

ORIGINAL RESEARCH ARTICLE

Impact of a BIS-monitored stepwise injection of etomidate for individualized sedation on ERAS in elderly patients with coronary heart disease undergoing thoracoscopic surgery

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Abstract

Introduction: Thoracoscopic surgery in elderly patients with coronary heart disease (CHD) requires careful anesthetic management to maintain hemodynamic stability. While etomidate is valued for its cardiovascular safety, conventional dosing may not provide sufficient individualization. Evidence on the use of bispectral index (BIS)-guided, stepwise etomidate sedation to optimize outcomes and support enhanced recovery after surgery (ERAS) remains limited.

Objective: This study assessed the efficacy, safety, and impact on ERAS of a BIS-guided sedation protocol using stepwise etomidate injections in elderly patients with CHD undergoing thoracoscopic surgery.

Methods: Ninety patients aged 60–80 years with CHD (classified as American Society of Anesthesiologists physical status I–II) were randomized into three groups ($n=30$). All received general anesthesia induction with remifentanyl through target-controlled infusion plus sevoflurane. The depth of anesthesia was monitored by BIS at thoracic opening and closure. Group I (control) received increased concentrations of sevoflurane; Group II received single intravenous doses of propofol; and Group III received single intravenous doses of etomidate guided by BIS. Hemodynamics, ST-T changes, BIS values, Ramsay sedation scores, post-operative adverse events, and anesthesia costs were compared.

Results: Baseline demographics were similar across groups. At thoracic opening and closure, Group I showed higher blood pressure and heart rate than Group II ($p<0.05$), but was comparable to Group III. Hemodynamic stability was greater in Group III than in Group II ($p<0.05$). ST-T depression was most severe in Group I and least in Group III. BIS values were higher in Group I, indicating lighter anesthesia. Respiratory depression and dizziness were more frequent in Group II, while nausea, vomiting, and agitation were more common in Group I. Anesthesia costs were highest in Group I.

Conclusion: Stepwise etomidate under BIS guidance provides stable hemodynamics, fewer complications, and lower costs, supporting its use in ERAS for elderly CHD patients undergoing thoracoscopic surgery.

Keywords: Bispectral index; Etomidate; Coronary heart disease; Thoracoscopy; Enhanced recovery after surgery

1. Introduction

The incidence of lung cancer is increasing annually. It has become one of the most common cancers worldwide and poses a serious threat to human life and health.¹⁻⁷ At present, China places great emphasis on early screening for lung cancer, enabling the detection of the disease in more elderly patients.⁸ This initiative aims to increase the clinical cure rate of lung cancer and improve patient prognosis. Elderly patients tend to have diminished organ functional reserves and disrupted self-regulatory mechanisms, making them prone to circulatory and respiratory suppression, including hypotension. For patients with coronary artery disease, this can lead to severe cardiovascular events. Moreover, many elderly patients have a history of cardiovascular disease, making them particularly vulnerable.⁹ Thoracoscopic surgery, which minimally impacts cardiac and lung function, is increasingly used in the diagnosis and treatment of thoracic diseases. However, its anesthesia technique is more complex, requiring precise intraoperative management and depth of anesthesia monitoring. At present, depth of anesthesia monitoring is widely used in general anesthesia procedures, especially in elderly patients, to prevent the stress responses caused by shallow anesthesia and reduce the occurrence of intraoperative awareness.

Given the characteristics of elderly patients and the anesthetic requirements for thoracoscopic surgery, this study developed an enhanced anesthesia plan incorporating sevoflurane, propofol, and etomidate. Sevoflurane is a volatile anesthetic that provides hypnosis, amnesia, analgesia, akinesia, and autonomic blockade during surgical and procedural interventions.¹⁰ Its safety and efficacy are well established, and ongoing research continues to define its effects on various patient populations and organ systems.¹¹ Both propofol and etomidate are short-acting intravenous anesthetics widely used in clinical anesthesia. They are known for their rapid onset, short duration, strong sedative effects, quick recovery, and favorable safety profiles.¹² Etomidate, in particular, is less likely to cause circulatory and respiratory suppression. Reports suggest that etomidate is increasingly used for anesthesia induction, outpatient surgery, and intensive care unit sedation due to its hemodynamic stability, and it is recommended for elderly and critically ill patients.^{13,14} In contrast, propofol allows for easier control of anesthesia depth and induces sleep more rapidly than etomidate.¹⁵ However, studies have shown that propofol has a more significant impact on hemodynamics and may cause respiratory suppression.¹⁶ Therefore, this study aimed to identify an optimal sedation strategy based on the pharmacological characteristics of these three anesthetics.

