of these drugs for adult laparoscopic herniorrhaphy may provide better anesthetic effect due to their synergy.

Materials and methods

Participant selection criteria

This retrospective study employed strict selection criteria. Eligibility: (1) clinically diagnosed inguinal hernia [15], (2) surgical candidacy, (3) American Society of Anesthesiologists (ASA) grade I-II, (4) no contraindications to anesthesia and no history of chronic pain, and (5) intact medical data.

Exclusion grounds: (1) being pregnant or lactating, (2) suffering from severe cardio-cerebrovascular pathologies, coagulopathy, acute/chronic infections, liver/kidney dysfunction, respiratory infections, or malignancies, (3) having sliding, incarcerated, giant scrotal, or recurrent hernia, (4) undergoing abdominal procedures before enrollment.

A systematic screening was conducted on adult patients who underwent laparoscopic herniorrhaphy (December 2022-December 2024). Eventually, 102 eligible participants were included and divided into two groups: the propofol group (n=50; sufentanil/remifentanil + propofol) and the sevoflurane group (n=52; sufentanil/remifentanil + sevoflurane). The Ethics Committee of Yiwu Central Hospital ratified this research.

Intervention protocol

All patients were subjected to fasting (8 h) and water was forbidden (4 h) before operation. Atropine (10 μg/kg) was injected intramuscularly 30 min before anesthesia to inhibit the secretion of the glands. Then an electrocardiography monitor was connected to monitor the heart rate (HR) and blood oxygen of patients in real time. The left radial artery was punctured after local anesthesia with lidocaine (0.5% annular infiltration anesthesia) in the left arm, and the changes in mean arterial pressure (MAP) and other basic values of patients were monitored.

Patients in the propofol group underwent propofol-sufentanil/remifentanil anesthesia. A target-controlled infusion (TCI) system targeting a 3 μg/mL propofol plasma concentration was utilized to induce anesthesia. Meanwhile, intravenous sufentanil (0.6 μg/kg) was delivered. Upon patient unresponsiveness and loss of consciousness, neuromuscular blockade using a 0.2 mg/kg cisatracurium besylate bolus was initiated. Following successful muscle paralysis, direct laryngoscopy-guided tracheal intubation was carried out. Then came propofol TCI lowering to 2 μg/mL to maintain anesthesia and appropriate anesthesia depth maintenance with a remifentanil (0.3 μg/kg) infusion. This combination was discontinued until procedure completion.

In the sevoflurane group, sevoflurane was co-administered with the same sufentanil/remifentanil analgesic protocol. Intravenous sufentanil plus facemask-based sevoflurane inhalation completed induction. Pre-induction preparation involved residual gas elimination through anesthetic circuit purging. The sevoflurane-saturated facemask was then sealed tightly over the patient's airway. For induction, a sufentanil (0.6 μg/kg) bolus was delivered intravenously. Cisatracurium besylate (0.2 mg/kg) was injected when the patient did not respond to to painful stimuli. After achieving optimal muscle relaxation, the endotracheal tube was inserted under direct laryngoscopy. After taking effect, the laryngoscope was used for endotracheal intubation. Following intubation, sevoflurane (3% volume fraction) inhalation and a 0.3 μg/kg remifentanil pump were used to maintain anesthesia, and the administration was stopped 5 min before the end of the operation.

Data collection and outcome measurements

To assess the impact of different anesthesia protocols on the outcomes, we employed a multi-dimensional approach for data collection and result evaluation.

(1) Surgical parameters: We documented operative duration, anesthesia induction time, and extubation time.

(2) Post-anesthetic recovery: It was monitored by recording emergence time (interval from anesthetic discontinuation to eye-opening or spontaneous respiration resumption), consciousness recovery time (duration from eye-opening to full reorientation), and agitation (Visual Analogue Scale [VAS]) incidence [16]. An at-rest VAS score of 5 or above (maximum: 7 points) defines agitation.

(3) Postoperative outcomes: The first postoperative ambulation time, total hospitalization duration, and gastrointestinal function restoration (return of bowel sounds, flatus, and oral liquid tolerance) were recorded.

(4) Adverse events: A recording was made of complications that occurred (laryngospasm, respiratory depression, cough, and nausea), with the incidence rate calculated.

(5) Haemodynamics: HR and MAP were measured at pre-induction baseline (T0), during intubation (T1), and post-extubation (T2).

(6) Stress response: Early-morning venous blood (5 mL) under fasting conditions was collected preoperatively and one day post-operation. Serum was separated via centrifugation and underwent radioimmunoassay for adrenaline (AD), norepinephrine (NE), and cortisol (Cor).

(7) Inflammatory markers: At preoperative and 24-hour postoperative intervals, an ELISA was performed to measure serum interleukin (IL)-1β/6 and tumor necrosis factor (TNF)-α levels.

(8) Pain mediators: Using ELISA, preoperative and postoperative (24-hour) substance P (SP), 5-hydroxytryptamine (5-HT), and β-endorphin (β-EP) were analyzed.

Statistical methods

This study utilized SPSS 26.0 for data analysis. Categorical variables were summarized as counts and percentages (n/%). Continuous variables were shown as the mean ± standard error of the mean (SEM; normally distributed) or the median (interquartile range) (M [Q1, Q3]; non-normally distributed). Differences were assessed by χ^2 tests for categorical data; for continuous variables, independent samples t-tests (between-groups), paired t-tests (within groups before and after intervention), and repeated measures ANOVA plus Bonferroni post-hoc analysis (among multiple time points) were used. $P<0.05$ was the statistical significance threshold.

Results

Baseline characteristics

Propofol and sevoflurane groups were similar in baseline parameters (gender distribution, age range, illness duration, hernia subtype classification, ASA physical status, hypertension, diabetes, and coronary artery disease; $P>0.05$; **Table 1**), ensuring comparability.

Surgical parameters

The sevoflurane and propofol cohorts showed comparable operative duration ((30.35±6.18) min VS. (28.64±5.15) min, P=0.133) and induction time ((1.56±0.34) min VS. (1.50±0.31) min, P=0.355), but the tracheal extubation ((13.00±1.96) min VS. (14.58±2.20) min, P<0.001) was markedly faster in the sevoflurane group (**Table 2**).

Recovery metrics

Sevoflurane-treated subjects exhibited reduced time to emergence ((10.58±2.66) min VS. (11.76±3.30) min, P=0.049) and consciousness recovery ((12.35±3.55) min VS. (14.80±4.19) min, P=0.002) than the propofol group, with fewer agitation episodes (15.38% VS. 34.00%, P=0.029; **Table 3**).

Postoperative outcomes

Earlier ambulation ((5.73±1.60) h VS. (6.46±1.51) h, P=0.020), faster gastrointestinal motility restoration ((17.52±6.50) d VS. (20.62±6.60) d, P=0.019), but comparable hospitalization duration (3.00 (3.00, 3.00) d VS. 3.00 (3.00, 3.00) d, P=0.127) were determined in the sevoflurane group versus the propofol cohort (**Table 4**).

Table 1. Baseline data

Factor	Propofol group (n=50)	Sevoflurane group (n=52)	t/χ^2	P
Gender			0.314	0.575
Male	32 (64.00)	36 (69.23)		
Female	18 (36.00)	16 (30.77)		
Age (years)	55.20±11.67	57.69±12.08	1.058	0.293
Duration of illness (months)	10.92±2.46	11.17±3.81	0.392	0.696
Hernia subtype classification			0.316	0.574
Indirect hernia	30 (60.00)	34 (65.38)		
Direct hernia	20 (40.00)	18 (34.62)		
ASA classification			0.745	0.388
I	33 (66.00)	30 (57.69)		
II	17 (34.00)	22 (42.31)		
Comorbidities				
Hypertension	10 (20.00)	13 (25.00)	0.546	0.365
Diabetes	8 (16.00)	9 (17.31)	0.031	0.859
Coronary heart disease	11 (22.00)	7 (13.46)	1.279	0.258

Note: ASA, American Society of Anesthesiologists.

Table 2. Surgical parameters

Factor	Propofol group (n=50)	Sevoflurane group (n=52)	t	P
Operative duration (min)	28.64±5.15	30.35±6.18	1.515	0.133
Induction time (min)	1.50±0.31	1.56±0.34	0.930	0.355
Time to tracheal extubation (min)	14.58±2.20	13.00±1.96	3.833	<0.001

Table 3. Recovery metrics

Factor	Propofol group (n=50)	Sevoflurane group (n=52)	t/χ^2	P
Time to emergence (min)	11.76±3.30	10.58±2.66	1.992	0.049
Time to consciousness recovery (min)	14.80±4.19	12.35±3.55	3.191	0.002
Agitation incidence (%)	17 (34.00)	8 (15.38)	4.774	0.029