In recent years, the concept of enhanced recovery after surgery (ERAS) has focused¹⁷ on reducing the physiological and psychological stress experienced by surgical patients. Achieving satisfactory anesthesia depth while ensuring the safety, stability, and comfort of elderly patients undergoing thoracoscopic surgery remains a challenge. In this study, we developed an individualized sedation plan using intermittent etomidate injections guided by the bispectral index (BIS) to address strong intraoperative stimuli. We compared this protocol with increased sevoflurane concentrations and intermittent propofol injections. Intraoperative hemodynamic stability, myocardial ischemia, adverse events, and average anesthetic costs were evaluated to assess the clinical efficacy, safety, and impact of intermittent etomidate injection on ERAS outcomes in elderly patients undergoing thoracoscopic surgery.

2. Methods

2.1. General information

The present study adopted a prospective design. The clinical registration platform is the Jilin Provincial Health Commission, Changchun, Jilin, China, with registration number 20240304059SF. Our study was approved by the Institutional Review Board of Jilin Province Cancer Hospital (approval number: 202108-024-01). Informed consent was obtained from all patients and/or their families. A total of 90 elderly patients (aged 60–80 years) with pre-operative coronary heart disease (CHD), classified as the American Society of Anesthesiologists physical status I–II, were enrolled in the study. These patients underwent thoracoscopic surgery at our hospital between September 2021 and January 2024 and were randomly and double-blindly assigned to three groups (30 patients per group). Exclusion criteria included: Patients with severe hypertension (grade >3), severe heart failure (New York Heart Association functional class >3), or severe pulmonary dysfunction (severe ventilatory impairment); those with significant arrhythmias, severe hepatic or renal dysfunction, a history of poorly controlled diabetes, coagulopathy, hypothyroidism, drug or lipid emulsion allergies, hyperkalemia, or incomplete examination results and medical records were excluded from the study.

2.2. Anesthesia monitoring

For all patients, body temperature was measured before surgery. Upon entering the operating room, patients were connected to standard monitoring equipment. Blood pressure (systolic blood pressure, diastolic blood pressure), heart rate, and oxygen saturation were monitored, and a four-lead limb electrocardiogram (ECG) with one chest lead was performed. In addition, BIS monitoring, muscle relaxant monitoring, and temperature monitoring

were conducted. Two peripheral intravenous lines were established in the lower limbs, and fluids (crystalloid and colloid) were administered at a 1:1 ratio. Intraoperatively, the following parameters were continuously monitored: Vital signs, ST-T depression on ECG, BIS values, concentrations of inhaled and exhaled sevoflurane, and end-tidal carbon dioxide pressure (EtCO₂).

2.3. Anesthesia methods

All patients were instructed to fast for 6–8 h and refrain from drinking water for 4 h before surgery. The same anesthesia induction regimen was used for all patients: 0.04–0.06 mg/kg midazolam, 0.3–0.4 µg/kg sufentanil, 1.5–2.0 mg/kg propofol, and 0.15–0.2 mg/kg cisatracurium besylate. Following general anesthesia induction, positive pressure ventilation and assisted breathing were initiated. Anesthesia depth was assessed using BIS values, and once adequate, tracheal intubation was performed under video laryngoscope guidance. A double-lumen endotracheal tube was inserted into the left (or right) main bronchus, and its position was immediately confirmed through fiberoptic bronchoscopy to ensure accurate placement for single-lung ventilation. During surgery, ventilator was used to control breathing, with the following settings: tidal volume of 6–8 mL/kg, positive end-expiratory pressure of 3–5 cmH₂O, and CO₂ pressure maintained within 35–45 mmHg. The respiratory rate was adjusted to 10–15 breaths/min based on CO₂.