Table 4. Postoperative outcomes

Factor	Propofol group (n=50)	Sevoflurane group (n=52)	t/Z	P
Postoperative ambulation (h)	6.46±1.51	5.73±1.60	2.368	0.020
Postoperative hospitalization (d)	3.00 (3.00, 3.00)	3.00 (3.00, 3.00)	-1.525	0.127
Restoration of gastrointestinal function (d)	20.62±6.60	17.52±6.50	2.390	0.019

Adverse events

Twelve incidents of adverse events (24.00%), including laryngospasm (3 cases), respiratory suppression (3 cases), nausea (3 cases), and cough (3 cases), were observed in the propofol group; which was higher compared to the sevoflurane cohort (4 adverse events (7.69%): cough (2 cases), respiratory suppression (1 case), and nausea (1 case); 7.69% VS. 24.00%, P=0.024; **Table 5**).

Hemodynamic parameters

For HR, the values at baseline (T0), during intubation (T1), and post-extubation (T2) were (77.16±7.72 vs. 77.19±5.76) times/min, (89.94±4.77 vs. 85.40±5.33) times/min, and (79.18±8.04 vs. 76.58±6.29) times/min, respectively, for the propofol and sevoflurane groups. The values for MAP were (78.90±7.59 vs. 78.71±7.81) mmHg at T0 between the propofol and sevoflurane groups, (95.70±7.55 vs.

Table 5. Adverse events

Factor	Propofol group (n=50)	Sevoflurane group (n=52)	χ^2	P
Laryngospasm	3 (6.00)	0 (0.00)		
Respiratory suppression	3 (6.00)	1 (1.92)		
Cough	3 (6.00)	2 (3.85)		
Nausea	3 (6.00)	1 (1.92)		
Total	12 (24.00)	4 (7.69)	5.126	0.024

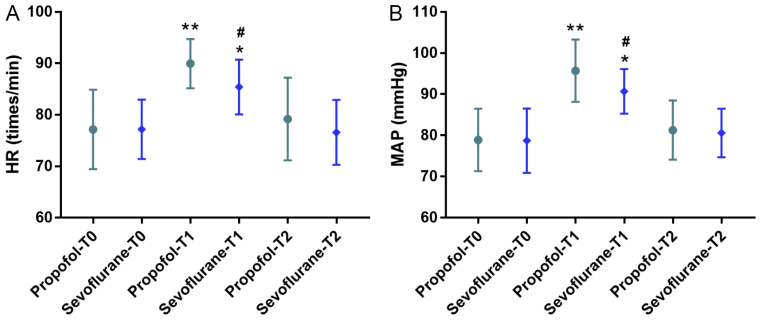

Figure 1. Hemodynamic parameter changes. A. Heart rate (HR) variations across groups. B. Mean arterial pressure (MAP) fluctuations. Notes: *P<0.05, **P<0.01 versus T0 (baseline); #P<0.05 versus propofol group at equivalent time intervals. T0: Pre-induction, T1: Intubation phase, T2: Post-extubation phase.

90.67±5.42) mmHg at T1, and (81.28±7.19 vs. 80.60±5.90) mmHg at T2. Through evaluation, no significant differences were found between the two anesthetic groups at T0 or T2 (P>0.05). However, at T1, both groups exhibited marked elevations in HR and MAP relative to baseline (P<0.05), with the sevoflurane group demonstrating significantly attenuated responses compared to the propofol group (P<0.05; **Figure 1**).

Stress markers

The ADR levels in the propofol and sevoflurane groups were (36.62±5.93) μg/L and (34.83±5.79) μg/L before surgery, and (51.72±6.52) μg/L and (45.48±4.88) μg/L after surgery, respectively; the NE levels in the propofol and sevoflurane groups rose from (229.44±37.91) μg/L and (221.67±39.68) μg/L at baseline to (344.72±40.51) μg/L and (302.67±28.98) μg/L following the operation, respectively; the Cor level in the propofol group increased from (118.64±10.63) μg/L before the operation to (160.98±9.67) μg/L after the operation, while in the sevoflurane group it rose from (120.40±9.64) μg/L to (146.19±8.68) μg/L. Through comparison, preoperative measurements of AD, NE, and Cor showed comparable levels between groups (P>0.05). The postoperative assessment revealed significant increases in all markers for both groups (P<0.05), with the sevoflurane group maintaining lower concentrations than the propofol group (P<0.05; **Figure 2**).