The intraoperative anesthesia regimen for all three groups consisted of combined intravenous and inhalational general anesthesia. Remifentanyl was administered through target-controlled infusion (TCI) at 1.5–2.0 ng/mL was administered, along with continuous inhalation of 1.5–2% sevoflurane for maintenance of sedation. Additional doses of cisatracurium besylate were administered as needed. BIS monitoring was used to assess anesthesia depth, and a muscle relaxant monitor was used to evaluate muscle relaxant metabolism.

The specific sedation strategies applied at key intraoperative time points differed among the three groups, as outlined below:

- Group I (control group): At two time points—during chest opening and closure—the sevoflurane concentration was increased by 0.5–1% to maintain anesthesia depth, without the use of additional intravenous sedatives.
- Group II (propofol group): At chest opening and closure, a single intravenous injection of 1.0–1.5 mg/kg propofol was administered to maintain anesthesia depth.
- Group III (etomidate group): Similarly, at chest opening and closure, a single intravenous injection of

0.1–0.2 mg/kg etomidate was given to maintain the depth of anesthesia.

At the end of surgery, all the patients were fully conscious, with reflexes restored and spontaneous respiratory rates of 10–15 breaths/min. Tidal volumes reached 350–500 mL. Once patients were naturally awake, the double-lumen endotracheal tube was removed. Auscultation revealed clear breath sounds, with no complications, such as atelectasis. Vital signs remained stable, and all patients were safely transferred to the recovery room. Post-operative pain management was managed using patient-controlled intravenous analgesia, consisting of a mixture of sufentanil 100 µg + tramadol 400 mg + 0.9% saline, diluted to a total volume of 100 mL.

2.4. Observations and recordings

The following parameters were observed and recorded at four key time points: At the start of surgery (T₁), during chest opening (T₂), during chest closure (T₃), and at the end of surgery (T₄).

- (i) Changes in blood pressure, heart rate, and other vital signs.
- (ii) ST-T depression on ECG.
- (iii) BIS values.
- (iv) Post-operative Ramsay sedation scores.
- (v) Incidence of post-operative adverse reactions.
- (vi) Average anesthesia cost per case.

2.5. Statistical analysis

Data were statistically analyzed using SPSS 29.0 software. Continuous variables with normal distribution are expressed as means ± standard deviations, and comparisons between groups were performed using *t*-tests. Categorical data were analyzed using the chi-square (χ²) test. A *p* < 0.05 was considered statistically significant.

3. Results

3.1. Comparison of general data between the three groups

There were no statistically significant differences among the three groups in terms of age, weight, height, body mass index (BMI), and surgical duration (*p* > 0.05). Results are presented in Table 1.

3.2. Comparison of blood pressure and heart rate at different time points

At time points T₂ and T₃, blood pressure and heart rate in Group I were significantly higher than those in Group II, with statistically significant differences (*p* < 0.05), but there was no significant difference compared to Group III (*p* > 0.05). Similarly, at T₂ and T₃, Group III had significantly

higher blood pressure and heart rate than Group II ($p<0.05$). Results are shown in Tables 2 and 3.

3.3. Amplitude of ST-T segment depression in the ECG

The degree of ST-T segment depression followed the order: Group I > Group II > Group III, with statistically

significant differences ($p<0.05$). In Group I, significant ST-T depression was observed at all time points (T_1 – T_4), with $p<0.05$. In Group II, significant ST-T depression occurred from T_2 to T_4 compared to T_1 ($p<0.05$). In Group III, no significant ST-T depression was observed at any time point ($p>0.05$). Results are illustrated in Figures 1 and 2.

3.4. Comparison of BIS values at various time points

At time points T_2 and T_3 , BIS values in Group I were significantly higher than those in Groups II and III, with statistically significant differences ($p<0.05$). There was no statistically significant difference between Group II and Group III ($p>0.05$). Results are shown in Figure 3.

3.5. Post-operative sedation scores (Ramsay)

Post-operative Ramsay sedation scores followed the order: Group I > Group II > Group III, with statistically significant differences. Results are illustrated in Figure 4.