Inflammatory cytokines

The IL-1β levels were (1.78±0.46) pg/mL and (1.68±0.48) pg/mL at baseline, and (3.97±1.21) pg/mL and (2.43±0.94) pg/mL post-operation in the propofol and sevoflurane groups, respectively. IL-6 expression was measured at (3.13±1.40) pg/mL and (2.97±1.28) pg/mL pre-intervention, which elevated to (5.68±2.13) pg/mL and (3.88±1.63) pg/mL post-operation in the propofol and sevoflurane groups, respectively. As to TNF-α, it rose from (0.91±0.24) ng/mL at baseline to (2.56±1.06) ng/mL post-operation in the propofol group, and from (0.89±0.24) ng/mL to (2.07±0.73) ng/mL in the sevoflurane group. According to the above data, baseline IL-1β, IL-6, and TNF-α levels were similar between groups (P>0.05). Post-surgical evaluation demonstrated elevated cytokine concentrations in both cohorts (P<0.05), though the sevoflurane group exhibited significantly reduced levels compared to the propofol group (P<0.05; **Figure 3**).

Pain mediators

In the propofol and sevoflurane groups, the preoperative SP levels were (62.52±6.97) pg/mL and (61.62±6.93) pg/mL, which increased to (100.62±11.54) pg/mL and (87.96±10.18) pg/mL after surgery, respectively. The 5-HT levels rose from (143.22±18.84) nmol/L and (148.52±22.81) nmol/L at baseline to (283.68±35.92) nmol/L and (239.67±29.10) nmol/L following the operation, respectively. β-EP decreased from preoperative levels of (143.00±18.76) ng/mL and (138.71±19.27)

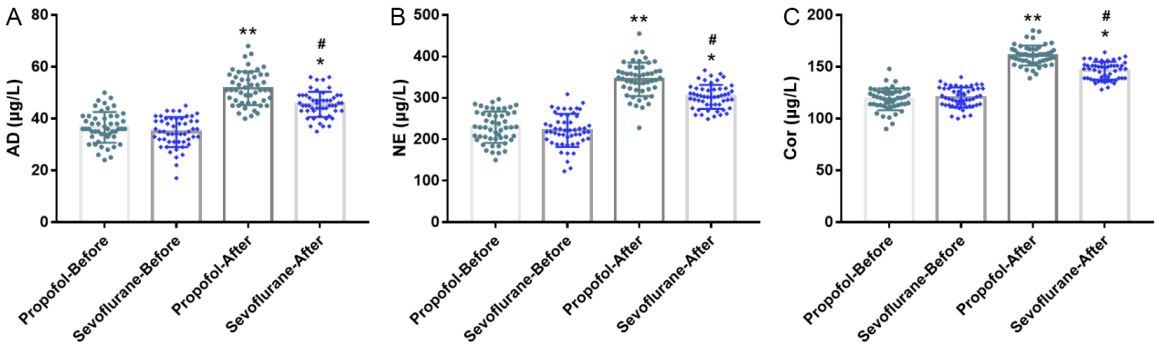

Figure 2. Comparative stress markers. A. Pre- and post-operative adrenaline (AD) changes. B. Pre- and post-operative noradrenaline (NE) alterations. C. Cortisol (Cor) changes pre- and post-surgery. Notes: *P<0.05, **P<0.01 versus T0 (baseline); #P<0.05 versus propofol group at equivalent time intervals.