Table 1. Comparison of the general data of patients

Parameter	Group I (n=30)	Group II (n=30)	Group III (n=30)
Age (years)	65.93±4.339	66.70±4.527	66.53±3.550
Height (cm)	163.03±5.840	164.63±7.946	162.57±6.740
Weight (kg)	64.57±9.311	62.72±11.081	65.00±9.738
BMI	24.28±3.161	23.05±3.292	24.61±3.445
Surgery duration (h)	2.20±1.235	2.39±1.129	2.45±1.182

Note: Data are expressed as means±standard deviations.
Abbreviation: BMI: Body mass index.

Table 2. Blood pressure at various time points in the three patient groups

Blood pressure	Group I	Group II	Group III	t (I, II)	p (I, II)	t (I, III)	p (I, III)	t (II, III)	p (II, III)
T_1 SBP	103.60±16.188	107.47±9.605	102.37±16.414	– 1.125	0.265	0.293	0.771	1.469	0.147
T_1 DBP	66.40±10.779	68.47±8.029	67.13±11.233	– 0.842	0.403	–0.258	0.797	0.529	0.599
T_2 SBP	121.87±14.894	103.03±13.190 ^a	116.10±11.300 ^c	5.185	<0.001	1.689	0.097	–3.878	<0.001
T_2 DBP	78.07±10.719	68.10±10.450 ^b	73.80±8.080 ^f	3.647	0.001	1.823	0.074	–2.281	0.026
T_3 SBP	108.63±19.454	99.73±8.038 ^c	112.67±11.300 ^g	2.316	0.024	–0.980	0.331	–5.087	<0.001
T_3 DBP	73.57±7.780	68.50±8.488 ^d	72.80±6.754 ^h	2.410	0.019	0.408	0.685	–2.171	0.034
T_4 SBP	117.90±13.089	125.50±16.351	119.63±17.730	– 1.987	0.052	–0.430	0.669	1.330	0.189
T_4 DBP	75.13±8.689	78.67±9.841	74.43±9.565	– 1.474	0.146	0.297	0.768	1.690	0.096

Notes: Data are expressed as means±standard deviations. Compared with group I: ^a $p<0.05$, ^b $p<0.05$, ^c $p<0.05$, ^d $p<0.05$. Compared with group II: ^e $p<0.05$, ^f $p<0.001$, ^g $p<0.05$, ^h $p<0.05$.

Abbreviations: DBP: Diastolic blood pressure; SBP: Systolic blood pressure; T: Time point.

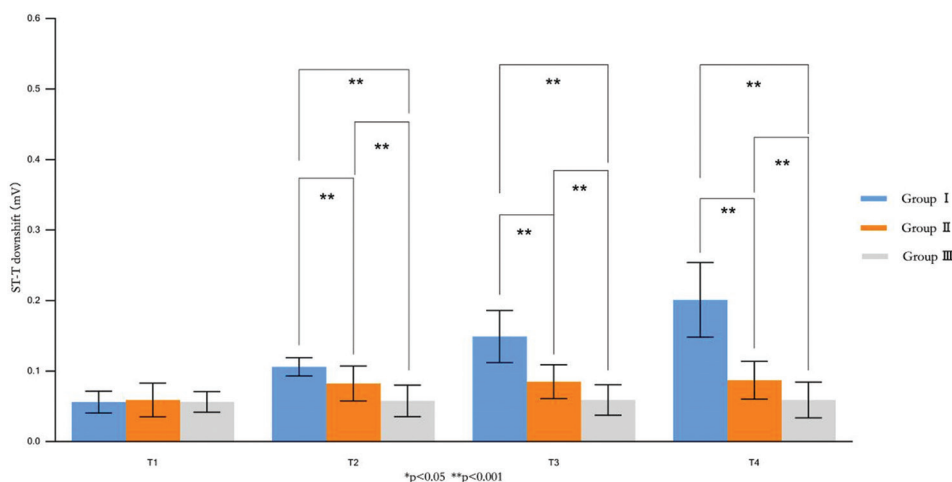


Figure 1. Amplitude of ST-T segment depression in the electrocardiogram in different groups

Notes: * $p<0.05$, ** $p<0.001$.

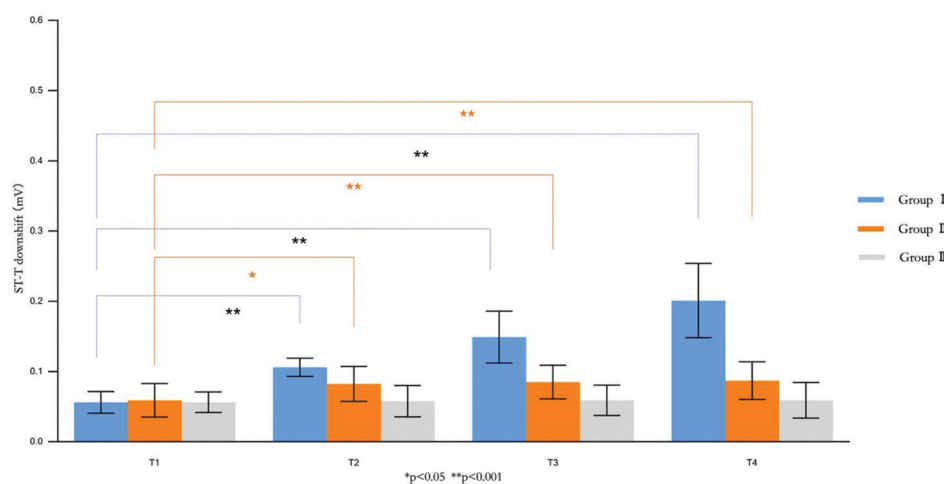


Figure 2. Amplitude of ST-T segment depression at different time points compared to T₁ in different groups
Notes: * $p<0.05$, ** $p<0.001$.

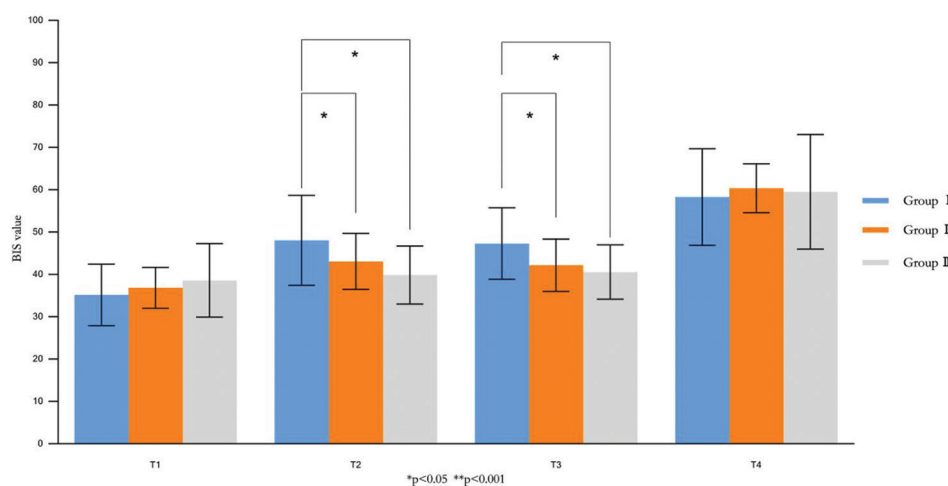


Figure 3. Comparison of bispectral index (BIS) values at various time points among the three different groups
Notes: * $p<0.05$, ** $p<0.001$.

Table 3. Heart rate at various time points in the three patient groups

Groups	T ₁	T ₂	T ₃	T ₄
I	68.87±14.500	68.83±11.462	76.27±8.690	74.93±9.989
II	74.63±13.252	61.93±10.248 ^a	62.57±10.311 ^b	70.33±10.138
III	68.70±11.957	71.73±11.083 ^c	76.33±16.276 ^d	71.83±13.921
t (I, II)	-1.608	2.458	5.565	1.770
p (I, II)	0.113	0.017	<0.001	0.082
t (I, III)	0.049	-0.996	-0.020	0.991
p (I, III)	0.961	0.323	0.984	0.326
t (II, III)	1.821	-3.556	-4.121	-0.477
p (II, III)	0.074	0.001	<0.001	0.635

Notes: Data are expressed as means±standard deviations. Compared with group I: ^a $p<0.05$, ^b $p<0.05$. Compared with group II: ^c $p<0.05$, ^d $p<0.05$.