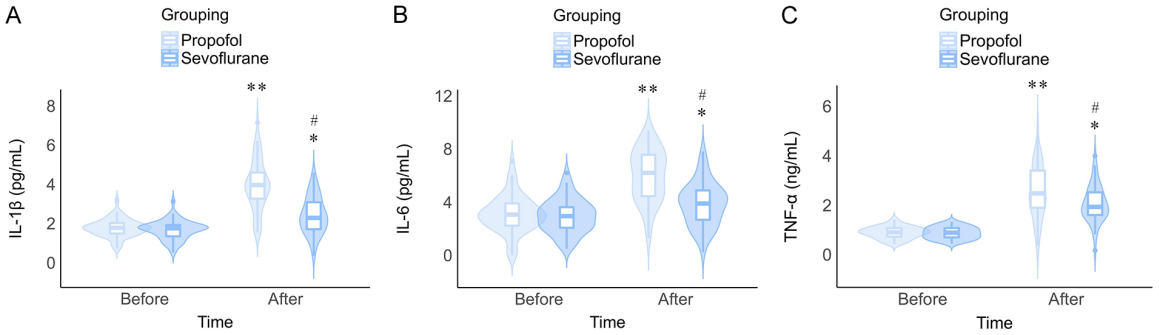

Figure 3. Inflammatory cytokine profiles. A. Interleukin-1β (IL-1β) level variations pre-operatively and 24 h post-operatively. B. Interleukin-6 (IL-6) level variations pre-operatively and 24 h post-operatively. C. Tumor necrosis factor-α (TNF-α) level variations pre-operatively and 24 h post-operatively. Notes: *P<0.05, **P<0.01 versus baseline (T0); #P<0.05 versus propofol group at the corresponding time point.

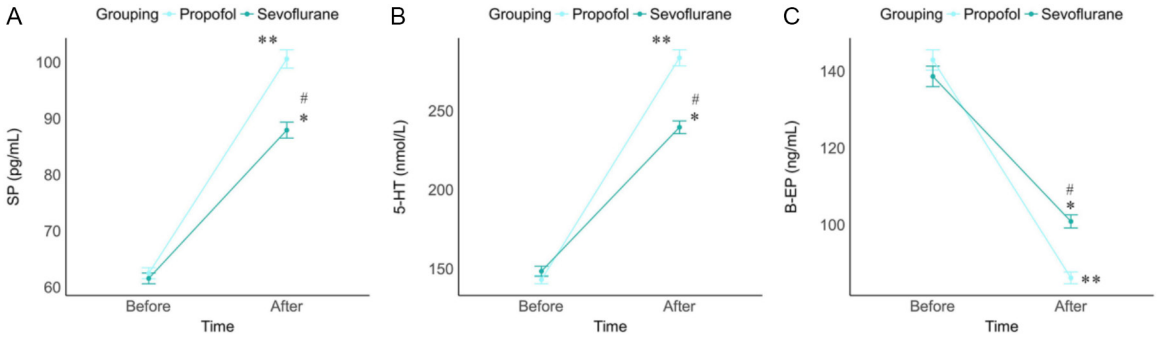

Figure 4. Postoperative pain mediator analysis. A. Substance P (SP) concentration changes pre-operatively and 24 h post-operatively. B. Serotonin (5-HT) concentration changes pre-operatively and 24 h post-operatively. C. β-endorphin (β-EP) concentration changes pre-operatively and 24 h post-operatively. Notes: *P<0.05, **P<0.01 versus baseline (T0); #P<0.05 versus propofol group at the corresponding time point.

ng/mL to post-operative concentrations of (86.20±10.87) ng/mL and (100.92±12.43) ng/mL, respectively. The data revealed no inter-group differences in SP, 5-HT, or β-EP at baseline (P>0.05). Postoperative analysis showed increased SP and 5-HT alongside decreased β-EP in both groups (P<0.05), with sevoflurane administration associated with more favorable profiles - lower SP and 5-HT and higher β-EP levels versus propofol (P<0.05; **Figure 4**).

Discussion

According to relevant studies, approximately 15%-20% of the global population is affected by hernias, among which inguinal hernia has a particularly high incidence in the male population [17]. Patients with inguinal hernia often have clinical symptoms such as inguinal swelling and pain, which have different degrees of negative impact on patients' daily life [18]. This study included 102 adult patients undergoing laparoscopic herniorrhaphy. All patients received sufentanil/remifentanil, in addition to propofol or sevoflurane. The comparative analysis was aimed at providing insights for improving the perioperative anesthesia protocol for adult laparoscopic hernia surgeries.

First of all, it was found that the sevoflurane group had significant clinical advantages in extubation time, anesthesia emergence time, consciousness recovery time, agitation rate, postoperative ambulation time, and gastrointestinal function recovery time, suggesting that sevoflurane combined with sufentanil/remifentanil has a certain anesthetic effect and postoperative recovery advantage for inguinal hernia patients undergoing laparoscopic herniorrhaphy. This may be attributed to the synergistic enhancement effect of sevoflurane combined with sufentanil/remifentanil on the anesthetic effect, which can accelerate the onset of anesthesia through different ways. The former takes effect quickly by virtue of its lower blood/gas partition coefficient and inhalation anesthetic properties compared with other inhalation anesthetics, while the latter takes effect quickly by virtue of its high lipophilicity through the blood-brain barrier [19, 20]. In this way, the extubation time of the sevoflurane group was relatively shorter, which accelerated anesthesia emergence and consciousness recovery. The sevoflurane group also showed certain clinical advantages in clinical safety, specifically showing significantly lower incidence of total adverse reaction events such as laryngospasm, respiratory depression, cough, nausea, etc.