3.6. Post-operative adverse reactions

The incidence of respiratory depression and dizziness was significantly higher in Group II than in Group I and Group III ($p<0.05$). Conversely, the incidence of nausea, vomiting, and agitation was significantly higher in Group I compared to Groups II and III ($p<0.05$). There was no statistically significant difference between Group II and Group III in these adverse reactions ($p>0.05$). Results are depicted in Figure 5.

3.7. Comparison of average anesthesia costs per procedure

Group I had significantly higher costs compared to Groups II and III ($p<0.05$). There was no statistically

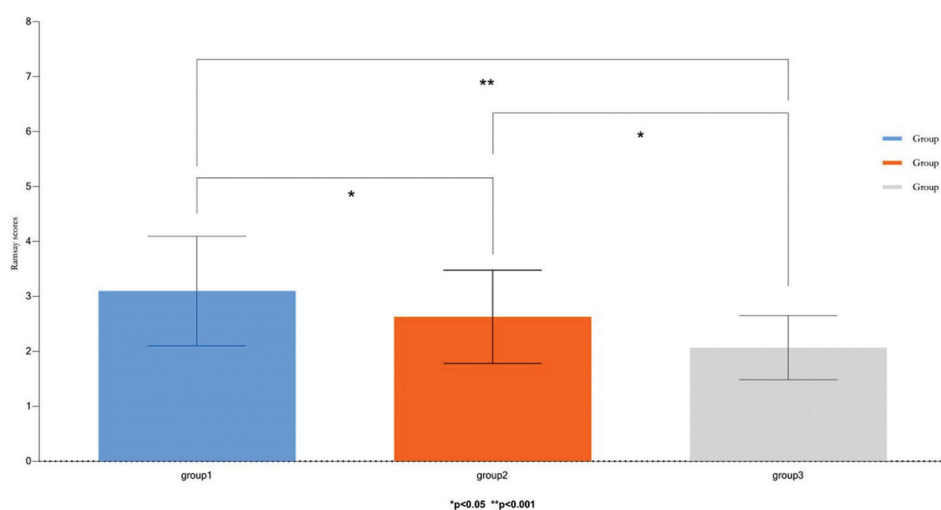


Figure 4. Post-operative sedation scores in the three groups

Notes: * $p < 0.05$, ** $p < 0.001$.

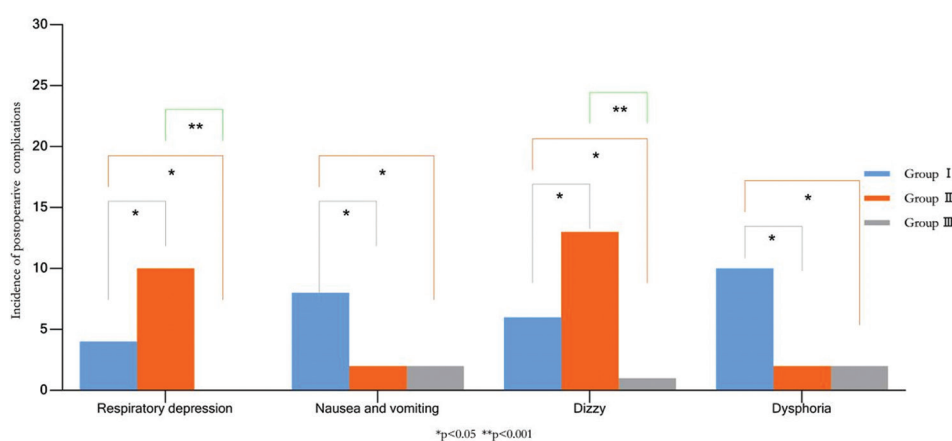


Figure 5. Post-operative adverse reactions in the three groups

Notes: * $p < 0.05$, ** $p < 0.001$.

significant difference between Group II and Group III ($p > 0.05$). Results are shown in [Figure 6](#).

4. Discussion

The primary treatment for lung cancer is surgical resection. However, traditional open-chest surgery involves rib retraction or cutting, causing significant trauma, which limits surgical treatment options for patients with comorbidities, such as coronary artery disease. Thoracoscopic surgery has revolutionized thoracic procedures, offering a viable alternative for elderly patients who cannot tolerate the trauma of open surgery. Studies have shown that aging alters pharmacokinetics and pharmacodynamics, significantly affecting drug metabolism and response.¹⁸ Therefore, careful selection of

the type and dosage of anesthetic agents in elderly patients is crucial. Maintaining perioperative circulatory stability in this population remains a key focus in modern anesthetic practice.

In this study, a multidisciplinary consultation was conducted pre-operatively, and BIS monitoring was used throughout the procedure. A standardized general anesthesia induction protocol was combined with an individualized and precise sedation strategy involving incremental etomidate injections. This approach not only allowed accurate assessment of anesthetic depth but also reduced the incidence of post-operative agitation and cognitive dysfunction in elderly patients. The recommended BIS value for adequate general anesthesia is 40–60,¹⁹ and neuromuscular monitoring should be

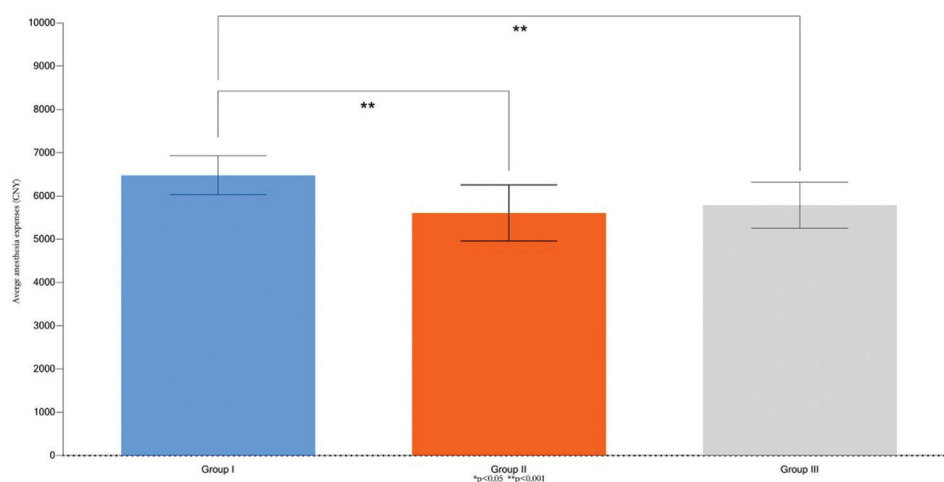


Figure 6. Comparison of average anesthesia costs per procedure among the three groups
Notes: * $p < 0.05$, ** $p < 0.001$.

used to guide the administration of muscle relaxants, minimizing residual neuromuscular blockade at the end of surgery.

There were no statistically significant differences in baseline characteristics, such as age, height, weight, BMI, or surgical duration among the three groups. At the time points of chest opening and closure, Group I exhibited significantly higher blood pressure and heart rate than Group II, but not significantly different from Group III. This suggests that propofol suppressed cardiovascular function, lowering heart rate and causing hypotension by inhibiting myocardial contractility and reducing vascular tone. This finding is consistent with previous reports indicating that propofol can cause circulatory dysfunction.²⁰⁻²² Similarly, blood pressure and heart rate in Group III were significantly higher than in Group II, indicating that etomidate exerts less cardiovascular suppression than propofol. This advantage contributes to improved hemodynamic stability, as demonstrated by relatively stable blood pressure and heart rate in Group III. These results are in agreement with previous studies showing that etomidate has minimal effects on hemodynamics.²³ Furthermore, the ST-T segment depression observed on ECG at chest opening and closure in the three groups showed that, under equivalent analgesic conditions, intravenous etomidate used to deepen anesthesia during intense surgical stimulation resulted in the least ST-T depression, thereby reducing the risk of myocardial ischemia. This supports the conclusion that the etomidate-based sedation protocol offers better circulatory stability in elderly patients. Etomidate does not significantly suppress the autonomic regulation of the heart and is considered safer than propofol when used in combination with opioids for anesthesia induction and

maintenance in elderly patients. In addition, etomidate mildly dilates coronary vessels, reduces vascular resistance, and increases coronary blood flow, thus lowering myocardial oxygen consumption. These effects are particularly beneficial for patients with compromised myocardial oxygen supply or coronary perfusion. In elderly patients with multiple comorbidities and reduced cardiovascular reserve, etomidate can effectively maintain stable hemodynamics.^{24,25}