The analysis of hemodynamics found that the sevoflurane group was relatively more stable. The HR and MAP of the two groups increased first and then decreased, but the increase of sevoflurane group was relatively smaller. Zhang et al. [21] reported that sevoflurane + sufentanil for adolescent idiopathic scoliosis surgery has more stable hemodynamics, and can also help patients recover rapidly from surgery, which is similar to our findings. The stabilizing effect of sevoflurane on hemodynamics may be related to its ability to avoid vascular sympathetic nerve excitation caused by intravenous administration [22].

Stress response assessment results showed that AD, NE and Cor of both cohorts were significantly increased at the end of the operation, with a lower increase amplitude in the sevoflurane group, suggesting that sevoflurane + sufentanil/remifentanil has a certain inhibitory effect on operation-related stress. Previous studies have mostly focused on the effect of sevoflurane plus block anesthesia on the stress response of surgical patients. For example, in the study of Wang Y et al. [23], the effect of sevoflurane + intercostal block on the regulation of stress response in patients undergoing lung cancer surgery was significantly better than that of propofol. As another example, Fan et al. [24] reported the effectiveness of sevoflurane + nerve block anesthesia in significantly reducing AD and Cor in patients undergoing hysteromyomectomy and reducing operation-related stress responses compared with propofol + remifentanil intravenous compound anesthesia. The stress-alleviating effect of sevoflurane may be attributed to its hyperpolarizing effect on neuronal membrane to some extent, which leads to the reduction of stress hormone release [25]. On the other hand, inhaled sevoflurane avoids the vascular sympathetic nerve excitation caused by intravenous administration, contributes to the maintenance of hemodynamic stability, and helps to inhibit neutrophil degranulation reaction and reduce oxidative stress, which is more helpful to reduce surgery-related stress than propofol [26, 27].

Furthermore, serum IL-1β, IL-6, and TNF-α were markedly elevated on postoperative day 1 in both arms, with lower levels in the sevoflurane group, which suggests the superior efficacy of sufentanil/remifentanil + sevoflurane in postoperative serum inflammation attenuation. This may be due to sevoflurane's modulation of the adenosine 5'-monophosphate (AMP)-activated protein kinase (AMPK) axis, which suppresses pro-inflammatory cytokine synthesis and secretion, thereby exerting anti-inflam-

matory effects [28]. Finally, better performance of pain mediators SP, 5-HT, and β-EP was determined in sevoflurane-treated patients. Ma et al. [29] reported that sevoflurane + remifentanil for pediatric patients undergoing laparoscopic inguinal hernia repair had a good effect on postoperative pain relief and sedation, while helping to stabilize hemodynamics, similar to our data.

There are some limitations in this study. First, the potential synergistic mechanism of sevoflurane + sufentanil/remifentanil anesthesia has not been analyzed yet. Supplementing the corresponding basic research will help further demonstrate the advantages of this anesthesia scheme. Second, our study subjects were patients who underwent laparoscopic hernia repair in a single center, which limits the applicability of our conclusions in a broader clinical setting. To verify the general applicability of this anesthesia combination, different invasive surgeries (e.g., various abdominal surgeries or open surgeries) need to be involved in future studies. The third limiting factor is the narrow range of outcome indicators, which mainly focus on the immediate indicators during the operation, rather than the long-term postoperative recovery. To evaluate its comprehensive value more comprehensively, outcome indicators such as postoperative cognitive status and more comprehensive quality-of-life indicators need to be included to have a deeper understanding of its real clinical impact.

To conclude, sufentanil/remifentanil + sevoflurane anesthesia for anesthesia in patients undergoing laparoscopic hernia repair can significantly shorten the time to extubation, anesthesia recovery, consciousness restoration, postoperative ambulation, and gastrointestinal function recovery. It reduces the rate of restlessness and the overall incidence of adverse reactions, while contributing to relatively stable hemodynamics. It also exerts positive effects on stress modulation, inflammation inhibition, and pain alleviation, deserving clinical promotion.

Disclosure of conflict of interest

None.

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