The BIS monitoring results revealed that, although increasing the sevoflurane concentration deepened anesthesia, its onset was slower than that of intravenous anesthetics, resulting in a failure to achieve satisfactory BIS values within a short time. Both propofol and etomidate are key sedatives in general anesthesia, with comparable sedative effects that are stronger than those of sevoflurane. Post-operative Ramsay sedation scores followed the order Group I > Group II > Group III, suggesting that sevoflurane accumulation prolongs recovery time as anesthesia duration increases. Propofol is known to strongly suppress the cardiovascular and respiratory systems in a dose-dependent manner.²⁶ Therefore, higher doses may be required to achieve the desired depth of sedation, increasing the risk of oversedation. In contrast, etomidate acts rapidly and is quickly metabolized and cleared from the body, allowing for faster recovery. The incidences of post-operative respiratory depression and dizziness were highest in Group II, followed by Group I and Group III. This was likely due to the need for higher doses of propofol, which may reduce tidal volume and lead to respiratory depression and dizziness. Etomidate, on the other hand, did not cause respiratory depression and significantly

reduced dizziness, demonstrating the most favorable outcomes. Previous studies also suggest that etomidate may offer protection against ischemia-reperfusion injury in both the brain and myocardium.²⁷ The incidences of nausea, vomiting, and agitation were higher in Group I than in Groups II and III, with no significant difference between Groups II and III. This finding aligns with prior reports indicating that inhalation anesthetics can cause post-operative nausea and vomiting. Although etomidate has been associated with side effects, such as myoclonus, nausea, and vomiting,²⁸ propofol has been shown to reduce the incidence of post-operative nausea and vomiting by approximately 19%.²⁹⁻³¹ Similarly, our study found that the use of high-concentration sevoflurane was associated with a higher rate of post-operative agitation compared to intravenous anesthesia, likely due to the accumulation of sevoflurane. When comparing average anesthetic costs, Group I incurred higher costs than Groups II and III did, likely due to prolonged use of high-concentration sevoflurane. While this approach deepened anesthesia, it also increased drug accumulation, delayed recovery, and resulted in longer post-anesthesia care unit stays and higher overall costs. Etomidate is widely valued for its cardiovascular stability; however, it has been linked to adrenal cortical suppression, particularly with prolonged or high-dose administration. In our study, we employed incremental bolus injections rather than continuous infusion, which may have reduced this risk. Nevertheless, we did not assess adrenal function (e.g., via adrenocorticotrophic hormone stimulation testing), and this omission represents an important limitation. Future investigations should incorporate endocrine assessments to more comprehensively evaluate the safety profile of etomidate, particularly in elderly and frail patients.

Our single-center design may also limit the generalizability of these findings. Local factors—including patient demographics, ethnic characteristics, and standardized surgical practices—may have influenced the results. Multicenter studies involving more diverse populations and surgical settings are needed to validate and expand our conclusions. Additional limitations should be acknowledged. Excluding individuals who were unable to read or write may have introduced selection bias, limiting the applicability of findings to older or less-educated populations. Moreover, several established risk factors for CHD—such as low-density lipoprotein cholesterol levels, hypertension, and smoking history—were not analyzed as primary variables. Future research should include a more comprehensive assessment of cardiovascular risk factors, along with structured post-operative follow-up and lifestyle evaluations, to better contextualize anesthesia outcomes in this population.

5. Conclusion

Our findings indicate that a BIS-guided, individualized sedation protocol using incremental etomidate injections during thoracoscopic surgery in elderly patients with coronary artery disease yields favorable clinical outcomes. These include improved hemodynamic stability, reduced myocardial ischemia, fewer adverse reactions, and greater patient satisfaction.

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Conflict of interest

The authors declare no conflicts of interest.

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Ethics approval and consent to participate

The study was approved by the Institutional Review Board of Jilin Province Cancer Hospital (approval number: 202108-024-01). Informed consent was obtained from all patients and/or their families.

Consent for publication

Written informed consent was obtained from all participants for inclusion in the study and publication of anonymized data.

Availability of data

Data presented in this study are available from the corresponding author upon reasonable request.

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